2018 Physical Activity Guidelines Advisory Committee Scientific Report

To the Secretary of Health and Human Services

The findings of this report are those of the 2018 Physical Activity Guidelines Advisory Committee. They do not necessarily reflect the views of the Office of Disease Prevention and Health Promotion or the U.S. Department of Health and Human Services.

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The Honorable Alex Azar
Secretary of Health and Human Services
200 Independence Avenue, S.W.
Washington, D.C. 20201

Dear Secretary Azar,

On behalf of the entire 2018 Physical Activity Guidelines Advisory Committee, we are very pleased to submit the *2018 Physical Activity Guidelines Advisory Committee Scientific Report*.

Our Committee was charged with reviewing the scientific literature on physical activity and health. The *2018 Physical Activity Guidelines Advisory Committee Scientific Report* provides a detailed summary of the disease prevention and health promotion benefits of a more physically active America that is firmly established by the latest scientific evidence. It builds on and significantly expands the scientific evidence summarized in the first *Physical Activity Guidelines Advisory Committee Report, 2008.* The Committee judged the 2008 Scientific Report to be an excellent document and used it as the foundation for the current report. It is clear, however, that the expansion of knowledge about the relationships between physical activity and health during the past 10 years has provided evidence of even more health benefits, demonstrated greater flexibility about how to achieve those benefits, and shown that a more physically active American population can be facilitated in a wide variety of ways.

The Scientific Report demonstrates that, across the full age spectrum, regular physical activity provides a variety of benefits that help us feel better, sleep better, and perform daily tasks more easily. The report also demonstrates that some benefits happen immediately. A single bout of moderate-to-vigorous physical activity can improve that night's sleep, reduce anxiety symptoms, improve cognition, reduce blood pressure, and improve insulin sensitivity on the day that it is performed. Most of these improvements become even larger with the regular performance of moderate-to-vigorous physical activity.

The newly documented health benefits also include reduced risk of excessive weight gain in adults, children, and pregnant women; improved cognitive function and a reduced risk of dementia; and reduced risk of cancer of the bladder, endometrium, esophagus, kidney, lung, and stomach. The report demonstrates, for the first time, physical activity-related health benefits for children ages 3 to 5 years. In addition, for the large number of adults who already have a chronic disease or condition such as osteoarthritis, hypertension, or type 2 diabetes, a reduced risk of developing a new chronic condition and reduced risk of progression of the condition they already have, plus improvements in quality of life and physical function.

Given Americans' low rates of participation in physical activity and high prevalence of chronic diseases and associated disabilities, this report is particularly timely. It provides the necessary foundation for the Department to revise the *2008 Physical Activity Guidelines for Americans*. Strong federal guidelines, policies, and programs on physical activity should be an essential component of any comprehensive disease prevention and health promotion strategy for Americans. Included in this report is a summary of evidence-based physical activity promotion interventions that hold promise for improving the nation's physical activity levels.

On behalf of the entire Committee, we thank you for the opportunity to support the prevention priorities of the Department. Over the past 20 months, the Committee members and consultants worked exceptionally long and hard to conduct the extensive scientific review that made this report possible. Despite this task being added to their usual busy schedules, they met tight deadlines, provided insight and education to one another, and unselfishly worked to develop a consensus report. Thus, we wish to thank you for assembling a Committee of outstanding professionals who are knowledgeable, dedicated, and highly productive. Committee members are committed to the broad dissemination of this report and the ensuing guidelines. Please do not hesitate to contact us or any of the Committee members if we can be of further service.

It is important to emphasize that this report could not have been completed without the outstanding support of all the HHS staff who assisted us throughout the entire process. We are very grateful for their substantial assistance throughout the process. Their excellent logistical and management support in all aspects of the Committee's work was essential. Special recognition goes to Lieutenant Commander Katrina Piercy of the Office of Disease Prevention and Health Promotion and Captain Richard Troiano of the National Cancer Institute for their tireless dedication to the coordination, and ultimate completion, of this project. This report greatly benefits from the expert editing provided by Anne Brown Rodgers, who helped us present information that is useful and readable, and from the rigorous literature review work overseen by Bonny Bloodgood at ICF.

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2018 Physical Activity Guidelines Advisory Committee Scientific Report

February 2018

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PART A. EXECUTIVE SUMMARY

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INTRODUCTION

The *2018 Physical Activity Guidelines Advisory Committee Scientific Report* abundantly demonstrates that physical activity is a "best buy" for public health. The report provides a detailed summary of the disease prevention and health promotion benefits of a more physically active America that is firmly established by the latest scientific evidence. It builds on and significantly expands the scientific evidence summarized in the first *Physical Activity Guidelines Advisory Committee Report, 2008.* The Committee judged the 2008 Scientific Report to be an excellent document and used it as the foundation for the current report. It is clear, however, that the expansion of knowledge about the relationships between physical activity and health during the past 10 years has provided evidence of even more health benefits, demonstrated greater flexibility about how to achieve those benefits, and shown that a more physically active American population can be facilitated in a wide variety of ways.

The 17 members of the 2018 Physical Activity Guidelines Advisory Committee were appointed in June 2016 and sworn into duty in July 2016. The Committee was instructed to examine the scientific literature, especially articles published in the 10 years since the publication of the 2008 Scientific Report, and to confirm, expand, or modify the recommendations in that report. The Committee conducted detailed searches of the scientific literature, evaluated and discussed at length the quality of the evidence, and developed conclusions based on the evidence as a whole. The quantity and quality of the report reflects this careful and diligent process.

MAJOR FINDINGS

Physically active individuals sleep better, feel better, and function better. The 2018 Scientific Report demonstrates that, in addition to disease prevention benefits, regular physical activity provides a variety of benefits that help individuals sleep better, feel better, and perform daily tasks more easily.

- Strong evidence demonstrates that moderate-to-vigorous physical activity improves the quality of sleep. It does so by reducing the length of time it takes to go to sleep and reducing the time one is awake after going to sleep and before arising in the morning. It also can increase the time in deep sleep and reduce daytime sleepiness.
- Single episodes of physical activity promote acute improvements in executive function for a period of time. Executive function includes the processes of the brain that help organize daily activities and plan for the future. Tasks such as one's ability to plan and organize, self-monitor and inhibit or facilitate behaviors, initiate tasks, and control emotions all are part of executive function. Physical activity also improves other components of cognition, including memory, processing speed, attention, and academic performance.
- Regular physical activity not only reduces the risk of clinical depression but reduces depressive symptoms among people both with and without clinical depression. Physical activity can reduce the severity of those symptoms whether one has only a few or many.
- Regular physical activity reduces symptoms of anxiety, including both chronic levels of anxiety as well as the acute feelings of anxiety felt by many individuals from time to time.
- Strong evidence also demonstrates that perceived quality of life is improved by regular physical activity.
- Physical activity improves physical function among individuals of all ages, enabling them to conduct their daily lives with energy and without undue fatigue. This is true for older adults, for whom improved physical function not only reduces risk of falls and fall-related injuries but contributes to their ability to maintain independence. It is also true for young and middle-aged adults, as improved physical function is manifested in the ability to more easily accomplish the tasks of daily living, such as climbing stairs or carrying groceries.

Some benefits happen immediately. A single bout of moderate-to-vigorous physical activity will reduce blood pressure, improve insulin sensitivity, improve sleep, reduce anxiety symptoms, and improve cognition on the day that it is performed. Most of these improvements become even larger with the regular performance of moderate-to-vigorous physical activity. Other benefits, such as disease risk reduction and physical function, accrue within days to weeks after adopting a new physical activity routine.

Physical activity reduces the risk of a large number of diseases and conditions. The past 10 years have greatly expanded the list of diseases and conditions for which greater amounts of physical activity reduce the risk. Some of the major results include:

- Strong evidence demonstrates that greater volumes of moderate-to-vigorous physical activity are associated with preventing or minimizing excessive weight gain in adults, maintaining weight within a healthy range, and preventing obesity. This is important because losing weight is difficult and costly.
- Strong evidence demonstrates that higher amounts of physical activity are associated with a reduced risk of excessive increases in body weight and adiposity in children ages 3 to 17 years.
- Strong evidence also demonstrates that more physically active women are less likely to gain excessive weight during pregnancy. They also are less likely to develop gestational diabetes or develop postpartum depression than their less active peers. Maternal and child health has been, appropriately, a priority in the United States for generations. These findings indicate that physical activity is an important tool in the maintenance of maternal health, and affects a key time period when establishing lifelong healthy behaviors can be beneficial to women and their children alike.
- Strong evidence demonstrates that greater volumes of physical activity reduce the risk of dementia and improve other aspects of cognitive function. Given the high and rising prevalence of older Americans and the expense and heartache of caring for individuals with dementia, the value of preventing dementia is high.
- For the first time, the 2018 Scientific Report demonstrates that regular physical activity provides health benefits to children as young as ages 3 to 5 years. The 2008 Committee was unable to reach a conclusion about this young age group because of insufficient information. A substantial increase in evidence since then has allowed the 2018 Committee to conclude that, in addition to the reduced risk of excessive gains in body weight and adiposity, regular physical activity improves bone health in this young age group. These findings call attention to the importance of establishing healthy physical activity behaviors at an early age.
- For older adults, strong evidence demonstrates a reduced risk of falls and fall-related injuries.

- The 2008 Committee concluded that regular moderate-to-vigorous physical activity reduced the risk of breast and colon cancer. The 2018 Committee expanded that list to include a reduced risk for cancers of the bladder, endometrium, esophagus, kidney, lung, and stomach.
- A large portion of the general population already has a chronic disease or condition. The 2018 Committee has concluded that, for many of these individuals, regular physical activity can reduce the risk of developing a new chronic condition, reduce the risk of progression of the condition they already have, and improve their quality of life and physical function. The conditions examined by the Committee included some of the most prevalent, including osteoarthritis, hypertension, and type 2 diabetes.

The benefits of physical activity can be achieved in a variety of ways. The public health target range suggested in the 2008 Scientific Report was 500 to 1,000 MET-minutes of moderate-to-vigorous physical activity (or 150 to 300 minutes per week of moderate-intensity physical activity). The 2018 Committee concurs with this target range. Unfortunately, half the U.S. adult population does not currently attain this level of physical activity. Thirty percent of the population reports doing no moderate-to-vigorous physical activity. Thus, for a large segment of the population, major improvements in health are available from modest increases in regular physical activity.

The 2008 Committee reported that inactive individuals can achieve substantial health gains by increasing their activity level even if they do not reach the target range. Since 2008, substantially more information in the scientific literature documents the value of reducing inactivity even if the 150- to 300-minute weekly target range is not achieved. Here is a brief review of the major findings.

- For individuals who perform no or little moderate-to-vigorous physical activity, replacing sedentary behavior with light-intensity physical activity reduces the risk of all-cause mortality, cardiovascular disease incidence and mortality, and the incidence of type 2 diabetes. Before this report, evidence that light-intensity physical activity could provide health benefits had not been clearly stated.
- Individuals who perform no or little moderate-to-vigorous physical activity, no matter how much time they spend in sedentary behavior, can reduce their health risks by gradually adding some or more moderate-intensity physical activity.
- For individuals whose amount of moderate-to-vigorous physical activity is below the current public health target range of 150 to 300 minutes of moderate-intensity physical activity, even

small increases in moderate-intensity physical activity provide health benefits. There is no threshold that must be exceeded before benefits begin to occur.

- For individuals whose physical activity is below the current public health target range, greater benefits can be achieved by reducing sedentary behavior, increasing moderate-intensity physical activity, or combinations of both.
- For any given increase in moderate-to-vigorous physical activity, the relative gain in benefits is greater for individuals who are below the current public health target range than for individuals already within the physical activity target range. For individuals below the target range, substantial reductions in risk are available with relatively small increases in moderate-intensity physical activity.
- Individuals already within the physical activity target range can gain more benefits by doing more moderate-to-vigorous physical activity. Individuals within the target range already have substantial benefits from their current volume of physical activity.
- Bouts, or episodes, of moderate-to-vigorous physical activity of any duration may be included in the daily accumulated total volume of physical activity. The *2008 Physical Activity Guidelines for Americans* recommended accumulating moderate-to-vigorous physical activity in bouts of 10 minutes or more. Research now shows that any amount of moderate-to-vigorous physical activity counts toward meeting the target range. Previously, insufficient evidence was available to support the value of bouts less than 10 minutes in duration. The 2018 Committee was able to conclude that bouts of any length contribute to the health benefits associated with the accumulated volume of physical activity.

Efforts to promote physical activity can be effective. The 2008 Scientific Report included no information about methods of promoting and facilitating healthy levels of physical activity. The 2018 Scientific Report includes a summary of major findings from the large body of scientific literature about promoting physical activity through different interventions.

- Strong evidence demonstrates that individual-level interventions can increase the volume of physical activity performed by youth and by adults, especially when the interventions are based on behavioral change theories and techniques.
- School-based, especially multi-component, programs and community-wide physical activity programs can be effective.

- Environmental and policy changes that improve access to places where people can be physically active, modify the built environment to better support physical activity behaviors (including physically active transport), and that, in general, make it easier for people to be physically active can be effective.
- Information and communication technologies, including wearable activity monitors, telephone and smartphone programs and applications, computer-tailored print interventions, and the Internet, can be used to enable self-monitoring, deliver messages, and provide support, all of which are helpful in promoting regular physical activity.

PUBLIC HEALTH IMPACT

The public health impact of insufficient physical activity and the potential gains from even small population-wide increases are substantial. Information contained in this report indicates that, in addition to a reduced risk of death, greater amounts of regular moderate-to-vigorous physical activity reduce the risk of many of the most common and expensive diseases or conditions in the United States. Heart disease, stroke, hypertension, type 2 diabetes, dementia, depression, postpartum depression, excessive weight gain, falls with injuries among the elderly, and breast, colon, endometrial, esophageal, kidney, stomach, and lung cancer are all less common among individuals who are or become more physically active. In addition, this report provides evidence that for some of these conditions, individuals who are or become more physically active, relative to their peers with the same condition, have a reduced risk of mortality, reduced risk of developing other chronic diseases or conditions, and reduced risk of progression of the disease they already have. They also have improved physical function and better quality of life.

Each of these conditions alone adds substantially to annual direct and indirect medical costs in the United States. Even small increases in regular moderate-to-vigorous physical activity, especially if made by the least physically active individuals, would appreciably reduce the nation's direct and indirect medical costs. Quantification of the costs attributable to insufficient physical activity was beyond the scope of this Committee. It is clear, however, that the cost reductions would be large by any standards.

More difficult to quantify, but equally as important, are the benefits associated with how individuals feel every day and the energy and vitality they have to carry out their daily lives. Placing dollar estimates on improved cognition across the full life span, better quality of life, fewer symptoms of depression and anxiety, enhanced quality of sleep, and improved physical function is difficult. In addition, monetizing these benefits likely cannot adequately describe the intangible societal benefits that derive from a happier and more energetic population.

THE FUTURE

The field of physical activity and public health has matured markedly in the past 10 years, and it will continue to develop at a rapid pace. Using the existing extensive scientific foundation and aided by recent technological advances, increases in knowledge about the relationships between physical activity and a wide variety of health and quality of life outcomes will surely continue. The Committee has described current evidence and recent gains in knowledge, but recognizes that in the near future, the field will generate more information about the benefits of physical activity and the types and volumes that provide those benefits. In addition, gains in the area of physical activity promotion are accumulating rapidly. Transferring this new knowledge into public health practice has the potential to improve the health of the American public to an unprecedented level.

At the same time, the Committee recognized that important gaps in knowledge still remain. It prepared a substantial list of topic-specific research recommendations. Six overarching recommendations are provided here.

- Determine the independent and interactive effects of physical activity and sedentary behavior on multiple health outcomes in youth, adults, and older adults.
- Determine the role and contribution of light-intensity physical activity alone or in combination with moderate-to-vigorous physical activity to health outcomes.
- Identify effective intervention strategies for increasing physical activity through actions in multiple settings in youth, adults, and older adults. Determine how the effectiveness of interventions differs by sex, age, race, ethnicity, socioeconomic status, and other factors.
- Strengthen the understanding of dose-response relationships between physical activity and multiple health outcomes in youth, adults, and older adults, and especially during the life transitions between these categories.
- Expand knowledge of the extent to which the relationships between physical activity and health outcomes are modified by demographic factors, including sex and race/ethnicity.
- Develop instrumentation and data collection systems that will enhance physical activity surveillance systems in the United States.

PART B. INTRODUCTION

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SETTING THE STAGE

In 2008, the U.S. Department of Health and Human Services (HHS) released the first edition of the *Physical Activity Guidelines for Americans*.[1] The Guidelines provides science-based advice on how physical activity can help promote health and reduce the risk of chronic disease. The Guidelines serves as the benchmark and primary, authoritative voice of the federal government for providing science-based guidance on physical activity, fitness, and health for Americans. It provides a foundation for federal recommendations and education for physical activity programs for Americans, including those at risk of chronic disease.

The Guidelines were developed using information from a Physical Activity Guidelines Advisory Committee,[2] similar to the expert committees formed for the *Dietary Guidelines for Americans*[3] process. This committee mechanism was recognized as an effective approach to obtain a comprehensive and systematic review of the science, which contributes to successful federal implementation as well as broad public acceptance of the Guidelines.

In 2013, five years after the Guidelines was released, HHS developed the *Physical Activity Guidelines Midcourse Report: Strategies to Increase Physical Activity Among Youth*.[4] This report built on the 2008 Guidelines[1] by focusing on strategies to help youth achieve the recommended 60 minutes of daily physical activity in a variety of settings, including school, preschool and childcare, community, family and home, and primary care.

The 2008 Guidelines[1] was developed because of strong evidence that regular physical activity promotes health and reduces risk of many chronic diseases, including heart disease, diabetes, and several cancers. This evidence base continues to grow; thus, in December 2015 HHS began the process of developing the second edition of the Physical Activity Guidelines by calling for nominations to the 2018 Physical Activity Guidelines Advisory Committee.

THE PHYSICAL ACTIVITY GUIDELINES ADVISORY COMMITTEE

The 2018 Physical Activity Guidelines Advisory Committee (Committee) was formed to provide independent advice and recommendations based on current scientific evidence for use by the federal government in developing the second edition of the *Physical Activity Guidelines for Americans*.

Nominations for nationally recognized experts in the field of physical activity and health were sought from the public through a *Federal Register* notice published on December 18, 2015. Criteria for Committee members included knowledge about current scientific research in human physical activity; familiarity with the purpose, communication, and application of federal physical activity guidelines; and demonstrated interest in the public's health and well-being through their research and/or educational endeavors. Expertise was sought in specific specialty areas related to physical activity and health promotion or disease prevention, including but not limited to: health promotion and chronic disease prevention; bone, joint, and muscle health and performance; obesity and weight management; physical activity and risk of musculoskeletal injury; physical activity and cognition; physical activity within specific settings, such as preschool or childcare, schools (e.g., activity breaks, physical education), the community, or built environment; physical activity dose-response; sedentary behavior; behavior change; systematic reviews; and special populations, including children, older adults, individuals with disabilities, and women who are pregnant or postpartum.

To ensure that recommendations of the Committee took into account the needs of the diverse groups served by HHS, membership was sought to include, to the extent practicable, a diverse group of men and women with representation from various geographic locations, racial and ethnic groups, and individuals with disabilities. Equal opportunity practices, in line with HHS policies, were followed in all membership appointments to the Committee. Appointments were made without discrimination on the basis of age, race and ethnicity, gender, sexual orientation, disability, or cultural, religious, or socioeconomic status. Individuals were appointed to serve as members of the Committee to represent balanced viewpoints of the scientific evidence and not to represent the viewpoints of any specific group. Members of the Committee were classified as Special Government Employees during their term of appointment, and as such were subject to the ethical standards of conduct for all federal employees. The Committee served without pay and worked under the regulations of the Federal Advisory Committee Act, known as FACA (Public Law 92-463 (5 U.S.C. Appendix 2, the Federal Advisory Committee Act of 1972), as amended).

The Secretary of HHS appointed 17 individuals for membership to the Committee in June 2016. The selected individuals are highly respected by their peers for their depth and breadth of scientific knowledge of the relationship between physical activity and health in all relevant areas of the current Physical Activity Guidelines. Biographical sketches of the Committee members are presented in Part H. Appendix 3. Biographical sketches.

CHARGE TO THE COMMITTEE

The Committee was established for the single, time-limited task of reviewing the 2008 *Physical Activity Guidelines for Americans* and developing physical activity and related health recommendations in this Scientific Report to the Secretary of HHS. The Committee's charge, which was described in the Committee's charter, is as follows:

The Committee, whose duties are time-limited and solely advisory in nature, will:

- Examine the first edition of the Physical Activity Guidelines for Americans and determine topics for which new scientific evidence is likely to be available that may reconfirm or inform revisions to the current guidance or suggest new guidance.

- Place its primary focus on the systematic review and analysis of the evidence published since the last Committee deliberations.
- Place its primary emphasis on the development of physical activity recommendations for the general population in the United States and for specific subgroups of the population where warranted by a public health need.
- Prepare and submit to the Secretary of HHS a scientific advisory report of technical recommendations with rationales to inform the development of the second edition of the Physical Activity Guidelines for Americans. The Committee is responsible for providing authorship for this scientific report; however, responsibilities do not include translating the recommendations into policy, developing a draft of the policy, or making recommendations for implementation, including communication and outreach strategies.
- Disband upon the submittal of the Committee's recommendations via the scientific advisory report to the Secretary of HHS.
- Complete all work within the two-year charter time frame.

COMMITTEE PROCESSES

The Committee operated under the regulations of the Federal Advisory Committee Act as outlined in its charter which was filed with Congress on June 1, 2016. This process ensures independent review in an open public manner, with opportunities for public participation.

Committee Meetings

The Committee held five public meetings over the course of 16 months. Meetings were held in July and October 2016, and March, July, and October 2017. The members met in person on the campus of the National Institutes of Health in Bethesda, Maryland, for each meeting. All meetings were publicly available live by videocast. In addition, the public was invited to attend the Committee's first two meetings in person. All meetings were announced through a *Federal Register* notice. Meeting summaries, presentations, archived recordings of all of the meetings, and other Committee related materials are available at https://health.gov/paguidelines.

Public Comments

Oral comments from the public were presented at the second public meeting, and written comments were accepted throughout the tenure of the Committee. Written comments were shared with the

Committee members as they were received. These comments are available for review at https://health.gov/paguidelines. The public comments process is described in *Part H. Appendix 4. Public Comments*.

Committee Organization and Work Process

During its first public meeting, the Committee decided that the work of reviewing the science would be best achieved by establishing subcommittees, each of which would review and interpret the literature for specific health outcomes and/or populations and summarize their findings as a chapter in the report. The Subcommittees, composed of Committee members and consultants, communicated by email and conference calls and met during public Committee meetings. Each Subcommittee was responsible for presenting to the full Committee its literature review process, grade and conclusion statement for each question, and research recommendations. During the public meetings, the Subcommittees responded to questions and made changes as indicated. The conclusions in this report represent the consensus of the entire Committee.

The Committee formed nine subcommittees: Aging, Brain Health, Cancer – Primary Prevention, Cardiometabolic Health and Prevention of Weight Gain, Exposure, Individuals with Chronic Conditions, Promotion of Physical Activity, Sedentary Behavior, and Youth. After its first public meeting, the Committee formed three Work Groups to consider additional topics: Physical Fitness, Youth to Adult Transition, and Pregnancy and Postpartum. The Subcommittee and Work Group organization are detailed in P*art H. Appendix 2. PAGAC Subcommittee and Work Group Assignments*. Each Committee member served on at least two Subcommittees, with the exception of the Co-Chairs, one of whom was a Subcommittee chair. The other Co-Chair participated in all of the other Subcommittees and Work Groups.

To assist in the review process, Subcommittee chairs identified consultants to fill knowledge gaps in one or more specific areas (see consultant list in *Membership List*). Consultants participated in Subcommittee discussions and decisions, but were not considered Committee members. Similar to Committee members, they completed ethics training and went through a federal review and clearance process. In addition, outside experts (see list in *Membership List*) provided information or a presentation to Subcommittees or Work Groups on a specific topic or question at one meeting.

A Designated Federal Officer (DFO) and Alternate DFO from the Office of Disease Prevention and Health Promotion (ODPHP) supported the Committee members. ODPHP served as the administrative lead for this project. The DFO and Alternate DFO also served as two of the seven Co-Executive Secretaries, who represented the various agencies responsible for federal physical activity policy and programs. These agencies include ODPHP, the Centers for Disease Control and Prevention (CDC), the National Institutes of Health (NIH), and the President's Council on Fitness, Sports & Nutrition (PCFSN). Each Subcommittee was supported by a federal staff liaison trained in the Federal Advisory Committee Act management and a systematic review liaison from the literature review team.

Approaches to Reviewing the Evidence

The Committee used the state-of-the-art methodology—systematic reviews—to address its 38 research questions and 104 subquestions. These reviews are publicly available on https://health.gov/paguidelines/second-edition/report/supplementary-material.aspx. *Part E. Systematic Review Literature Search Methodology* of this report details the process used by the Committee to evaluate the scientific evidence. This section also describes the grading rubric the Committee used to grade the level of evidence available to answer its questions. Each Subcommittee drafted a chapter that summarizes and synthesizes the results of its review and includes the evidence grades and conclusion statements for each question (see *Part F. The Science Base*). Research recommendations to address gaps that could advance knowledge related to the question posed and inform future federal physical activity guidance, as well as other policies and programs, are included at the end of each chapter and in *Part G. Needs for Future Research*. At least two Committee members who were not members of the drafting Subcommittee and federal staff liaisons reviewed each chapter.

Report Structure

Reflecting the Subcommittee and Work Group structure, the bulk of the report consists of 11 science-based chapters that summarize the evidence assessed and evaluated by the Committee. Ten chapters correspond to the work of the nine Subcommittees—the Exposure Subcommittee's findings are split into two chapters—and one chapter covers the work of the Pregnancy and Postpartum Work Group.

In addition to summarizing the evidence relating physical activity to individual health outcomes, one of the Committee's major goals was to integrate the scientific information on the relationship between physical activity and health and to summarize it in a manner that could be used effectively by HHS to develop the Physical Activity Guidelines and related statements. This information is contained in Part D. Integrating the Evidence.

CONTENTS AND ORGANIZATION OF THE SCIENTIFIC REPORT

The report starts with a *Membership List* of the Physical Activity Guidelines Advisory Committee members, consultants, and federal staff to acknowledge the individuals involved in the development of this report. There are four major components in the report. The first component provides essential background and synthesis information and includes:

- *Part A. Executive Summary* provides an executive summary of the entire report.
- *Part B. Introduction* provides a brief background on the rationale for updating the *Physical Activity Guidelines for Americans* and an explanation of the Committee's formation, structure, and process to develop its report.
- *Part C. Background and Key Physical Activity Concepts* explains the concepts and terminology that provide the foundation for the report's content and framing, including those relating to physical activity, sedentary behavior, dimensions of physical activity, physical fitness, and measurement.
- *Part D. Integrating the Evidence* synthesizes the Committee's findings about the relation of physical activity to a broad array of health outcomes.
- *Part E. Systematic Review Literature Search Methodology* explains the process used to systematically review the literature review questions.

The second component, *Part F. The Science Base*, includes 11 chapters organized into four sections that review and summarize the scientific literature relating physical activity to individual health-related outcomes and populations:

New Issues in Defining Physical Activity

- Chapter 1. Physical Activity Behaviors: Steps, Bouts, and High Intensity Training
- Chapter 2. Sedentary Behavior

Physical Activity and Selected Health Outcomes

- Chapter 3. Brain Health
- Chapter 4. Cancer Prevention
- Chapter 5. Cardiometabolic Health and Prevention of Weight Gain
- Chapter 6. All-cause Mortality, Cardiovascular Mortality, and Incident Cardiovascular Disease

Physical Activity Considerations for Selected Populations

- Chapter 7. Youth
- Chapter 8. Women Who are Pregnant or Postpartum
- Chapter 9. Older Adults
- Chapter 10. Individuals with Chronic Conditions

Promoting Physical Activity

- Chapter 11. Promoting Regular Physical Activity

The third component, *Part G. Needs for Future Research* provides the Committee's collective recommendations about key areas of research that could address gaps they encountered and further enhance the science base on physical activity and health.

The fourth component, *Part H. Appendices*, includes 1) glossary of terms, 2) list of Subcommittee and Work Group assignments, 3) biographical sketches of Committee members, and 4) description of the public comment process with a link to the public comment database.

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PART C. BACKGROUND AND KEY PHYSICAL ACTIVITY CONCEPTS

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HISTORICAL PERSPECTIVE

The field of physical activity and public health has been developing at a rapid pace during the past several decades. During the 1950s and 1960s, two scientific areas – exercise science and epidemiologic science – converged in an effort to understand and address the heart disease epidemic. In the United States, the percentage of all deaths caused by heart disease had risen from 8 to 10 percent in the early 1900s to slightly less than 40 percent by 1960.[1] By the late 1980s, scientific evidence had clearly shown that regularly performed moderate-to-vigorous physical activity reduced the risk of heart disease.[2] Evidence of other health benefits soon followed.[3] This *2018 Physical Activity Guidelines Advisory Committee Scientific Report* adds to the lengthening list of health benefits of regular physical activity.

Less well recognized has been a third area of influence beyond exercise science and epidemiologic science. In 1974, the Canadian government published a report titled *A New Perspective on the Health of Canadians*.[4] More commonly referred to as "The Lalonde Report," after the Canadian Minister of Health and Welfare, the report made a clear distinction between the clinical health care system and the arena of disease prevention and health promotion. Within disease prevention and health promotion, it called attention to the importance of "lifestyle," including physical activity. The Canadian report was followed by the U.S. report, *Healthy People: The Surgeon General's Report on Health Promotion and Disease Prevention*, which had a similar message.[5] These documents called attention to the important impact of lifestyle behaviors on the risk of disease, an observation that is now well accepted. Also widely recognized is the fact that individual behaviors, including physical activity behaviors, are determined not solely by individual choice but by social and cultural factors as well as environmental impediments or opportunities.

Thus, while exercise science and epidemiologic science remain central to the field of physical activity and public health, the field now includes an array of other scientific disciplines. Behavioral science, clinical science, recreation science, transportation science, city planning, political science, and other disciplines are now recognized to be essential for the proper study and practice of physical activity and public health.

The widening range of scientific fields currently contributing to this topic reflects the recognition that physical activity is embedded and intricately connected to every aspect of daily life. No longer viewed only as distinct and prolonged bouts of "vigorous physical exercise,"[6] physical activity is recognized as encompassing the accumulation of movement occurring throughout the day, regardless of location, type, or purpose. This broader view of physical activity complicates the study, understanding, and discussion of this key health behavior. The purpose of this chapter is to provide a brief discussion of physical activity-related terminology and issues that may help readers understand the concepts, evidence, and interpretations that are presented elsewhere in this report.

The *Physical Activity Guidelines Advisory Committee Report, 2008*[7] and the *2008 Physical Activity Guidelines for Americans*[8] demonstrated that the importance and value of physical activity and public health had been recognized at the highest level of government. The 2018 Scientific Report is further evidence of the importance of physical activity to the national interest.

PHYSICAL ACTIVITY TERMS AND DIMENSIONS

As the field has matured and the complexity of physical activity has become more apparent, applying clear definitions and descriptions of relevant concepts and issues has become increasingly important. In this document, the Committee has endeavored to use the most appropriate terms for the physical activity behaviors and concepts being discussed.

Core Terms

Physical activity is bodily movement produced by skeletal muscles that results in energy expenditure.[9] The term, physical activity, does not require or imply any specific aspect or quality of movement. The term encompasses all types, intensities, and domains. Although the term “physical activity” has been used often as a short-hand description for moderate-to-vigorous-intensity forms of physical activity, given current interest and discussions about physical activity of intensities less than moderate-intensity (i.e., <3 METs, see description below), the term “physical activity” should be used when discussing the full range of intensities. More specific descriptors such as sedentary behavior, light, moderate, vigorous, or moderate-to-vigorous should be used when talking about a specific range of intensities.

Exercise is physical activity that is planned, structured, repetitive, and designed to improve or maintain physical fitness, physical performance, or health.[9] Exercise, like physical activity, encompasses all intensities. The word exercise, like the term physical activity, has been used often to mean moderate-to-vigorous-intensity physical activity. However, it is preferable to specify the intensity when discussing or describing exercise.

Sedentary behavior is any waking behavior characterized by an energy expenditure 1.5 or fewer METs while sitting, reclining, or lying.[10] Most office work, driving a car, and sitting while watching television are examples of sedentary behaviors.

Non-exercise physical activity is a phrase that encompasses all physical activity that is not exercise. It has been used to mean various types and intensities of physical activity, mostly light intensity physical activity. Given its ambiguity, however, clearer descriptions of the physical activity behavior of interest are preferable.

Types of Physical Activity

Specific Types of Activity

A common way of describing physical activity type is to specify the activity under discussion. Walking, bicycling, tai chi, bocce ball, gardening, and vacuuming are examples of specific activities.

Activity by Predominant Physiologic Effect

Aerobic Physical Activity

Aerobic physical activity includes forms of activity that are intense enough and performed long enough to maintain or improve an individual's cardiorespiratory fitness. Aerobic activities such as walking, basketball, soccer, or dancing, commonly require the use of large muscle groups. The connection between aerobic activities such as these and cardiorespiratory fitness is sufficiently close that the term "aerobic capacity" is considered equivalent to cardiorespiratory fitness. Technically, aerobic physical activity includes any activity that could be maintained using only oxygen-supported metabolic energy pathways and could be continued for more than a few minutes. However, since the publication of *Aerobics* in 1969[11] in both common and scientific usage, "aerobic" activity has come to mean physical activity that would be expected to maintain or improve cardiorespiratory fitness or aerobic capacity.

Anaerobic Physical Activity

Anaerobic physical activity refers to high-intensity activity that exceeds the capacity of the cardiovascular system to provide oxygen to muscle cells for the usual oxygen consuming metabolic pathways. Anaerobic activity can be maintained for only about 2 to 3 minutes. Sprinting and power lifting are examples of anaerobic physical activity.

Muscle-strengthening Activities

Muscle-strengthening activities maintain or improve muscular strength (how much resistance can be overcome), endurance (how many times or for how long resistance can be overcome), or power (how fast can the resistance be overcome). Muscle-strengthening activities include everyday behaviors, such as carrying heavy groceries, shoveling snow, lifting children, or climbing stairs, as well as the use of exercise equipment, such as weight machines, free weights, or elastic bands.

Bone-strengthening Activities

Bone-strengthening activities are movements that create impact and muscle-loading forces on bone. These forces stress the bone, which adapts by modifying its structure (shape) or mass (mineral content), thereby increasing its resistance to fracture. Jumping, hopping, skipping, and dancing are activities that are good for bone strengthening, as are muscle-strengthening activities.

Balance Training

Balance training activities are movements that safely challenge postural control. If practiced regularly, they improve the ability to resist intrinsic or environmental forces that cause falls whether walking, standing, or sitting. Standing on one foot, walking heel-to-toe, the balance walk, and using a wobble board are examples of balance training activities.[12, 13]

Flexibility Training

Flexibility training, also called stretching, improves the range and ease of movement around a joint. Dynamic stretching, such as the movements of tai chi, qigong, and yoga, and static stretching are examples of flexibility training.

Yoga, Tai Chi, and Qigong

These activities, whose origins lie outside of Western culture, typically combine muscle-strengthening, balance training, light-intensity aerobic activity, and flexibility in one package. Some variations of yoga, tai chi, and qigong emphasize relaxation, meditation, or spirituality as well. As a result, are sometimes referred to as “mind-body” activities.

Domains of Physical Activity

As noted above, physical activity occurs throughout the day, for a variety of purposes, and in many types of settings. Occupational forms of physical activity were the focus of most of the initial epidemiologic studies on physical activity and health.[14, 15] As occupations requiring high levels of physical activity declined, the research focus shifted to leisure-time or recreational physical activity.[16, 17] Most of the research findings summarized for this report are based on studies of leisure-time physical activities. For many individuals, physical activity during leisure-time is more easily modified than during other domains and includes the majority of moderate-to-vigorous intensity activities.

Nevertheless, physical activity can and does occur throughout all portions of the day, and, with few exceptions, the health-enhancing value of physical activity is independent of the purpose for performing it. As a result, non-leisure forms of physical activity, such as transport-related physical activities like cycling to work, are now recognized as options for physical activity promotion. There are many ways of grouping physical activity. One popular method categorizes physical activity into four domains, as follows:

- **Occupational physical activity** is performed while one is working. Stocking shelves in a store, delivering packages in an office, preparing or serving food in restaurant, or carrying tools in a garage are examples of occupational physical activity.
- **Transportation physical activity** is performed in order to get from one place to another. Walking or bicycling to and from work, school, transportation hubs, or a shopping center are examples.
- **Household physical activity** is done in or around one's home. It includes household tasks such as cooking, cleaning, home repair, yardwork, or gardening.
- **Leisure-time physical activity** is performed at one's discretion when one is not working, transporting to a different location, and not doing household chores. Sports or exercise, going for a walk, and playing games (hopscotch, basketball) are examples of leisure-time physical activity.

Body Position

The rising interest and recognized importance of low energy expenditure activities call attention to body position during physical activity. Physical activity occurs in any body position. Some positions, notably, lying, reclining, and sitting, facilitate less bodily movement and energy expenditure than do standing or ambulating. Recently developed motion sensors can measure low levels of physical activity more accurately than previously possible and have enabled research in this area. Given the large amount of awake time that is spent sitting, much of the research has focused upon sitting. To promote standard terminology and improve communication, researchers have collaborated in the development of a proposed set of definitions for research in this area.[10] The definition of sedentary behavior, "any waking behavior characterized by an energy expenditure ≤1.5 metabolic equivalents (METs), while in a sitting, reclining or lying posture," is used throughout this report.

Absolute and Relative Intensity

Absolute Intensity

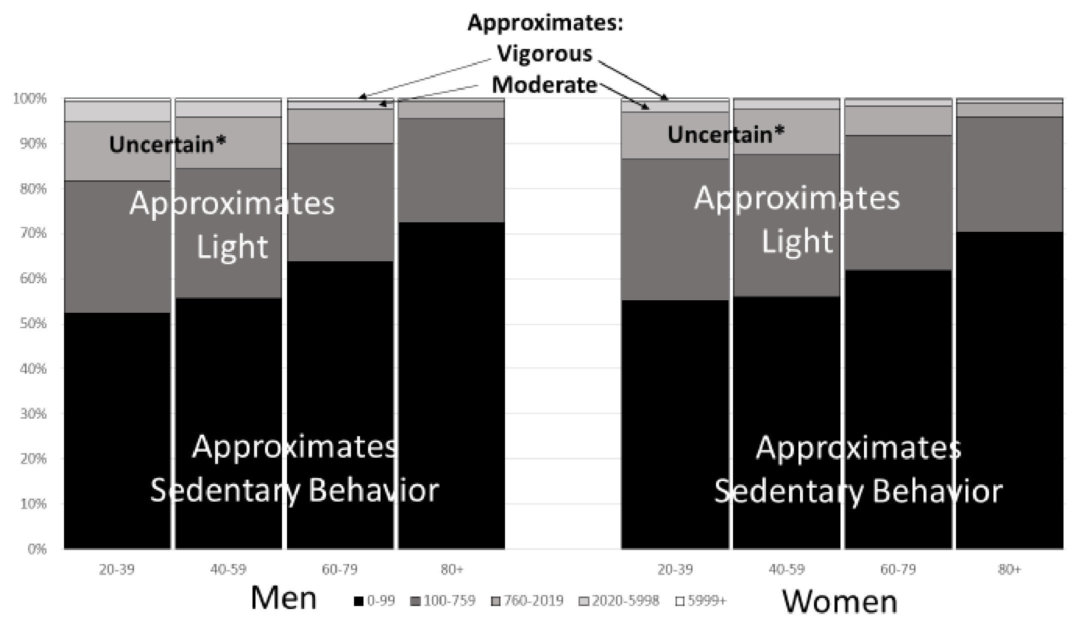
Absolute intensity is the rate of energy expenditure required to perform any physical activity. It can be measured in METs, kilocalories, joules, or oxygen consumption. The most commonly mentioned unit in this report is the MET. One MET is the rate of energy expenditure while sitting at rest, which, for most people approximates an oxygen uptake of 3.5 milliliters per kilogram per minute. The energy expenditure of other activities is expressed in multiples of METs. For example, for the average adult, sitting and reading requires about 1.3 METs. Strolling or walking slowly requires about 2.0 METs. Walking at about 3.0 miles per hour requires about 3.3 METs, and running at 5 miles per hour requires about 8.3 METs. The average rate of energy expenditure for a substantial number of activities has been documented for the general adult population[18] and for children and youth ages 6 to 18.[19]

Absolute rates of energy expenditure commonly have been divided into 4 categories.

- **Vigorous-intensity activity** requires 6.0 or greater METs; examples include walking very fast (4.5 to 5 mph), running, carrying heavy groceries or other loads upstairs, shoveling snow by hand, mowing grass with a hand-push mower, or participating in an aerobics class. Adults generally spend less than 1 percent of waking time in vigorous activity (Figure C-1).[20]
- **Moderate-intensity activity** requires 3.0 to less than 6.0 METs; examples include walking briskly or with purpose (3 to 4 mph), mopping or vacuuming, or raking a yard.
- **Light-intensity activity** requires 1.6 to less than 3.0 METs; examples include walking at a slow or leisurely pace (2 mph or less), cooking activities, or standing while scanning groceries as a cashier.
- Physical activity requiring 1.0 to 1.5 METs have, in the past, been referred to as "sedentary activity." Almost all these physical activities are included in the term "sedentary behavior," defined earlier to be any waking behavior characterized by an energy expenditure 1.5 or fewer METs while sitting, reclining, or lying.[10] The one common activity with an energy expenditure of 1.5 METs not included within sedentary behavior is standing quietly. Continued use of the term "sedentary activity" is sure to be confusing, especially because standing is the only behavior within it not covered by "sedentary behavior." In this report, the Committee has simply used the

word standing whenever necessary. These low-intensity physical activity behaviors are very common. Accelerometer-based estimates indicate that adults in the United States spend more than 50 percent of their waking time in physical activities requiring an estimated 1.0 to 1.5 METs (Figure C-1).[21]

Figure C-1. Proportion of Time-awake at Different Categories of Accelerometer Counts for U.S. Adults, by Sex and Age Group, 2003-2004



Note: *=Some researchers categorize counts in this range as light-intensity, others as moderate-intensity.
Source: Adapted from data found in Matthew, 2005,[22] and Troiano et al., 2008.[20]

Relative Intensity

For the general young to middle-aged adult population, the terms used to describe the rate of energy expenditure – light, moderate, vigorous – adequately represent the perceived level of effort to perform an activity. Older individuals, those with certain physical impairments, or individuals who have been very inactive may have a lower aerobic capacity and, as a result, may perceive the activity to be relatively more difficult to perform,[23] thereby creating a mismatch between the word used to describe the absolute rate of energy expenditure and the individual's perceived level of effort.

Relative intensity refers to the ease or difficulty with which an individual performs any given physical activity. It has a physiologic basis and can be described using physiologic parameters, such as percent of aerobic capacity (VO_2max) or percent of maximal heart rate. Relative intensity can also be measured with tools that assess an individual's perception about how difficult it is to perform an activity. A variety of tools have been developed to help individuals self-regulate the relative intensity of their aerobic physical activity. For ease of use in non-clinical settings, the sing-talk test is the simplest. During light-intensity activities most people are able to sing, during moderate-intensity they can talk but not sing, and during vigorous activities, even talking is difficult.[24] Also simple to use is a 10-point scale, originally designed as a communication tool, where 0 is sitting and 10 is the greatest effort possible.[8] Moderate-intensity physical activity is about half way (five or six points), with vigorous higher (seven or eight). In general, an individual's subjective assessment of how hard he or she is working corresponds well with laboratory-based assessments of capacity.

The contrast between absolute and relative intensities can be highlighted by noting that the focus of absolute intensity is the activity, whereas the focus of relative intensity is the individual's level of effort during the activity. Observational population-based studies typically determine what an individual has done and estimate the energy required to do it, so the measurement is absolute. Experimental studies typically use relative intensity in prescribing a program of physical activity to ensure the desired level of effort is appropriate for the individual.

Dose, Volume, and Dose-response for Aerobic Activities

Dose

Dose of aerobic physical activity is the type and amount of reported or prescribed physical activity. Physical activity may be prescribed for improving health, rehabilitation, training, or research. As devices to measure physical activity become more common and functional in both research and popular use, modifications in the components and summary descriptors of dose are likely.

The components of dose for aerobic physical activity are the frequency, duration, and intensity of the physical activity:

- **Frequency** is usually counted as sessions or bouts of moderate-to-vigorous physical activity per day or per week.
- **Duration** is the length of time for each session or bout.
- **Intensity** is the rate of energy expended during the physical activity session or bout, usually in METs.

Dose is commonly calculated for a specific period of time, such as per day or per week, and, for aerobic activity, has been limited to moderate-to-vigorous physical activity because those are the intensities known to provide benefits. Increasingly, the acronym FITT, standing for frequency, intensity, time (duration), and type of activity (e.g., aerobic, muscle-strengthening) has been used to describe physical activity dose.[25]

Volume

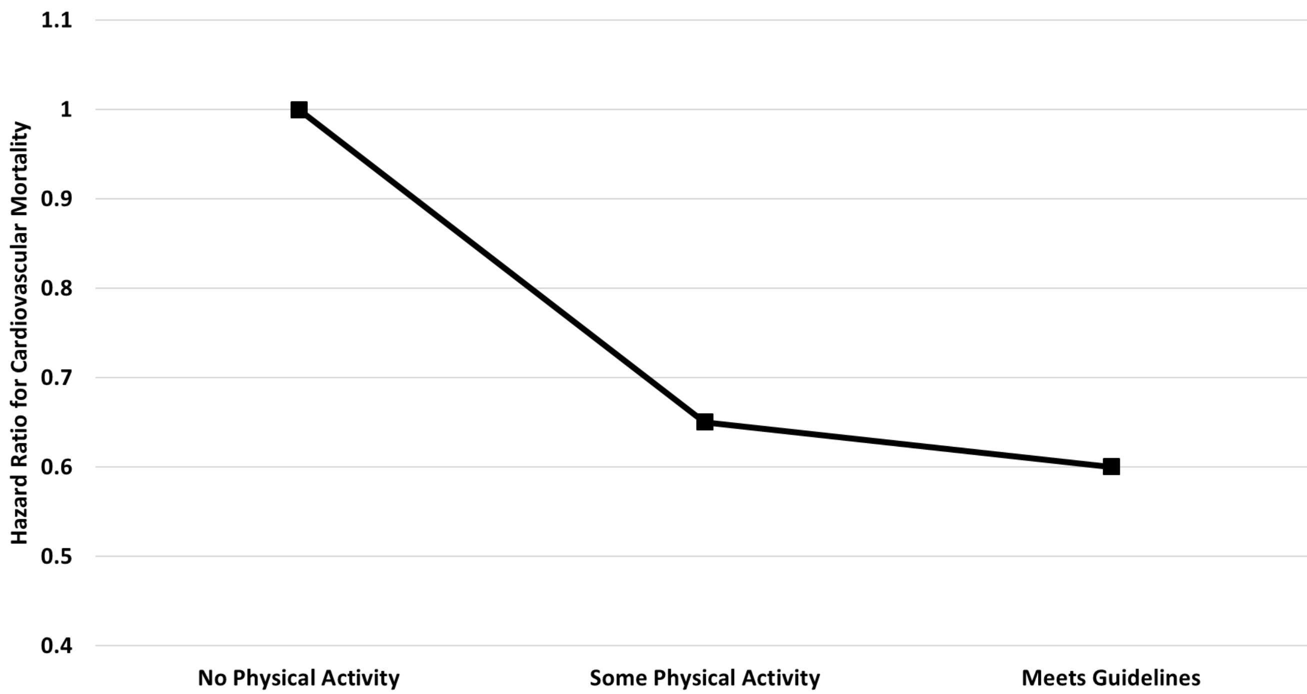
Volume is the quantification of the dose of activity accumulated over a specified length of time. Volume is usually expressed in MET-minutes or MET-hours per day or week. It is calculated by multiplying the physical activity frequency and duration by the MET values corresponding to that physical activity. For activities, such as walking or running, where a rate of energy expenditure at any given speed is a fixed amount, volume is sometimes simplified to minutes or hours of the activity, such as minutes per week of walking. Kilocalories per day or per week is used is used less frequently.

As the use of personal devices (see Devices, below) to measure physical activity has increased, volume is sometimes expressed as activity counts or step counts during a set period of time. Steps are easily counted. Step counts are easily understood by individuals and the media. They are a useful prescription tool for health care providers and trainers. Step counts blend well with public health messages encouraging the use of stairs rather than elevators, walking in airports rather than taking the train or shuttle, or parking at a distance from the final destination. Step counts include light- as well as moderate- and vigorous-intensity physical activity. As a result, the number of steps that would be equivalent to 150 to 300 minutes per week of moderate-to-vigorous physical activity varies from individual to individual and it may be less than the commonly suggested 10,000 steps.[26,27] Regardless, step counts are simple to use, can be tailored to meet individual needs, and appear to be useful for monitoring progress toward personal goals.[8]

Dose-response

Dose-response is the relationship between the dose or volume of physical activity and the magnitude of change, if any, in the health outcome or physiologic change. A graduated response—small dose with small response, large dose with large response—is evidence of the truth of the relationship. For ordinal data, a dose-response relationship requires at least three levels of exposure, in this case three volumes of physical activity (Figure C-2). For data collected as a continuous variable, differing shapes of the relationship can be examined. The shape of a dose response curve adds importantly to the understanding of the relationship. For example, in Figure C-2, the shape indicates that the majority of the reduction in mortality risk among individuals with type 2 diabetes is achieved by moving from "no activity" to "some activity", and that meeting the Guidelines confers additional benefits.

Figure C-2. Risk of Cardiovascular Mortality Among People with Type 2 Diabetes by Dose of Physical Activity



Source: Adapted from data found in Sadarangani et al., 2014.[28]

MEASURING PHYSICAL ACTIVITY

Measuring physical activity with reasonable accuracy and acceptable cost is vital to the understanding of the relationship between physical activity and health. Because of the complexity of physical activity, measuring it may be the most difficult aspect of the study and promotion of physical activity.

Over time, the preferred method of measuring physical activity behavior has changed. Early epidemiologic studies commonly relied upon job categories to categorize workers into higher or lower levels of physical activity. As mechanization reduced the number of jobs requiring substantial amounts of physical activity, questionnaires to assess primarily leisure-time physical activity became the predominant method. Recently, technological advances have made possible the development of devices to assess bodily movement. The accuracy of devices has improved and the cost has declined such that devices are now the preferred measurement tool in many epidemiologic studies.

Occupational Categories

Estimates of the energy requirements for various job categories provided an inexpensive and simple method of dividing individuals into higher and lower physical activity categories. Only employed individuals, mostly men, were included and the method assumes all workers in the same category expend about the same energy on the job. The decline in physically demanding jobs has made job categories a less useful measurement tool than they were 60 to 70 years ago. Nevertheless, the method provided persuasive evidence that individuals who were more physically active had lower rates of cardiovascular disease than did their co-workers who had less physically demanding jobs.

Questionnaires

Information for questionnaires usually comes from individuals reporting on their own physical activity behavior. It may also come from proxy reporters, such as parents of young children, or observers watching the physical activity of others. Several general categories of questionnaires have been developed, as have large numbers of specific questionnaires within each category. Global questionnaires strive to place individuals into physical activity categories using one or more questions. Quantitative history questionnaires use more questions to inquire about participation in specific activities or activities of specific intensity, almost always moderate-to-vigorous intensity. Physical activity diaries are another form of questionnaire. Many recent questionnaires have begun to inquire about sedentary or sitting behaviors but, for the most part, questionnaires have focused upon moderate-to-vigorous physical activity because those activities are most easily remembered. Questionnaires generally do an adequate job of ranking individuals from high to low physical activity volumes. They are less accurate determining the actual volume of moderate-to-vigorous physical activity performed. Questionnaires are capable of determining the specific activities performed and the domains for those activities. Individuals can also report the relative intensity of their activities. The use of the Internet to administer questionnaires and to collate the responses has reduced the burden on both respondents and researchers.

Devices

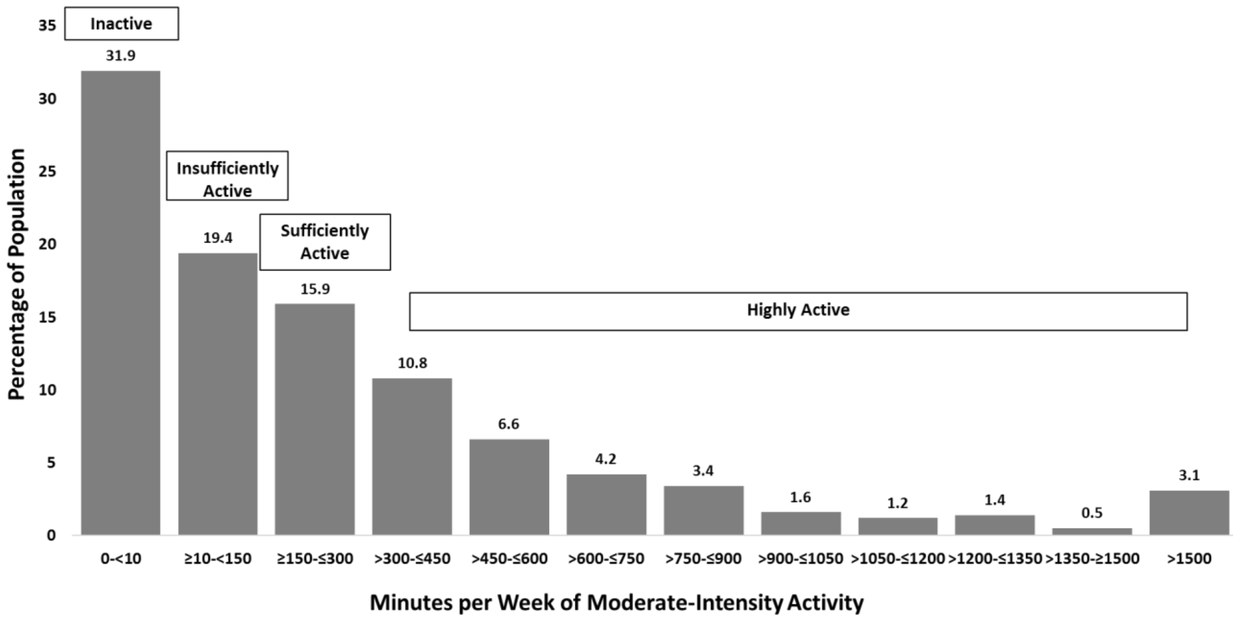
The types and accuracy of devices to measure physical movement have been improving rapidly and their cost has steadily declined. Formerly, devices were one of two general types: pedometers, devices that counted steps, and accelerometers, devices that measured truncal or limb movement. With current technology, accelerometers are now available as smart phone apps and components of wrist watches. They have become more accurate at assessing upper body as well as lower body movements and some are waterproof, enabling the assessment of water activities. Many of these systems use a variety of sensors and technologies and are referred to as “multi-sensor systems.” They measure steps, often are paired with global positioning systems providing estimates of speed and distance, and some include heart rate monitors, making estimates of relative as well as absolute energy expenditure possible. The advances in measurement of bodily movement, especially light-intensity physical activities, will continue to improve knowledge and understanding of the relationship between physical activity and health.

MONITORING PHYSICAL ACTIVITY

Monitoring the status of selected health indicators is a vital function of public health agencies and a critical factor in the allocation of public health resources. Public health agencies now monitor, in addition to causes of death, disease incidence and prevalence, and the prevalence of important health-related behaviors, such as physical activity. They now also recognize the importance of monitoring factors that facilitate or impede physical activity, such as policies and environments. As indicated in the previous section, physical activity is difficult to measure and monitor precisely. Until recently, public health monitoring systems used only self-report instruments. Device-measured physical activity monitoring systems are becoming more available, and already provide useful supplements to existing national systems. The increasing use and capacity of devices that measure physical activity is likely to both enable and require flexibility and change in public health physical activity monitoring systems in the near future.

This section provides examples of useful information provided by public health monitoring systems. One simple and important use of monitoring data is to describe the proportion of individuals performing different amounts of physical activity (Figure C-3). About half of the U.S. adult population reports that they accumulate less than the target range of 150 to 300 minutes of leisure-time moderate-intensity equivalent physical activity each week. Nearly one-third are classified as “inactive,” meaning that they report doing less than 10 minutes of moderate-to-vigorous physical activity. Because the benefits for several important health outcomes, such as cardiovascular disease, type 2 diabetes, and all-cause mortality, accrue rapidly at the lower end of the physical activity range, facilitating more physical activity among the individuals who are inactive would be expected to produce substantial reductions in morbidity and mortality.

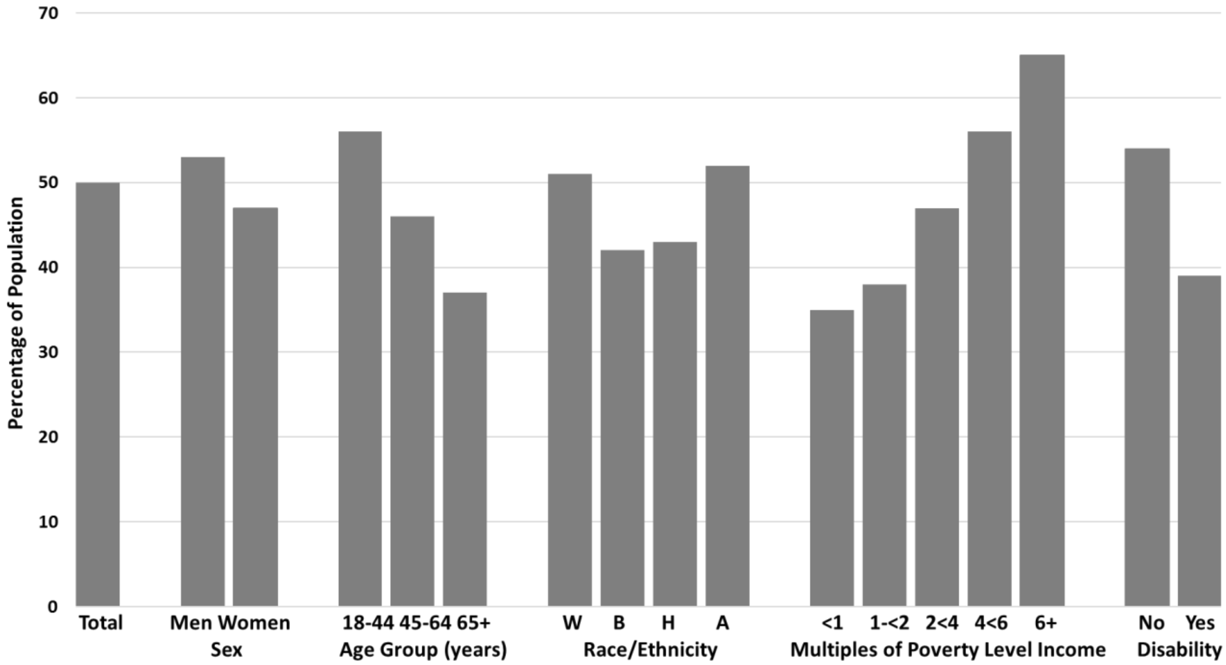
Figure C-3. Distribution of Self-Reported Volume of Moderate-to-Vigorous Physical Activity, 150 Minutes per Week Increments, U.S. Adults, 2015



Source: Adapted from data found in the National Health Interview Survey, 2015.[29]

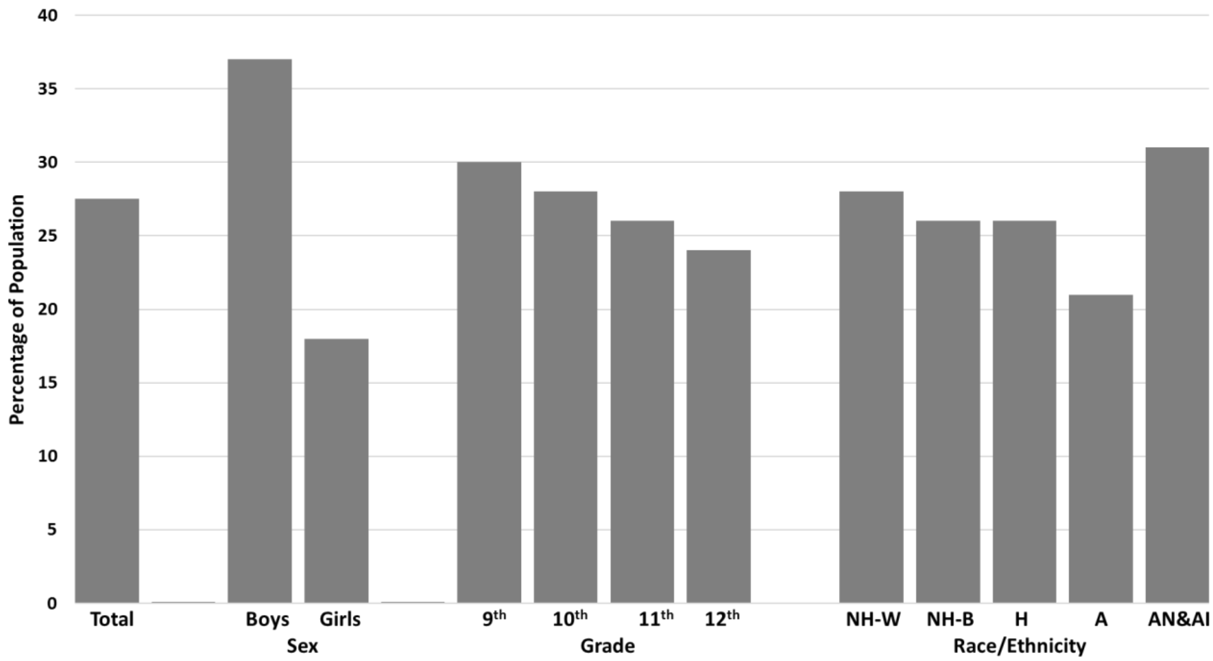
Another important use of monitoring data is to identify population subgroups who stand to benefit the most from increasing their physical activity level (Figure C-4). The proportion of adults in or above the target range differ substantially and systematically across age groups, income groups, and by disability status. Similar information is available for high school students (Figure C-5).

Figure C-4. Percentage Adults within or above Target Range for Moderate-to-Vigorous Physical Activity by Population Subgroup, 2015



Legend: W=White, B=Black, H=Hispanic, A=Asian.
Note: Estimates are age-adjusted using the year 2000 standard population.
Source: Adapted from data found in the National Health Interview Survey, 2015.[29]

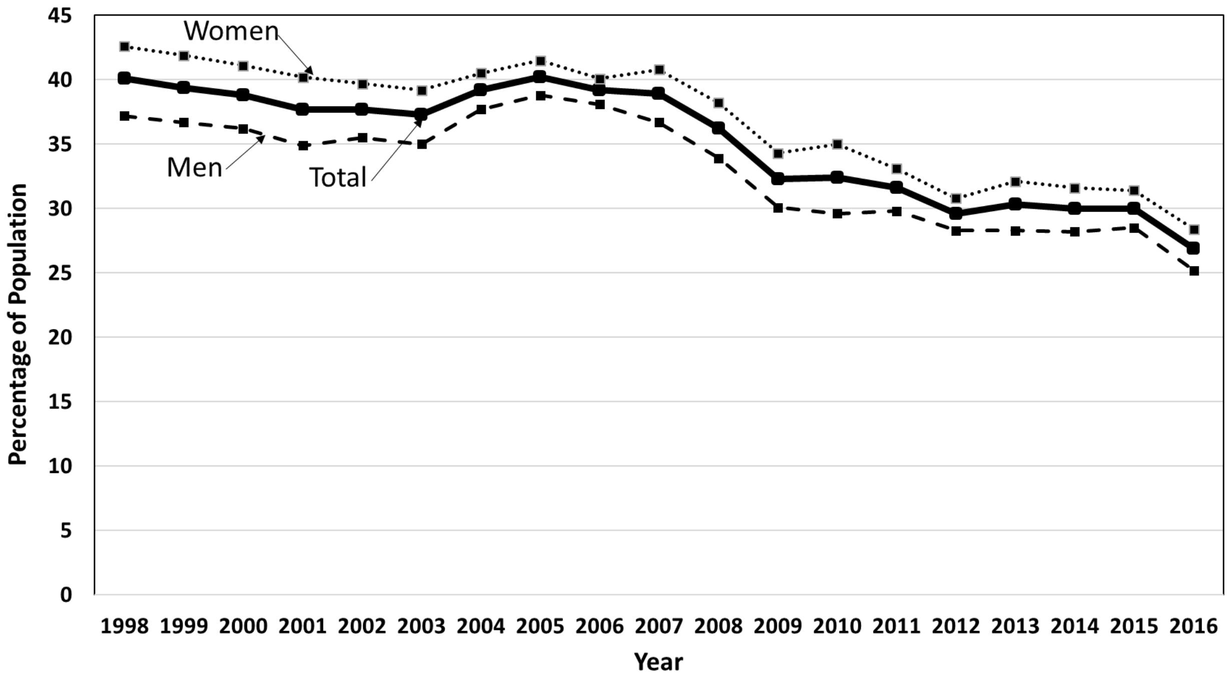
Figure C-5. Percentage of High School Students Meeting Aerobic Target Range, 2013



Legend: NH-W=Non-Hispanic White, NH-B=Non-Hispanic Black, H=Hispanic, A=Asian, AN&AI=Alaska Native and American Indian.
Source: Adapted from data found in the Youth Risk Behavior Survey, 2013.[30]

In addition to information about the current prevalence of physical activity behaviors overall and among subgroups, public health monitoring systems also provide information about changes, if any, over time (Figure C-6). National estimates of changes in prevalence over time provide information about the overall impact of the multiple factors that influence physical activity behaviors. Data from the National Health Interview Survey suggest that from 1998 through 2015 the prevalence of individuals who report doing no leisure-time moderate-to-vigorous physical activity has declined from about 40 percent to 30 percent.[29] The decline has occurred for both women and men.[29]

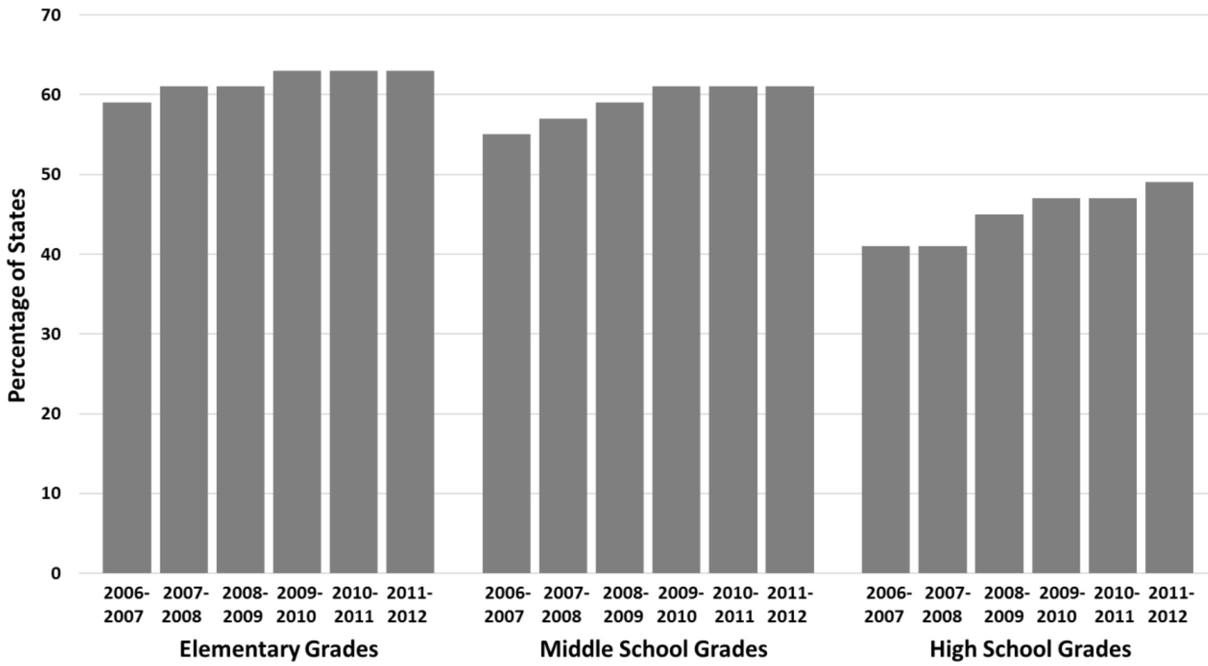
Figure C-6. Prevalence of Adults Who Engage in No Leisure-time Moderate-to-Vigorous Physical Activity, by Sex and Year, 1998 to 2015



Note: Estimates are age-adjusted using the year 2000 standard population.
Source: Adapted from data found in the National Health Interview Survey, 1998-2015.[29]

In addition to monitoring the prevalence of physical activity among population subgroups and over time, current surveillance systems are beginning to monitor the prevalence of policies and environmental characteristics that facilitate regular physical activity participation. For example, the number of states with clear physical education curriculum policies in elementary, middle, and high schools has slowly risen between 2006 and 2012 (Figure C-7).[31]

Figure C-7. Percentage of States with a Clear Physical Education Policy, by Level of School, School Years 2006-2007 to 2011-2012



Source: Adapted from data found in Institute of Medicine, 2013.[31]

PHYSICAL FITNESS

Physical fitness is a physiologic attribute determining a person's ability to perform muscle-powered work. A fundamental manifestation of this attribute is the ability to move—for example, to walk, run, climb stairs, and lift heavy objects. As a result, physical fitness is an important factor in the ability of individuals to perform routine daily activities and an important issue from a public health perspective. Physical fitness has been defined as "the ability to carry out daily tasks with vigor and alertness, without undue fatigue, and with ample energy to enjoy leisure-time pursuits and respond to emergencies."[32]

The concept of physical fitness typically has been operationalized as a multicomponent construct including cardiorespiratory endurance (aerobic power), musculoskeletal fitness, flexibility, balance, and speed of movement (see Table C-1). For the purposes of this report, to the term "fitness" refers to this general sense.

Table C-1. Components of Physical Fitness

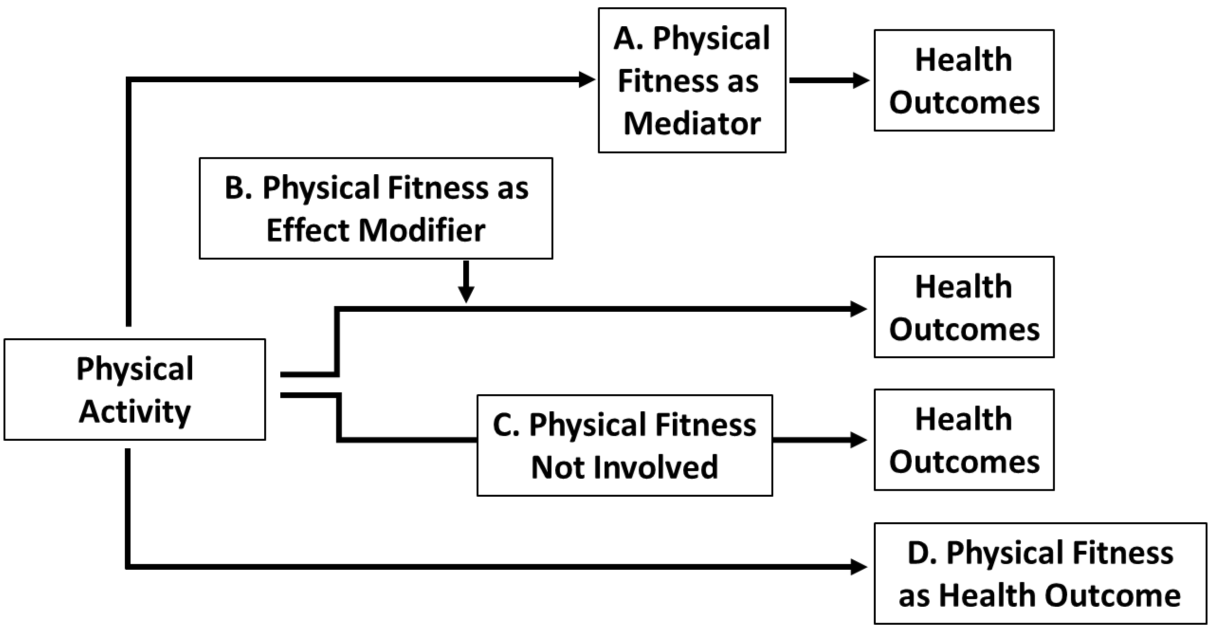
Cardiorespiratory Endurance	The ability to perform large-muscle, whole-body exercise at moderate to high intensities for extended periods of time.
Musculoskeletal Fitness	The integrated function of muscle strength, muscle endurance, and muscle power to enable performance of work.
Flexibility	The range of motion available at a joint or group of joints.
Balance	The ability to maintain equilibrium while moving or while stationary.
Speed	The ability to move the body quickly.

A large volume of research has focused on the relationship between physical activity and health. The findings of that research, summarized elsewhere throughout this report, identify multiple health benefits associated with maintaining greater amounts of physical activity. In addition, a substantial body of research has examined the relationship between physical fitness—cardiorespiratory fitness and, in some cases, musculoskeletal fitness—and health outcomes. The findings show that greater physical fitness is associated with reduced all-cause mortality, cardiovascular disease mortality, and risk of developing a wide range of non-communicable diseases.[33] To date, the majority of this information has been acquired in men, but some data now indicate that these relationships also exist in women.[33]

Thus, compelling scientific evidence indicates that both physical activity and physical fitness provide important health benefits. In addition, it is clear that physical activity and physical fitness are positively correlated,[34] and it is well documented that increases in the amounts and intensities of physical activity typically produce increases in physical fitness, particularly in those who are less physically active at baseline.[35] Accordingly, it is reasonable to question the independence of the relationships between physical activity and physical fitness with health outcomes. In some epidemiological studies it has been possible to examine, independently, the associations of both physical activity and fitness on the incidence of disease outcomes.[36] This research shows that physical activity behavior accounts for only a portion of the impact of physical fitness on health.[37] Similarly, the impact of physical activity on health is partially explained by its effect on physical fitness.[37]

The available evidence suggests that physical activity and physical fitness interact in their effects on a variety of health outcomes. Given that both physical activity and physical fitness are complex multicomponent concepts, it is likely that they interact in a variety of ways to influence health. Figure C-8 is a simple conceptual framework for observational studies. Figure C-9 is a simple conceptual framework for intervention studies.[38, 39] Both are intended to stimulate thought, discussion, and research into the mechanisms of greatest importance to the field of physical activity and public health. The models will be improved by future investigations.

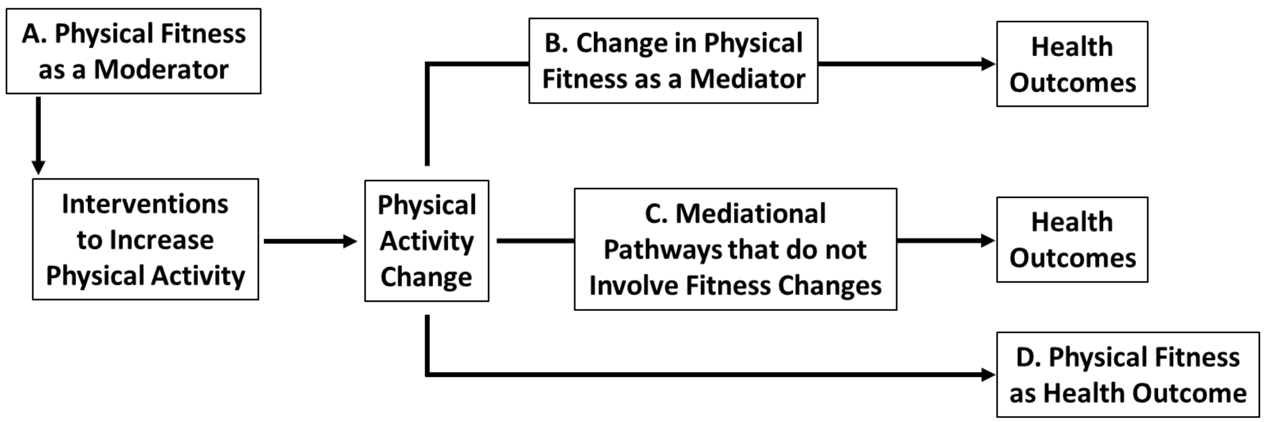
Figure C-8. The Role of Physical Fitness along Various Pathways between Physical Activity and Health Outcomes, Observational Studies



- **Pathway A:** Physical fitness may serve as an intermediate variable along the pathway between physical activity and health outcomes. Synonyms for intermediate variable include contingent variable, intervening (causal) variable, and mediator variable.[40] Intermediate variables lie along the pathway between the exposure and outcome of interest. In this case, physical activity induces changes in physical fitness and physical fitness causes changes in the health outcome.
- **Pathway B:** Physical fitness may serve as an effect modifier. Synonyms for effect modifier include moderator variable or antecedent moderator.[40] Effect modifiers operate outside of the causal chain to influence the effect of the exposure variable on the outcome. If, in an observational study, the participants are stratified according a component of physical fitness and the beneficial effect of a greater volume of physical activity compared to a lower volume differs between strata of physical fitness, then physical fitness is an effect modifier.

- **Pathway C:** Physical activity may be associated with health outcomes through pathways that do not involve physical fitness.
- **Pathway D:** Physical fitness may be considered as an outcome itself. Individuals who are more physically fit are better able "to carry out daily tasks with vigor and alertness, without undue fatigue, and with ample energy to enjoy leisure time pursuits and to meet unforeseen emergencies"—in other words, the definition of fitness suggested above.

Figure C-9. The Role of Physical Fitness along Various Pathways between Physical Activity and Health Outcomes, Intervention Studies



- **Pathway A:** This pathway represents the potential moderating influence of initial physical fitness on interventions to increase physical activity. Baseline physical fitness can exert an important influence on responses to interventions aimed at increasing physical activity. For example, individuals with low baseline fitness may not respond behaviorally as well as individuals with high baseline fitness to interventions emphasizing vigorous physical activity,[41] or may require a more gradual increase in intensity to achieve comparable effects.
- **Pathway B:** This pathway represents the potential mediating influence of changes in physical fitness on the health effects derived from physical activity increases. With an increase in physical activity, a change in physical fitness can mediate some of the resultant health effects, such that the health effects accrue directly in relation to the increases in fitness. In theory, for some health outcomes, an increase in physical activity may produce change in a health outcome only if physical fitness is increased.
- **Pathway C:** Physical activity may be associated with health outcomes through pathways that do not involve changes in physical fitness.

- **Pathway D:** An increase in physical fitness represents an important health outcome in its own right.

Although physical activity is the primary exposure of public health concern, physical fitness is an appropriate addition to the list of outcomes important to public health. For many years, physical fitness has been used as an appropriate public health outcome for children and youth, and physical function has been recognized as an important health outcome for older adults. Missing has been the recognition that improved physical fitness is important in the everyday lives of young and middle-aged adults, as well. Depending upon the physical activity regimen and population, physical fitness can change relatively quickly in response to an increase in physical activity.[42] As such changes are typically readily detected by individuals who have increased their physical activity, physical fitness can serve as an important source of positive reinforcement for individuals who have adopted a higher level of activity. It is important to note that, like many other physiologic characteristics, an individual's physical fitness is affected by both genetic factors and behavior. Accordingly, it is to be expected that the extent to which physical fitness is enhanced by an increase in physical activity varies from individual to individual.

PHYSICAL ACTIVITY ACROSS THE LIFE COURSE

Physical activity capacity, preferences, and needs vary substantially across the life course. This creates a tension between the need for public health guidelines to be simple and the need to properly account for the variation among age groups. Current practice is to divide the population into three primary age-groups—youth, adults, and older adults—with several subcategories for the youth group (Table C-2). The break between youth and adults represents the transition from secondary school to higher education or full-time work; the break between adults and older adults is less clear-cut but generally centers on retirement. These breaks represent significant changes in social and environmental factors that influence physical activity participation and are, therefore, important in understanding and designing successful physical activity promotion strategies. These breaks also represent changes in the health outcomes associated with physical activity. Specifically, the youth guidelines are designed to ensure healthy growth and development, the adult guidelines primarily address disease prevention, and the older adult guidelines center on slowing the loss of function due to aging. The differences in these three paradigms (growth and development, disease prevention, maintenance of function) are reflected in the differences in recommended volumes and types of health-related physical activity across the life course.

Table C-2. Age Groups in National Physical Activity Guidelines or Recommendations from Five Developed Nations

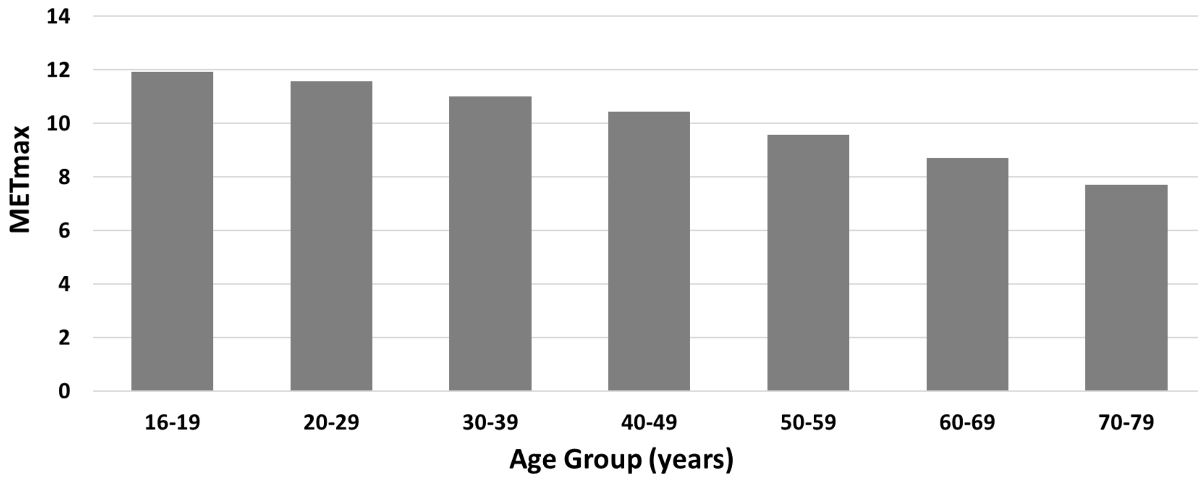
Age Group	Australia (2014)[43]	Canada (2011 and 2017)[44, 45]	Germany (2016)[46]	United Kingdom (2011)[47]	United States (2008)[8]
Children and adolescents	0-5 years 5-12 years 13-17 years	0-4 years 5-11 years 12-17 years	0-3 years 4-6 years 6-11 years 12-18 years	<5 years not walking <5 years walking 5-18 years	6-17 years
Adults	18-64 years	18-64 years	18-65 years	19-64 years	18-64 years
Older adults	Older Australians	65+ years	65+ years	65+ years	65+ years

Legend: <=less than, +=more than.

The normal decline in maximal aerobic capacity across the life course (Figure C-10) suggests that guidelines set for the "average" adult my not be challenging enough for the youngest adults and too challenging for many older adults. The *2008 Physical Guidelines for Americans* acknowledged this problem for older adults and modified the older adult guidelines to emphasize relative rather than absolute intensity to guide the level of effort.[8] The 2018 Advisory Committee recognized that similar adjustments might be appropriate for younger adults, namely that intensity for younger adults should be relative to their aerobic capacity. This would mean a higher absolute intensity and perhaps a higher accumulated volume than for middle-aged and older-adults. In addition, the Committee recognized that the health outcomes influenced by physical activity during young adulthood shared features with the growth and development needs of younger individuals and the disease prevention needs of middle-aged and older adults. As examples, the brain is not fully developed and the skeleton not fully mineralized until well into the third decade, and maintenance of normal blood pressure and body weight is important for younger as well as older adults. After discussion and preliminary research examining physical activity and health outcomes during young adulthood, the Committee felt the issue to be important but set it aside because the available literature did not appear to be strong enough to either confirm or support a change to the current approach. For the present, the age groups used by the

Committee are the same as in the *2008 Physical Activity Guidelines for Americans*,[8] the guidelines from other countries (Table C-2), as well as Healthy People data.[48]

Figure C-10. Maximal Oxygen Uptake in METs, by Age Group



Legend: METmax=maximal oxygen uptake.
Source: Adapted from data in Pate et al., 2006[49] for ages 16 to 19 and American College of Sports Medicine (ACSM)[50] for all other age groups.

SAFETY DURING PHYSICAL ACTIVITY

At the start of their deliberations, the Committee recognized the importance of physical activity-related adverse events. Although the benefits of regular physical activity outweigh the inherent risk of adverse events, adverse events can happen and, though usually not severe, they are an impediment to continued and more widespread participation in regular physical activity. The Committee judged the basic principles and messages of the chapter on adverse events in the *Physical Activity Guidelines Advisory Committee Report, 2008*[7] to still apply in 2018. Rather than prepare a chapter that would duplicate the material in the prior report, each subcommittee looked for information about adverse events uncovered by their searches and, when appropriate, included the information in their chapters. (See, for example, *Part F. Chapter 9. Older Adults*). Included here is a brief summary of the material about adverse events from the 2008 Advisory Report.[7]

The 2008 Advisory Report[7] concluded that the benefits of physical activity outweigh the risks. It acknowledged a wide range of types of physical activity-associated adverse events, including musculoskeletal injuries, cardiac events, heat injuries, and infectious diseases. All types were addressed but the focus was on the prevention of musculoskeletal injuries. The 2008 Scientific Report[7] noted that physical activity-related musculoskeletal injuries are directly related to the type of activity, the volume of physical activity performed, and the rate of progression or change in volume of physical activity.

Type of activity is important because the risk of musculoskeletal injury is directly related to the force and frequency of contact or collisions with other people, the ground, or other objects. Activities are commonly divided into four categories: Collision (e.g., football, ice hockey), contact (e.g., basketball, soccer), limited-contact (e.g., baseball, ultimate frisbee), and non-contact (e.g., running, swimming). "Activities with fewer and less forceful contact with other people or objects have appreciably lower injury rates than do collision or contact sports. Walking for exercise, gardening or yard work, bicycling or exercise cycling, dancing, swimming, and golf, already popular in the United States, are activities with the lowest injury rates."[7]

The risk of injury is directly related to a person's usual dose or volume of physical activity. Dose is determined by the frequency, duration, and intensity of the activity (see the section on "Dose, Volume, and Dose-response for Aerobic Activities," above). Runners, for example, who run 40 miles per week are more likely to be injured than those who run 15 miles per week.

The risk of injury is directly related to the rate of progression or change in volume of physical activity.[7] Military recruits, for example, are commonly prescribed a specific type and volume of exercise. The type may change and the volume may increase over time, but all recruits are expected to do the same type and volume. Recruits who, before enrollment in the military, were doing lesser amounts of physical activity, incur more injuries than do recruits who had been doing greater amounts. Students in physical education classes and participants in aerobic dance classes have similar experiences; those who were less active before the classes are more likely to have a class-related injury than are those who were more active. A few experimental studies have assigned different doses of physical activity to groups of individuals with similar baseline physical activity practices. Injury rates are higher among those assigned the higher volumes.

"The findings in military recruits, students, and runners are consistent with the two major principles of exercise training programs: 1) overload and adaptation, and 2) specificity of response. The overload and adaptation principle states that function is improved when tissues (e.g., muscles) and organs (e.g., heart) are exposed to an overload (i.e., a stimulus greater than usual) and provided time to recover and adapt. Repeated exposures to a tolerable overload are followed by adaptation of the tissues and organs to the new load and improvements in performance and function. Too large an overload or insufficient time for adaptation, however, leads to injury and malfunction. The principle of specificity states that the adaptation and improved function is limited to the tissues and organs that have been overloaded. Training the muscles of the legs, for example, does not improve strength in the arms and shoulders."[7]

The 2008 Advisory Report[7] noted that research determining the safest rate of change for individuals at differing habitual levels of physical activity is not available. That observation remains today. The 2008 Advisory Report did conclude, however, that "adding a small and comfortable amount of walking, such as 5 to 15 minutes 2 to 3 times per week, to one's usual daily activities has a low risk of musculoskeletal injury and no known risk of sudden severe cardiac events. Frequency and duration of aerobic activity should be increased before intensity. Increases in activity level may be made as often as weekly among youth, whereas monthly is more appropriate for older or unfit adults. Attainment of the desired level of activity may require a year or more, especially for elderly, obese, or habitually sedentary individuals."[7]

For more information about other aspects of physical activity-related adverse events, such as sudden adverse cardiac events, the value of proper equipment and safe environments, please see *Part G. Section 10: Adverse Events* in the 2008 Scientific Report.[7]

PROMOTION OF PHYSICAL ACTIVITY

The public health importance of developing approaches and programs to increase participation by the general public in regular moderate-to-vigorous physical activity grew from two observations. First was the evidence that regular physical activity reduced the incidence and mortality of cardiovascular disease, the leading cause of death in the United States. Second was the recognition that mechanization at worksites was reducing the prevalence of jobs requiring much moderate-to-vigorous physical activity.

Over the past 30 to 35 years, the field of health education and promotion has advanced considerably in its knowledge about the complex factors that underlie physical activity behaviors and the approaches most likely to increase population levels of physical activity. Major theories and conceptual frameworks that have been instrumental in this progress include the Health Belief Model,[51] Social Cognitive Theory,[52] the Transtheoretical Model,[53] and applications of a Social Ecological framework.[54] The application of such theoretical models and conceptual frameworks to the study of health behavior change, including physical activity behavior change, has led to several general conclusions, which include the following[55]:

- Physical and social environmental influences are important determinants of health behavior change.
- Behavior change is a process rather than an event, with factors that influence behavior changing over time.
- There is a difference between behavioral intention and action.
- Changing behavior initially and maintaining behavior change over longer periods of time are often two different challenges that may be governed by different factors.

Given that less than half of U.S. adults and high school aged youth perform moderate-to-vigorous physical activity within the public health target range (see earlier information in this chapter), the promotion of physical activity has high public health importance. The 2018 Scientific Report includes, for the first time, a review of the recent evidence pertaining to physical activity promotion. Given the complexity and breadth of the physical activity promotion literature, a Social Ecological framework was applied in reviewing the evidence base in this area (see *Part F. Chapter 11. Promoting Regular Physical Activity*). The literature was divided into the following levels of intervention and impact: the individual, community settings, environmental and policy approaches, and information and communication technology approaches. These different levels are defined further in the chapter. In addition, interventions aimed specifically at reducing sedentary behavior were reviewed.

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INTRODUCTION

This chapter, *Part D. Integrating the Evidence*, is the final step in the development of this report. *Part F. The Science Base* contains the findings from the Subcommittees' reviews of the scientific literature about the relationships between physical activity and selected health outcomes or conditions, about the importance of physical activity for selected age groups or populations, about the types of physical activity that influence health outcomes, and about the promotion of physical activity. Each chapter in Part F provides a review of the scientific literature on one or more specific topics. The conclusions of each chapter were discussed and approved at the public meetings over the course of the Committee's deliberations. The purpose of this chapter is to summarize findings from the various chapters in Part F that share a similar feature, such as improved health or reduced risk of disease, a common population group, such as youth or older adults, or that pertain to the types and amounts of physical activity associated with the observed benefits. The chapter uses a question-and-answer format to address questions typically raised by the public, policy makers, and health and fitness professionals.

OVERALL BENEFITS

Question 1. What does current scientific evidence reveal about the relationship between moderate-to-vigorous physical activity and risk of developing a variety of chronic diseases and other conditions?

Current evidence from large numbers of peer-reviewed scientific articles expands the previously documented health benefits that accrue to more physically active individuals when compared to less physically activity individuals[1] (Table D-1). Notably, a greater volume of moderate-to-vigorous physical activity is associated with a reduced risk of excessive weight gain for both the general population and for pregnant women. Regular moderate-to-vigorous physical activity also reduces feelings of anxiety and depression, and improves sleep and quality of life. A single episode provides temporary improvements in cognitive function. Current evidence demonstrates that even young children, ages 3 to 5 years, have greater bone strength and a healthier weight status if they are more physically active. Among older adults, regularly performed physical activity reduces the risk of dementia, improves physical function (the ability to accomplish routine tasks) and reduces the risk of falling and the risk of injury if a fall does occur. Current evidence also demonstrates that more physical activity reduces the risk of cancers of the bladder, breast, colon, endometrium, esophagus (adenocarcinoma), kidney, stomach, and lung. For people with colorectal cancer, women with breast cancer, and men with prostate cancer, greater amounts of physical activity are associated with reduced risk of mortality from the original type of cancer; for people with colorectal cancer or women with breast cancer, greater amounts of physical activity are associated with reduced risk of all-cause mortality. Physical activity-related benefits also have been demonstrated for the large number of individuals who already have one or more chronic conditions, such as osteoarthritis, hypertension, type 2 diabetes, dementia, multiple sclerosis, spinal cord injury, stroke, Parkinson's disease, schizophrenia, attention deficit hyperactivity disorder, and recent hip fracture. Individuals considered to be frail also benefit from regular physical activity.

Table D-1. Physical Activity-Related Health Benefits for the General Population and Selected Populations Documented by the 2018 Physical Activity Guidelines Advisory Committee

Children	
3 to <6 Years of Age	**Improved bone health and weight status**
6 to 17 years of age	**Improved cognitive function (ages 6to 13 years)** Improved cardiorespiratory and muscular fitness Improved bone health Improved cardiovascular risk factor status Improved weight status or adiposity Fewer symptoms of depression
Adults, all ages	
All-cause mortality	Lower risk
Cardiometabolic conditions	Lower cardiovascular incidence and mortality (including heart disease and stroke) Lower incidence of hypertension Lower incidence of type 2 diabetes
Cancer	Lower incidence of **bladder,** breast, colon, **endometrium, esophagus, kidney, stomach, and lung cancers**
Brain health	**Reduced risk of dementia** Improved cognitive function **Improved cognitive function following bouts of aerobic activity** **Improved quality of life** **Improved sleep** **Reduced feelings of anxiety and depression in healthy people and in people with existing clinical syndromes** Reduced incidence of depression
Weight status	**Reduced risk of excessive weight gain** Weight loss and the prevention of weight regain following initial weight loss when a sufficient dose of moderate-to-vigorous physical activity is attained An additive effect on weight loss when combined with moderate dietary restriction
Older Adults	
Falls	Reduced incidence of falls **Reduced incidence of fall-related injuries**
Physical function	**Improved physical function in older adults with and without frailty**
Women who are Pregnant or Postpartum	
During pregnancy	**Reduced risk of excessive weight gain** **Reduced risk of gestational diabetes** No risk to fetus from moderate-intensity physical activity
During postpartum	**Reduced risk of postpartum depression**

Individuals with Pre-Existing Medical Conditions	
Breast cancer	**Reduced risk of all-cause and breast cancer mortality**
Colorectal cancer	**Reduced risk of all-cause and colorectal cancer mortality**
Prostate cancer	**Reduced risk of prostate cancer mortality**
Osteoarthritis	**Decreased pain** **Improved function and quality of life**
Hypertension	**Reduced risk of progression of cardiovascular disease** **Reduced risk of increased blood pressure over time**
Type 2 diabetes	**Reduced risk of cardiovascular mortality** **Reduced progression of disease indicators: hemoglobin A1c, blood pressure, blood lipids, and body mass index**
Multiple sclerosis	**Improved walking** **Improved physical fitness**
Dementia	**Improved cognition**
Some conditions with impaired executive function (attention deficit hyperactivity disorder, schizophrenia, multiple sclerosis, Parkinson's disease, and stroke)	**Improved cognition**

Note: Benefits in **bold font** are those added in 2018; benefits in normal font are those noted in the 2008 Scientific Report.[1] Only outcomes with strong or moderate evidence of effect are included in the table.

Question 2. Does current evidence indicate that people who habitually perform greater amounts of moderate-to-vigorous physical activity feel better and sleep better?

People who are more physically active feel better and sleep better (see *Part F. Chapter 3. Brain Health*). In addition to reductions in risk for a variety of chronic health diseases and conditions, strong evidence demonstrates that more physically active people consistently report better quality of life, reduced anxiety, and reduced feelings of depression. The improved feelings have been observed in both observational cohort studies and experimental trials. Strong evidence also demonstrates that people who are more physically active sleep better. Laboratory assessments of sleep using polysomnography demonstrate that greater volumes of moderate-to-vigorous physical activity are associated with reduced sleep latency (taking less time to fall asleep), improved sleep efficiency (higher percentage of time in bed actually sleeping), improved sleep quality, and more deep sleep. Research using standardized self-reported assessments of sleep demonstrate that a greater volume of moderate-to-vigorous physical activity is associated with significantly less daytime sleepiness, better sleep quality, and a reduced frequency of use of medication to aid sleep. These improvements in sleep are reported by people with chronic insomnia as well as by people without diagnosed sleep disorders. Evidence also indicates that, in general, the number of hours before bed time at which the activity is performed does not matter; benefits are equivalent for bouts of activity performed more than 8 hours before bedtime, 3 to 8 hours before, and less than 3 hours before bedtime.

Question 3. Does the evidence indicate that people who are more physically active are better able to perform everyday tasks without undue fatigue?

People who are more physically active are better able to perform everyday tasks without undue fatigue. Increased amounts of moderate-to-vigorous physical activity are associated with improved cardiorespiratory and muscular fitness and improved physical function for adults of all ages. (For more details, see *Part C. Background and Key Physical Activity Concepts*). Climbing stairs, carrying heavy packages, performing household chores, and carrying out other daily tasks are all accomplished more easily by individuals who are more physically active because of a higher capacity to perform work. More physically active children and adolescents have higher cardiorespiratory and muscular fitness. Among older adults, both observational and experimental studies demonstrate that greater amounts of physical activity are associated with improved physical function and slowing of age-related loss of physical function. The improvements include faster gait speed, better balance, improved ability to get up from a seated position, and greater ability to carry out activities of daily living, such as bathing, dressing, toileting, and eating. At all ages, for a given amount of physical activity, the relative gains in physical fitness and physical function are greatest for individuals who have not been physically active.

Question 4. How soon do the benefits of physical activity accrue?

Some benefits occur immediately after a session of moderate-to-vigorous physical activity, commonly referred to as the "last bout effect." Reduced feelings of anxiety, improved sleep, and improved cognitive function are examples of benefits that can occur after a single episode of moderate-to-vigorous physical activity. If participation in physical activity becomes regular, reductions in routine (baseline) feelings of anxiety occur, the last bout effect on deep sleep becomes more pronounced, and components of executive function continue to improve. Executive function includes the processes of the brain that help organize daily activities and plan for the future. Tasks such as the ability to plan and organize; monitor, inhibit, or facilitate behaviors; initiate tasks; and control emotions all are part of executive function.

The cardiometabolic profile also shows improvements soon after an episode of moderate-to-vigorous physical activity. Blood pressure is reduced, and insulin sensitivity is increased. These cardiometabolic benefits persist for hours to days after the last bout. They also may be sufficient to lower the blood pressure of people with pre-hypertension and hypertension into normal ranges for a major portion of the day.

Other benefits, such as reduced risk of cardiovascular disease (CVD), diabetes, falls, and fall-related injuries among older adults, and improved physical function accrue as the physiologic adaptations to greater physical activity transpire. Improved cardiorespiratory and muscular fitness and biomarkers of disease risk start to accrue within days, and for a given amount of physical activity, maximize after a few months. Additional benefits accrue if physical activity volume is further increased. The reductions in risk apply every day and at all ages, including young adults, even though their risk for chronic disease is lower than for middle-aged and older adults.

Question 5. What does the evidence indicate about the public health target range, or "dose," of moderate-to-vigorous physical activity that is likely to provide many of the health benefits listed in Table 1?

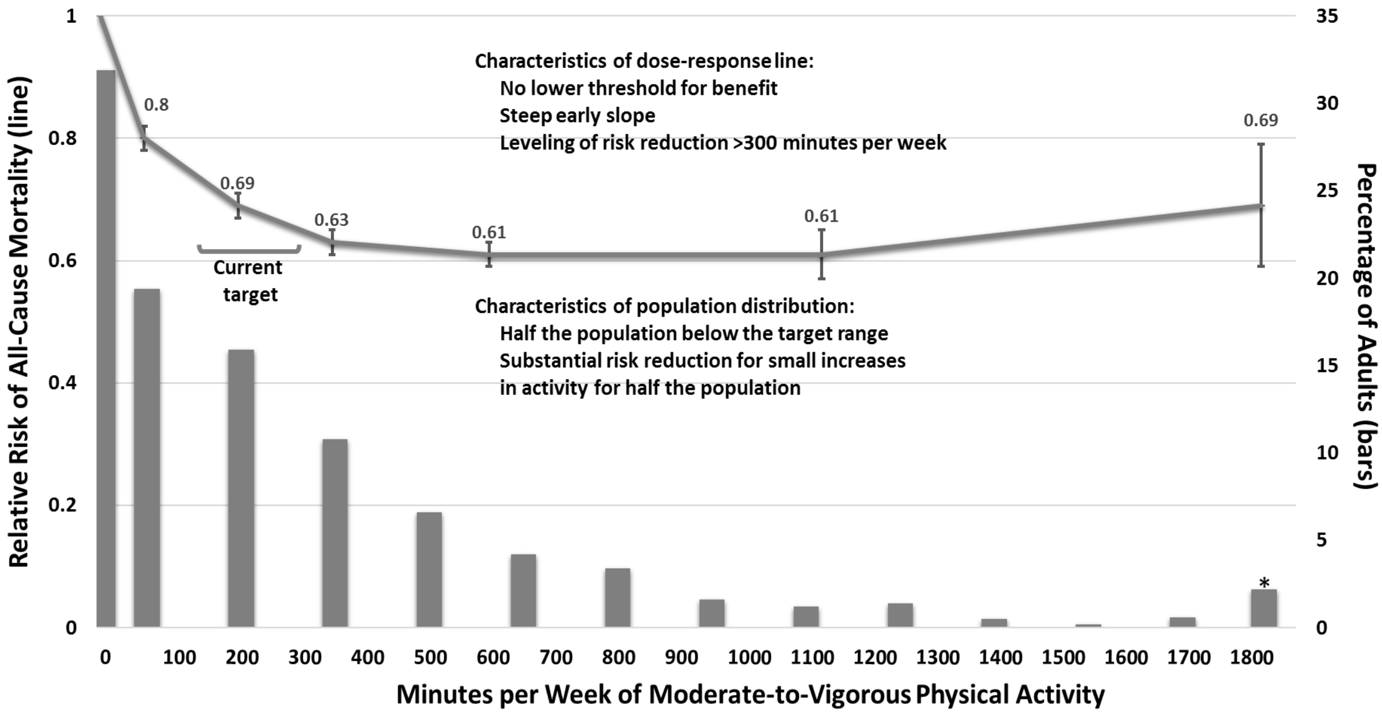
Current evidence continues to indicate that the majority of potential benefit or risk reduction is achieved by people who perform in the range of 500 to 1,000 MET-minutes per week of aerobic physical activity. Because MET-minutes is a unit of measure unfamiliar to most people, the target range has been commonly expressed as 150 to 300 minutes of moderate-intensity physical activity per week. Because vigorous-intensity physical activities (6 or more METs) require roughly twice the energy expenditure of moderate-intensity activities (3 to less than 6 METs), the time required to perform 500 to 1,000 MET-minutes of vigorous-intensity physical activity is roughly half that for moderate-intensity physical activity. As a result, about 75 to 150 minutes of vigorous-intensity physical activity per week is considered within the target range. Combinations of moderate- and vigorous-intensity activity that sum to within 500 to 1,000 MET-minutes per week are also in the target range. As an example, most healthy adults walking at about 3 miles per hour for 150 minutes during a week, or about a total of 7.5 miles, will expend about 500 MET-minutes of energy; if they walk for 300 minutes, or about 15 miles, they will expend about 1,000 MET-minutes of energy. Fewer minutes are needed to be in the target range for more vigorous activities. For example, running at 5 miles per hour would require about 60 minutes to reach 500 MET-minutes per week, or 120 minutes to reach 1,000 MET-minutes per week.

Question 6. What does the evidence indicate about the benefits of moderate-to-vigorous physical activity below or above the target range?

People do not need to reach the lower end of the 150 to 300-minute target range to benefit from regular physical activity. Individuals who exceed the target range usually achieve even greater health benefits. For example, the line in Figure D-1 displays a typical dose-response curve for moderate-to-vigorous physical activity and the relative risk of all-cause mortality. The dose-response curve indicates no lower threshold and a steep early decline in relative risk. It also suggests some additional reduction in risk at volumes of physical activity above the current target range. In addition, the bars on the figure display the percentage of adults reporting different amounts of moderate-to-vigorous physical activity. The population distribution of self-reported moderate-to-vigorous physical activity indicates that about half of the adult population could reduce their risk substantially by modestly increasing their moderate-to-vigorous physical activity.

The shape of the dose-response curves for cardiovascular disease incidence and mortality, and for the incidence of type 2 diabetes are similar to the shape of the dose-response curve for all-cause mortality depicted in Figure D-1. The evidence is currently insufficient to depict dose-response curves for other health outcomes listed in Table D-1, such as reduction in risk of dementia, several cancer sites, or excessive weight gain.

Figure D-1. Risk of All-Cause Mortality and Self-Reported Physical Activity, by Minutes of Moderate-to-Vigorous Physical Activity per Week



Note: *Includes all adults reporting greater than 1800 minutes per week of moderate-to-vigorous physical activity.
Source: Adapted from data found in Arem et al., 2015[2] and National Center for Health Statistics, 2015.[3]

Question 7. What does current evidence indicate about the importance of the intensity, duration, and frequency of moderate-to-vigorous physical activity that comprise the weekly target volume of physical activity?

Intensity

The Committee did not specifically examine the relative value of different levels of intensity of physical activity, such as moderate- versus vigorous-intensity physical activity. Volume is accumulated more quickly when performing activities at greater intensity, reducing the number of minutes required to reach a desired volume. Greater intensity also brings greater levels of cardiorespiratory fitness, but also has greater risk of injury, especially if one is unaccustomed to vigorous physical activity. Greater intensity is inversely associated with pleasure during moderate-to-vigorous physical activity, so displeasure is higher during vigorous- than during moderate-intensity activity. This unpleasant affective experience dissipates soon after the episode of moderate-to-vigorous physical activity ends. For public health purposes, total volume of physical activity is a more important target than the specific intensity at which it is accumulated.

High intensity interval training (HIIT), sometimes called sprint interval training, has been a recent topic of discussion in both lay and scientific publications. HIIT consists of short periods of high intensity anaerobic exercise, commonly less than 1 minute, alternating with short periods of less intense recovery. The length of time spent at high intensity and recovery intensity varies among regimens, as does the total duration of a training session. Current evidence indicates that HIIT is an efficient method for increasing cardiorespiratory fitness, providing equal fitness benefits with about half the energy expenditure when compared with continuous moderate-to-vigorous intensity exercise. There may also be some benefits on insulin-mediated glucose control. The unpleasant affective response associated with increased intensity is greatest above the lactate and ventilatory thresholds. Current information is insufficient about other potential health benefits, the risks of adverse events, and the long-term sustainability of HIIT training regimens.

Please see Question 9 for a broader consideration of the issue of intensity.

Duration

The total volume of accumulated moderate-to-vigorous physical activity is a more important determinant of health benefits than the duration of the episodes that comprise the total. The *Physical Activity Guidelines Advisory Committee Report, 2008,*[1] accepted prior conclusions that bouts as short as 10 minutes added benefit and should be included in the accumulated total. At the time, evidence was not reviewed to determine if bouts shorter than 10 minutes also contributed, largely because the available data collection systems could not accurately collect information about the multiple short bouts of moderate-to-vigorous physical activity scattered throughout normal daily activity. The evidence from recent observational studies of cardiometabolic risk factors using device-measured physical activity indicates that bouts of moderate-to-vigorous physical activity of any duration contribute to the total volume of physical activity that determines benefit. These findings do not support the previous recommendation that only bouts of 10 or more minutes provide health benefits.

Frequency

Total volume of moderate-to-vigorous physical activity is more important than the number of days per week on which individuals perform the activity. For benefits derived from single episodes, such as reduced anxiety, improved sleep and executive function, blood pressure reductions, and improved insulin sensitivity, regular participation throughout the week would likely be more beneficial. A limited amount of evidence suggests that individuals who accumulate all or almost all of their weekly moderate-to-vigorous physical activity on 1 or 2 days per week experience reductions in all-cause and cardiovascular mortality commensurate with individuals who accumulate an equivalent total volume on 3 or more days per week. If time for moderate-to-vigorous physical activity is available only 1 or 2 days per week, doing it on those days is better than not doing it.

Question 8. What does current scientific evidence demonstrate about the relationship between sedentary behavior and the risk of developing various chronic diseases or conditions?

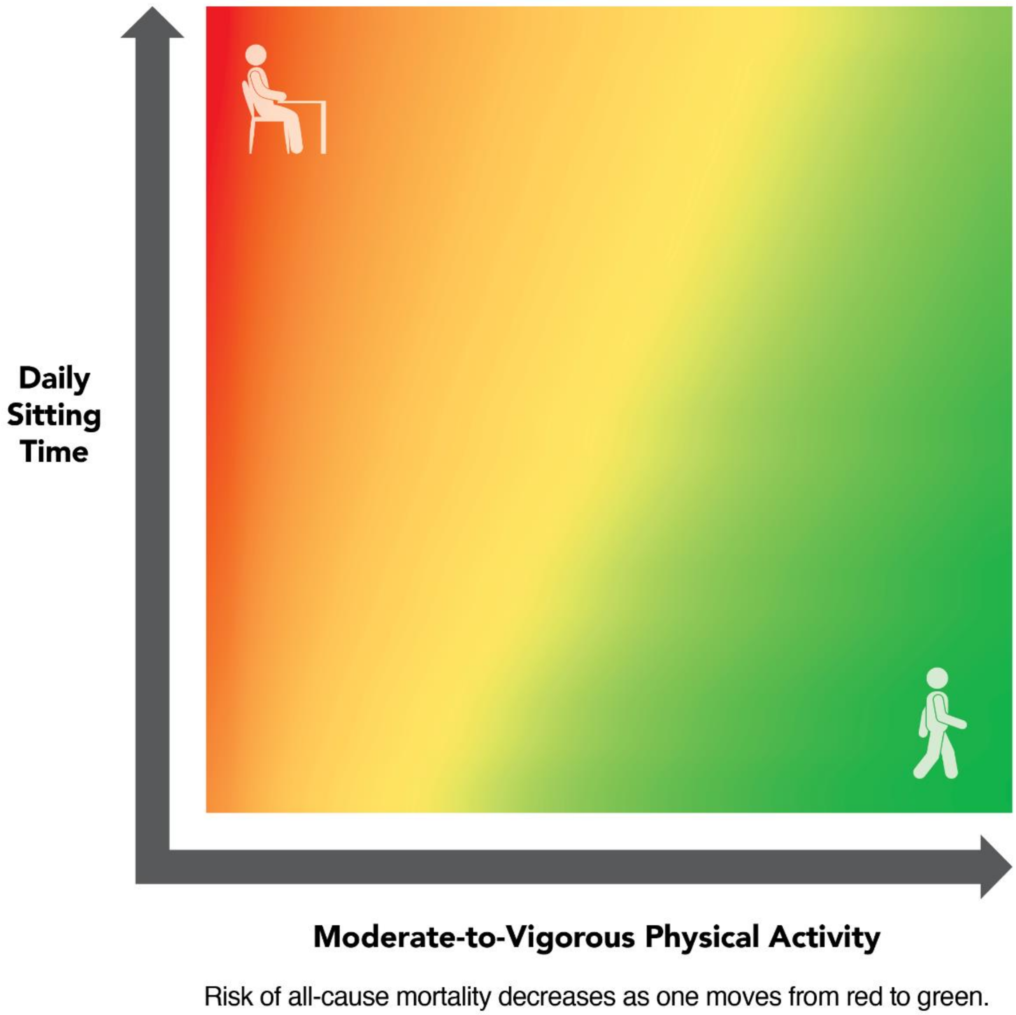
Scientific evidence demonstrates that more time spent in sedentary behavior is related to greater all-cause mortality, CVD mortality and incidence, type 2 diabetes incidence, and the incidence of colon, endometrial, and lung cancer. Evidence is insufficient to determine whether breaks in sedentary behavior reduce the risk. For inactive adults, replacing sedentary behavior with light-intensity physical activities is likely to produce some health benefits. Among all adults, replacing sedentary behavior with higher intensity (moderate-to-vigorous) physical activities may produce even greater benefits.

Question 9. What does current scientific evidence indicate about how the risks of sedentary behavior and the benefits of moderate-to-vigorous physical activity interact to determine overall risk or benefit?

Evidence indicates that the volume of moderate-to-vigorous physical activity affects the level of risk of all-cause mortality and cardiovascular disease mortality associated with sedentary behavior time. The Committee developed a “heat map” depicting the risk of all-cause mortality associated with various combinations of sitting time and moderate-to-vigorous physical activity using regression techniques to interpolate the hazard ratios between four levels of sitting time and four levels of moderate-to-vigorous physical activity[4] (Figure D-2).

In the heat map, red represents higher risk of all-cause mortality, and green represents lower risk. The greatest risk of mortality is borne by individuals who sit the most and who do the least moderate-to-vigorous physical activity (the upper left corner of the heat map). The lowest risk of mortality is achieved by individuals who sit the least and do the most moderate-to-vigorous physical activity (lower right corner of the heat map).

Figure D-2. Relationship Among Moderate-to-Vigorous Physical Activity, Sitting Time, and Risk of All-Cause Mortality



Source: Adapted from data found in Ekelund et al., 2016.[4]

At the greatest time spent sitting (the top row), the risk of all-cause mortality begins to decrease (color becomes orange) even with small additions of moderate-to-vigorous physical activity. At the greatest volume of moderate-to-vigorous physical activity, the risk is low even for those who sit the most. The best currently available estimate of this volume is about 37 to 38 MET-hours per week, equal to about 80 to 90 minutes per day of moderate-intensity activities, such as walking or yard work at a moderate level of effort, or 40 to 45 minutes per day of vigorous-intensity activities, such as running at 4 to 5 miles per hour, bicycling at 10 or more miles per hour, climbing hills with 20-pound pack, or vigorous dancing.

At the lowest volume of moderate-to-vigorous physical activity (the ordinate), the risk of all-cause mortality increases as time spent sitting increases. This suggests that for individuals who do not perform any moderate-to-vigorous physical activity, replacing sitting time with light-intensity physical activities, such as walking at 2 miles per hour, dusting or polishing furniture, or easy gardening, reduces the risk of all-cause mortality. Although the risk of all-cause mortality is reduced as the time spent in sedentary behavior is reduced, even the individuals who sit the least have an elevated risk if they perform no moderate-to-vigorous physical activity. High volumes of moderate-to-vigorous physical activity appear to remove the risk of all-cause mortality associated with high volumes of sitting. Very low time spent sitting reduces but does not eliminate the risk of no moderate-to-vigorous physical activity.

The heat map demonstrates that many combinations of less sitting time and more moderate-to-vigorous physical activity are associated with reduced risk of all-cause mortality. Figure D-2 is based on firm evidence for all-cause and cardiovascular mortality, outcomes with well-established dose-response relationships with sedentary behavior and moderate-to-vigorous physical activity. The dose-response relationships for various combinations of sedentary behavior and moderate-to-vigorous physical activity with other health outcomes are unknown. A similar pattern seems likely, but other patterns may emerge as additional research on other outcomes is conducted.

Question 10. How do different types of physical activity contribute to health outcomes?

Aerobic Activity

Although other types of physical activity contribute to positive health outcomes, moderate-to-vigorous aerobic activity is associated with nearly all the benefits listed in Table D-1. Aerobic activity leads to improved cardiorespiratory fitness (VO_2max) with an increase in the capacity and efficiency of the cardiorespiratory system to transport oxygen to skeletal muscles and for muscles to use this oxygen. Cardiorespiratory fitness also is associated with improvements in biomarkers for CVD and type 2 diabetes (e.g., atherogenic lipoprotein profile, blood pressure, insulin sensitivity) in adults and older adults with and without these diseases. Although generally not considered muscle-strengthening behavior, aerobic activity leads to improved strength and endurance of the major muscle groups used to perform the chosen behavior, such as running or swimming. The high impact of some aerobic activities, such as running or playing tennis, and the strong muscular forces of others, such as rowing or wrestling, improve bone health.

Muscle Strengthening

Muscle-strengthening activities involve contracting muscles against resistance. Greater muscular strength is associated with greater ease performing daily tasks for people of all ages, and provides reductions in blood pressure equivalent to aerobic activities. Muscle-strengthening activities for older adults, often in combination with balance training, are associated not only with improved physical function but also with reduced risk of falls and reduced risk of injury due to falls. Muscle-strengthening activities can help maintain lean body mass during a program of weight loss, but by themselves result in little weight loss.

Muscles are strengthened according to the exercise science principles of overload, adaptation, and specificity. *Overload* indicates that a resistance slightly greater than usual is applied. If applied on a regular basis and the overload is not too large, the muscles *adapt* to the new load and become stronger. The improvements in strength are *specific* to the muscles to which the overload has been applied.

Most evidence supports a muscle-strengthening program with the following characteristics: progressive muscle strengthening exercises that target all major muscle groups (legs, hips, back, abdomen, chest, shoulders, arms), performed on two to three nonconsecutive days per week. To enhance muscle strength, 8 to 12 repetitions of each exercise should be performed to volitional fatigue. One set of 8 to 12 repetitions is effective at increasing muscular strength; limited evidence suggests that 2 or 3 sets is more effective.

The most commonly prescribed methods for increasing muscular strength, endurance, and power involve calisthenics (e.g., push-ups, sit-ups, chin-ups) or specific types of equipment, including weight machines, free weights, resistance bands, and similar devices. Essentially all types of aerobic activity, such as walking, swimming, or sporting activities, contribute to the strength of the involved muscles, as do many household activities such as raking leaves, vacuuming, carrying laundry baskets, or lifting heavy packages. The improvements or maintenance of muscular strength are specific to the muscles used during the activity, so a variety of activities is necessary to achieve balanced muscular strength.

Bone Strengthening

Bone-strengthening activities reduce the risk of osteoporosis and fractures. Bone-strengthening activities involve significant impact or muscular forces, both of which apply stress to bone, which adapts by increasing its strength. Activities such as hopping, jumping, skipping, and running provide significant impact forces. Standing on one’s toes and suddenly dropping to one’s heels also provides helpful impact forces. Activities such as dancing, stair climbing, or push-ups, all of which require quick and strong muscle contractions, provide significant muscle forces.

Balance Training

Balance training helps maintain a steady posture against anticipated or unanticipated perturbations while walking or standing. It is commonly combined with muscle-strengthening activities, with sessions about 3 times per week, for the prevention of falls and fall injuries among older adults. Examples of balance training activities include standing on one foot, walking heel-to-toe, and using a wobble board.

Flexibility Training (Stretching)

Dynamic and static stretching improve the range and ease of movement around joints. Flexibility training is a common component of multicomponent physical activity programs but has not been sufficiently studied by itself, precluding assessment of its independent benefits, if any, on health. If joint flexibility is limited and impedes the performance of daily activities, flexibility training can increase range of motion, thereby facilitating activities such as getting dressed or getting into and out of cars.

Yoga, Tai Chi, Qigong

These forms of physical activity are potentially beneficial because they typically combine muscle strengthening, balance training, light-intensity aerobic activity, and flexibility in one package. Yoga, tai chi, and qigong each have several forms or styles of activity. Some of the forms include components that emphasize relaxation, mindfulness, meditation, and/or spiritual thinking. The purposeful combination of mental and physical components, sometimes referred to as “mind-body” activity, may provide mental or physical health benefits but prevents an assessment of the contribution of either component by itself.

Question 11. What does the scientific evidence indicate about the association between walking and health benefits?

Walking, the most commonly performed aerobic activity, is associated with the wide range of benefits listed in Table D-1. Although some medical conditions or disabilities prevent individuals from walking, for most people walking is a normal and frequent component of everyday life. Walking is one of the safest and most readily accessible physical activities. Adding 5 to 10 minutes of walking to one’s usual daily physical activities and increasing the time and then intensity (speed) slowly over several weeks or months is an excellent way to become more physically active. Daily step count is another way to monitor gradual increases toward a final goal. Modern technological devices (e.g., pedometers, smart phones, activity trackers) can help individuals monitor their daily step counts to ensure that they are progressing at a safe and steady pace to meet their goals.

BRAIN HEALTH

Question 12. Is there evidence that moderate-to-vigorous physical activity influences brain-related health outcomes?

Moderate-to-vigorous physical activity positively influences several brain-related health outcomes, including cognition, anxiety, depression, sleep, and quality of life (Table D-2). Tools enabling assessments of the brain's structure and function are progressing rapidly and have enabled much to be learned in the past decade, with more new knowledge expected in the next several years. Current evidence indicates a beneficial effect of regular moderate-to-vigorous physical activity on various components of cognition. The evidence is strongest for a reduced risk of dementia and improved executive function. Single episodes of physical activity promote acute improvements in executive function for a brief period of time. Executive function includes the processes of the brain that help organize daily activities and plan for the future. Tasks such as one's ability to plan and organize, self-monitor and inhibit or facilitate behaviors, initiate tasks, and control emotions all are part of executive function. Physical activity also improves other components of cognition, including memory, processing speed, attention, and academic performance.

Strong evidence demonstrates that moderate-to-vigorous physical activity reduces the risk of developing major depression. It also reduces the symptoms of depression among individuals with and without clinical levels of depression. Similarly, moderate-to-vigorous physical activity reduces general feelings of anxiety (trait anxiety) among individuals with and without anxiety disorders. Acute episodes of moderate-to-vigorous physical activity also can reduce immediate feelings of anxiety (state anxiety). Moderate-to-vigorous physical activity also can raise perceptions of one's quality of life and improves a variety of sleep outcomes among the general population as well as for individuals with symptoms of insomnia or sleep apnea.

Table D-2. Summary of Conclusion Statements Regarding Strength* of the Evidence for Relationships Between Physical Activity and Cognition, Depression, Anxiety, Affect, Quality of Life, and Sleep

Outcome	Population	Benefit	Strength of Evidence
Cognition	General population and children 5 to 13 years of age: habitual moderate-to-vigorous physical activity	Improved cognition	Moderate
		Reduced risk of dementia	Strong
		Improved performance on academic achievement tests	Moderate
		Improved neuropsychological performance (executive function, processing speed, memory)	Moderate
	General population and children 5 to 13 years of age: acute episodes of moderate-to-vigorous physical activity	Improved cognition (executive function, attention, academic performance, memory, crystalized intelligence, processing speed)	Strong
	Individuals with dementia and some other conditions that affect cognition (attention deficit hyperactivity disorder, schizophrenia, multiple sclerosis, Parkinson’s disease, stroke)	Improved cognition	Moderate
Quality of life	Adults, ages 18 years and older	Improved quality of life	Strong
	Individuals with schizophrenia	Improved quality of life	Moderate
Depressed mood and depression	Adults, ages 18 years and older	Reduced risk of depression	Strong
		Fewer depressive symptoms for individuals with and without major depression	Strong
		Dose-related reduction in depressive symptoms (i.e., present at low levels, increases with greater frequency, intensity, volume)	Strong
Anxiety	Adults, ages 18 years and older: Acute episodes of moderate-to-vigorous physical activity	Reduced state anxiety	Strong
	Adults, ages 18 years and older: habitual moderate-to-vigorous physical activity	Reduced trait anxiety for individuals with and without anxiety disorders	Strong

Outcome	Population	Benefit	Strength of Evidence
Affect	Adolescents through middle-aged adults	In experimental studies, direct relationship between feelings of negative affect and intensity of moderate-to-vigorous physical activity	Strong
Sleep	Adults, ages 18 years and older: acute and habitual moderate-to-vigorous physical activity	Improved sleep outcomes Size of benefit directly related to duration of episode	Strong Moderate
	Individuals with symptoms of insomnia or sleep apnea	Improved sleep outcomes with greater amounts of moderate-to-vigorous physical activity	Moderate

Note: "Strength of the evidence" refers to the strength of the evidence that a relationship exists and not to the size of the effect of the relationship. Only populations and outcomes with strong or moderate evidence of effect are included in the table.

YOUTH

Question 13. Does current evidence indicate health and fitness benefits from physical activity for children and youth?

In 2008, insufficient evidence was available to comment on the impact of physical activity on the health of children younger than age 6 years. New evidence has emerged since then, and now, strong evidence indicates that greater volumes of physical activity among children ages 3 through 5 years are associated with a reduced risk of excessive weight gain and favorable indicators of bone health.

Among older children and youth through high school age, the evidence continues to demonstrate that moderate-to-vigorous physical activity improves cardiovascular and muscular fitness, bone health, weight status, and cardiometabolic risk factor status. For children ages 5 through 13, the evidence indicates that both acute bouts and regular moderate-to-vigorous physical activity improve cognition, including memory, processing speed, attention, and academic performance. Information on the effect on cognition for younger children and adolescents is not yet sufficient.

Question 14. What does the evidence indicate about the type and dose of physical activity most likely to produce these health benefits among children?

For children 3 through 5 years, little information is available currently on the type or volume of activity most likely to be associated with weight status. Until such information becomes available, a prudent target would be for all children to achieve the current median estimated volume of three hours per day of physical activity at intensities that include light, moderate, and vigorous physical activity. The type of physical activity associated with bone health consists of high-impact, dynamic, short duration exercise, such as hopping, skipping, jumping, tumbling; the volume of such activity needed is not currently known.

For school-aged children, sufficient evidence indicates health benefits accrue with 60 minutes per day of moderate-to-vigorous physical activity. Because different benefits derive from different types of activity, the 60 minutes will be most healthful if different types of activity are performed. Vigorous-intensity physical activity will enhance cardiovascular health. A variety of play, games, exercise, sports, or chores can strengthen major muscle groups, and activities with high-impact forces, such as hopping, skipping, and jumping, will improve bone strength. These findings are consistent with the findings in the *Physical Activity Guidelines Advisory Committee Report, 2008,* and the recommendations in the *2008 Physical Activity Guidelines for Americans* stating that within the 60 minutes of daily physical activity, children and adolescents should engage in muscle-strengthening, bone-strengthening, and vigorous intensity physical activities at least three days per week.[1, 5]

OLDER ADULTS

Question 15. Is there evidence that the target range for moderate-to-vigorous physical activity should differ for older adults?

The target range of 150 to 300 minutes per week of moderate relative intensity activities remains an appropriate target for older adults. However, because older adults expend more energy than younger adults for the same task, such as walking, and because aerobic capacity declines with age, relative intensity is a better guide for beneficial activity for older adults than estimates of absolute intensity developed for young and middle-aged adults. The use of relative intensity rather than absolute intensity as a guide to level of effort applies also to individuals who have been very inactive and who have a low aerobic capacity as a result. Activities performed at a moderate relative intensity are commonly described as being "somewhat hard." (See *Part C. Background and Key Physical Activity Concepts*, for more information about absolute and relative intensity of physical activity and ratings of perceived (relative) exertion. For both older and younger individuals, some activity is better than none, and appreciable benefits accrue from regular physical activity at levels below the target range.

Question 16. Is there evidence of health benefits of particular importance for older adults?

Strong evidence demonstrates that physically active older adults are less likely to experience falls, less likely to be seriously injured if they do fall, and more likely to maintain independence and functional ability compared to those who are inactive. Strong evidence also demonstrates that physically active older adults have a lower risk of dementia, better perceived quality of life, and reduced symptoms of anxiety and depression. Experimental trials have demonstrated that even individuals with frailty and with Parkinson's disease can improve their physical function, thus minimizing and delaying aging-related declines. Aerobic, muscle-strengthening, and multicomponent physical activity programs all demonstrate benefits. The improvements appear to be somewhat greater with activity programs that include specific muscle strengthening and balance training activities.

SELECTED COMMON CHRONIC CONDITIONS

Question 17. Does the evidence indicate that habitual moderate-to-vigorous physical activity provides preventive health benefits to individuals with some common chronic conditions?

The benefits of habitual physical activity likely vary from condition to condition, but for several prevalent diseases or conditions studied by the Committee, one or more health benefits were evident (Table D-3). For example, for people with colorectal cancer, women with breast cancer, and men with prostate cancer, greater amounts of physical activity are associated with reduced risk of mortality from the original type of cancer; for people with colorectal cancer or women with breast cancer, greater amounts of physical activity are associated with reduced risk of all-cause mortality. Habitual physical activity also reduces the risk of mortality from CVD among people with hypertension or type 2 diabetes. Adults with osteoarthritis who are more physically active experience less pain, improved physical function, and better quality of life relative to less active adults with osteoarthritis. Similarly, more physically active individuals who have Parkinson's disease, multiple sclerosis, spinal cord injury, stroke, recent hip fracture, and frailty have better physical function, including walking ability, relative to less active adults with the same condition. For individuals with some of these conditions, muscle strength and balance are improved as well (Table D-3). Except for the mortality outcomes, evidence regarding the type of physical activity associated with these reductions often comes from intervention studies in which the physical activity exposure was a multicomponent program including aerobic activity (commonly walking), strength, and balance training. These findings emphasize that preventive effects of physical activity are relevant and important for both healthy adults and for adults with chronic conditions. Indeed, for adults with conditions where physical activity is recommended for its therapeutic effects, the evidence indicates that physical activity typically provides both therapeutic and preventive benefits.

Table D-3. Evidence of Health Benefits from Habitual Physical Activity Among People with One of Several Common Chronic Diseases or Conditions

RISK REDUCTION OUTCOMES INVESTIGATED FOR SURVIVORS OF THREE COMMON CANCERS			
Disease or Condition	**Risk of All-cause Mortality**	**Risk of Cancer-specific Mortality**	**Risk of Developing Recurrence of Primary Cancer or New Type of Cancer**
Breast cancer	Reduced	Reduced	IE
Colorectal cancer	Reduced	Reduced	IE
Prostate cancer	IE	Reduced	IE

RISK REDUCTION OR HEALTH IMPROVEMENT INVESTIGATED FOR SELECTED COMMON CONDITIONS					
Disease or Condition	**Risk of Mortality**	**Quality of Life**	**Physical Function**	**Progression of Disease**	**Cognition**
Osteoarthritis	IE	Less pain, improved quality of life, and improved physical function among people with hip or knee osteoarthritis		No evidence of progression of osteoarthritis up to 10,000 steps per day	-
Hypertension	Reduced cardiovascular mortality	IE	IE	Reduced progression of blood pressure	-
Type 2 diabetes	Reduced cardiovascular mortality	IE	IE	Improved HbA1c, BP, BMI, and lipids IE for neuropathy, nephropathy, retinopathy, foot sores	-
Multiple sclerosis	IE	IE	Improved walking, strength, fitness	IE	Improved cognition
Spinal cord injury	IE	IE	Improved walking, wheelchair skills	IE	-

RISK REDUCTION OR HEALTH IMPROVEMENT INVESTIGATED FOR SELECTED COMMON CONDITIONS					
Disease or Condition	**Risk of Mortality**	**Quality of Life**	**Physical Function**	**Progression of Disease**	**Cognition**
Intellectual disabilities	IE	IE	IE	IE	-
Parkinson's disease	-	-	Improved walking, strength, balance	-	Improved cognition
Stroke	-	-	Improved walking	-	Improved cognition
Recent hip fracture	-	-	Improved walking, balance, activities of daily living	-	-
Frailty	-	-	Improved walking, balance, activities of daily living	-	-
Dementia	-	-	-	-	Improved cognition
Schizophrenia	-	Improved quality of life	-	-	Improved cognition
Attention deficit hyperactivity disorder	-	-	-	-	Improved cognition

Legend: IE=Insufficient evidence found in systematic reviews and meta-analyses to reach a conclusion, -=question did not address this outcome for this condition, HbA1c=hemoglobin A1c, BP=blood pressure, BMI=body mass index.

PREGNANCY

Question 18. Is there evidence regarding the benefits or risks of light-to-moderate intensity physical activity during pregnancy and the postpartum period?

Strong evidence demonstrates that more physically active women with a normally progressing pregnancy have a reduced risk for excessive weight gain, gestational diabetes, and postpartum depression relative to their less physically active counterparts. The amount of physical activity in most of the experimental trials included in the evidence consisted of light- to moderate-intensity physical activity accumulating to about 120 to 150 minutes per week. Insufficient information about the adoption of vigorous-intensity physical activity during pregnancy was available to reach a conclusion about its benefits or risks during pregnancy and the postpartum period. The 2008 Advisory Committee reported that women who habitually performed vigorous-intensity physical activity prior to pregnancy could continue as long as "they remain asymptomatic and maintain open communication with their health care providers.[1] The 2018 Committee concurs. The 2018 Committee did not perform specific literature searches to investigate the association between physical activity and specific benefits or risks related to labor and delivery, date of delivery, weight status of the newborn, or other outcomes. However, the conclusions and information provided in the *Physical Activity Guidelines Advisory Committee Report, 2008*[1] and the *2008 Physical Activity Guidelines for Americans*[5] are consistent with the information provided on these topics in the articles included in the specific searches performed by the Committee.

WEIGHT STATUS

Question 19. Does the evidence demonstrate that moderate-to-vigorous physical activity contributes to preventing or minimizing excessive weight gain?

Strong evidence demonstrates that greater volumes of moderate-to-vigorous physical activity are associated with preventing or minimizing excessive weight gain in adults, being able to maintain weight within a healthy range of body mass index, and preventing obesity. The 2018 Advisory Committee did not examine literature addressing the association between physical activity and weight loss or the prevention of weight regain following initial weight loss. The 2008 Advisory Committee,[1] however, did address these important issues and concluded that when a sufficient dose of moderate-to-vigorous physical activity is attained, it will result in weight loss and the prevention of weight regain following initial weight loss. The 2008 Advisory Committee also reported that physical activity has an additive effect on weight loss when combined with moderate dietary restriction compared to moderate dietary restriction alone.[1]

Question 20. Does moderate-to-vigorous physical activity provide health benefits for people with overweight or obesity even if their weight status remains the same?

Strong evidence demonstrates that physically active adults with overweight or obesity experience benefits generally similar to those with normal body weight. Regardless of weight status, the relative reduction in risk of all-cause mortality, incidence and mortality of cardiovascular disease, and incidence of type 2 diabetes are essentially equivalent. For endometrial cancer, the risk reduction is greater for individuals with overweight of obesity than for individuals with normal weight status. Adults with overweight or obesity are more responsive than adults with normal weight to high intensity interval training's effects on improving insulin sensitivity, blood pressure, and body composition.

INFLUENCE OF RACE OR ETHNICITY, AND SOCIOECONOMIC STATUS ON HEALTH OUTCOMES

Question 21. Is there evidence that the volume of moderate-to-vigorous physical activity associated with health benefits differs by race or ethnicity, or socioeconomic status?

Race or Ethnicity

The 2008 Committee reported that "based on the currently available scientific evidence, the dose of physical activity that provides various favorable health and fitness outcomes appears to be similar for adults of various races and ethnicities."[1] The 2018 Committee concurs. In the studies used to address the questions asked by the 2018 Committee, the effect of race or ethnicity was uncommonly reported and, when it was, the studies showed little evidence of effect modification by race or ethnicity on the relationship between moderate-to-vigorous physical activity and health outcomes.

Socioeconomic Status

Information on the effect of socioeconomic status on the relationship between moderate-to-vigorous physical activity was even more sparse than for race or ethnicity, and, therefore, this Committee was unable to state any conclusions about the role, if any, of socioeconomic status.

ADVERSE EVENTS

Question 22. What does the scientific evidence indicate about the pattern of physical activity that is most likely to produce the fewest adverse medical events while providing benefits?

The 2018 Committee determined that the basic principles and messages in the *Physical Activity Guidelines Advisory Committee Report, 2008* and the *2008 Physical Activity Guidelines for Americans* still apply.[1, 5] The information in those reports indicates that activities with fewer and less forceful contact with other people or objects have appreciably lower rates of musculoskeletal injuries than do collision or contact sports. Walking for exercise, gardening or yard work, bicycling or exercise cycling, dancing, swimming, and golf are popular activities in the United States, and they are associated with the lowest injury rates. Risk of musculoskeletal injury during activity increases with the total volume of activity (e.g., MET-hours per week). Intensity, frequency, and duration of activity all contribute to the risk of musculoskeletal injuries, but their relative contributions are unknown. Sudden cardiac adverse events are rare, are associated with relatively vigorous physical activity, and are inversely associated with the volume of regularly performed vigorous physical activity. The limited data available for medical risks during moderate-intensity activity indicate that the risks are very low for activities like walking and that the health benefits from such activity outweigh the risks.

Question 23. What does the scientific evidence say about actions that can be taken to reduce the risk of injury during physical activity?

Information in the *Physical Activity Guidelines Advisory Committee Report, 2008,* and the *2008 Physical Activity Guidelines* indicates that injuries are more likely when people are much more physically active than they are accustomed to.[1, 5] The key point to remember is that when individuals do more activity than usual, the risk of injury is related to the size of the increase. Gradual progression, a series of small increments in physical activity each followed by a period of adaptation, is associated with less risk of musculoskeletal injuries than an abrupt increase to the same final level. Although the safest method of increasing one's physical activity has not been empirically established, for individuals who have been performing little or no moderate-to-vigorous physical activity, adding a small and comfortable amount of light- to moderate-intensity activity, such as walking an additional 5 to 15 minutes 2 to 3 times per week, has a low risk of musculoskeletal injury and no known risk of sudden severe cardiac events. Frequency and duration should be increased before raising the intensity.

The risk of adverse events is also reduced by using proper equipment, such as helmets, eyewear or goggles, elbow or knee pads; choosing safe environments, such as those with good lighting, smooth surfaces, and away from traffic; following rules and policies; and making sensible choices, such as avoiding extreme heat or cold.

Warming up before and cooling down after exercise are commonly recommended to prevent injuries and adverse cardiac events. Limited evidence does suggest that various combinations of warm up, muscle-strengthening, conditioning, and stretching are associated with lower rates of musculoskeletal injuries. Also based on limited evidence, careful warming up and cooling down are standard practice in cardiac rehabilitation programs. Guidelines typically recommend 10 to 20 minutes of stretching and progressive warm up activity before the main activity session and 10 to 20 minutes of gradually diminishing activity at the end.

Question 24. Is there evidence regarding who should see a physician or have a medical examination before increasing the amount or intensity of physical activity they perform?

The *Physical Activity Guidelines Advisory Committee, 2008*, and the *2008 Physical Activity Guidelines for Americans* noted, and the 2018 Physical Activity Guidelines Advisory Committee agrees, that the protective value of a medical consultation for persons with or without chronic diseases who are interested in increasing their physical activity level is not established.[1, 5] No evidence is available to indicate that people who consult with their medical provider receive more benefits and suffer fewer adverse events than people who do not. Also unknown is whether official recommendations to seek medical advice before augmenting one's regular physical activity practices reduce participation in regular moderate physical activity by implying that being active may be less safe and provide fewer benefits than being inactive.

PROMOTION OF PHYSICAL ACTIVITY

Question 25. What interventions are effective for promoting regular physical activity participation?

The extensive body of evidence in the physical activity promotion field shows that interventions at different levels of impact, including at the individual, community, environment and policy, and information and communication technology levels, can promote increased participation in regular physical activity (Table D-4). For example, at the individual level of impact, interventions that include behavior change theories and techniques as well as interventions specifically targeted at youth and at older adults have demonstrated success in promoting regular physical activity. At the level of community settings, multi-component school interventions and those that have successfully revised the structure of physical education classes are effective in promoting increased school-based physical activity in children and adolescents. At the level of environment and policy, the evidence on physical activity promotion among children and adults supports the utility of built environment characteristics and infrastructure that support active transportation, indoor and outdoor facilities for physical activity, and access to such facilities. At the level of information and communication technologies, the types of technologies that have been found consistently to promote regular physical activity among adults include wearable activity monitors, telephone-assisted interventions, internet-delivered interventions that include educational components, text-messaging programs, and computer-tailored print interventions. Among children and adolescents, information and communication technologies interventions involving systematically developed smartphone applications have been found to be effective.

Table D-4. Summary of Conclusion Statements Regarding Strength* of the Evidence that Varying Types of Interventions Increase the Amount of Physical Activity Among Those Who Are Exposed to the Intervention

Level	Type of Intervention	Strength of Evidence
Individual	Older adults	Strong
	Youth	Strong: Especially when family is included or intervention delivered during school
	Behavior change theories and techniques	Strong
	Peer led	Moderate
Community-based	School-based	Strong: Multiple components Strong: Revised physical education classes
	Community wide	Moderate: If intervention has intensive contact with majority of population over time
Environmental and Policy	Point-of-decision prompts	Strong
	Built environment and infrastructure that promotes active transportation	Moderate
	Community design that supports physical activity, including active transportation	Moderate
	Access to indoor or outdoor facilities	Moderate

Level	Type of Intervention	Strength of Evidence
Information and Communications Technologies	Wearable activity monitors (accelerometers and pedometers)	Strong: General adult population Moderate: Individuals who are overweight or obese
	Telephone-assisted	Strong
	Web-based or internet-delivered, with educational component	Strong: General adult population
	Computer-tailored print interventions	Strong
	Mobile phone programs	Strong: Smart phone applications, children and adolescents Moderate: Text messaging, general population

Level	Type of Intervention to Reduce Sedentary Behavior	Strength of Evidence
Community-based	Youth, primarily school-based interventions	Moderate
	Worksite interventions	Moderate

Note: "Strength of the evidence" refers to the strength of the evidence that a relationship exists and not to the size of the effect of the relationship.

Question 26. What interventions are effective for reducing sedentary behavior?

Current evidence indicates that several types of interventions can be effective in reducing sedentary behavior in different age groups. For youth, evidence suggests that school-based interventions targeting reductions in television viewing and other screen-time activities can have a positive impact on reducing sedentary behavior. Among adults working primarily while seated, interventions targeting sedentary activities have resulted in reduced sedentary behavior at the workplace. Effective interventions have included those aimed at physical modifications to work stations (e.g., sit-stand workstations) in combination with educational and behavioral support.

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PART E. SYSTEMATIC REVIEW LITERATURE SEARCH METHODOLOGY

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OVERVIEW

Under the direction of the Office of Disease Prevention and Health Promotion (ODPHP), the National Institutes of Health (NIH), the Centers for Disease Control and Prevention (CDC), and the President's Council on Fitness, Sports and Nutrition (PCFSN), ICF (a contractor), herein referred to as the literature review team, was responsible for supporting the 2018 Physical Activity Guidelines Advisory Committee in reviewing the scientific literature used to support the development of its report.

The literature review team used a methodology informed by best practices for systematic reviews (SRs) developed by the United States Department of Agriculture's (USDA) Nutrition Evidence Library (NEL),[1] the Agency for Healthcare Research and Quality (AHRQ),[2] the Cochrane Collaboration,[3] and the Health and Medicine Division of the National Academies of Sciences, Engineering, and Medicine SR standards[4] to review, evaluate, and synthesize published, peer-reviewed physical activity research. The literature review team's rigorous, protocol-driven methodology was designed to maximize transparency, minimize bias, and ensure the SRs conducted by the Committee were relevant, timely, and of high quality. Using this evidence-based approach enabled compliance with the Data Quality Act,[5] which states that federal agencies must ensure the quality, objectivity, utility, and integrity of the information used to form federal guidance. Strict quality control processes were implemented throughout the Committee's process to ensure transparency, integrity, reproducibility, and research excellence in design, implementation, and synthesis of the SRs.

The 2018 Scientific Report process was led by the Committee, with support from a federal leadership team. All work completed by the literature review team was under the direction and review of the Committee members. The literature review team[i] comprised several groups:

- A training and quality control team that developed an abstraction tool and accompanying abstraction guide, developed and implemented training and quality control protocols, and ensured overall quality and integrity of the Committee's SRs,
- SR liaisons, who managed the literature review team's workflow for their designated Subcommittee(s) and/or Work Group,
- Librarians, who reviewed search strategies, confirmed search results, and retrieved full text articles,
- A triage team that participated in a 5-hour triage training before conducting title and abstract triage of original articles, existing reports, SRs, meta-analyses (MAs), and pooled analyses identified through the literature searches, and
- Abstractors, who participated in a three-phase, five-week virtual training before abstracting data from original articles, existing reports, SRs, MAs, and pooled analyses. They also assessed

[i] All literature review team staff were required to disclose potential conflicts of interest or professional bias before working on this team. No conflicts of interest or bias were identified.

bias of original articles and assessed the quality of existing reports, SRs, MAs, and pooled analyses.

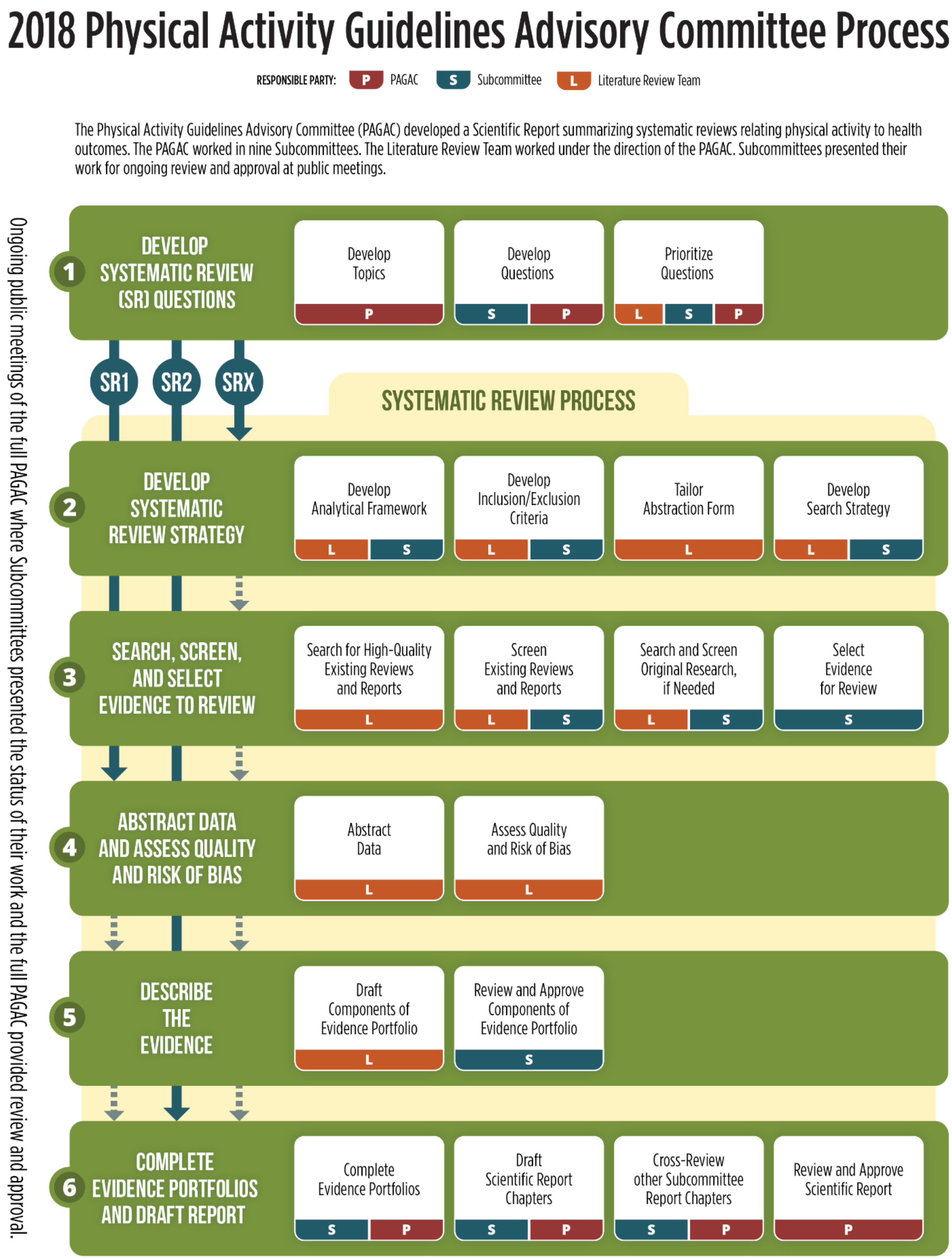
A six-step process was used to develop the Scientific Report:

- Step 1: Develop systematic review questions
- Step 2: Develop systematic review strategy
- Step 3: Search, screen, and select evidence to review for each question
- Step 4: Abstract data and assess the quality and risk of bias of the research
- Step 5: Describe the evidence
- Step 6: Complete evidence portfolios and draft Scientific Report

Figure E-1 provides a visual representation of this process. The model displays the six overarching steps and the associated tasks within each step. It also shows that at any given time, multiple SRs were being executed. For each SR, Steps 2 through 6 were completed sequentially. Throughout the life of the Committee Subcommittees presented the status of their work at in-person public meetings for review and approval by the full Committee. The responsible parties for each task (full Committee, Subcommittee, and/or literature review team[ii]) are included in the model.

[ii] Because federal staff served in an support role, specific tasks were not assigned to them.

Figure E-1. 2018 Physical Activity Guidelines Advisory Committee Process Model



SYSTEMATIC REVIEW PROCESS

Step 1: Develop Systematic Review Questions

In 2014, a federal planning group led by ODPHP, NIH, CDC, and PCFSN organized a potential scope and state of the science meeting with experts from around the country to gather information on whether sufficient new evidence was available to update the *2008 Physical Activity Guidelines for Americans.*[6] Based on the *Physical Activity Guidelines Advisory Committee Report, 2008,*[7] and a summary of areas of rapidly developing science, the group identified a number of key areas with new research available: youth younger than age 6 years, older adults, brain health across the life span, dose-response, and sedentary behavior. In early 2016, the literature review team conducted a scoping exercise to determine the amount of literature published on topics included in the 2008 Scientific Report[7] since the completion of that report. The Committee used the list of key topics from 2014, the summary of the scoping exercise, and their expertise to determine the final list of topics to examine.

At their first public meeting, the Committee decided on topics and formed Subcommittees. The Subcommittee members then developed and refined clearly focused SR questions and subquestions within each topic, which were used to systematically search the existing literature. The development of the SR questions took place during Subcommittee calls.

Prioritize SR Questions

After formulating a list of SR questions, Subcommittee members ranked the questions based on the following:

- Potential for greatest public health impact
- Potential to inform public health policy and/or programs
- Existence of mature scientific evidence
- Potential generalizability

The SR questions and their prioritization were reviewed and revised by the full Committee during their second public meeting. Any refinements to the questions or questions developed after the second public meeting were presented to leaders of all the Subcommittees for their review and approval.

Step 2: Develop Systematic Review Strategy

Develop Analytical Frameworks

The Subcommittees developed an analytical framework for each of their SR questions. Analytical frameworks are a visual representation of the search that provided the foundation for each search strategy. The frameworks were used throughout the process to clearly define key variables and terms, help determine the inclusion and exclusion criteria, inform the development of the literature search strategy, and control the scope. For each question, Subcommittee members were asked to develop the components of the analytical framework using the PICO (Population, Intervention or Exposure, Comparison, and Outcomes) method. The analytical frameworks specified the criteria for the types of population (participants), types of interventions (and comparisons), and the types of outcomes of interest. The frameworks were discussed and refined during Subcommittee calls. In some cases, these discussions resulted in refinements to the SR questions. The development of the analytical framework was often done in conjunction with the next step in the process (developing the inclusion and exclusion criteria).

Develop Inclusion and Exclusion Criteria

SR liaisons developed a template to draft inclusion and exclusion criteria for each search to determine whether studies were eligible to be included in the SR and ensure that the evidence being considered in the SRs was relevant to the U.S. population. The template was shared with Subcommittee members for review, feedback, and approval. To promote consistency, all the SRs included four basic criteria, with additional criteria used as appropriate. The four constant criteria were:

- Publication language: Studies had to be published with full text in English.
- Publication status: Studies had to be published in peer-reviewed journals or a high-quality report identified by the Committee.
- Research type: Studies had to be existing SRs, MAs, pooled analyses, reports, or original research, determined to have appropriate suitability and quality by the Committee.
    - Existing reviews, including SRs, MAs, and pooled analyses, were considered if they met the inclusion criteria for the SR question; no priority was given to the selection of any specific type of review.
- Study subjects: Studies had to include human subjects

As appropriate, Subcommittee members considered additional criteria to identify the optimal evidence to answer each of their SR questions. These criteria related to the following:

- Age of study subjects
- Health status of study subjects
- Comparison groups included or excluded
- Date of publication
- Study design
- Intervention/exposure
- Outcome

Develop Search Strategies

A search strategy was created to identify peer-review literature for each SR conducted. Each search strategy included the following items:

- Search terms
- Boolean logic used to combine search terms
- Databases searched
- Limits: Search date range, languages searched, types of articles included (e.g., peer-reviewed articles, database-specific filters)

The search strategy also recorded the date(s) the searches were conducted and the number of articles identified with each search.

Three databases (PubMed®, CINAHL, and Cochrane) were used for each SR. These databases were identified because they represented comprehensive repositories of citations, abstracts, and full articles in fields relevant to the Committee's SRs.

The SR liaisons and librarians (from both ICF and the National Institutes of Health Library), and Subcommittee members worked together in an iterative process to develop each strategy. A list of core physical activity search terms was developed and shared with the Committee. Each Subcommittee could add or remove physical activity terms, as appropriate for each of their SR questions. Core terms were: "Aerobic activities," "Aerobic activity," "Cardiovascular activities," "Cardiovascular activity," "Endurance activities," "Endurance activity," "Exercise," "Physical activities," "Physical activity," "Physical conditioning," "Resistance training," "Sedentary lifestyle," "Strength training," "Walking," and

“Sedentary.” Population- and/or health outcome-specific search terms were developed for each SR question. As appropriate, population- or health outcome-specific search terms (e.g., cancer, all-cause mortality) were shared among the SR liaisons for consistency across Subcommittees.

Once the search terms were approved by the Subcommittee members, the SR liaisons conducted a draft search to get an estimate of how many results (articles) were identified using the search strategy. If the number of results seemed unreasonable or inaccurate to the Subcommittee members based on their expertise, the SR liaisons worked with Subcommittee members to refine the search strategy to ensure that it adequately captured articles that addressed the SR question. If the Subcommittee members considered the number of results to be reasonable and accurate, the SR liaisons shared the list of articles identified through the search for Subcommittee review, feedback, and approval.

The analytical framework, inclusion and exclusion criteria, and search strategy for each SR question can be found in the question-specific evidence portfolios, and can be accessed at www.health.gov/paguidelines.

Step 3: Search, Screen, and Select Evidence to Review

Searching, screening, and selecting scientific literature was an iterative process that sought to objectively identify the most complete and relevant body of evidence to answer each SR question. Working from the analytical frameworks, search strategies, and inclusion and exclusion criteria, the SR liaisons searched, screened, and selected the scientific literature in a systematic way to provide transparent evidence for each Subcommittee’s deliberations.

Identify Sources of Evidence to Answer SR Questions

Each SR question was answered using:

- Existing reviews and/or reports,
- Original research (de novo SR),or
- A combination of both existing reviews and/or reports and original research.

For each SR, existing reviews and reports were searched and screened first. These documents are valuable sources of summarized evidence that were used to prevent duplication of effort and promote efficient time and resource management. The decision to use existing reviews and/or reports, original research, or a combination of both existing reviews and/or reports and original research was made by

Subcommittee members for each SR after their review of the initial search results or the title, abstract, or full-text triage results.

Search for High-Quality Existing Reviews

Existing reviews were identified by using the search strategy, which specifically was restricted to identify only publications that were SRs, MAs, and pooled analyses. Two librarians independently reviewed the search strategies carried out by the SR liaisons to ensure quality and comprehensiveness, providing recommendations as needed. The librarians also duplicated each search to identify any errors in searching procedures and reviewed documentation of each search strategy.

After completing each search, duplicates were removed, resulting in a set of articles for triage. The list of articles identified for triage was shared with Subcommittee members, who provided review, feedback, and approval.

Search for High-Quality Existing Reports

The SR liaisons conducted a search of nine resources and websites[iii] using the search terms "physical activity," "exercise," and "sedentary" to identify and gather high-quality existing reports with potential relevance to SR questions that were not identified through the search for high-quality existing reviews. The search resulted in 1,277 titles that were reviewed for relevance independently by two SR liaisons, resulting in a pool of 195 potentially relevant reports. When discrepancies were identified, a third SR liaison reviewed the titles to help reach consensus.

The SR liaisons reviewed the list of report titles and descriptions and shared with their Subcommittee(s) any they thought might be relevant. If the Subcommittee members agreed that an existing report was relevant to a SR question, the report moved to triage.

Search for Original Research Articles

If the Subcommittee determined that a complete (de novo) SR or partial (supplemental de novo) SR was necessary because, for example, of a lack of relevant existing reviews, SR liaisons developed a strategy for a complete or partial search that was specifically tailored to the Subcommittee's needs for

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[iii] Resources and websites searched to identify high-quality reports included: AHRQ Evidence Reports: http://www.guideline.gov/resources/ahrq-evidence-reports.aspx; Campbell Collaboration Library of Systematic Reviews: http://www.campbellcollaboration.org/lib/; Cochrane Library: Accessed through NIH Library; Grey Literature Report: http://www.greylit.org/; Health and Medicine Division: http://www.nationalacademies.org/hmd/Reports.aspx; National Guideline Clearinghouse: http://www.guideline.gov; NICE: http://www.evidence.nhs.uk/; Rand Corporation: Accessed through NIH Library; and World Health Organization: http://www.who.int/gho/publications/en/.

Subcommittee review. SR liaisons then implemented the approved search strategy. Librarians reviewed the search strategies to ensure quality and comprehensive nature, and the searches were duplicated to identify any errors in searching procedures.

After completing the search, duplicates were removed, resulting in the set of articles for triage. The list of articles identified for triage was shared with Subcommittee members, who provided review, feedback, and approval.

Triage Articles

Once the literature search was complete, all article titles and abstracts were independently screened, or triaged by two members of the triage team, by one triage team member and one Subcommittee member, or by two or more Subcommittee members. When discrepancies were identified, an additional screener reviewed the titles or abstracts to help reach consensus.

- Title and abstract triage: Two screeners independently reviewed each article's title, then reviewed each remaining article's abstract, to determine whether it met the criteria for inclusion in the review. The list of articles identified and the triage results were shared with Subcommittee members. Subcommittee members were asked to provide review, feedback, and approval. The triage process was conducted and recorded in the online database developed for the Committee, which recorded all triage and abstraction data.
- Full-text triage: Full text was retrieved for the remaining articles after title and abstract triage and shared with Subcommittee members. Subcommittee members conducted triage on the full-text articles and excluded articles that did not meet the inclusion criteria. In addition, during the abstraction process, abstractors identified any concerns about inclusion, which the SR liaison brought to Subcommittee members for review and final decision. Any changes to the initial triage determinations based on full-text review were updated in the online database. SR liaisons shared the final list of included and excluded articles with the associated rationale for exclusion with Subcommittee members for their review.

Conduct Supplemental Searching Activities

Subcommittee members and federal support staff were encouraged to share additional articles that may have contributed to the evidence after the search strategy was executed. Subcommittee members and staff identified these articles through their expertise and familiarity with the literature or through hand searching of included article reference lists.

- If an article was identified that met the inclusion criteria (i.e., was published during the time frame searched and used existing search terms or reasonable variations of the included search terms) but had not been captured by the search strategy, it went through article triage.
- If an article was identified that had not been captured by the search strategy and did not meet the time frame requirement, the search could be "re-opened" to allow the article and other relevant articles published since the search was conducted into the potential body of evidence for consideration. Before re-opening the search, Subcommittee members had to confirm that the article would meet the inclusion criteria, provide evidence that it would alter the conclusion statement and/or the evidence grade, and request approval from the leaders of all the Subcommittees.

Determine Sources of Evidence

After reviewing the full text of all the included existing reviews and reports, the Subcommittee members decided whether these sources of evidence could be used to answer the SR question in full, in part, or not at all.

- If the existing reviews and reports selected could be used to answer the SR question in full, the literature review team proceeded to Step 4: Abstract Data and Assess Quality and Risk of Bias.
- If the existing reviews and reports selected could be used to answer the SR question in part (i.e., in combination with a de novo SR), the literature review team proceeded to Step 4 for the selected existing reviews and reports. Concurrently, the Subcommittee members discussed which components of the SR question were not addressed by the selected existing reviews and/or reports. SR liaisons developed and implemented a search strategy to answer the remaining components of the question, as described in the Search for Original Research Articles section. The revised search strategy was shared with the Subcommittee members for feedback and approval before implementation.
- If none of the existing reviews and reports could be used to answer the SR question (or if no existing reviews and/or reports were identified by the search strategy), the SR liaison implemented a search strategy to search for original research articles.

Step 4: Abstract Data and Assess Quality and Risk of Bias

An objective data abstraction approach was used to present and summarize the characteristics of studies that addressed a SR question. The goals of data abstraction were to accurately identify and concisely describe the key elements of each study, while capturing consistent information from each article across the whole body of evidence. Abstractors were hired, trained, and certified to perform all abstracting duties, and strict quality control procedures were used throughout the abstraction process.

Conduct Abstraction Training and Quality Control

Abstractor candidates participated in a three-phase, five-week virtual training that culminated in a certification process. All abstractors were certified before abstracting articles for the Committee. The training was supported by an abstractor training manual that contained detailed instructions, definitions, reporting instructions, response options, and examples (including screen shots of the online database), as well as annotated versions of the articles used in the training. In addition to initial training sessions, the training and quality control team provided group retraining and recalibration and one-on-one consultation and training to abstractors. On an ongoing basis, the training and quality control team provided feedback and developed guidance documents (e.g., FAQs) based on frequently asked questions and common errors.

Two abstractors (referred to as a "pair") independently conducted all data abstraction tasks. Abstractors were assigned batches of articles to review in the online database. After both abstractors completed the batch, the pair reviewed their entries, discussed discrepancies, and reached agreement:

- When abstractors were able to settle discrepancies, the online database was updated to reflect the decision.
- When needed, the abstractors contacted a training and quality control team member to discuss their disagreements or gain clarification. A training and quality control team member conducted an independent review of the specific data elements where discrepancies existed and provided guidance. After a decision was reached by abstractors, the online database was updated to reflect the decision.

Concurrent with abstraction, the training and quality control team independently abstracted data for 12.5 percent (at a minimum) of existing reviews, reports, and original research and then compared their entries with those of the abstractor pair to identify discrepancies. A higher percentage of articles were reviewed by the training and quality control team when abstractors moved from abstracting SRs, MAs, pooled analyses, or reports to abstracting original articles and when new research questions required changes in the abstraction form.

Abstract Data

Data were entered into an online database using standard abstraction items, one for existing reviews and reports and another for original research (Standard Abstraction Items – SR, MA, Pooled Analyses, and Reports and Standard Abstraction Items—Original Research). The forms were modeled after similar forms used for the 2008 Advisory Committee and the Guide to Community Preventive Services SRs, and were tailored for each SR based on input from Subcommittee members. The pair of abstractors independently read and reviewed each article, abstracted key information, and entered it into the online database, which was prepopulated with basic information about the article (e.g., citation, abstract). After all quality control processes were conducted, complete abstraction data were used to populate individual article evidence summary tables.

Assess Quality for Existing SRs, MAs, and Pooled Analyses[iv]

In addition to abstracting key information from SRs, MAs, and pooled analyses, the pair of abstractors independently assessed each existing review's quality. Quality for each SR, MA, or pooled analysis was assessed using $AMSTAR_{ExBP}$.[8] $AMSTAR_{ExBP}$, a modified version of "A Measurement Tool to Assess Systematic Reviews" (AMSTAR),[9] was used to assess the methodological quality of SRs and MAs. $AMSTAR_{ExBP}$ is an adaptation of AMSTAR that focuses on MAs that examine the effects of exercise training on blood pressure. The training and quality control team made additional revisions to adapt $AMSTAR_{ExBP}$ for the Committee (SR, MA, and Pooled Analysis Quality Assessment Using Tailored AMSTARExBP Instrument). The adaptation made by the training and quality control team for the Committee was based on a methodology improvement publication for AMSTAR.[10] The main revisions clarified reporting instructions for scoring quality items in different types of reviews and were not intended to modify the tool itself. The results of the SR, MA, and pooled analysis quality assessment were used to develop quality assessment charts and were shared with Subcommittee members for review.

[iv] If authors of a publication conducted an SR followed by an MA, the study was classified as an MA. If authors referred to a study as a pooled analysis, the publication was classified as pooled analysis, independently of being accompanied by a SR or not. Publications that consisted only of SRs, for which the authors did not also conduct a meta-analysis, were classified as an SR. Subcommittee members classified existing reviews as SRs, MAs, or pooled analyses consistent with abstractions and the evidence portfolio.

Assess Quality for Existing Reports

In addition to abstracting key information from existing reports, pairs of abstractors also independently assessed each report's quality. The literature review team developed, with feedback from the USDA NEL, a set of questions that assessed the integrity and appropriateness of the methodology, recommendations, and references in existing reports (Existing Reports Quality Assessment Instrument). The results of each reports' quality assessment were used to develop quality assessment charts and were shared with Subcommittee members for review.

Assess the Risk of Bias for Original Research

In addition to abstracting key information from each original research article, pairs of abstractors assessed each study's risk of bias. Risk of bias, or internal validity, was assessed for each original study using an adapted version of the USDA NEL Bias Assessment Tool (BAT).[11] The NEL BAT uses a domain-based evaluation to help determine whether any systematic error exists that could either over- or underestimate the study results. Selection, performance, detection, and attrition bias are addressed in the NEL BAT.

The NEL BAT is tailored by study design, with different sets of questions applying to randomized controlled trials (RCTs) (14 questions), non-randomized controlled trials (14 questions), and observational studies (12 questions). To adapt the NEL BAT for the Committee, the training and quality control team made minor revisions to expand the reporting instructions to facilitate decision making and provide examples relevant to the Committee's topics, questions, and study designs (Original Research Bias Assessment using Adapted Nutrition Evidence Library Bias Assessment Tool Instrument). The results of studies' risk of bias assessments were used to develop the risk of bias summary charts and were shared with Subcommittee members for review.

Step 5: Describe the Evidence

To facilitate the Committee's review and analysis of the evidence, the literature review team prepared evidence portfolios for each SR question. For transparency, the evidence portfolios documented the full process followed for each of the SRs, including the sources of evidence, conclusions, evidence grades, description of evidence, populations analyzed, individual evidence summary tables, risk of bias and quality assessment charts, search strategy, literature tree, references, and rationale for exclusion of articles excluded at abstract or full-text triage. After the SR liaison compiled the evidence portfolios, all evidence portfolios and reference lists were edited and reviewed for consistency. SR liaisons submitted evidence portfolios to the corresponding Subcommittee for review, feedback, and approval.

This step was often done concurrently with Step 6: Complete Evidence Portfolio and Draft Advisory Committee Scientific Report.

The evidence portfolio for each SR question can be accessed at www.health.gov/paguidelines.

Step 6: Complete Evidence Portfolios and Draft Scientific Report

Develop Conclusion Statements

Subcommittee members reviewed and deliberated on the body of evidence (i.e., included existing reviews, original research articles included in existing reviews, and/or included original research) to develop conclusion statements that answered each of their SR questions and any subquestions. Conclusion statements were tightly associated with the evidence, focused on general agreement among the studies around the independent variable(s) and outcome(s), and acknowledged areas of disagreement or limitations, where they existed. The conclusion statement(s) reflected only the evidence reviewed and not information Subcommittee members might have known from another source.

Grade the Evidence

Along with the SR evidence portfolios, the Committee members were given a rubric, the 2018 Physical Activity Guidelines Advisory Committee Grading Criteria (Table E-1), to guide their assessment and grading of the strength of the evidence supporting each conclusion statement. The rubric was adapted from the USDA NEL Conclusion Statement Evaluation Criteria rubric[12] and revised slightly by Committee members to reflect the specific characteristics of physical activity literature. Grading the strength of the evidence was based on applicability of the populations, exposures, and outcomes studied; generalizability to the population of interest; risk of bias and study limitations; quantity and consistency of findings across studies; and magnitude and precision of effect.

Subcommittees presented their conclusion statements and strength of evidence grades to the full Committee during public meetings for deliberation and approval. When necessary, Subcommittee members revised the conclusion statements and grades. Any changes to conclusion statements and strength of evidence grades had to be re-presented to the full Committee during public meetings.

Develop Narrative Summary and Research Recommendations

After the Subcommittee members developed a conclusion statement and grade for a SR question and any SR subquestions, they developed a narrative summary of their analysis and research recommendations related to the question. The summary included a review and synthesis of the evidence, rationale for evidence grades, and limitations. The research recommendations listed key areas where additional research could enhance the evidence base by addressing gaps identified in the existing research, advancing the field of physical activity research, and informing future editions of the Physical Activity Guidelines.

Draft the PAGAC Scientific Report

Subcommittee members drafted a summary for each SR question using the body of evidence. The SR question summaries were compiled into the Committee's Scientific Report.

PAGAC EVIDENCE ASSESSMENT TOOLS

Standard Abstraction Items – SR/MA/Pooled Analyses/Reports[v]

Summary of Individual SR/MA/Pooled Analysis/Report

- Type of Review/Source
  - Systematic Review/Meta-Analysis/Pooled-Analysis
    - Total Number of Studies
  - Report
    - Report Organization/Sponsor
    - Report Type
- Purpose of the Review/Report
- Author Stated Funding Source
- Exposure Definition
  - Measures Steps?
  - Measures Bouts?
  - High Intensity Interval Training (HIIT)?
- Timeframe[vi]

[v] All items ending with a question mark have yes/no responses.
[vi] Records the years covered in the search of the SR, MA, or report. If authors searched from the earliest date available in a database (e.g., from the database's inception) it was abstracted as "inception to end date of search."

- Description of Outcomes
    - Measures Change in Fitness?
- Report's Conclusions

Study Population[vii]

- Sex
- Race/Ethnicity
- Age
- Socioeconomic Status
- Population Density
- Weight Status
- Disability Status
- Pregnancy Status
- Cancer
- Chronic Condition
- Other

Standard Abstraction Items—Original Research[viii]

Study Overview

- Purpose
- Study Design
- Do the authors refer to supplementary material or previous publications for detailed methods?
- Country
- Author Stated Funding Source
- Author Stated Sample Power
- Sample Size - Initial
- Final Sample Size
- Attrition (%)
- Was the study an intervention?
- Type of Intervention
    - Provision of Information/Education
    - Behavioral
    - Environmental
    - Policy/Legislation/Regulation
    - Laboratory-based
    - Technology
    - Other

[vii] All populations analyzed and presented in the data related to the outcome of interest are recorded.
[viii] All items ending with a question mark have yes/no responses.

- Physical Activity Exposure Assessment
    - Self-reported
    - Device-measured
    - Direct Observation
    - Other
    - Measures Steps?
    - Measures Bouts?
- Outcomes and Measurement
    - Measures Change in Fitness?
    - Addresses Adverse Events?

Study Population[ix]

- Sex
- Race/Ethnicity
- Age
- Socioeconomic Status
- Population Density/Urbanicity
- Weight Status
- Disability Status
- Pregnancy Status
- Cancer
- Chronic Condition
- Other

Intervention Components

- Length of Overall Physical Activity Intervention
- Frequency of Physical Activity
- Intensity of Physical Activity
- Duration of Physical Activity
- Physical Activity Type
    - Cardiorespiratory
    - Strength
    - Balance
    - Flexibility
    - Active Play, Free Play, or Outdoor Play
    - Other
- High Intensity Interval Training (HIIT)?
- Was Intention to Treat Analysis Conducted?

[ix] All populations analyzed/presented in the data related to the outcome of interest are recorded.

SR, MA, and Pooled Analyses Quality Assessment Using Tailored AMSTAR$_{ExBP}$ Instrument

- Were the review questions and inclusion and exclusion criteria clearly delineated prior to executing the search strategy?
- Were the population variables defined and considered in the methods?
- Was a comprehensive literature search performed?
- Was there duplicate study selection and data extraction?
- Was the search strategy clearly described?
- Was relevant grey literature included in the review?
- Was a list of studies (included and excluded) provided?
- Were the characteristics of the included studies provided?
- Was Frequency, Intensity, Time, and Type (FITT) defined for each study and examined in relation to the outcome effect sizes?
- Was the scientific quality (risk of bias) of the included studies assessed and documented?
- Did results depend on study quality, either overall, or in interaction with moderators?
- Was the scientific quality of the included studies used appropriately in formulating conclusions?
- Were the data appropriately synthesized in a qualitative manner and if applicable, was heterogeneity assessed?
- Was the effect size index chosen justified, statistically?
- Was individual-level meta-analysis used?
- Were practical recommendations clearly addressed?
- Was the likelihood of publication bias assessed?
- Was the conflict of interest disclosed?

Existing Reports Quality Assessment Instrument

- Were the review questions and inclusion and exclusion criteria clearly delineated prior to executing the search strategy?
- Did the inclusion criteria permit grey literature?
- Was a comprehensive literature search performed?
- Was the scientific quality of the included source assessed and documented?
- Are limitations reported and discussed?
- Are the conclusions substantiated by and logically connected to the evidence and findings presented?
- Was there a clear list of practical recommendations provided for future research or work on the topic?
- Are the recommendations relevant to the purpose of the report and supported by the evidence, findings, and conclusions?
- Were the potential conflicts of interest among report funders, authors, expert, or stakeholders assessed and explained?
- Was a reference list or a bibliography for the cited literature provided?

Original Research Bias Assessment using Adapted Nutrition Evidence Library Bias Assessment Tool Instrument[x]

- Were the inclusion and exclusion criteria similar across study groups?
- Was the strategy for recruiting or allocating participants similar across study groups?
- Was the allocation sequence randomly generated?
- Was the group allocation concealed (so that assignments could not be predicted)?
- Was distribution of health status, demographics, and other critical confounding factors similar across study groups at baseline? If not, does the analysis control for baseline differences between groups?
- Did the investigators account for important variations in the execution of the study from the proposed protocol or research plan?
- Was adherence to the study protocols similar across study groups?
- Did the investigators account for the impact of unintended or unplanned concurrent interventions or exposures that were differentially experienced by study groups and might bias results?
- Were participants blinded to their intervention or exposure status?
- Were investigators blinded to the intervention or exposure status of participants?
- Were outcome assessors blinded to the intervention or exposure status of participants?
- Were valid and reliable measures used consistently across all study groups to assess inclusion and exclusion criteria, interventions and exposures, outcomes, participant health benefits and harms, and confounding?
- Was the length of follow-up similar across study groups?
- In cases of high or differential loss to follow-up, was the impact assessed (e.g., through sensitivity analysis or other adjustment method)?
- Were other sources of bias taken into account in the design and/or analysis of the study (e.g., through matching, stratification, interaction terms, multivariate analysis, or other statistical adjustment such as instrumental variables)?
- Were the statistical methods used to assess the primary outcomes adequate?

[x] Item relevance depended on the study design reported.

Table E-1. 2018 Physical Activity Guidelines Advisory Committee Grading Criteria

Criteria	Strong	Moderate	Limited	Not Assignable
Applicability	Study populations, exposures, and outcomes are directly related to the question	Some of the study populations, exposures, or outcomes, are directly related to the question	Most of study populations, exposures, and outcomes relate to the question indirectly	All of the study populations, exposures, and outcomes relate to the question indirectly
Generalizability (to the U.S. population of interest)	Studied population, exposure, and outcomes are free from serious doubts about generalizability	Minor doubts about generalizability	Serious doubts about generalizability due to narrow or different study population, exposure, or outcomes studied	Highly unlikely that the studied population, exposure, and/or outcomes are generalizable to the U.S. population
Risk of bias or study limitations (as determined by NEL BAT and/or $AMSTAR_{ExBP}$)	Studies are of strong design; free from methodological concerns, bias, and execution problems	Studies are of strong design with minor methodological concerns OR studies of weaker study design	Studies of weak design OR inconclusive findings due to design flaws, bias, or execution problems	Serious design flaws, bias, or execution problems across the body of evidence
Quantity and Consistency (of the results across the available studies)	Many studies have been published and the results are highly consistent in direction and approximate size of effect	A moderate number of studies have been published with some inconsistency in direction or size of effect	Few studies have been published with some inconsistency in direction or size of effect	Findings are too disparate to synthesize OR single small study unconfirmed by other studies
Magnitude and precision of effect	The magnitude and precision of the estimated effect provide considerable confidence in the accuracy of the findings	The magnitude and precision of the estimated effect provide confidence in the accuracy of the findings	The magnitude and precision of the estimated effect provide some but not a lot of confidence in the accuracy of the findings	Magnitude and precision of effect cannot be determined

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PART F. CHAPTER 1. PHYSICAL ACTIVITY BEHAVIORS: STEPS, BOUTS, AND HIGH INTENSITY TRAINING

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INTRODUCTION

The *Physical Activity Guidelines Advisory Committee Report, 2008*[1] demonstrated that moderate-to-vigorous physical activity is associated with a wide range of health benefits. Most of the literature on which the conclusions were based used survey and questionnaire data, where physical activity exposures were assessed using self-reported estimates of time spent in aerobic continuous moderate-to-vigorous physical activity accumulated in bouts of at least 10 minutes. In the 2008 Scientific Report, all other physical activity—sedentary behavior, light-intensity physical activity, and bouts of moderate-to-vigorous intensity physical activity of less than 10 minutes duration—was considered “baseline” physical activity. The physical activity that counted toward health benefits—moderate-to-vigorous physical activity in bouts of 10 minutes or more—was on top of baseline physical activity.

The conclusions of the 2008 Scientific Report[1] were solidly based on the existing scientific information, and the findings and conclusions of the *2018 Physical Activity Guidelines Advisory Committee Report* mostly extend the range of beneficial outcomes described in the 2008 Scientific Report. However, 10 additional years of scientific inquiry, aided by substantial advances in measuring physical activity, have improved and refined the understanding of the types of physical activity that influence health outcomes. These include topics such as:

- Are there simpler metrics—such as step counts—for estimating the volume of health-promoting behavior?
- Do short episodes of activity—bouts less than 10 minutes in duration—contribute to accumulated beneficial physical activity, such as parking distant from the entrance to a place of work (as suggested in most public health statements about physical activity); walking into the coffee shop instead of using the drive-through; getting up from chairs at work to walk around the office; getting up from the couch during the breaks in a TV program to do a chore; climbing a flight of stairs?
- How does the newly popularized high intensity interval training (HIIT) mode of exercise fit into health recommendations?
- What, if any, is the value of light-intensity physical activity?
- At any given volume of moderate-to-vigorous physical activity, does the composition of baseline physical activity influence health outcomes?

The Committee considered it important to address these questions and anticipate the ones that might arise following the publication of the 2018 Scientific Report by investigating the current data and further research needs of three particularly relevant issues: the role of daily step counts in the assessment of daily accumulated physical activity across all intensity levels, including light-intensity activity; the impact on health benefits of moderate-to-vigorous physical activity in bouts lasting less than 10 minutes; and the effect of and contribution of HIIT to the prescribed amount of weekly moderate-to-vigorous physical activity, and whether HIIT is associated with cardiometabolic health benefits.

All the dose-response data used to develop the physical activity targets for the 2008 Guidelines[2] were developed using epidemiologic data from longitudinal cohort studies with the condition as the outcome and moderate-to-vigorous physical activity as the exposure. One well-accepted limitation of reported data is the inability to incorporate light-intensity physical activity. With the advent of devices to objectively measure physical activity of community-dwelling individuals during daily life activities in addition to exercise, it is becoming increasing clear that light-intensity physical activity contributes to favorable health benefits, independent of those provided by moderate-to-vigorous physical activity.[3]

Since the 2008 Scientific Report,[1] several developments have occurred in the means by which physical activity and exercise are measured, quantified, and prescribed to individuals seeking exercise-associated health benefits. The proliferation and popularity of smart phones and other wearable devices containing accelerometers have facilitated the measurement of daily steps counts (see *Part F. Chapter 11. Promoting Regular Physical Activity* for additional details). Current consumer devices have three-dimensional accelerometers, which permit assessments of step cadence; this permits the assessment of physical activity as light intensity or as moderate-to-vigorous physical activity. It is now possible to assess the contribution of light-intensity physical activity to total step counts and, therefore, to better estimate total energy expenditure (see *Part C. Background and Key Concepts* for additional details). Because step counts incorporate both light-intensity and moderate-to-vigorous physical activity, the Subcommittee considered it important to better understand how the measurement of steps might fit into the assessment of daily or weekly physical activity exposures and its relationship to health outcomes.

The persistence of the seeming need to accumulate moderate-to-vigorous physical activity in episodes (bouts) of at least 10 minutes, which dates to the physical activity recommendations from the Centers for Disease Control and Prevention and the American College of Sports Medicine,[4] has provided a barrier to research investigating how episodes of less than 10 minutes might contribute to the accumulation of the recommended moderate-to-vigorous physical activity. In addition, it creates dissonance with recommendations such as “take the stairs,” “move more, sit less,” and “park your car in the parking lot further from your place of work,” which can incorporate more physical activity into an individual’s lifestyle but typically take less than 10 minutes to execute. Therefore, the Subcommittee considered it important to examine data regarding whether accumulated episodes of less than 10 minutes have health benefits and whether those benefits are similar to those of accumulated episodes of greater than 10 minutes.

Since the 2008 Scientific Report, high intensity interval training (HIIT) has become a popular research topic. The media also presents HIIT as an alternative means by which individuals can achieve health benefits similar to those of classical continuous moderate-to-vigorous physical activity. Some have suggested that HIIT may be a better alternative than traditional amounts of exercise because it consumes less overall time per week and might be more attractive as a long-term strategy by which to achieve the health benefits of regular physical activity. The Subcommittee considered it important to examine scientific evidence regarding the use of HIIT for health benefits, the sustainability of HIIT programs, and the rate of adverse events relative to classical continuous aerobic training.

REVIEW OF THE SCIENCE

Overview of Questions Addressed

This chapter addresses three major questions and related subquestions.

1. What is the relationship between step count per day and (1) all-cause and cardiovascular disease mortality, and (2) incidence of cardiovascular disease events and type 2 diabetes?
    a) Is there a dose-response relationship? If yes, what is the shape of the relationship?
    b) Does the relationship vary by age, sex, race/ethnicity, socioeconomic status, or weight status?
2. What is the relationship between bout duration of physical activity and health outcomes?
    a) Does the relationship vary by age, sex, race/ethnicity, socioeconomic status, or weight status?
3. What is the relationship between high intensity interval training and reduction in cardiometabolic risk?
    a) Is there a dose-response relationship? If yes, what is the shape of the relationship?
    b) Does the relationship vary by age, sex, race/ethnicity, socioeconomic status, or weight status?

Data Sources and Process Used to Answer Questions

One search and triage process was conducted for existing reviews (systematic reviews, meta-analyses, pooled analyses, and reports) for all three questions. The Exposure Subcommittee determined that systematic reviews, meta-analyses, and pooled analyses provided sufficient literature to answer Question 3. The existing reviews did not provide sufficient evidence to answer Questions 1 and 2. Separate de novo searches for original research were conducted for Questions 1 and 2. For complete details on the systematic literature review process, see *Part E. Systematic Review Literature Search Methodology*.

Question 1. What is the relationship between step count per day and all-cause and cardiovascular disease mortality and (2) incidence for cardiovascular disease events and risk of type 2 diabetes?

a) Is there a dose-response relationship? If yes, what is the shape of the relationship?
b) Does the relationship vary by age, sex, race/ethnicity, or socio-economic status, and weight status?

Source of evidence: Original research articles

Conclusion Statements

Insufficient evidence is available to determine whether a relationship exists between step counts per day and all-cause and cardiovascular disease mortality. **PAGAC Grade: Not assignable.**

Limited evidence suggests that step count per day is associated with reduced incidence of cardiovascular disease events and risk of type 2 diabetes. **PAGAC Grade: Limited.**

Limited evidence suggests a dose-response relationship between the measure of steps per day and cardiovascular disease events and type 2 diabetes risk. **PAGAC Grade: Limited.**

Insufficient evidence is available to determine whether the relationship between the measure of steps per day and cardiovascular disease events and type 2 diabetes risk is influenced by age, sex, race/ethnicity, socioeconomic status, or weight status. **PAGAC Grade: Not assignable.**

Review of the Evidence

The committee reviewed evidence from nine manuscripts that reported on five original research studies. Of the nine reports, four used a cross-sectional design,[5-8] four used a prospective design,[9-12] and one used a randomized controlled design where control and intervention groups were compared, as well as pooled, to examine steps per day in relationship to insulin resistance.[13] The Navigator study, a multicenter trial of 9,306 individuals with impaired glucose recruited from 40 countries, provided four manuscripts (three longitudinal and one cross-sectional). All four Navigator papers examined health outcomes after pooling intervention and control groups. Therefore, the Navigator study design was considered cross-sectional[5] or longitudinal prospective.[9, 11, 12] Participants in all nine reviewed studies were middle-age or older. Males and females, multiple races and ethnicities, a continuum of body sizes, and diverse geographical areas were represented, supporting the generalizability of conclusions.

Cross-sectional studies cannot control for bi-directional relationships, i.e., the outcome causing the exposure as well as the exposure causing the outcome. Because it is likely that individuals with undiagnosed disease may take fewer steps per day than healthy individuals, the reviewed cross-sectional studies were used only to understand usual step counts per day across sample populations.

The longitudinal studies reported health outcomes that included blood glucose levels,[10, 12, 13] metabolic syndrome,[9] and a composite of CVD incidence, which included cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke.[11]

The baseline number of steps per day varied across studies but the median was approximately 5,000 steps per day. One report[13] showed that 80 percent of the steps taken in a day were of light-intensity physical activity. Samples of older adults accumulated fewer daily steps than did younger middle-aged adults. An Australian sample of Tasmanian adults (mean age at baseline 50 years)[10] accumulated nearly twice as many daily steps at baseline as other samples (approximately 10,000, whereas most study baseline steps per day were approximately 5,000).

Evidence on the Overall Relationship

No study was found that examined the relationship between step counts per day and all-cause or cardiovascular mortality. Therefore, the Subcommittee was unable to draw a conclusion about this relationship.

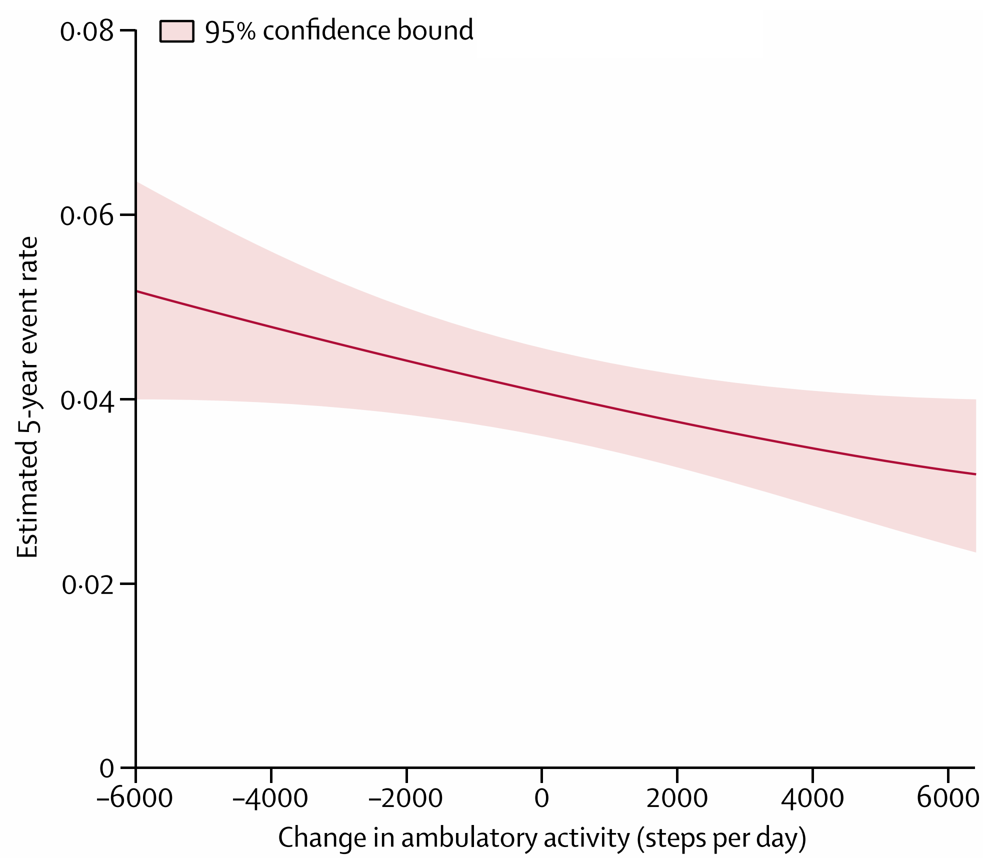
Several longitudinal studies examined the relationship between step counts per day and disease incidence or risk. One study examined cardiovascular disease events, defined as cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke.[11] The other four longitudinal studies addressed type 2 diabetes risk.[9, 10, 12, 13]

Yates et al[11] provided evidence of the benefit of increasing steps per day to reduce cardiovascular event incidence as well as the effect of baseline step count on subsequent cardiovascular disease events. This study included more than 45,000 person-years of follow-up in which 531 cardiovascular events occurred. Change in steps per day and baseline steps were positively associated with reduced risk for cardiovascular disease events.

Herzig et al,[13] Huffman et al,[9] Ponsonby et al,[10] and Yates et al[12] focused on markers of type 2 diabetes risk. Following a 3-month intervention in which 78 participants who already had an abnormal glucose profile participated in 3 days a week of supervised walking or usual physical activity, step count per day for intervention and control groups were pooled.[13] This measure was not associated with improved glucose profiles. Huffman et al[9] analyzed Navigator data and showed an incremental reduction in the 6-year metabolic syndrome score with baseline step count. Also using Navigator data, Yates et al[12] reported previous steps per day to be weakly and negatively associated with 2-hour glucose levels after adjustment for glucose levels in the preceding 3 years. Ponsonby et al[10] followed 458 adults with a normal glucose profile and showed that higher steps per day at baseline were associated with a lower incidence risk for dysglycemia (impaired fasting glucose or impaired glucose tolerance) after 5 years.

Dose-response: In Yates et al[11] a yearly 2,000 steps per day increase resulted in an 8 percent yearly reduction in cardiovascular event rate in individuals with impaired glucose tolerance. In addition, baseline level of steps per day was inversely associated with cardiovascular event incidence. Specifically, at baseline each 2,000 steps per day increment was associated with a 10 percent lower cardiovascular event rate (Figure F1-1).

Figure F1-1. Association Between Change in Daily Step Count and Cardiovascular Events in Individuals with Impaired Glucose Tolerance



Source: Reprinted with permission from Elsevier (The Lancet, Yates et al., 2014,[11] 383, 1059-1066).

Huffman et al[9] also analyzed Navigator data and showed for every incremental 2,000 step increase in baseline steps per day a 0.29 percent reduction in the 6-year metabolic syndrome score was expected. Ponsonby et al[10] estimated that for any average daily step count, an additional 2,000 steps would be associated with a 25 percent reduction in developing incident dysglycemia over the succeeding 5 years.

Similar to the Navigator studies,[9, 11] the relationship between step count per day and health outcome appeared linear in Ponsonby et al.[10]

Evidence on Specific Factors

Demographic factors and weight status: The difference in risk reduction reported in Yates et al[11] was not affected by weight status, sex, age, geographical region, or level of baseline steps per day. Despite these findings, the evidence on these factors was not sufficient enough for the Subcommittee to draw a conclusion about any relationship. Negative associations between steps and metabolic syndrome score reported in Huffman et al[9] were independent of weight status. Ponsonby et al[10] reported associations that were also independent of weight status when examining steps per day and dysglycemia.

For additional details on this body of evidence, visit: https://health.gov/paguidelines/second-edition/report/supplementary-material.aspx for the Evidence Portfolio.

Public Health Impact

Steps are a basic unit of locomotion and as such, provide an easy-to-understand metric of ambulation—an important component of physical activity. Measuring step counts has been shown to motivate diverse samples of individuals to increase physical activity levels (see *Part F. Chapter 11. Promoting Regular Physical Activity* for more details). Increasingly, the self-assessment of steps can be accomplished through device-based, readily obtainable technology such as pedometers, smartphones, and physical activity trackers. Unlike the measure of moderate-to-vigorous physical activity minutes per week, the metric of step counts per day provides a comparable measure to how caloric intake in most dietary guidance is standardized, i.e., per day. As a result, steps per day would provide a useful tool for researchers and the public to address a variety of health and physical activity issues. In addition, steps can be at light-, moderate-, and vigorous-intensity levels, providing a range of exertion choice to promote walking at all ages and for all levels of fitness. For these reasons, the measure of steps per day has the potential to significantly improve the translation of research findings into public health recommendations, policies, and programs.

Question 2. What is the relationship between bout duration of physical activity and health outcomes?

a) Does the relationship vary by age, sex, race/ethnicity, socioeconomic status, or weight status?

Source of evidence: Original research articles

Conclusion Statements

Moderate evidence indicates that bouts of any length of moderate-to-vigorous physical activity contribute to the health benefits associated with accumulated volume of physical activity. **PAGAC Grade: Moderate.**

Insufficient evidence is available to determine whether the relationship between physical activity accumulated in bouts with a duration of less than 10 minutes and health outcomes varies by age, sex, race/ethnicity, or socioeconomic status. **PAGAC Grade: Not assignable.**

Historical Context

Physical activity recommendations have traditionally focused on moderate-to-vigorous physical activity performed in a continuous manner. The historical perspective of these recommendations was summarized in the U.S. Surgeon General's *Report on Physical Activity and Health.*[14] In 1995, the Centers for Disease Control and Prevention and the American College of Sports Medicine provided the first contemporary recognition of the recommendation for moderate-to-vigorous physical activity to be "accumulated" in order to achieve a specific threshold of daily physical activity that, in turn, could result in health and fitness benefits.[4] This recommendation stated that "intermittent bouts of physical activity, as short as 8 to 10 minutes, totaling 30 minutes or more on most days provided beneficial health and fitness effects." This resulted in a new paradigm, and the 2008 Guidelines continued to support this recommendation for adults, stating that "aerobic activity should be performed in episodes of at least 10 minutes".[2] However, free-living physical activity is also performed in episodes typically less than 10 minutes in duration; these shorter episodes of physical activity also may have health-related benefits. Thus, the Subcommittee was interested in examining the available scientific literature to determine whether physical activity episodes of less than 10 minutes in duration have health-related benefits; or, alternatively, if the benefits are only realized when the duration of physical activity episodes is at least 10 minutes.

Review of the Evidence

To answer this question, the Subcommittee reviewed evidence from 25 manuscripts that reported on 23 original research studies.[15-39] Two pairs of these studies reported on different outcomes from the same studies.[16-19] Of the 23 studies, 11 used a cross-sectional design,[18-21, 25-27, 30, 31, 35, 36, 38] 2 used a prospective design,[22, 37] 9 used a randomized design,[15-17, 23, 24, 28, 29, 32, 33, 38] and 1 used a non-randomized design.[34]

These studies reported on either one or numerous outcomes. A variety of health outcomes were covered, including body weight or body composition,[15-18, 20, 23-25, 27-35, 37, 38] blood pressure,[16, 23, 24, 29, 31, 32, 37, 38] blood lipids,[16, 19, 22, 23, 27, 31-33, 38, 39] glucose or insulin,[16, 23, 26, 30, 38] metabolic syndrome,[21, 30] inflammatory biomarkers,[31, 38] or a composite of CVD risk.[36]

The duration of intermittent bouts also varied across studies. Cross-sectional[18-21, 25-27, 30, 31, 35, 36, 38] and prospective studies[22, 37] reported on bouts of physical activity that were less than 10 minutes, whereas randomized studies[15-17, 23, 24, 28, 29, 32-34, 39] reported only on intermittent bouts that were at least 10 minutes.

Evidence on the Overall Relationship

As reported in 11 manuscripts, 10 of the 23 unique studies examined used randomized designs that only included bouts of physical activity that were at least 10 minutes in duration.[15-17, 23, 24, 28, 29, 32-34, 39] These studies demonstrated that intermittent bouts resulted in similar or enhanced effects when compared to continuous bouts of physical activity of longer duration for outcomes of weight and body composition,[15-17, 23, 24, 28, 29, 32-34, 39] blood pressure,[16, 23, 24, 29, 32] blood lipids,[16, 23, 32, 33, 39] or glucose or insulin.[16, 23] However, these studies do not provide information to evaluate bouts of physical activity of less than 10 minutes in duration.

Evidence of overall health benefits resulting from bouts of physical activity less than 10 minutes in duration is provided primarily by studies that used a cross-sectional design,[18-21, 25-27, 30, 31, 35, 36, 38] with a few studies using a prospective design[22, 37] (Table F1-1). This evidence supports that physical activity accumulated in bouts less than 10 minutes in duration is associated with body mass index (BMI) or body fatness,[18, 20, 25, 27, 30, 31, 35, 37, 38] blood pressure,[31, 37, 38] blood lipids,[19, 22, 27, 31, 38] glycemic control,[19, 26, 30, 31, 38] metabolic syndrome,[21, 30] inflammatory markers,[31, 38] or Framingham Cardiovascular Disease Risk Score.[36]

Table F1-1. Summary of the Association Between Physical Activity Bout Duration and Health Outcomes from Prospective and Cross-Sectional Studies that Included Bouts of Less than 10-minute Duration

Citation	Study Type	Sample Size	Weight	BMI	Percent Body Fat, Body Composition	Visceral Adiposity	Blood Pressure	Total Cholesterol	HDL Cholesterol	LDL Cholesterol	Triglycerides	Fasting Glucose	Fasting Insulin	2-hour insulin during a glucose tolerance test	HbA1c	Metabolic Syndrome	CRP	Framingham CVD Risk Score
White et al., 2015[37]	Prospective	2076		≥10			Both											
Di Blasio et al., 2014[22]	Prospective	67							≥10									
Loprinzi and Cardinal, 2013[31]	Cross-Sectional	6321		Both	Both		Both	Both	Both	Both	Both	Both					Both	
Wolff-Hughes et al., 2015[38]	Cross-Sectional	5668		≥10	<10		<10		<10		<10	<10	<10				<10	
Gay et al., 2016[26]	Cross-Sectional	5302													<10			
Fan et al., 2013[25]	Cross-Sectional	4511		Both														
Strath et al., 2008[35]	Cross-Sectional	3250	≥10		≥10													
Glazer et al., 2013[27]	Cross-Sectional	2109		Both	Both				Both		Both							

Citation	Study Type	Sample Size	Weight	BMI	Percent Body Fat, Body Composition	Visceral Adiposity	Blood Pressure	Total Cholesterol	HDL Cholesterol	LDL Cholesterol	Triglycerides	Fasting Glucose	Fasting Insulin	2-hour insulin during a glucose tolerance test	HbA1c	Metabolic Syndrome	CRP	Framingham CVD Risk Score
Vasankari et al., 2017[36]	Cross-Sectional	1398																1-5, 6-10, 11-15, 20-120 min
Clarke and Janssen, 2014[21]	Cross-Sectional	1119														1-9, 4-9, 7-9 min		
Jefferis et al., 2016[30]	Cross-Sectional	1009		Both	Both								Both			Both		
Cameron et al., 2017[20]	Cross-Sectional	298		<10	Both	Both												
Ayabe et al., 2013[18]	Cross-Sectional	42				>3 min												
Ayabe et al., 2012[19]	Cross-Sectional	42							≥32 sec			≥3 min						

Legend: BMI=body mass index, HDL=high-density lipoprotein, LDL=low-density lipoprotein, CRP=C-reactive protein, and Both=both bouts of greater than or equal to 10 minutes versus less than 10 minutes in duration showed an association.
Note: Values shown indicate the duration of physical activity bouts at which a significant association was shown with selected health outcomes. Empty cells indicate the outcome was not reported.

Obesity. One cohort study examined incidence of obesity.[37] This study reported that physical activity accumulated in bouts of at least 10 minutes in duration was associated with lower incidence of obesity, whereas physical activity accumulated in less than 10 minutes was not associated with lower incidence of obesity. For cross-sectional studies that examined BMI, two favored physical activity accumulated in bouts of at least 10 minutes compared to physical activity accumulated in bouts less than 10 minutes,[31, 38] one favored physical activity accumulated in less than 10 minute bouts,[20] and three did not report a difference between physical activity accumulated in bouts less than 10 minutes versus bouts of at least 10 minutes.[25, 27, 30] Of the seven cross-sectional studies that examined measures of body fatness, one favored physical activity accumulated in bouts of at least 10 minutes,[35] one reported that the association between total volume of physical activity was more strongly associated with cardiometabolic health than physical activity accumulated in bouts of at least 10 minutes,[38] and five studies showed no difference between physical activity accumulated in bouts of at least 10 minutes versus physical activity not accumulated in bouts of at least 10 minutes.[18, 20, 27, 30, 31]

Resting Blood Pressure. For resting blood pressure, the Subcommittee reviewed one cohort study and two cross-sectional studies. The cohort study[37] demonstrated that physical activity in bouts of either at least 10 minutes or less than 10 minutes in duration was associated with lower incidence of hypertension. Both cross-sectional studies showed that physical activity accumulated in bouts less than 10 minutes was associated with lower resting blood pressure.[31, 38]

Total Cholesterol. One cross-sectional study showed that physical activity accumulated in bouts of at least 10 minutes or less than 10 minutes in duration was associated with lower total cholesterol.[31] The one cross-sectional study that examined low-density lipoprotein (LDL) cholesterol showed that both physical activity accumulated in bouts of at least 10 minutes in duration and in less than 10 minutes in duration were inversely associated with LDL cholesterol.[31]

HDL-cholesterol. For high-density lipoprotein (HDL) cholesterol, the one prospective study, which was only 14 weeks in duration, reported that physical activity accumulated in bouts of at least 10 minutes in duration predicted increase in HDL, whereas when the threshold was reduced to include bouts of at least 5 minutes this pattern of physical activity was not predictive of increase in HDL.[22] Of the four cross-sectional studies reviewed, two showed similar associations between HDL and physical activity accumulated in bouts of at least 10 minutes and less than 10 minutes,[27, 31] one showed that physical activity accumulated in bouts as short as 32 seconds was associated with higher HDL,[19] and one showed physical activity accumulated in bouts less than 10 minutes was more strongly associated with HDL than physical activity accumulated in at least 10 minutes.[38]

Triglycerides. Three cross-sectional studies examined the association between physical activity and triglycerides. Two of these studies showed similar associations between triglycerides and physical activity accumulated in bouts of at least 10 minutes in duration or in bouts less than 10 minutes.[27, 31] One of these studies showed physical activity accumulated in bouts of less than 10 minutes was more strongly associated with lower triglycerides than physical activity accumulated in bouts of at least 10 minutes.[38]

Glucose Control Measures. Three cross-sectional studies examined the association between physical activity and fasting glucose,[19, 31, 38] two with fasting insulin,[30, 38] and one with Hemoglobin A1c (HbA1c).[26] For fasting glucose, one study showed that bouts of physical activity that were at least 3 minutes in duration were associated with lower fasting glucose,[19] one study showed no difference in the association between fasting glucose and moderate-to-vigorous physical activity accumulated in bouts of less than 10 minute versus bouts of at least 10 minutes,[31] and one study showed that physical activity accumulated in bouts of less than 10 minutes was more strongly associated with lower fasting glucose when compared to physical activity accumulated in bouts of at least 10 minutes.[38] For fasting insulin, one study showed no difference in the association when comparing moderate-to-vigorous physical activity accumulated in less than 10 minutes and at least 10 minutes,[30] and one study showed physical activity accumulated in bouts of less than 10 minutes was more strongly associated when compared to physical activity accumulated in bouts of at least 10 minutes in duration.[38] The one study that examined HbA1c showed that physical activity accumulated in bouts less than 10 minutes predicted lower HbA1c, whereas physical activity accumulated in bouts of at least 10 minutes in duration was not predictive of lower HbA1c.[26]

Metabolic Syndrome. Two cross-sectional studies were reviewed that reported on the association between physical activity and metabolic syndrome.[21, 30] One study showed that moderate-to-vigorous physical activity accumulated in bouts of either 1 to 9 minutes, 4 to 9 minutes, or 7 to 9 minutes in duration predicted lower odds of having metabolic syndrome independent of moderate-to-vigorous physical activity accumulated in bouts of at least 10 minutes.[21] An additional study reported that the odds of having metabolic syndrome did not differ when comparing physical activity accumulated in bouts of less than 10 minutes versus at least 10 minutes.[30]

C-reactive Protein. Two cross-sectional studies examined the association between physical activity and c-reactive protein.[31, 38] One study showed no difference in the association between c-reactive protein and physical activity accumulated in bouts of less than 10 minutes in duration and bouts of at least 10 minutes.[31] One study showed that physical activity accumulated in bouts of less than 10 minutes was more strongly associated with lower c-reactive protein when compared to physical activity accumulated in bouts of at least 10 minutes.[38]

Framingham Cardiovascular Disease Risk Score. One cross-sectional study examined the association between physical activity and the Framingham Cardiovascular Disease Risk Score.[36] This study showed that physical activity accumulated in bouts of 1 to 5 minutes, 6 to 10 minutes, 11 to 15 minutes, or 20 to 120 minutes in duration and during total waking time were negatively associated with Framingham Cardiovascular Disease Risk Score.

Evidence on Specific Factors

Demographic factors and weight status: The literature examined included studies that included participants representing a range of ages, sex, race/ethnicity, and likely socioeconomic status. This literature also included participants representing a range of weight status. However, the results presented in this literature did not specifically present results from analyses to compare whether the association between physical activity that varied in bout duration varied by these demographic characteristics.

For additional details on this body of evidence, visit: https://health.gov/paguidelines/second-edition/report/supplementary-material.aspx for the Evidence Portfolio.

Public Health Impact

The *2008 Physical Activity Guidelines for Americans*[2] recommended that physical activity be accumulated in bouts of at least 10 minutes in duration to influence a variety of health-related outcomes. The evidence reviewed continues to support that physical activity accumulated in bouts of at least 10 minutes in duration can improve a variety of health-related outcomes. However, additional evidence, mostly from cross-sectional studies, suggests that physical activity accumulated in bouts that are less than 10 minutes is also associated with favorable health-related outcomes. Although published too late to include in our literature review, a recent study with device-based measures of physical activity and mortality as an outcome, demonstrates that bouts of less than even five minutes result in mortality benefits.[40] These findings are of public health importance because it suggests that engaging in physical activity, regardless of length of the bout, may have health-enhancing effects. This is of particular importance for individuals who are unwilling or unable to engage in physical activity bouts that are at least 10 minutes in duration. Therefore, public health initiatives to enhance health should recommend including physical activity as an important lifestyle behavior regardless of the duration.

Question 3. What is the relationship between high intensity interval training (HIIT) and reduction in cardiometabolic risk?

a) Is there a dose-response relationship? If yes, what is the shape of the relationship?
b) Does the relationship vary by age, sex, race/ethnicity, socioeconomic status, or weight status?

Sources of evidence: Systematic reviews and/or meta-analyses

Conclusion Statements

Moderate evidence indicates that high intensity interval training can effectively improve insulin sensitivity, blood pressure, and body composition in adults. These high intensity interval training-induced improvements in cardiometabolic disease risk factors are comparable to those resulting from continuous, moderate-intensity aerobic exercise and are more likely to occur in adults at higher risk of cardiovascular disease and diabetes, compared to healthy adults. **PAGAC Grade: Moderate.**

Insufficient evidence is available to determine whether a dose-response relationship exists between the quantity of high intensity interval training and several risk factors for cardiovascular disease and diabetes. **PAGAC Grade: Not assignable.**

Insufficient evidence is available to determine whether the effects of high intensity interval training on cardiometabolic risk factors are influenced by age, sex, race/ethnicity, or socioeconomic status. **PAGAC Grade: Not assignable.**

Moderate evidence indicates that weight status influences the effectiveness of high intensity interval training to reduce cardiometabolic disease risk. Adults with overweight or obesity are more responsive than adults with normal weight to high intensity interval training's effects on improving insulin sensitivity, blood pressure, and body composition. **PAGAC Grade: Moderate.**

Review of the Evidence

The 2018 Advisory Committee based its conclusions on evidence published before May 2017, specifically from three existing systematic reviews and/or meta-analyses.[41-43] Participants were males and females predominantly ages 18 years and older. The exposure was physical activity performed as high intensity interval training (HIIT).

For the purposes of this review, we used the following definition. HIIT is a form of interval training consisting of alternating short periods of intense anaerobic exercise with less intense aerobic recovery periods. There are no universally accepted lengths for either the anaerobic period, the recovery period, nor the ratio of the two; no universally accepted number of cycles for any HIIT session or the entire duration of the training bout; and no universally accepted relative intensity at which the intense anaerobic component should be performed.

The outcomes of interest were all-cause and CVD mortality, CVD and type 2 diabetes incidences, cardiorespiratory fitness, and cardiometabolic disease risk factors. The Subcommittee's assessment and evaluation specifically focused on outcomes related to cardiometabolic disease risk factors (e.g., blood pressure, fasting blood lipids and lipoproteins, fasting blood glucose and insulin, and BMI), due to a lack of information regarding mortality and cardiometabolic morbidities.

Evidence on the Overall Relationship

Results from these systematic reviews and/or meta-analyses of clinical intervention studies consistently support that HIIT can effectively improve cardiorespiratory fitness (increase VO_2max) in adults with varied body weight and health status.[41-43] HIIT-induced improvements in insulin sensitivity,[42, 43] blood pressure,[41, 43] and body composition[41-43] more consistently occur in adults who have overweight or obesity with or without high risk of CVD and diabetes, especially if these individuals train for 12 or more weeks. These HIIT-induced improvements in cardiometabolic disease risk are comparable in magnitude to those achievable with continuous, moderate-intensity aerobic training.[42] Healthy adults who have normal weight and lower risk of cardiometabolic disease do not typically show improvements in insulin sensitivity, blood pressure, and body composition with HIIT. Blood lipids and lipoproteins apparently are not influenced by HIIT.[41]

Batacan et al[41] reported findings based on 65 individual studies involving 2,164 participants (including 936 individuals who performed HIIT). Participants were predominantly ages 18 years and older. This meta-analysis included randomized controlled trials (RCTs) and non-randomized controlled trials and comparative studies in groups of individuals without (46 of 65 studies) or with (19 of 65 studies) a diagnosed, current medical condition. Batacan et al[41] defined high-intensity interval training "as activities with intermittent bouts of activity that were performed at maximal effort, great than or equal to 85% VO_2 max, greater than or equal to 85% heart rate reserve or the relative intensity of at least 90% heart rate max." The modes of exercise included treadmill running, cycling, and swimming. The 65 studies were categorized with respect to exercise training intervention duration and participant BMI classification. Among groups of participants with normal weight (BMI 18.5–24.9 kg/m^2), short-term (<12 weeks) and long-term (≥12 weeks) HIIT interventions increased VO_2max, but did not significantly or consistently influence clinical indexes of cardiometabolic disease risk (systolic and diastolic blood pressures; total cholesterol, HDL, LDL, and triglycerides; or fasting glucose and insulin). Among groups of participants classified as having overweight (BMI 25-29.9 kg/m^2) or obesity (BMI ≥30 kg/m^2), short-term and long-term HIIT significantly and consistently increased VO_2 max and decreased diastolic blood pressure and waist circumference. Long-term HIIT also decreased resting heart rate, systolic blood pressure, and body fat percentage among groups with overweight or obesity.

Jelleyman et al[42] conducted a meta-analysis of 50 studies involving 2,033 participants (including 1,383 individuals who performed HIIT) to assess the effect of HIIT interventions on indexes of blood glucose control and insulin resistance, compared with continuous training or control conditions. Both controlled (N=36, 72%) and uncontrolled (N=14, 28%) studies were included. HIIT was defined as "at least two bouts of vigorous or higher intensity exercise interspersed with periods of lower intensity exercise or complete rest".[42] Participants were ages 18 years and older and the HIIT intervention was 2 weeks or longer. Subgroup analyses were performed after stratifying participants based on health characteristics: healthy (well-trained, recreationally active, or sedentary); weight status (overweight or obese); metabolic syndrome (metabolic syndrome or type 2 diabetes); or with another chronic disease. VO_2 max increased after HIIT by 0.30 liters per minute (95% CI: 0.25-0.35, P<0.001), compared to baseline. The increase in VO_2 max was greater for HIIT than for non-exercising control conditions (weighted mean difference (WMD)=0.28 liters per minute, 95% CI: 0.12-0.44, P=0.001) and attenuated but still significant compared with continuous training (WMD=0.16 liters per minute (95% CI: 0.07-0.25, P=0.001). HIIT reduced body weight, compared to baseline, by 0.7 kg (95% CI: -1.19 to -0.25, P=0.002). Compared to non-exercise control, the HIIT-induced weight loss was 1.3 kg (95% CI: -1.90 to -0.68, P<0.001). HIIT-induced weight loss was not different than weight loss from continuous training. HIIT decreased fasting glucose, compared to baseline, by 0.13 mmol per liter (95% CI: -0.19 to -0.07, P<0.001). This response over time was not statistically different compared with non-exercise control and continuous training. Subgroup analysis showed that for the groups of individuals with metabolic syndrome or type 2 diabetes, fasting glucose was reduced by HIIT, compared to non-exercise control, by 0.92 mmol per liter (95% CI: -1.22 to -0.63, $P<0.001$). HIIT decreased fasting insulin from baseline by 0.93 µU per liter (95% CI: -1.39 to -0.48, $P<0.001$), but this response was not different than the non-exercise control. HIIT decreased insulin resistance compared to baseline (change in Homeostasis Model Assessment of Insulin Resistance score, -0.33; 95% CI: -0.47 to -0.18, $P<0.001$). Reduction in insulin resistance (results from multiple insulin resistance models combined) was greater for HIIT versus non-exercise control (-0.49; 95% CI: -0.87 to -0.12) and HIIT versus continuous training (-0.35; 95% CI: -0.68 to -0.02). Within the metabolic syndrome or type 2 diabetes grouping, HIIT did not change HbA1c, compared to baseline, among all 13 studies reporting these data. Subgroup analyses showed that HIIT reduced HbA1c by 0.25% (95% CI: -0.27 to -0.23, $P<0.001$), compared to baseline. Among all studies, the HbA1c response over time (no change) was not statistically different between HIIT and control and continuous training groups. Subgroup analyses based on health (physical activity) status or other chronic diseases were either not significant or inconclusive due, in part, to limited available data.

Kessler et al[43] conducted a quasi-systematic, qualitative review of 24 RCTs assessing the effects of HIIT interventions on changes in cardiometabolic disease risk factors. Fourteen of the 24 trials included a continuous moderate-intensity exercise control group, and the other 14 studies included a non-exercise control group. Participants had varied weight status (normal weight, overweight or obese) and health status (healthy (17 studies), CVD (5 studies), metabolic syndrome (1 study), type 2 diabetes (1 study). Intervention durations ranged from two weeks to six months. HIIT was categorized into two subtypes: aerobic interval training (19 studies) and sprint interval training (5 studies). For the purpose of the Subcommittee's assessment, results only from aerobic interval training studies are described. This was done because of the low number of sprint interval training studies included in the Kessler et al[43] review. Compared to baseline (i.e., changes over time), aerobic interval training increased VO_2 max (14 of 14 studies), increased insulin sensitivity (4 of 4 studies), and decreased blood pressure in participants not ingesting anti-hypertensive medication (5 of 5 studies with intervention periods ≥12 weeks). Other indexes of cardiometabolic disease risk were not influenced by aerobic interval training, including fasting glucose, total cholesterol, HDL, LDL, and triglycerides. Results for body weight, BMI, body fat percent, and waist circumference were mixed, with improvements observed more consistently for aerobic interval training interventions of 12 weeks or longer in participants with overweight or obesity. Collectively, these aerobic interval training responses were comparable with continuous moderate-intensity exercise, except VO_2max, which was greater for aerobic interval training versus continuous moderate-intensity exercise.

Dose-Response: Among the three review articles the Committee systematically reviewed,[41-43] results were not presented from RCTs designed to assess dose-response relationships between duration of HIIT and changes in cardiometabolic disease risk factors. Using meta-regression techniques, Batacan et al[41] reported that VO_2max was predicted by longer HIIT intervention duration (β coefficient 0.77; 95% CI: 0.35-1.18) and BMI (β coefficient 0.84; 95% CI: 0.29-1.38), but not by total time performing HIIT (minutes) (β coefficient 0.0002; 95% CI: -0.0017-0.0021) among groups of participants with overweight or obesity. Intervention duration, total time performing HIIT, and BMI did not predict the improvements observed in systolic blood pressure and diastolic blood pressure among groups with overweight or obesity. Other cardiometabolic risk factors were not assessed due to lack of heterogeneity of responses. Regarding indexes of glucose control, Jelleyman et al[42] (also using meta-regression techniques) reported that HIIT characteristics, interval intensity, and weekly high-intensity exercise did not predict the improvements (over time) in insulin resistance, fasting glucose, fasting insulin, or HbA1c.

Evidence on Specific Factors

Age, sex, race/ethnicity, socioeconomic status: Information on the race/ethnicity and socioeconomic status of participants was limited, inconsistently presented, and not statistically assessed. As a result, no conclusions about these relationships were possible.

Weight status: Weight status significantly influenced the effect of HIIT on several risk factors of cardiometabolic disease, with groups of adults classified as having overweight or obesity, but not normal weight, reducing blood pressure and body fat[41] and improving insulin sensitivity.[42, 43]

Evidence on Participant Safety

Participant safety is central to using HIIT as a tool to reduce the risk of cardiometabolic disease among adults, especially those who have overweight or obesity, with cardiometabolic disease risk factors, diagnosed CVD or type 2 diabetes, or another chronic disease. Although the Subcommittee did not address participant safety among adults performing HIIT, the issue is highly relevant with respect to using HIIT for health promotion. Jelleyman et al[42] documented adverse events reported in the 50 studies included in their meta-analysis. Among the 19 total adverse events reported from the 17 studies (34% of the total) that included this type of information, 18 adverse events were attributable to musculoskeletal injuries incurred with exercise, with 14 of 18 occurring with HIIT. None of the reported injuries was a serious adverse event or necessitated the participant to discontinue the intervention or drop out of the study. Perhaps consistent with the very low incidence of adverse events, mean participant dropout rate was 10 ± 10 percent among the 36 (72%) of studies that documented attrition. The health and disease characteristics of the participants who experienced an adverse event were not presented or discussed.

For additional details on this body of evidence, visit: https://health.gov/paguidelines/second-edition/report/supplementary-material.aspx for the Evidence Portfolio.

Public Health Impact

The Subcommittee has identified moderate evidence to indicate that HIIT can effectively improve insulin sensitivity, blood pressure, and body composition in adults. These HIIT-induced improvements in cardiometabolic disease risk factors are comparable to those resulting from continuous, moderate-intensity aerobic exercise and are more likely to occur in adults with overweight and obesity.

NEEDS FOR FUTURE RESEARCH

Question 1. Step Count Per Day and Question 2. Bout Duration

1. Conduct additional longitudinal research, either in the form of prospective studies or randomized controlled trials, to examine the dose-response relationship between:

    a) Steps per day and health outcomes, and

    b) Whether physical activity accumulated in bouts of less than 10 minutes in duration enhances health outcomes.

    Rationale: This information is critical for setting target volumes of physical activity using steps per day as the metric and for firmly establishing that steps per day predicts the incidence of future disease outcomes. In this review, only one randomized controlled trial was identified and it did not include multiple arms to examine the effects of various doses of steps per day on outcomes.

    The majority of studies reviewed supporting the health benefits of physical activity accumulated in bouts of less than 10 minutes in duration used a cross-sectional design, with none of the randomized studies reporting on the effects of physical activity accumulated in bouts of less than 10 minutes. Having this knowledge will inform potential cause and effect rather than simply associations.

2. Include measurement methods in prospective and randomized controlled studies that will examine:

   a) Whether the rate of stepping and the length (bouts) of continuous steps influence the relationship between steps per day and disease outcomes

   b) Whether physical activity performed in a variety of bout lengths has differential effects on health outcomes

   Rationale: The studies reviewed used simple pedometers providing accumulated steps and could neither address patterns nor intensity of steps per day. Additional physical activity assessment methods collecting these data should provide a better target for recommending physical activity volume. Based on the studies reviewed, randomized studies did not report on physical activity accumulated in bouts less than 10 minutes in duration, and only two prospective studies were identified that reported on physical activity accumulated in bouts less than 10 minutes. This may be a result of the methods used to assess physical activity in randomized and prospective studies, and suggests the need to include physical activity assessment methods that allow for these data to be available for analysis.

Question 3. High Intensity Interval Training

1. Conduct longer-term randomized controlled trials to assess the adherence to and the effects of high intensity interval training, compared to other types of physical activity programs, on physiological, morphological, and cardiometabolic health outcomes. They should address issues of dose-response and be of at least 6 months in duration. These randomized controlled trials should include diverse groups of adults who have overweight or obesity and/or who are at high risk of cardiovascular disease or type 2 diabetes. They should systematically assess adverse events, including musculoskeletal injuries, attributable to high intensity interval training, compared to other types of exercise training, among adults with a wide variety of health and disease characteristics.

   Rationale: Most high intensity interval training intervention periods are less than 12 weeks, which may be insufficient time to assess the magnitude and sustainability of clinically-important changes in some physiological, morphological, and cardiometabolic health outcomes. The willingness and ability of individuals to adhere to high intensity interval training programs is currently unknown. Prescriptively designing these studies to include participants who have overweight or obesity and/or who are at high risk of cardiovascular disease or type 2 diabetes is important to inform health promotion practitioners and policy leaders on the utility of recommending high intensity interval training for health among a large proportion of the U.S. adult population. At present, evaluation of the safety of high intensity interval training among adults with varied health and disease characteristics is compromised by the limited data available, in part, due to the low proportion of studies reporting adverse events.

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PART F. CHAPTER 2. SEDENTARY BEHAVIOR

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INTRODUCTION

In general, sedentary behavior refers to any waking behavior characterized by an energy expenditure of 1.5 METs or less while in a sitting, reclining, or lying posture.[1] Most previous physical activity research has focused on the association between higher intensity (i.e., moderate-to-vigorous) physical activity and health outcomes. However, sedentary behavior has received an increasing amount of attention as a public health problem because: 1) it appears to have negative associations with health outcomes, and 2) it is a highly prevalent behavior in the U.S. population. Data collected by accelerometry in the U.S. National Health and Nutrition Examination Survey indicate that children and adults spend approximately

7.7 hours per day (55% of their monitored time) being sedentary.[2] Thus, the potential population health impact of sedentary behavior is substantial.

Given that much of the scientific evidence for an association between sedentary behavior and health has been published after 2008, the 2008 Physical Activity Guidelines Advisory Committee did not systematically assess the effects of sedentary behavior on health outcomes. Since then, a considerable amount of research has been conducted, and the 2018 Physical Activity Guidelines Advisory Committee decided to systematically review this literature to assess the effect of sedentary behavior on health outcomes.

The Sedentary Behavior Subcommittee operationalized the definition of sedentary behavior to include self-reported sitting (leisure-time, occupational, total), television (TV) viewing or screen time, and data from objective, device-based assessments (accelerometry or inclinometry). Although these operational definitions do not capture all aspects of the definition of sedentary behavior (i.e., both posture and energy expenditure), they are widely used in the scientific literature as measures of time spent in sedentary behavior.

The Subcommittee examined the relationship between sedentary behavior and major causes of mortality and also assessed the relationship between sedentary behavior and weight status in addition to the incidence of common chronic diseases, including type 2 diabetes, cardiovascular disease, and cancer. In addition to the relationship between the total duration of daily or weekly sedentary behavior and health outcomes, it is of interest to understand the associations between patterns of sedentary behavior, including bouts and breaks, and health outcomes. A bout of sedentary behavior can be operationalized as a period of uninterrupted sedentary time, whereas a break in sedentary behavior can be operationalized as a non-sedentary bout in between two sedentary bouts.[1] The potential health effects associated with sedentary bouts and breaks are also addressed in this chapter.

REVIEW OF THE SCIENCE

Overview of Questions Addressed

This chapter addresses five major questions:

1. What is the relationship between sedentary behavior and all-cause mortality?

2. What is the relationship between sedentary behavior and cardiovascular disease mortality?
3. What is the relationship between sedentary behavior and cancer mortality?
4. What is the relationship between sedentary behavior and (1) type 2 diabetes, (2) weight status, (3) cardiovascular disease, and (4) cancer?
5. Does the effect of moderate-to-vigorous physical activity on all-cause mortality vary by amount of sedentary behavior?

Questions 1 through 4 each have the following subquestions:

a) Is there a dose-response relationship? If yes, what is the shape of the relationship?
b) Does the relationship vary by age, sex, race/ethnicity, socioeconomic status, or weight status?
c) Is the relationship independent of amounts of light, moderate, or vigorous physical activity?
d) Is there any evidence that bouts or breaks in sedentary behavior are important factors?

Data Sources and Process Used to Answer Questions

A single literature search strategy was conducted to answer Questions 1, 2, and 3. Subsets of the resulting body of evidence were used to answer each question or subquestion. The databases searched included PubMed, Cochrane, and CINAHL. The systematic literature search to address Questions 1, 2, and 3 was conducted in three steps. Step 1 involved a search for existing systematic reviews and meta-analyses that could address the question. Step 2 involved reviewing the original research articles contained in the systematic reviews and meta-analyses to identify those that could provide evidence to address the questions, especially the subquestions related to dose-response and variation in the relationship by age, sex, race/ethnicity, socioeconomic status, or weight status. Original research articles contained in the systematic reviews and meta-analysis identified in Step 2 are not included as evidence in the evidence portfolio. Step 3 involved a de novo literature search of more recent original research studies published after the systematic reviews and meta-analyses.

The systematic literature search to address Question 4 was conducted in two steps. The databases searched included PubMed, Cochrane, and CINAHL. Step 1 involved a search for existing systematic reviews and meta-analyses that could address the question. Step 2 involved a de novo literature search of more recent original research studies published after the systematic reviews and meta-analyses.

The evidence used to address Question 5 was obtained from the evidence base compiled for Question 1.

Question 1: What is the relationship between sedentary behavior and all-cause mortality?

a) Is there a dose-response relationship? If yes, what is the shape of the relationship?

b) Does the relationship vary by age, sex, race/ethnicity, socioeconomic status, or weight status?
c) Is the relationship independent of amounts of light, moderate, or vigorous physical activity?
d) Is there any evidence that bouts or breaks in sedentary behavior are important factors?

Sources of evidence: Systematic reviews, meta-analyses, original research articles

Conclusion Statements

Strong evidence demonstrates a significant relationship between greater time spent in sedentary behavior and higher all-cause mortality rates. **PAGAC Grade: Strong.**

Strong evidence demonstrates the existence of a direct, curvilinear dose-response relationship between sedentary behavior and all-cause mortality, with an increasing slope at higher amounts of sedentary behavior. **PAGAC Grade: Strong.**

Limited evidence suggests that the relationship between sedentary behavior and all-cause mortality does not vary by age, sex/ethnicity, or weight status. **PAGAC Grade: Limited.**

Insufficient evidence is available to determine whether the relationship between sedentary behavior and all-cause mortality varies by socioeconomic status. **PAGAC Grade: Not assignable.**

Strong evidence demonstrates that the relationship between sedentary behavior and all-cause mortality varies by amount of moderate-to-vigorous physical activity. **PAGAC Grade: Strong.**

Insufficient evidence is available to determine whether bouts or breaks in sedentary behavior are important factors in the relationship between sedentary behavior and all-cause mortality. **PAGAC Grade: Not assignable.**

Review of the Evidence

Sources of evidence included: 1) systematic reviews and meta-analyses published from January 2000 to December 5, 2016, 2) the relevant original research articles cited by the systematic reviews and meta-analyses, and 3) recent original research articles published between January 2014 and January 30, 2017.

The search for systematic reviews and meta-analyses returned a total of 201 articles and the titles were reviewed by two members of the Subcommittee. A total of 48 articles were deemed potentially relevant based on the title search and the abstracts of these papers were reviewed by two members of the Subcommittee. Of these, 16 articles were deemed to be potentially relevant and the full papers were retrieved. A review of the full texts of these papers by two members of the Subcommittee identified nine systematic reviews and meta-analyses that addressed Question 1 (Supplementary Table S-F2-1). These 9 systematic reviews included information on 25 original research articles that included all-cause mortality as an outcome. After excluding one study in breast cancer survivors,[3] one study of occupational sitting and physical activity that included a mix of sitting and physical activity exposures,[4] one study that only presented data on changes in sitting time,[5] and two studies that presented only baseline descriptions of cohorts,[6, 7] the Subcommittee was able to identify 20 original articles that addressed Question 1 (Supplementary Table S-F2-2).

The de novo literature search of original research studies returned a total of 1,214 articles and the titles were reviewed by two members of the Subcommittee. A total of 62 articles were deemed potentially relevant based on the title search, and the abstracts of these papers were reviewed by two members of the Subcommittee. Of these, 38 articles were deemed to be potentially relevant and the full papers were retrieved. A review of the full texts of these papers by two members of the Subcommittee identified 30 original studies that addressed Question 1. Note that three of the papers[8-10] identified in the search for original articles were duplicates of those identified from the systematic reviews and meta-analyses and they appear only in Supplementary Table S-F2-2. Supplementary Table S-F2-3 presents the 27 new original studies that address Question 1.

Evidence on the Overall Relationship

A total of nine systematic reviews and meta-analyses[11-19] that reviewed a total of 20 original studies have addressed the relationship between sedentary behavior and all-cause mortality, and they provide strong evidence demonstrating a significant relationship. The number of studies that addressed all-cause mortality encompassed by each of the reviews ranges from 3 to 16, with newer reviews reporting on a greater number of studies as they appear in the literature. The meta-analysis of Biswas et al[18] analyzed 14 prospective cohort studies and reported a hazard ratio of 1.22 (95% confidence interval (CI): 1.09-1.41) for the relationship between sedentary behavior and all-cause mortality. The available studies represent several population cohorts that apply broadly to the U.S. population and the results are consistent in direction and the size of the effect.

Based on the review of the more recent original research articles, 9 of 10 studies found a significant relationship between self-reported total or leisure sitting time and all-cause mortality, 3 out of 5 studies of TV viewing or screen time found a significant relationship between TV viewing or screen time and all-cause mortality, and 0 out of 2 studies found a significant relationship between occupational sitting time and all-cause mortality.

Thirteen studies have reported on relationships between device-based objectively measured sedentary behavior (using accelerometry) and all-cause mortality. Of these, 11 studies relied on data from the National Health and Nutrition Examination Survey (NHANES). Although the analytical strategies differed, 10 of the 13 studies reported a significant relationship (1 in men only) between sedentary time and all-cause mortality (8 out of the 11 NHANES studies). Among the 3 NHANES studies that did not find a significant relationship, one stratified their analysis by level of visual acuity,[20] one compared risk for below-median to above-median sedentary time,[21] and the third compared risk across quartiles of sedentary time.[22] The 8 NHANES studies that reported a significant association between sedentary behavior and all-cause mortality used a variety of analysis strategies, including comparisons of quartiles of sedentary behavior,[23] comparing above-median to below-median sedentary time,[24] continuous variable analysis,[25, 26] latent class analysis,[27] and isotemporal substitution analysis.[28-30]

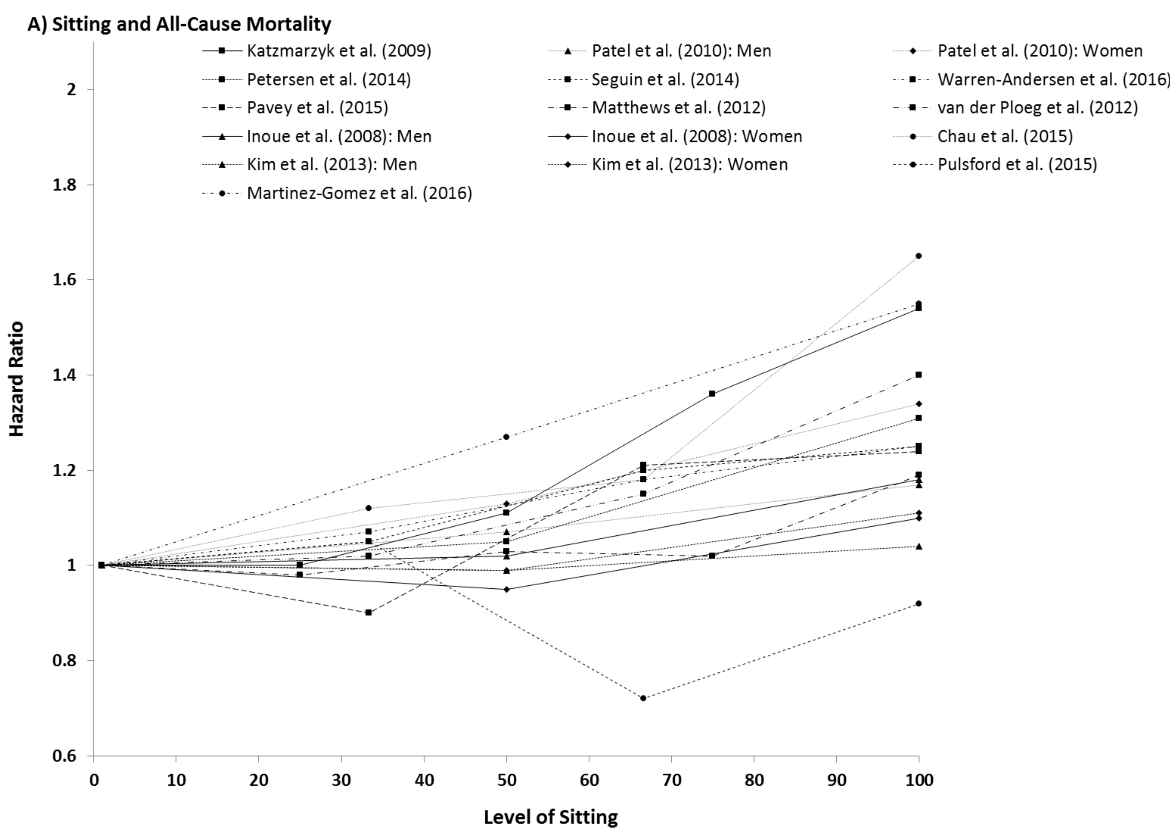
Given the confines of the 24-hour period, interest is increasing in understanding inter-relationships among time spent in different aspects of daily living, such as sleep, sedentary behavior, and light-, moderate-, and vigorous-intensity physical activity, with outcomes such as all-cause mortality. To this end, several studies have used isotemporal substitution analyses to model the effects of replacing time spent in sedentary behavior with time spent in other behaviors such as standing, light-intensity activity, moderate-to-vigorous physical activity, or exercise.[28-33] The results invariably show a reduction in mortality risk when sedentary behavior is replaced with higher intensity activities. Models in which an equivalent duration of sedentary behavior is replaced with light-intensity physical activity predict a reduction in mortality, and models in which sedentary behavior is replaced with moderate- or vigorous-intensity physical activity predict an even greater reduction in mortality. Because the models are “isotemporal,” it cannot be determined whether the increase in predicted benefit is due to the higher intensity of the physical activity per se or the higher volume of energy expended.

Dose-response: Strong evidence also demonstrates the existence of a dose-response relationship between sedentary behavior and all-cause mortality. Two meta-analyses were used to provide evidence for dose-response relationships between daily sitting[15] or TV viewing,[17] and all-cause mortality. Chau et al[15] found that a spline model of best fit had hazard ratios of 1.00 (95% CI: 0.98-1.03), 1.02 (95% CI: 0.99-1.05) and 1.05 (95% CI: 1.02-1.08) for every 1-hour increase in daily sitting time in intervals between 0 to

3, more than 3 to 7, and more than 7 hours per day total sitting, respectively. Thus, the dose-response curve was curvilinear, and the slope of the relationship increased beyond 7 hours per day of sitting. Similarly, Sun et al[17] reported that TV viewing time was statistically significantly associated with all-cause mortality risk in a curvilinear, direct fashion that increases steadily and more rapidly as length of exposure increases ($P_{nonlinearity}$=0.001).[17]

Of the 47 original studies identified through the systematic reviews and meta-analyses and the de novo search, 29 tested for the existence of a dose-response relationship, and 24 studies found a significant dose-response relationship. Figure F2-1 presents the dose-response curves from studies of self-reported sitting (Panel A) and TV viewing (Panel B) that included at least three amounts of sedentary behavior as the exposure. The pattern of results generally mirrors those of the two previous meta-analyses,[15, 17] with increasing risk at higher amounts of sedentary behavior following a curvilinear relationship.

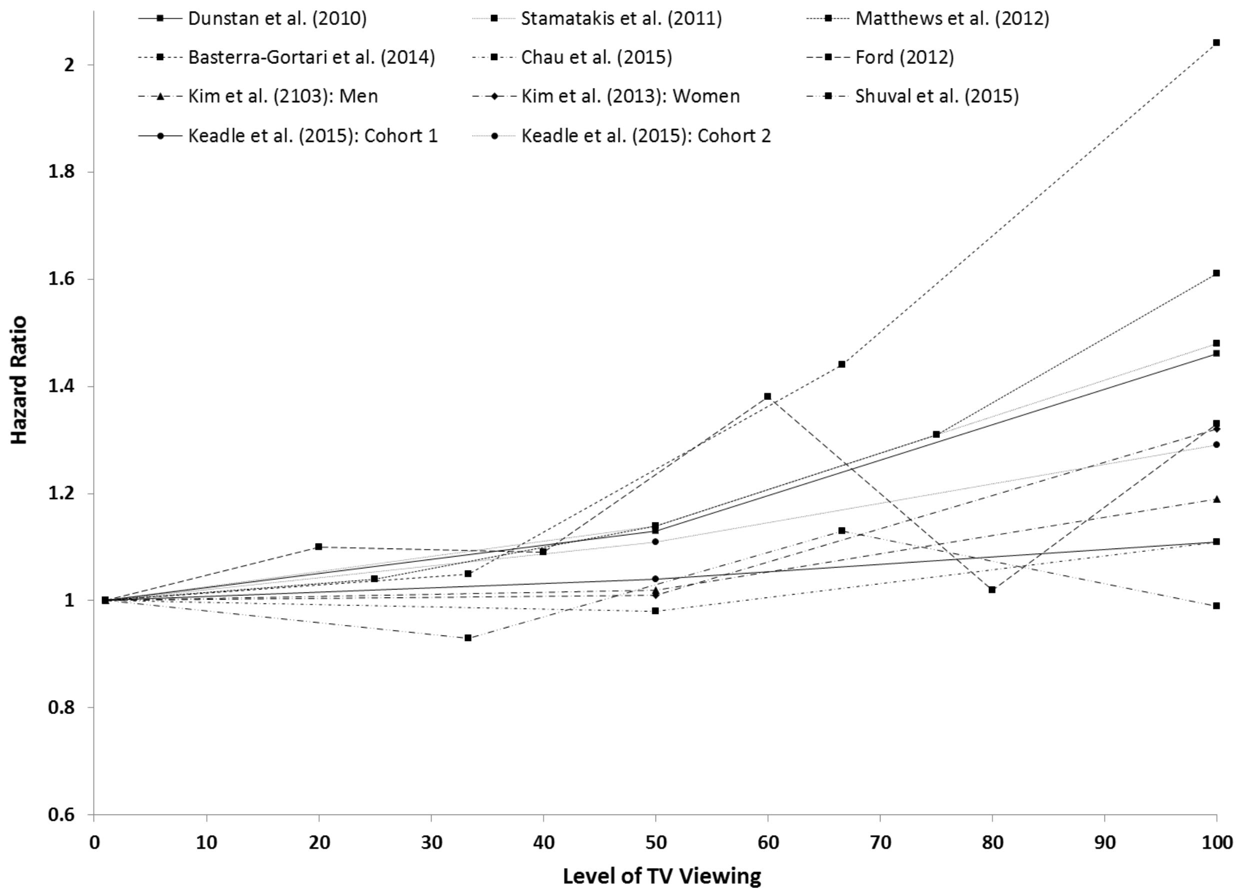
Figure F2-1. Dose-Response Curves Showing Relationship Between Sedentary Behavior and All-Cause Mortality



Note: The figure shows the reported hazard ratio for each category of sitting with the lowest category of sitting assigned as the referent at zero on the X-axis and the highest value assigned at 100. The original categories of

sitting from the studies (tertiles, quartiles, quintiles, etc.) have been rescaled from 0 to 100 using an ordinal scale. For example, for a study with three categoires, the points were plotted at 0, 50 and 100.
Source: Adapted from data found in Katzmarzyk et al., 2009,[34] Patel et al., 2010,[35] Petersen et al., 2014,[10] Seguin et al., 2014,[36] Warren Andersen et al., 2016,[37] Pavey et al., 2015,[9] Matthews et al., 2012,[38] van de Ploeg et al., 2012,[39] Inoue et al., 2008,[40] Chau et al., 2015,[8] Kim et al., 2013,[41] Pulsford et al., 2015,[42] and Martinez-Gomez et al., 2016.[43]

B) TV Viewing and All-Cause Mortality



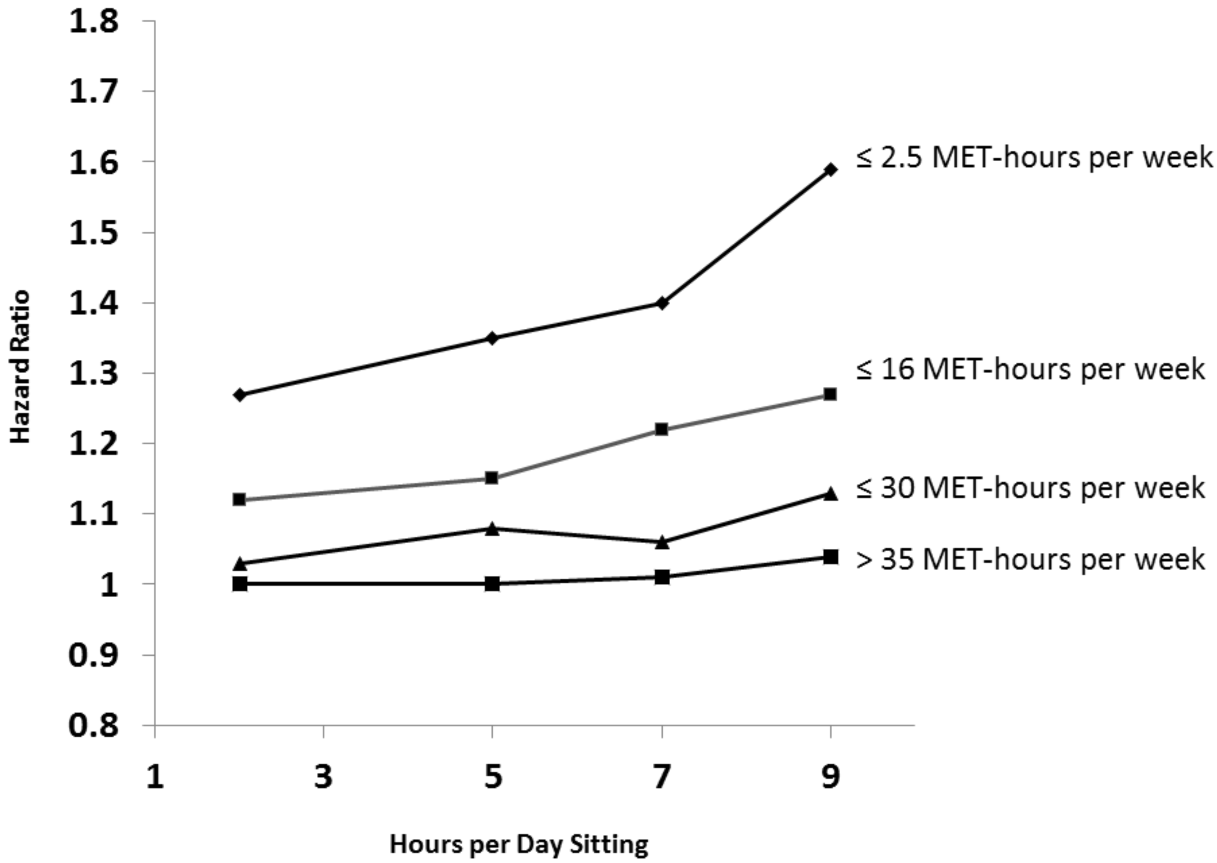
Note: The figure shows the reported hazard ratio for each category of TV viewing with the lowest category of TV viewing assigned as the referent at zero on the X-axis and the highest value assigned at 100. The original categories of TV viewing from the studies (tertiles, quartiles, quintiles, etc.) have been rescaled from 0 to 100 using an ordinal scale. For example, for a study with three categoires, the points were plotted at 0, 50 and 100.
Source: Adapted from data found in Dunstan et al., 2010,[44] Stamatakis et al., 2011,[32] Matthews et al., 2012,[38] Basterra-Gortari et al., 2014,[45] Chau et al., 2015,[8] Ford, 2012,[46] Kim et al., 2013,[41] Shuval et al., 2015,[47] and Keadle et al., 2015.[48]

Evidence on Specific Factors

Demographic factors and weight status: Limited evidence suggests that the relationship between sedentary behavior and all-cause mortality does not vary by age, sex, race/ethnicity, or weight status. Available evidence is insufficient to determine whether the relationship between sedentary behavior and all-cause mortality varies by socioeconomic status. In general, studies reported no significant effect modification by age,[35, 36, 44, 49, 50] sex,[31, 35, 44, 49] or weight status,[35, 36, 44, 49] and stratified analyses generally showed similar results across age,[28, 38, 39, 41, 49] sex,[28, 34, 37, 39, 41, 49] race/ethnicity,[37, 38, 41, 51] and weight status,[28, 34, 35, 38, 39, 41, 49] with varying levels of significance. In general, data are lacking on the variation in the observed associations by level of socioeconomic status. The available evidence suggests that the observed relationship between sedentary behavior and all-cause mortality applies broadly to the general adult population of the United States.

Amount of physical activity: Strong evidence demonstrates that the relationship between sedentary behavior and all-cause mortality varies by the amount of moderate-to-vigorous physical activity. The effect of sedentary behavior on all-cause mortality is stronger among people who have low amounts of moderate-to-vigorous physical activity. For example, in the meta-analysis of Biswas et al[18] the risk of all-cause mortality was 1.16 (95% CI: 0.84-1.56) among those with high physical activity and 1.46 (95% CI: 1.22-1.75) among those with low physical activity. Further, Ekelund et al[19] conducted a harmonized meta-analysis using individual-level data from more than 1 million adults and reported that increasingly higher amounts of moderate-to-vigorous physical activity attenuated the relationship between sedentary behavior and all-cause mortality (Figure F2-2), and the relationship between self-reported sitting and mortality was not significant among those who reported participating in at least moderate-intensity physical activity for 60 to 75 minutes per day. Similar results were observed for TV viewing, although high amounts of physical activity did not completely attenuate the relationship between TV viewing and all-cause mortality. Evidence is insufficient to determine whether the association between sedentary behavior and all-cause mortality varies by level of light- or vigorous-intensity activity.

Figure F2-2. Relationship Between Sitting and All-Cause Mortality, Stratified by Amount of Moderate-to-Vigorous Physical Activity



Source: Adapted from data found in Ekelund et al., 2016.[19]

Bouts and breaks: Insufficient evidence is available to determine whether bouts or breaks in sedentary behavior are important factors in the relationship between sedentary behavior and all-cause mortality. Only one study was identified that included bouts of sedentary behavior in their definition of the exposure. Using accelerometry data from NHANES, Evenson et al[27] defined sedentary bouts as 30 or more minutes with at least 80 percent of the minutes falling below 100 counts per minute, allowing for less than 5 consecutive minutes above the threshold. Based on latent class analysis, the class with the highest percentage of the day in sedentary bouts had a higher risk of all-cause mortality compared to the class with fewer sedentary bouts (hazard ratio (HR)=2.10; 95% CI: 1.11-3.97). However, further research is required to replicate these results. No studies were identified that examined the associations between breaks in sedentary behavior and all-cause mortality. Thus, a grade was not assignable for this question.

For additional details on this body of evidence, visit: Supplementary Tables S-F2-1, S-F2-2, and S-F2-3 and https://health.gov/paguidelines/second-edition/report/supplementary-material.aspx for the Evidence Portfolio.

Question 2: What is the relationship between sedentary behavior and cardiovascular disease mortality?

a) Is there a dose-response relationship? If yes, what is the shape of the relationship?
b) Does the relationship vary by age, sex, race/ethnicity, socioeconomic status, or weight status?
c) Is the relationship independent of amounts of light, moderate, or vigorous physical activity?
d) Is there any evidence that bouts or breaks in sedentary behavior are important factors?

Sources of evidence: Systematic reviews, meta-analyses, original research articles

Conclusion Statements

Strong evidence demonstrates a significant relationship between greater time spent in sedentary behavior and higher mortality rates from cardiovascular disease. **PAGAC Grade: Strong.**

Strong evidence demonstrates the existence of a direct, positive dose-response relationship between sedentary behavior and mortality from cardiovascular disease. **PAGAC Grade: Strong.**

Limited evidence suggests that the relationship between sedentary behavior and cardiovascular disease mortality does not vary by age, sex, race/ethnicity, or weight status. **PAGAC Grade: Limited.**

Insufficient evidence is available to determine whether the relationship between sedentary behavior and mortality from cardiovascular disease varies by socioeconomic status. **PAGAC Grade: Not assignable.**

Moderate evidence indicates that the relationship between sedentary behavior and mortality from cardiovascular disease varies by amount of moderate-to-vigorous physical activity. **PAGAC Grade: Moderate.**

Insufficient evidence is available to determine whether bouts or breaks in sedentary behavior are important factors in the relationship between sedentary behavior and mortality from cardiovascular disease. **PAGAC Grade: Not assignable.**

Review of the Evidence

Sources of evidence included: 1) systematic reviews and meta-analyses published from January 2000 to December 5, 2016, 2) the relevant original research articles cited by the systematic reviews and meta-analyses, and 3) recent original research articles published between January 2014 and January 30, 2017.

The search for systematic reviews and meta-analyses returned a total of 201 articles and the titles were reviewed by two members of the Subcommittee. A total of 48 articles were deemed potentially relevant based on the title search and the abstracts of these papers were reviewed by two members of the Subcommittee. Of these, 16 articles were deemed to be potentially relevant and the full papers were retrieved. A review of the full texts of these papers by two members of the Subcommittee identified five systematic reviews and meta-analyses that addressed Question 2 (Supplementary Table S-F2-4). These 5 systematic reviews and meta-analyses included information on 12 original research articles that included cardiovascular disease mortality as an outcome. After excluding one study that presented only a baseline description of a cohort,[7] 11 original articles addressed Question 2 (Supplementary Table S-F2-5).

The de novo literature search of original research studies returned a total of 1,214 articles and the titles were reviewed by two members of the Subcommittee. A total of 62 articles were deemed potentially relevant based on the title search and the abstracts of these papers were reviewed by two members of the Subcommittee. Of these, 38 articles were deemed to be potentially relevant and the full papers were retrieved. A review of the full texts of these papers by two members of the Subcommittee identified seven original studies that addressed Question 2 (Supplementary Table S-F2-6).

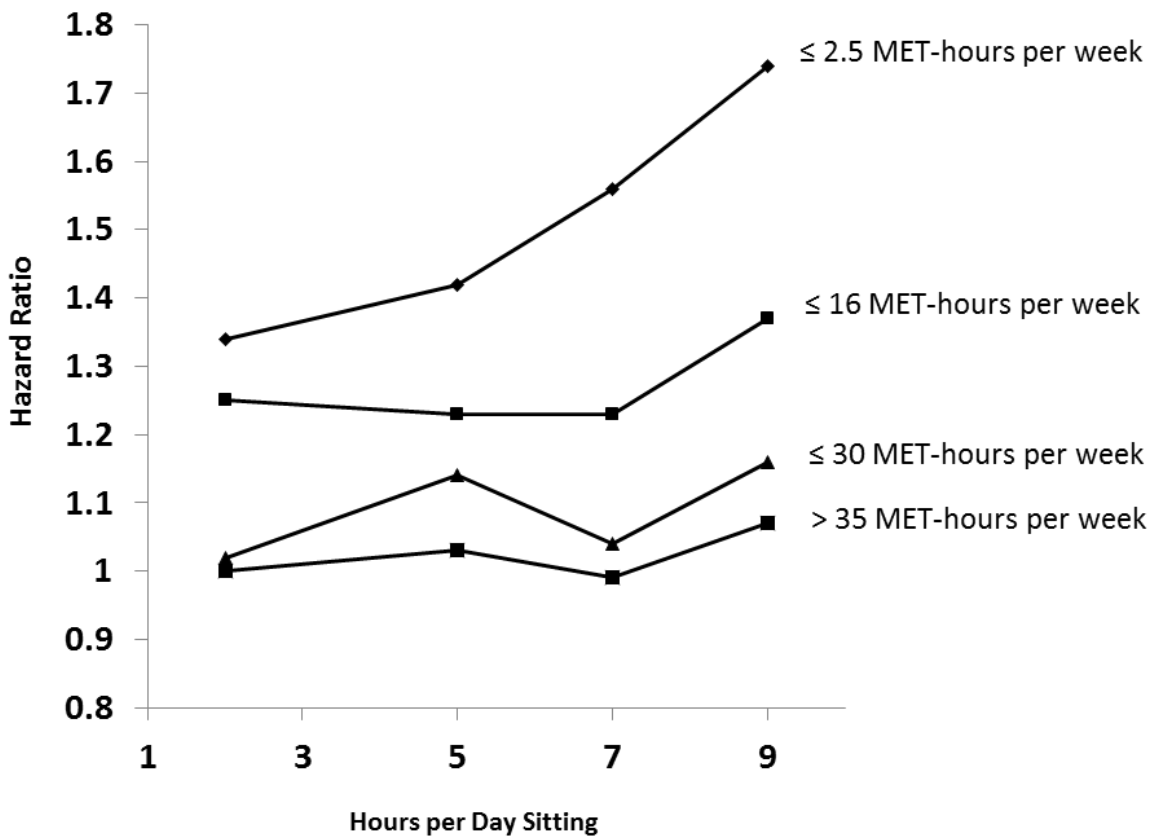
Evidence on the Overall Relationship

A total of 5 systematic reviews and meta-analyses that reviewed 11 original studies have addressed the relationship between sedentary behavior and cardiovascular disease mortality, and they provide strong evidence demonstrating a significant relationship between sedentary behavior and cardiovascular disease mortality. The meta-analysis of Biswas et al[18] analyzed seven prospective cohort studies and reported a hazard ratio of 1.15 (95% CI: 1.11-1.20) for the relationship between sedentary behavior and cardiovascular disease mortality. Further, a meta-analysis by Wilmot et al[14] reported a relative risk of 1.90 (95% CI: 1.36-2.66) for the relationship between sedentary behavior and cardiovascular disease mortality. Both meta-analyses reported a statistically significant summary risk estimate. However, the magnitude of the effect was quite different. The main reasons for the difference in the summary hazard ratios between these two meta-analyses relate to the selection of studies included in each review and differences in the exposure categories and types of sedentary behavior among the included studies.

A total of 18 original studies were identified through the meta-analyses and systematic reviews (N=11) and the de novo search (N=7). Nine studies reported on the association with sitting or total sedentary time, eight reported on the association with TV or screen time, and three studies used device-based measures of sedentary time (accelerometry or arm band). A total of 13 of these 18 studies found a significant positive relationship between sedentary time and cardiovascular disease mortality. The available studies represent several population cohorts that apply broadly to the U.S. population and the results are consistent in direction and the size of the effect.

Dose-response: Strong evidence also demonstrates the existence of a dose-response association between sedentary behavior and cardiovascular disease mortality. Seventeen original research studies tested for the existence of a dose-response association, and 10 reported a significant association. Except for one study of TV viewing among Japanese adults,[52] the studies that did not detect a significant dose-response association had small sample sizes (N< 10,000).[22, 28, 46, 50, 53, 54] The results of the pooled analysis of 11 prospective cohort studies by Ekelund et al[19] demonstrated that the associations among sedentary behavior, moderate-to-vigorous physical activity, and cardiovascular disease mortality were similar to those observed for all-cause mortality. Figure F2-3 presents the dose-response associations between sedentary time and cardiovascular disease mortality, stratified by amount of moderate-to-vigorous physical activity.[19]

Figure F2-3. Relationship Between Sitting and Cardiovascular Disease Mortality, Stratified by Amount of Moderate-to-Vigorous Physical Activity



Source: Adapted from data found in Ekelund et al, 2016.[19]

Evidence on Specific Factors

Demographic factors and weight status: Limited evidence suggests that the relationship between sedentary behavior and cardiovascular disease mortality does not vary by age, sex, race/ethnicity or weight status. Among the available studies that tested for interaction effects,[34, 36, 44, 49] no significant effect modification was observed for age,[36, 44, 49] sex,[34, 36, 44, 49] race/ethnicity,[36] or weight status.[36, 44, 49] In general, data are lacking on variation in the observed associations by level of socioeconomic status. The available evidence suggests that the observed relationship between sedentary behavior and mortality from cardiovascular disease applies broadly to the general adult population of the United States.

Amount of physical activity: Moderate evidence suggests that the relationship between sedentary behavior and cardiovascular disease mortality varies by amount of moderate-to-vigorous physical activity. Several individual studies reported the interaction between sedentary behavior and physical activity was not significant. However, the meta-analysis of Ekelund et al[19] provided convincing evidence that the association between sedentary time and cardiovascular disease mortality was influenced by moderate-to-vigorous physical activity. Some of the individual studies may have been underpowered to detect significant interaction effects, whereas the pooled analysis overcomes this limitation. Figure F2-3 presents the relationship between sedentary behavior and mortality rates from cardiovascular disease, stratified by amount of moderate-to-vigorous physical activity.[19] The strongest association between sitting and cardiovascular disease mortality is observed among those who are physically inactive (moderate-to-vigorous physical activity ≤ 2.5 MET-hours per week), and the slope of the association diminishes across increasing categories of moderate-to-vigorous physical activity. Evidence is insufficient to determine whether the association between sedentary behavior and cardiovascular disease mortality varies by amount of light- or vigorous-intensity activity.

Bouts and breaks: Insufficient evidence is available that bouts or breaks in sedentary behavior are important factors in the relationship between sedentary behavior and mortality from cardiovascular disease. No studies were identified that examined the relationship between breaks and/or bouts of sedentary behavior and mortality rates from cardiovascular disease.

For additional details on this body of evidence, visit: Supplementary Tables S-F2-4, S-F2-5, and S-F2-6 and https://health.gov/paguidelines/second-edition/report/supplementary-material.aspx for the Evidence Portfolio.

Question 3: What is the relationship between sedentary behavior and cancer mortality?

a) Is there a dose-response relationship? If yes, what is the shape of the relationship?
b) Does the relationship vary by age, sex, race/ethnicity, socioeconomic status, or weight status?
c) Is the relationship independent of amounts of light, moderate, or vigorous physical activity?
d) Is there any evidence that bouts or breaks in sedentary behavior are important factors?

Sources of evidence: Systematic reviews, meta-analyses, original research articles

Conclusion Statements

Limited evidence suggests a direct relationship between greater time spent in sedentary behavior and higher mortality rates from cancer. **PAGAC Grade: Limited.**

Limited evidence suggests the existence of a direct, positive dose-response relationship between sedentary behavior and mortality from cancer. **PAGAC Grade: Limited.**

Insufficient evidence is available to determine whether the relationship between sedentary behavior and cancer mortality varies by age, sex, race/ethnicity, socioeconomic status, or weight status. **PAGAC Grade: Not assignable.**

Insufficient evidence is available to determine whether the relationship between sedentary behavior and mortality from cancer varies by amount of moderate-to-vigorous physical activity. **PAGAC Grade: Not assignable.**

Insufficient evidence is available to determine whether bouts or breaks in sedentary behavior are important factors in the relationship between sedentary behavior and mortality from cancer. **PAGAC Grade: Not assignable.**

Review of the Evidence

Sources of evidence included: 1) systematic reviews and meta-analyses published from January 2000 to December 5, 2016, 2) the relevant original research articles cited by the systematic reviews and meta-analyses, and 3) recent original research articles published between January 2014 and January 30, 2017.

The search for systematic reviews and meta-analyses returned a total of 201 articles and the titles were reviewed by two members of the Subcommittee. A total of 48 articles were deemed potentially relevant based on the title search and the abstracts of these papers were reviewed by two members of the Subcommittee. Of these, 16 articles were deemed to be potentially relevant and the full papers were retrieved. A review of the full texts of these papers by two members of the Subcommittee identified five systematic reviews and meta-analyses that addressed Question 3 (Supplementary Table S-F2-7). These 5 systematic reviews included information on 10 original research articles that included cancer mortality as an outcome. After excluding one study in colorectal cancer survivors[55] and one study that presented a baseline description of a cohort,[7] eight original articles addressed Question 3 (Supplementary Table S-F2-8).

The de novo literature search of original research studies returned a total of 1,214 articles and the titles were reviewed by two members of the Subcommittee. A total of 62 articles were deemed potentially relevant based on the title search and the abstracts of these papers were reviewed by two members of the Subcommittee. Of these, 38 articles were deemed to be potentially relevant and the full papers were retrieved. A review of the full texts of these papers by two members of the Subcommittee identified five original studies that addressed Question 3 (Supplementary Table S-F2-9).

Evidence on the Overall Relationship

The five systematic reviews/meta-analyses suggest that only a weak association exists between sedentary behavior and all-cancer mortality. For example, the meta-analysis of eight studies by Biswas et al[18] reported a summary hazard ratio of 1.13 (95% CI: 1.05-1.21). A total of 13 original research studies were identified that addressed the association between sedentary behavior and cancer mortality. Five of the 13 studies reported a significant association, and the results were not always consistent (one in women only; one for TV viewing but not sitting; one in current smokers only). Cancer is a heterogeneous disease, and the major risk factors differ by cancer site. Further, associations between specific risk factors and cancer mortality are affected by cancer screening and treatment availability and efficacy. A limitation of most studies of sedentary behavior and cancer mortality is a failure to take these factors into account.

Dose-response: Limited evidence suggests the existence of a dose-response association between sedentary behavior and cancer mortality. Thirteen original research studies tested for the existence of a dose-response association, and five reported a significant dose-response association in the total sample or in one or more subgroups.

Evidence on Specific Factors

Demographic factors and weight status: Insufficient evidence is available to determine whether the relationship between sedentary behavior and cancer mortality varies by age, sex, race/ethnicity, socioeconomic status, or weight status. Of the five studies that reported a significant association between sedentary behavior and cancer mortality,[35, 36, 38, 53, 56] only one tested for effect modification, and the results indicated no significant interactions with body mass index (BMI) and race/ethnicity.[36] The study showed a significant interaction with age, with a significant association observed in women ages 50 to 69 years but not in women ages 70 to 79 years. However, this finding needs to be replicated in other studies before any definitive statements can be made about the effects of age on the observed associations. In general, data on variations in the observed associations by level of socioeconomic status are lacking.

Amount of physical activity: Insufficient evidence is available to determine whether the relationship between sedentary behavior and cancer mortality is modified by physical activity. The pooled meta-analysis by Ekelund et al[19] did not specifically test for an interaction between sedentary behavior and moderate-to-vigorous physical activity on cancer mortality, and there did not appear to be a relationship between sedentary behavior (either sitting or TV time) and cancer mortality within quartiles of moderate-to-vigorous physical activity. Further, the study by Seguin et al[36] reported no significant interaction between sedentary time and physical activity (*P*=0.51). Evidence is insufficient to determine whether the association between sedentary behavior and mortality from cancer varies by amount of light or vigorous activity.

Bouts and breaks: Available evidence is insufficient to determine whether bouts or breaks in sedentary behavior are important factors in the relationship between sedentary behavior and mortality from cancer. No studies were identified that examined the relationship between breaks and/or bouts of sedentary behavior and mortality rates from cancer.

For additional details on this body of evidence, visit: Supplementary Tables S-F2-7, S-F2-8, and S-F2-9 and https://health.gov/paguidelines/second-edition/report/supplementary-material.aspx for the Evidence Portfolios. For information on the relationship of physical activity and cancer, see Part F. Chapter 4: Cancer Prevention.

Question 4: What is the relationship between sedentary behavior and (1) type 2 diabetes, (2) weight status, (3) cardiovascular disease, and (4) cancer?

a) Is there a dose-response relationship? If yes, what is the shape of the relationship?
b) Does the relationship vary by age, sex, race/ethnicity, socioeconomic status, or weight status?
c) Is the relationship independent of amounts of light, moderate, or vigorous physical activity?
d) Is there any evidence that bouts or breaks in sedentary behavior are important factors?

Sources of evidence: Systematic reviews, meta-analyses, original research articles

Conclusion Statements

Type 2 Diabetes

Strong evidence demonstrates a significant relationship between greater time spent in sedentary behavior and higher risk of type 2 diabetes. **PAGAC Grade: Strong.**

Limited evidence suggests the existence of a direct, graded dose-response relationship between sedentary behavior and risk of type 2 diabetes. **PAGAC Grade: Limited.**

Insufficient evidence is available to determine whether the relationship between sedentary behavior and type 2 diabetes varies by age, sex/ethnicity, socioeconomic status, or weight status. **PAGAC Grade: Not assignable.**

Insufficient evidence is available to determine whether the relationship between sedentary behavior and type 2 diabetes varies by amount of moderate-to-vigorous physical activity. **PAGAC Grade: Not assignable.**

Insufficient evidence is available to determine whether bouts or breaks in sedentary behavior are important factors in the relationship between sedentary behavior and incidence of type 2 diabetes. **PAGAC Grade: Not assignable.**

Weight Status

Limited evidence suggests a positive relationship between greater time spent in sedentary behavior and higher levels of adiposity and indicators of weight status. **PAGAC Grade: Limited.**

Limited evidence suggests the existence of a direct, graded dose-response relationship between greater sedentary behavior and higher levels of adiposity and indicators of weight status. **PAGAC Grade: Limited.**

Insufficient evidence is available to determine whether the relationship between sedentary behavior and weight status varies by age, sex/ethnicity, socioeconomic status, or baseline weight status. **PAGAC Grade: Not assignable.**

Insufficient evidence is available to determine whether the relationship between sedentary behavior and weight status varies by amount of moderate-to-vigorous physical activity. **PAGAC Grade: Not assignable.**

Insufficient evidence is available to determine whether bouts or breaks in sedentary behavior are important factors in the relationship between sedentary behavior and weight status. **PAGAC Grade: Not assignable.**

Cardiovascular Disease

Strong evidence demonstrates a significant relationship between greater time spent in sedentary behavior and higher risk of incident cardiovascular disease. **PAGAC Grade: Strong.**

Strong evidence demonstrates the existence of a direct, graded dose-response relationship between sedentary behavior and risk of incident cardiovascular disease. **PAGAC Grade: Strong.**

Insufficient evidence is available to determine whether the relationship between sedentary behavior and incident cardiovascular disease varies by age, sex/ethnicity, socioeconomic status, or weight status. **PAGAC Grade: Not assignable.**

Insufficient evidence is available to determine whether the relationship between sedentary behavior and incident cardiovascular disease varies by amount of moderate-to-vigorous physical activity. **PAGAC Grade: Not assignable.**

Insufficient evidence is available to determine whether bouts or breaks in sedentary behavior are important factors in the relationship between sedentary behavior and incidence of cardiovascular disease. **PAGAC Grade: Not assignable.**

Cancer

Moderate evidence indicates a significant relationship between greater time spent in sedentary behavior and higher risk of incident endometrial, colon, and lung cancers. **PAGAC Grade: Moderate.**

Limited evidence suggests the existence of a direct dose-response relationship between sedentary behavior and incident endometrial, colon, and lung cancers. **PAGAC Grade: Limited.**

Insufficient evidence is available to determine whether the relationship between sedentary behavior and incident cancer varies by age, sex/ethnicity, socioeconomic status, or weight status. **PAGAC Grade: Not assignable.**

Insufficient evidence is available to determine whether the relationship between sedentary behavior and incident cancer varies by amount of moderate-to-vigorous physical activity. **PAGAC Grade: Not assignable.**

Insufficient evidence is available to determine whether bouts or breaks in sedentary behavior are important factors in the relationship between sedentary behavior and incident cancer. **PAGAC Grade: Not assignable.**

Review of the Evidence

Sources of evidence included: 1) systematic reviews and meta-analyses published from January 2000 to February 21, 2017, and 2) recent original research articles published between January 2014 and April 25, 2017.

The systematic literature search to address Question 4 was conducted in two steps. Step 1 involved a search for existing systematic reviews and meta-analyses that could address the question. The search strategy (from January 1, 2000 to February 21, 2017 returned a total of 201 articles and the titles were reviewed by two members of the Subcommittee. A total of 48 articles were deemed potentially relevant based on the title search and the abstracts of these papers were reviewed by two members of the Subcommittee. Of these, 22 articles were deemed to be potentially relevant and the full papers were retrieved. A review of the full texts of these papers by two members of the Subcommittee identified 11 systematic reviews and meta-analyses that addressed Question 4 (five for type 2 diabetes, two for weight status, five for cardiovascular disease, and eight for cancer) (Supplementary Table S-F2-10).

Step 2 involved a de novo literature search of original research studies published between January 1, 2014, and April 25, 2017. The search strategy returned a total of 1,877 articles and the titles were reviewed by two members of the Subcommittee. A total of 200 articles were deemed potentially relevant based on the title search and the abstracts of these papers were reviewed by two members of the Subcommittee. Of these, 44 articles were deemed to be potentially relevant and the full papers were retrieved. A review the full texts of these papers by two members of the Subcommittee identified 34 original studies that addressed Question 4 (Supplementary Table S-F2-11).

Type 2 Diabetes

Evidence on the Overall Relationship

Two systematic reviews[12, 13] and three meta-analyses[11, 14, 18] addressed the issue of sedentary behavior and the incidence of type 2 diabetes (Supplementary Table S-F2-10). All three meta-analyses reported significant pooled estimates of risk for incident type 2 diabetes associated with sedentary behavior. The pooled relative risk per 2 hours of TV viewing per day was 1.20 (95% CI: 1.14-1.27) among four original papers analyzed by Grontved and Hu.[11] The summary relative risk (from five cross-sectional and five prospective studies) for type 2 diabetes reported by Wilmot et al[14] was 2.12 (95% CI: 1.61-2.78) for highest versus lowest sedentary time. Finally, the summary hazard ratio for type 2 diabetes was 1.91 (95% CI: 1.64-2.22) from five studies analyzed by Biswas et al.[18]

Eight original research articles were retrieved from the de novo literature search for incident type 2 diabetes (Supplementary Table S-F2-11).[57-64] Three[57, 59, 61] of the eight studies reported significant effects of higher sedentary behavior and greater risk of type 2 diabetes from fully adjusted models. An additional three studies[58, 62, 64] reported significant effects of sedentary behavior on risk of type 2 diabetes in minimally adjusted models (e.g., age, sex) but the effects were attenuated to the null when additional covariates, including BMI, were added to the models. These results are supported by the meta-analysis of Grontved and Hu[11] who reported a that pooled relative risk per 2 hours of TV viewing per day on risk of type 2 diabetes was 1.20 (95% CI: 1.14-1.27), which was reduced to a relative risk of 1.13 (95% CI: 1.08-1.18) when the relative risk was calculated from models that included BMI or another obesity measure. These results suggest that BMI may be on the causal pathway between sedentary behavior and increased risk of type 2 diabetes. In other words, the effects of sedentary behavior on risk of type 2 diabetes may be operating, in part, through its association with BMI.

Dose-response: Limited evidence suggests a graded, positive association between sedentary behavior and incident type 2 diabetes. The meta-analysis of Grontved and Hu[11] reported a significant, positive linear dose-response association between TV viewing and type 2 diabetes. Further, two[57, 61] of four original research studies[57, 58, 60, 61] that tested for linear dose-response associations reported a significant finding.

Evidence on Specific Factors

Demographic factors and weight status: Available evidence is insufficient to determine whether the relationship between sedentary behavior and incident type 2 diabetes varies by age, sex, race/ethnicity, socioeconomic status, or weight status. A single study stratified the analysis by race/ethnicity and reported a significant graded association only among Non-Hispanic Whites and not in Chinese Americans, African Americans, or Hispanic Americans.[61] Two studies reported a significant interaction between sedentary behavior and BMI on risk of diabetes,[57, 62] with significant effects of sedentary behavior observed only among individuals with obesity. On the other hand, a single study[64] reported no significant interaction between sedentary behavior and BMI on risk of diabetes (P=0.65).

Amount of physical activity: Insufficient evidence is available to determine whether the relationship between sedentary behavior and incident type 2 diabetes varies by amount of moderate-to-vigorous physical activity. Four of the original research studies considered the potential interactions between sedentary behavior and physical activity on incident type 2 diabetes.[57, 58, 62, 64] Manini et al[57] reported significant effects of daily sitting on incident type 2 diabetes among people with different amounts of physical activity (all P-values for trends <0.01). On the other hand, Smith and Hamer[58] reported that active participants who reported high TV viewing were not at elevated risk of type 2 diabetes, in comparison to inactive participants who reported high TV viewing, who were at significantly elevated risk. Petersen et al[62] reported a non-significant interaction between sitting time and moderate-to-vigorous physical activity (*P*=0.68). However, the association between sitting time and incident type 2 diabetes was only significant in those who were inactive. Asvold et al[64] reported a significant interaction between daily sitting time and leisure-time physical activity (*P*=0.01), with a significant effect observed only in inactive participants. Thus, the evidence from these four studies is not consistent.

Bouts and breaks: Insufficient evidence is available that bouts or breaks in sedentary behavior are important factors in the relationship between sedentary behavior and incident type 2 diabetes. No studies were identified that addressed this topic.

Weight Status

Evidence on the Overall Relationship

Two systematic reviews[12, 13] each reviewed 10 original research studies and concluded that evidence was insufficient or limited, respectively, that sedentary behavior was related to changes in body weight or other indicators of weight status, such as BMI, waist circumference, body fat, or overweight (BMI ≥25 kg/m^2) or obesity (BMI ≥30 kg/m^2) (Supplementary Table S-F2-10). Fourteen original research articles were identified that were published between 2014 and 2017[65-78] (Supplementary Table S-F2-11) that explored associations between sedentary behavior and indicators of adiposity or weight status.

Of the 14 original studies, 11 reported a significant positive association between at least one sedentary behavior and at least one indicator of adiposity or weight status,[67, 68, 70-78] whereas three studies reported no significant results.[65, 66, 69] However, the relationships observed among the studies that reported significant effects showed considerable heterogeneity. For example, among adults in the United Kingdom, the relationship between TV viewing and incident abdominal obesity (high waist circumference) was significant, but the relationship with incident obesity (high BMI) was not.[72] Among Swedish adults followed for 5 years, the association between computer gaming and incident overweight was significant in women, but not in men.[73] Among Finnish adults, the association between screen time and 6-year weight change was significant in men ages 24 to 27 years but not in men ages 30 to 39 years or in women.[74] Saidj et al[76] reported that occupational sitting time was associated with changes in waist circumference over 5 years, but not with changes in BMI. In the same study, the authors found no association between leisure-time sitting and either BMI or waist circumference.[76] Finally, among Chinese adults, the relationship between daily sedentary time and the incidence of obesity was significant in men but not in women.[78] However, the association with weight change per se was significant in both men and women.

Several indicators of adiposity and weight status have been employed as outcomes in the available studies. Many studies included multiple analyses of subgroups (e.g., in men, in women, and total sample). Significant results were reported in five[70, 71, 74, 78] out of seven analyses[65, 70, 71, 74, 78] for body weight; four[67, 68, 73, 75] out of nine analyses[67, 68, 73, 75, 76] for BMI; 3[67, 68, 77] out of 10 analyses[65, 67-69, 71, 75-77] for waist circumference; one out of one analysis[71] for fat mass; one[75] out of two analyses[71, 75] for percent body fat; one[71] out of one analysis[71] for fat mass index; 2[73, 78] out of 10 analyses[66, 72, 73, 78] for incident overweight or obesity; and one out of one analysis[72] for incident central obesity (high waist circumference).

The results for weight status differed by the exposure variable used to measure sedentary behavior. However, some significant results were reported regardless of the exposure variable used. For example, significant results were reported for one or more of the indicators of weight status in one[71] out of two analyses[69, 71] in studies that used accelerometry to measure sedentary time; significant results were reported for one or more of the indicators of weight status in three[76, 78] out of six analyses[65, 66, 76, 78] in studies that relied on self-reported measures of sitting time or total sedentary time; and significant results were reported for one or more indicators of weight status for 8[67, 68, 70, 72-74, 77] out of 10 analyses[67-70, 72-75, 77] in studies that used TV viewing or screen time as the exposure.

The associations between measures of sedentary behavior and indicators of adiposity are complex. For example, four studies explored the existence of a reciprocal relationship between sedentary behavior and weight status[67, 71, 75, 76]—i.e., does weight status at baseline predict changes in sedentary behavior? Three of the four studies reported significant reciprocal effects[71, 75, 76] and one did not.[67] Helajarvi et al[67] reported that consistently low TV viewing was associated with a smaller increase in BMI and waist circumference over approximately 10 years of follow-up in young Finnish adults, with no evidence of a reciprocal relationship. On the other hand, Menai et al[75] also reported a significant association between increased TV viewing over follow-up and increases in BMI and percent fat. However, a reciprocal relationship also was observed, with positive associations between baseline BMI, percent fat, and waist circumference and increases in TV viewing. Positive associations between accelerometer-determined sedentary time and increases in weight, fat mass, and fat mass index were observed among U.K. adults, and significant positive associations also were seen between the obesity indicators at baseline and increases in sedentary time over follow-up.[71] Similarly, association between baseline leisure-time sitting and changes in BMI or waist circumference was seen over 5 years of follow-up in Danish adults. However, higher BMI and waist circumference were both positively associated with greater increases in leisure-time sitting (P<0.0001).[76]

Dose-response: The issue of dose-response was addressed in 12 of the original research studies, mainly by testing for linear associations in regression models, or testing for linear trends across categorical exposures.[65-72, 74-77] A statistically significant linear dose-response association was observed in 9 of the 12 studies for at least one subgroup for one of the weight-related outcomes.[67, 68, 70-72, 74-77]

Evidence on Specific Factors

Demographic factors and weight status: Insufficient evidence is available to determine whether age, sex, race/ethnicity, or baseline weight status are important factors in the relationship between sedentary behavior and weight status.

Amount of physical activity: Insufficient evidence is available to determine whether the association between sedentary behavior and weight status varies by amount of moderate-to-vigorous physical activity. Shibata et al[77] found no significant interaction between change in moderate-to-vigorous physical activity and change in TV viewing on 12-year changes in waist circumference among Australian adults. Although Bell et al[66] found no main effect of leisure-time sitting on incident obesity in the study of U.K. adults, a significant interaction between sitting time and physical activity was seen at a 5-year (P=0.02) but not at a 10-year (P=0.37) follow-up. At the 5-year follow-up, the combination of high physical activity and low sedentary time was associated with an odds ratio of 0.26 (95% CI: 0.11-0.64) for incident obesity.[66]

Bouts and breaks: Insufficient evidence is available that bouts or breaks in sedentary behavior are important factors in the relationship between sedentary behavior and weight status. No studies were identified that addressed this topic.

Cardiovascular Disease

Evidence on the Overall Relationship

One systematic review[13] and four meta-analyses[11, 14, 18, 79] were identified that addressed the association between sedentary behavior and incident cardiovascular disease (Supplementary Table S-F2-10). All four meta-analyses reported a statistically significant pooled estimate of risk. Grontved and Hu[11] reported a pooled relative risk of 1.15 (95% CI: 1.06-1.23) per 2 hours of TV viewing per day. Similarly, Biswas et al[18] and Pandey et al[79] reported summary hazard ratios of 1.14 (95% CI: 1.00-1.30) and 1.14 (95% CI: 1.09-1.19), respectively, for high versus low sedentary behavior and incident cardiovascular disease. Finally, Wilmot et al[14] reported a significant summary relative risk for cardiovascular events of 2.47 (95% CI: 1.44-4.24). Taken together, the results of these meta-analyses indicate that sedentary behavior is significantly associated with incident cardiovascular disease risk.

Three[10, 80, 81] of the six original research studies[10, 80-84] published between 2014 and 2017 found a significant association between sedentary behavior and incident cardiovascular disease (Supplementary Table S-F2-11). Petersen et al[10] reported that daily sitting time was significantly associated with incident myocardial infarction but not with incident coronary heart disease. Young et al[80] reported a significant association between sedentary time and incident heart failure in U.S. men, and Borodulin et al[81] reported a significant association between daily sitting time and incident fatal and nonfatal cardiovascular disease among Finnish adults.

Dose-response: Two meta-analyses addressed the issue of dose-response in the association between sedentary behavior and incident cardiovascular disease.[11, 79] Grontved and Hu[11] reported a significant linear dose-response association between TV viewing and incident fatal and nonfatal cardiovascular disease. In a similar vein, Pandey et al[79] reported a significant, curvilinear dose-response association with increasing slope of risk at increasingly higher levels of sedentary time. Three of the recent research studies published between 2014 and 2017 reported significant dose-response associations between sedentary behavior and incident cardiovascular disease.[10, 80, 81]

Evidence on Specific Factors

Demographic factors and weight status: Insufficient evidence is available to determine whether the relationship between sedentary behavior and cardiovascular disease varies by age, sex, race/ethnicity, socioeconomic status, or weight status, as few studies examined these interactions. Young et al[80] reported that the association between sedentary time and incidence of heart failure was elevated in all ethnic groups, but was statistically significant only in Non-Hispanic White and Hispanic men. The association also was significant in men with normal weight, overweight, and obesity. McDonnell et al[83] reported no significant interactions between TV viewing and age, race or sex on risk of incident stroke.

Amount of physical activity: Available evidence is insufficient to determine whether the relationship between sedentary behavior and cardiovascular disease varies by amount of moderate-to-vigorous physical activity. Two of the original research studies identified in the de novo literature search considered the potential interactions between sedentary behavior and physical activity on incident cardiovascular disease. Petersen et al[10] found no significant interaction between sitting time and leisure-time physical activity for myocardial infarction or coronary heart disease. On the other hand, Young et al[80] reported a small additive interaction effect between low physical activity and high sedentary time on incident heart failure (relative risk (RR)=0.08; 95% CI: 0.03-0.14).

Bouts and breaks: Insufficient evidence is available that bouts or breaks in sedentary behavior are important factors in the relationship between sedentary behavior and incident cardiovascular disease. No studies were identified that addressed this topic.

Cancer

Evidence on the Overall Relationship

Four systematic reviews[12, 13, 85, 86] and four meta-analyses[18, 87-89] addressed the relationship between sedentary behavior and cancer incidence (Supplementary Table S-F2-10). Two meta-analyses addressed associations with total cancer incidence,[18, 88] two meta-analyses examined associations with incidence of several-site-specific cancers,[87, 88] and one meta-analysis addressed breast cancer incidence only.[89] The research studies included in the meta-analyses generally reported relative risks that were adjusted for several covariates, including physical activity. Six original research studies, published between 2014 and 2017, that addressed the relationship between sedentary behavior and incident cancer were identified[90-95] (Supplementary Table S-F2-11). These studies considered the relationship between sedentary behavior and total cancer and site-specific cancers,[94] breast cancer,[91, 93] ovarian cancer,[92] prostate cancer,[90] and lung cancer.[95]

Total Cancer: Two meta-analyses examined the association between sedentary behavior and total cancer incidence.[18, 88] Shen et al[88] reported a summary relative risk of 1.20 (95% CI: 1.12-1.28) and Biswas et al[18] reported a summary hazard ratio of 1.13 (95% CI: 1.05-1.21) for highest versus lowest levels of sedentary behavior and all-cancer incidence. Further, an original research study in a large cohort (American Cancer Prevention Study II Nutrition Cohort) reported a significant association between leisure-time sitting and total cancer incidence in women but not in men.[94] The results of studies that use total cancer incidence as the outcome should be interpreted with caution, given that cancer is a heterogeneous disease and specific cancers vary widely in their etiology and progression, as well as geographic distribution.

Breast Cancer: Three meta-analyses examined the association between sedentary behavior and breast cancer incidence.[87-89] Zhou et al[89] reported non-significant associations between highest and lowest amounts of sitting time and breast cancer incidence (odds ratio (OR)=1.05; 95% CI: 0.99-1.11) and highest versus lowest amounts of TV viewing and breast cancer (OR=1.07; 95% CI: 0.96-1.20), respectively. Similarly, Schmid and Leitzmann[87] also reported no relationship between highest versus lowest amounts of sedentary behavior and breast cancer incidence in their meta-analysis (RR=1.03; 95% CI: 0.95-1.12). On the other hand, Shen et al[88] reported a significant association between the highest versus the lowest amounts of sedentary behavior and breast cancer incidence (RR=1.17; 95% CI: 1.03-1.33). The Shen et al[88] meta-analysis used three prospective cohort studies in their analysis, whereas Schmid and Leitzmann[87] relied on 13 case-control and prospective studies, and Zhou et al[89] also relied on both case-control and prospective studies (9 studies for sitting and 6 studies for TV viewing). Of the two newer original research studies that were found, one reported a significant association with breast cancer[93] and the other did not.[91]

Endometrial Cancer: Two meta-analyses examined the association between sedentary behavior and endometrial cancer, and both reported a significant association.[87, 88] Comparing the highest versus lowest levels of sedentary time, Schmid and Leitzmann[87] reported a summary relative risk of 1.36 (95% CI: 1.15-1.60); whereas Shen et al[88] reported a summary relative risk of 1.28 (95% CI: 1.08-1.53).

Colorectal Cancer: The meta-analysis by Shen et al[88] reported a significant association comparing the highest versus lowest amounts of sedentary behavior and combined colorectal cancer (RR=1.30; 95% CI: 1.12-1.49); whereas Schmid and Leitzmann[87] reported a significant association for the highest versus lowest amounts of sedentary behavior and colon cancer (relative risk = 1.28; 95% CI: 1.13-1.45) but not for rectal cancer (RR=1.03; 95% CI: 0.89-1.19).

Lung Cancer: Two meta-analyses examined the association between sedentary behavior and lung cancer, and both reported a significant association.[87, 88] Comparing the highest versus lowest levels of sedentary time, Schmid and Leitzmann[87] reported a summary relative risk of 1.21 (95% CI: 1.03-1.43); whereas Shen et al[88] reported a summary relative risk of 1.27 (95% CI: 1.06-1.52).

Other Cancers: The two meta-analyses that examined site-specific cancers[87, 88] did not find significant associations between sedentary behavior and risk of ovarian cancer, prostate cancer, stomach cancer, testicular cancer, renal cell carcinoma, or non-Hodgkin lymphoid neoplasms. In a more recent original research study using data from the American Cancer Prevention Study II Nutrition Cohort, the authors reported significant associations between leisure-time sitting and risk of multiple myeloma, invasive breast cancer, and ovarian cancer in women, but found no associations in men between sedentary behavior and site-specific cancers.[94]

Dose-response: One meta-analysis examined dose-response associations between sedentary behavior and cancer risk by modelling the association according to 2-hour increments per day of time spent being sedentary.[87] Each 2-hour per day of sitting time was related to significantly increased risk of colon cancer (RR=1.08; 95% CI: 1.04-1.11), endometrial cancer (RR=1.10; 95% CI: 1.05-1.15), and a borderline statistically increased risk of lung cancer (RR=1.06; 95% CI: 1.00-1.11).

Evidence on Specific Factors

Demographic factors and weight status: None of the identified meta-analyses stratified its analysis by demographic factors or weight status. Only three original studies tested for interactions between sedentary behavior and BMI, with varying results.[90, 93, 94] Therefore, the evidence is insufficient to determine whether the association between sedentary behavior and cancer risk varies by age, sex/ethnicity, socioeconomic status, or weight status.

Amount of physical activity: None of the identified meta-analyses stratified its analysis by amount of physical activity. Three of the six original research studies tested for an interaction between sedentary behavior and physical activity, and none was significant.[90, 93, 94] Therefore, the evidence is insufficient to determine whether the association between sedentary behavior and cancer risk varies by amount of moderate-to-vigorous physical activity.

Bouts and breaks: Insufficient evidence is available that bouts or breaks in sedentary behavior are important factors in the relationship between sedentary behavior and incident cancer. No studies were identified that addressed this topic.

For additional details on this body of evidence, visit: Supplementary Tables S-F2-10 and S-F2-11, and https://health.gov/paguidelines/second-edition/report/supplementary-material.aspx for the Evidence Portfolio. For information on the relationship of physical activity and cancer, see Part F. Chapter 4: Cancer Prevention.

Question 5. Does the effect of moderate-to-vigorous physical activity on all-cause mortality vary by amount of sedentary behavior?

Sources of evidence: Meta-analyses, original research articles

Conclusion Statement

Moderate evidence indicates that the beneficial effect of moderate-to-vigorous physical activity on all-cause mortality varies by amount of sedentary behavior. Importantly, the relative reductions in risk are larger for those who are the most sedentary. **PAGAC Grade: Moderate.**

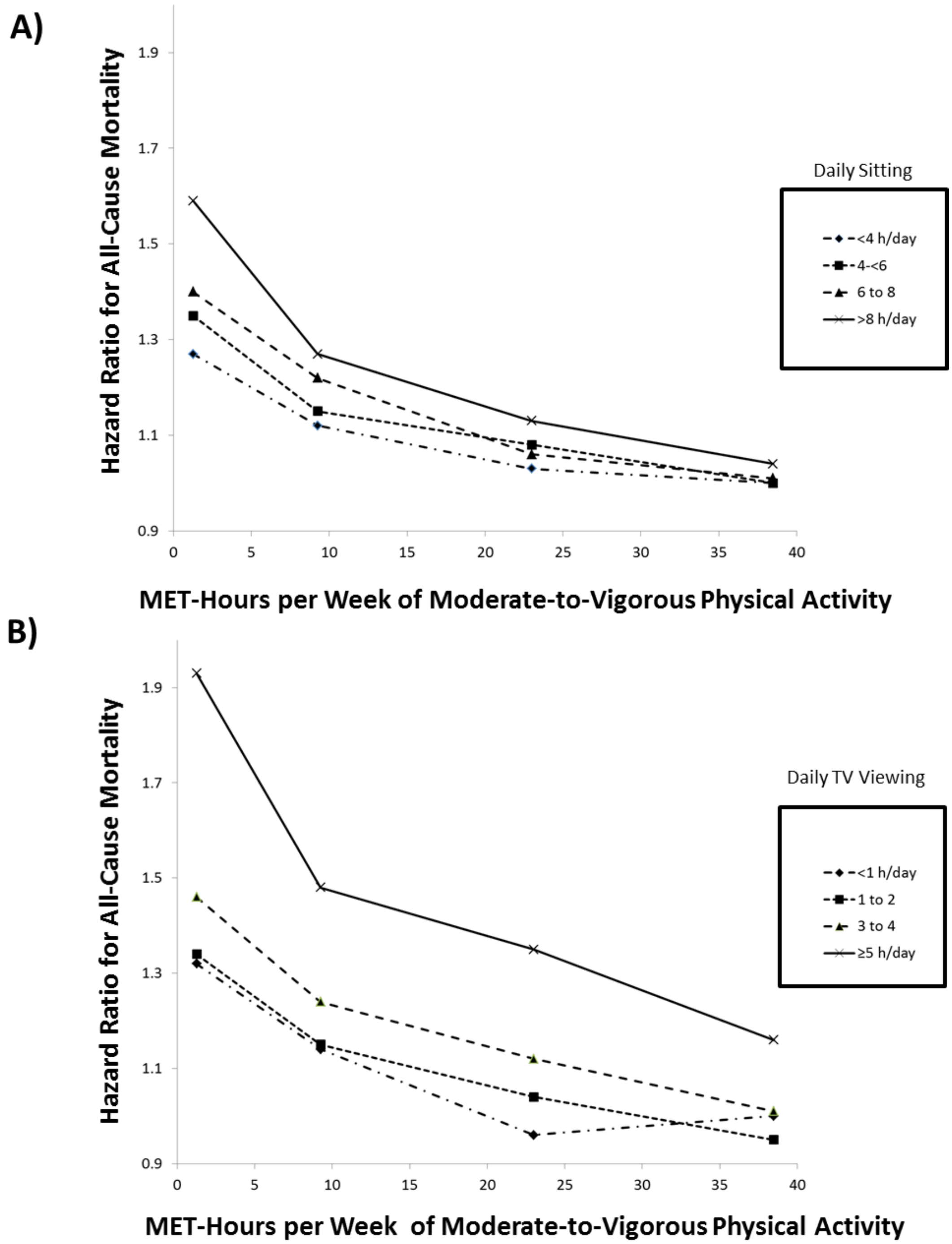
Review of the Evidence

The evidence used to address Question 5 was obtained from the evidence compiled for Question 1. The evidence base is described in greater detail in the section for Question 1. All systematic reviews/meta-analyses and original research articles were reviewed for potential inclusion in the evidence for Question 5. Cohort studies that included multiple amounts of moderate-to-vigorous physical activity as the exposure, in addition to at least two categories of sedentary time, were included in the evidence base. One meta-analysis of data from more than 1 million participants from 16 cohort studies was identified[19] in addition to two original research articles.[35, 38] An additional three original research studies[36, 39, 51] provided graphical representations of death rates or hazard ratios across combined categories of sedentary behavior and moderate-to-vigorous physical activity. However, the purpose of these figures was to examine the shape of the association between sedentary behavior within different amounts of moderate-to-vigorous physical activity, and the point estimates were not provided in the figures. Finally, one study reported similar non-linear associations between moderate-to-vigorous physical activity in those who had more than 10.9 hours per day of sedentary behavior versus those who had 10.9 hours or less per day of sedentary behavior. However, estimates of relative risk were not provided.[26]

The joint associations of moderate-to-vigorous physical activity with daily sitting and TV viewing from the meta-analysis of Ekelund et al[19] are plotted in Figure F2-4. In general, the overall shapes of the dose-response relationships between moderate-to-vigorous physical activity and all-cause mortality are generally similar when stratified by level of sitting or TV viewing. However, the relative risks at every level of moderate-to-vigorous physical activity are consistently higher in the high sitting and high TV viewing groups. The reduction in risk of all-cause mortality is relatively greater for those who are the most sedentary. This is especially apparent at the lower amounts of moderate-to-vigorous physical activity. For example, among those who sit more than 8 hours per day, the risk for individuals in the second quartile (about 9.25 MET-hours per week) is 20 percent lower than the risk for individuals in the first quartile (≤2.5 MET-hours per week). In contrast, among those who sit less than 4 hours per day, the risk for individuals in the second quartile is 12 percent lower than the risk for individuals in the first quartile.

The level of risk associated with accumulating approximately 20 to 25 MET-hours per week of moderate-to-vigorous physical activity in the low sitting (<4 h/day) group is similar to the risk associated with accumulating 35 to 40 MET-hours per week in the high sitting (>8 h per day) group (Figure 4a). Similar results are observed across categories of TV viewing, except that the level of relative risk associated with high amount of moderate-to-vigorous physical activity in the high TV viewing (≥5 h/day) never achieves that of moderate or high amounts of moderate-to-vigorous physical activity in the low TV viewing (<1 h/day) group (Figure F2-4B). These observations are supported by the results of two original research studies in U.S. adults.[38, 94] It should be noted that both original research studies contributed data to the pooled meta-analysis by Ekelund et al.[19] Further research is required to determine why the associations differ somewhat for self-reported sitting versus self-reported TV viewing.

Figure F2-4. Relationship Between Moderate-to-Vigorous Physical Activity and All-cause Mortality, Stratified by Amounts of A) Sitting Time and B) TV Viewing



Source: Adapted from data found in Ekelund et al., 2016.[19]

For additional details on this body of evidence, visit: https://health.gov/paguidelines/second-edition/report/supplementary-material.aspx for the Evidence Portfolio.

OVERALL SUMMARY, CONCLUSIONS, AND PUBLIC HEALTH IMPACT

Strong scientific evidence demonstrates that exposure to high amounts of sedentary behavior significantly increases the risk of all-cause mortality, cardiovascular disease incidence and mortality, and type 2 diabetes incidence. Moderate evidence indicates that high amounts of sedentary behavior are associated with the incidence of cancer, particularly for endometrial, colon and lung cancer. Further, limited evidence exists that sedentary behavior is associated with cancer mortality and weight status. Currently, sedentary behavior is highly prevalent in the U.S. population. Therefore, limiting excessive time spent sitting would reduce the population health impact associated with premature mortality and several major chronic diseases such as type 2 diabetes, cardiovascular disease, and cancer. For physically inactive adults, replacing sedentary behavior with light intensity physical activities is likely to produce some health benefits. Among all adults, replacing sedentary behavior with higher intensity (moderate-to-vigorous) physical activities may produce even greater benefits.

Strong evidence demonstrates that the association between sedentary behavior and all-cause mortality varies by amount of moderate-to-vigorous physical activity, such that the hazardous effects of sedentary behavior are more pronounced in physically inactive people. Moderate evidence also indicates that the effects of moderate-to-vigorous physical activity vary by amount of sedentary behavior, such that those who are the most sedentary experience the greatest relative reductions in mortality risk associated with increases in physical activity. Further, individuals who are highly sedentary appear to require even higher amounts of physical activity to achieve the same level of absolute mortality risk as people who are less sedentary. Therefore, moderate-to-vigorous physical activity should be part of every adult’s lifestyle, especially for those who sit for large portions of the day.

NEEDS FOR FUTURE RESEARCH

1. Conduct research using prospective cohorts on the interactive effects of physical activity and sedentary behavior on all-cause and cardiovascular disease mortality and incident cardiovascular disease, especially on the role of light-intensity physical activity on attenuating the relationship between sitting and mortality.

   Rationale: Evidence on the role of physical activity in displacing the mortality risks associated with sedentary behavior is limited. A better understanding of these interactive effects will allow for more specific recommendations regarding the amount and intensity of physical activity required to maximize health benefits among people with higher or lower levels of sedentary behavior. Given that associations between specific risk factors and cancer mortality are affected by cancer screening and treatment availability and efficacy, studies of the associations between sedentary behavior and all-cancer mortality are not a priority.

2. Conduct research using prospective cohorts on the role of bouts and breaks in sedentary behavior in relation to all-cause and cardiovascular disease mortality.

   Rationale: The preponderance of the existing evidence on prospective associations between sedentary behavior and health is based on the association between daily or weekly duration of sedentary behavior. More research is needed on the relationship between patterns of sedentary behavior and mortality and other health outcomes, especially the role of sedentary bouts and breaks. This information will contribute to the development of recommendations on how sedentary behavior patterns should be modified to maximize related health benefits. Given that associations between specific risk factors and cancer mortality are affected by cancer screening and treatment availability and efficacy, studies of the associations between sedentary behavior and all-cancer mortality are not a priority.

3. Conduct research on how factors such as sex, age, race/ethnicity, socioeconomic status, and weight status relate to the association between sedentary behavior and cardiovascular disease incidence and cardiovascular disease mortality.

   Rationale: Compared to the evidence base for all-cause mortality, fewer studies have addressed issues of effect modification by these factors on the relationship between sedentary behavior and cardiovascular disease incidence and mortality. This information will help determine how generalizable the potential benefits of reducing sedentary behavior are in preventing cardiovascular disease and whether different recommendations are required based one’s sex, age, race/ethnicity, socioeconomic status, or weight status. Given that associations between specific risk factors and cancer mortality are affected by cancer screening and treatment availability and efficacy, studies of the associations between sedentary behavior and all-cancer mortality are not a priority.

4. Conduct research using prospective cohorts to disentangle the independent effects of sedentary behavior and adiposity on risk of type 2 diabetes.

Rationale: Given that the association between sedentary behavior and type 2 diabetes is attenuated when body mass index is a covariate in the statistical models, this suggests that body mass index may be in the causal pathway between sedentary behavior and risk of type 2 diabetes. However, further research is required to understand the nature and direction of this relationship to better understand whether the relationship between sedentary behavior and type 2 diabetes is truly causal.

5. Conduct randomized controlled trials to test the health effects of interventions to replace time spent in sedentary behaviors with standing and light-, moderate-, and vigorous-intensity physical activity.

   Rationale: The preponderance of the evidence on the health effects of sedentary behavior has come from observational epidemiological studies. To develop public health guidelines and develop effective intervention strategies, more evidence is required on the positive and negative consequences associated with replacing sedentary behavior with greater intensity activities for short or long durations.

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Physical Activity and Selected Health Outcomes

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PART F. CHAPTER 3. BRAIN HEALTH

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INTRODUCTION

Maintaining or improving brain health is a universal goal across the lifespan. In youth, we seek to enhance brain maturation and development, reach expected developmental milestones relative to thoughts and actions, and achieve academic goals, including school readiness and achievement. In late adulthood, we aim to avoid dementia and cognitive impairment. Across the lifespan, we strive to ensure high-quality brain health, as manifested by optimally functioning cognition, low levels of anxiety and feelings of depression, a positive assessment of perceptions of quality of life, and comfortable and effective sleep patterns. Despite these common goals, and the fact that recent research has provided much important information on these topics, the effects of physical activity on brain health remain poorly understood by the public. Additionally, physical activity is infrequently prescribed by health care professionals for prevention or treatment of medical conditions affecting the brain. The *Physical Activity Guidelines Advisory Committee Report, 2008*[1] focused on several mental health outcomes and this literature has substantially grown over the past decade. Drawing from this expanded evidence base, the

2018 Physical Activity Guidelines Advisory Committee Scientific Report addresses this important topic and examines the strength of the scientific evidence that would be the basis for public health guidelines.

The term "Brain Health" can be broadly conceptualized as the optimal or maximal functioning of behavioral and biological measures of the brain and the subjective experiences arising from brain function (e.g., mood). This includes measurements of biological markers of the brain (e.g., structural brain morphology) or the subjective manifestations of brain function, including mood and anxiety, perceptions of quality of life, cognitive function (e.g., attention and memory), and sleep. Several decades of non-human animal research conclude that unequivocal evidence shows that physical activity positively affects behavioral and biological measures of brain health. This research has been supported by a rapidly expanding investigation of physical activity on brain health in humans. As such, for the first time, the scientific field is well-positioned for a comprehensive assessment of this broad and quickly maturing area of science with the aim of understanding and describing the public health implications regarding the relationship between physical activity and the benefits of maintaining brain health throughout the lifespan.

The 2008 Scientific Report[1] concluded that physical activity "reduces the risk of depression and cognitive decline in adults and older adults." In addition, it indicated that "there was some evidence that physical activity would improve sleep" and described "limited evidence that physical activity would reduce distress/well-being and anxiety".[1] In the past 10 or more years, significant advancements have occurred in both the sophistication of instruments and approaches to study brain health and the quality of research examining the influence of physical activity on brain health outcomes.

This 2018 Scientific Report greatly expands on the statements made in 2008 by examining whether regular and long-term engagement in physical activity, as well as brief bouts of activity, are capable of improving cognitive function, perceptions of quality of life, affect, anxiety and depression, and sleep across the lifespan and in disorders and conditions with common deficits (e.g., dementia). This report goes beyond the mental health definition used in the 2008 Scientific Report[1] by further examining physical activity on other aspects of the brain, thus requiring a broader view that is more properly encompassed by the term "brain health." Question 1 examines whether physical activity is an effective method for improving cognitive function across the lifespan or reducing the risk for dementia. In addition, it examines the effects of physical activity on cognitive function in conditions that are often associated with cognitive deficits or problems (e.g., schizophrenia). Question 2 focuses on the influence of physical activity on perceptions of quality of life. The Brain Health Subcommittee approached this problem from a perspective of differentiating quality of life from well-being, with the term "well-being" encompassing both cognitive-evaluative and affective components. The Subcommittee focused on the cognitive-evaluative components and assessed whether physical activity improves general quality of life and health-related domains of quality of life, which are defined as "a reflection of the way that individuals perceive and react to their health status and to other, nonmedical aspects of their lives".[2] Question 3 focuses on the affective components of well-being, and examines the effect of physical activity on core affective responses (i.e., how pleasant and activated people feel during and after activity), state and trait anxiety, depressive symptoms, and clinical depression. Question 4 addresses the research on the influence that physical activity has on sleep outcomes, including in individuals with sleep disorders. In each of these areas, the Subcommittee also examined whether evidence was available for dose-response effects between the physical activity exposure and the outcome, and whether the relationship varied by age, race, sex, weight status, or sociodemographic characteristics.

REVIEW OF THE SCIENCE

Overview of Questions Addressed

This chapter addresses four major questions and related subquestions:

1. What is the relationship between physical activity and cognition?
    a) Is there a dose-response relationship? If yes, what is the shape of the relationship?
    b) Does the relationship vary by sex, race/ethnicity, socioeconomic status, or weight status?
    c) Does the relationship exist across the lifespan?
    d) Does the relationship vary for individuals with normal to impaired cognitive function (i.e., dementia)
    e) What is the relationship between physical activity and biomarkers of brain health?

2. What is the relationship between physical activity and quality of life?
    a) Is there a dose-response relationship? If yes, what is the shape of the relationship?
    b) Does the relationship vary by age, sex, race/ethnicity, socioeconomic status, or weight status?

3. What is the relationship between physical activity and (1) affect, (2) anxiety, and (3) depressed mood and depression?
    a) Is there a dose-response relationship? If yes, what is the shape of the relationship?
    b) Does the relationship vary by age, sex, race/ethnicity, socioeconomic status, or weight status?
    c) Does the relationship exist across a continuum of mood and affective disorders (e.g., depression)?
    d) What is the relationship between physical activity and brain structure and function?

4. What is the relationship between physical activity and sleep?
    a) Is there a dose-response relationship for either acute bouts of physical activity, or regular physical activity? If yes, what is the shape of the relationship?
    b) Does the relationship vary by age, sex, race/ethnicity, socioeconomic status, or weight status?
    c) Does the relationship vary for individuals with normal to impaired sleep behaviors? If yes, for which sleep disorders?

Data Sources and Process Used to Answer Questions

The Brain Health Subcommittee determined that systematic reviews, meta-analyses, pooled analyses, and reports provided sufficient literature to answer all four research questions. The databases searched included PubMed, Cochrane, and CINAHL.

Question 1: What is the relationship between physical activity and cognition?

a) Is there a dose-response relationship? If yes, what is the shape of the relationship?
b) Does the relationship vary by age, sex, race/ethnicity, socioeconomic status, or weight status?
c) Does the relationship exist across the lifespan?
d) Does the relationship vary for individuals with normal to impaired cognitive function (i.e., dementia)
e) What is the relationship between physical activity and biomarkers of brain health?

Sources of Evidence: Systematic reviews and meta-analyses

Conclusion Statements

During the course of the review, it was determined that an accurate description of the state of the science for addressing this question would require several additional subcategories. As such, separate grades were assigned for acute bouts of physical activity (subquestion a), different age groups (subquestion c), and medical conditions with cognitive impairment (subquestion d).

Moderate evidence indicates a consistent association between greater amounts of physical activity and improvements in cognition, including performance on academic achievement tests; performance on neuropsychological tests, such as those involving processing speed, memory, and executive function; and risk of dementia. Such evidence has been demonstrated across numerous populations and individuals representing a gradient of normal to impaired cognitive health status. These effects are found across a variety of forms of physical activity, including aerobic activity (e.g., brisk walking), muscle-strengthening activity, yoga, and play activities (e.g., tag or other simple low organizational games). **PAGAC Grade: Moderate.**

Insufficient evidence is available to determine whether a dose-response relationship exists between physical activity and cognition because of conflicting findings across populations, cognitive outcomes, and experimental approaches. **PAGAC Grade: Not assignable.**

Strong evidence demonstrates that acute bouts of moderate-to-vigorous physical activity have a transient benefit for cognition, including attention, memory, crystalized intelligence, processing speed, and executive control during the post-recovery period following a bout of exercise. The findings indicate that the effects are larger in preadolescent children and older adults relative to other periods of the lifespan. **PAGAC Grade: Strong.**

Insufficient evidence is available to determine the effects of moderate-to-vigorous physical activity on cognition in children younger than age 5 years. **PAGAC Grade: Not assignable.**

Moderate evidence indicates an effect of both acute and long-term moderate-to-vigorous physical activity interventions on brain, cognition, and academic outcomes (e.g., school performance, psychometric profile of memory and executive function) in preadolescent children ages 5 to 13 years. **PAGAC Grade: Moderate.**

Insufficient evidence is available to determine whether a relationship exists between moderate-to-vigorous physical activity and cognition in adolescents ages 14 to 18 years. **PAGAC Grade: Not assignable.**

Insufficient evidence exists regarding the effect of long-term moderate-to-vigorous physical activity on cognition in young or mid-life adults ages 18 to 50 years. **PAGAC Grade: Not assignable.**

Moderate evidence indicates an effect of long-term moderate-to-vigorous physical activity interventions on cognitive and brain outcomes in adults ages 50 years and older. **PAGAC Grade: Moderate.**

Limited evidence suggests that moderate-to-vigorous physical activity has a stronger effect on cognition in older compared to middle-aged and younger adults. Limited evidence also suggests a stronger effect of moderate-to-vigorous physical activity in older adult women compared to older adult men. **PAGAC Grade: Limited.**

No evidence was observed for an effect of physical activity on cognition as a function of socioeconomic status, race/ethnicity, or weight status. **PAGAC Grade: Not assignable**

Strong evidence demonstrates that greater amounts of physical activity are associated with a reduced risk of developing cognitive impairment, including Alzheimer’s disease. **PAGAC Grade: Strong.**

Moderate evidence indicates that moderate-to-vigorous physical activity interventions can improve cognition in individuals with dementia. **PAGAC Grade: Moderate**

Moderate evidence indicates that moderate-to-vigorous physical activity can have beneficial effects on cognition in individuals with diseases or disorders that impair cognitive function, including attention deficit hyperactivity disorder, schizophrenia, multiple sclerosis, Parkinson’s disease, and stroke. However, data are lacking for several other major conditions that are clinically associated with impaired cognitive function (i.e., autism, cancer). **PAGAC Grade: Moderate.**

Moderate evidence indicates that moderate-to-vigorous physical activity positively affects biomarkers of brain health and cognition. Physical activity-induced changes to these biomarkers have been observed across much of the lifespan, with considerably more evidence in children and older adults than in other age groups. **PAGAC Grade: Moderate.**

Limited evidence suggests that moderate-to-vigorous physical activity has a stronger effect on cognition in older compared to middle-aged and younger adults. Limited evidence also suggests a stronger effect of moderate-to-vigorous physical activity in older adult women compared to older adult men. No evidence was observed for an effect of physical activity on cognition as a function of socioeconomic status, race/ethnicity, or body mass index. **PAGAC Grade: Limited.**

Strong evidence demonstrates that acute bouts of moderate-to-vigorous physical activity have a transient benefit for cognition, including attention, memory, crystalized intelligence, processing speed, and executive control during the post-recovery period following a bout of exercise. The findings indicate that the effects are larger in preadolescent children and older adults relative to other periods of the lifespan. **PAGAC Grade: Strong.**

Review of the Evidence

Cognitive and brain health are important to many facets of life, including educational and academic attainment, job performance, quality-of-life, and for diseases and disorders that directly or indirectly influence these outcomes. For this question, measurement of cognition includes a broad range of outcomes, including academic achievement, performance on neuropsychological tests that assess several processes, such as attention, memory, processing speed, and executive function (an umbrella term that represents a number of goal-directed processes that support thinking, reasoning, and problem solving), and dementia diagnoses. However, cognition—as defined in this question—does not include measurement of intelligence, motor function, personality, mood (addressed below in Question 3), and sensory and perceptual function.

To address this question, the Subcommittee used 32 meta-analyses and systematic reviews of the literature that examined whether results from randomized controlled trials (RCTs) and prospective longitudinal studies are associated with cognitive outcomes. These reviews included results from healthy young (N=3[3-5]) and older adults (N=3[6-8]), children (N=4[9-12]), and adolescents (N=2[13, 14]) as well as populations with impaired cognition, such as children and adults with attention deficit hyperactivity disorder (ADHD) (N=3[15-17]), adults with mild cognitive impairment or dementia (N=4[18-21]), multiple sclerosis (N=1[22]), Parkinson's disease (N=1[23]), schizophrenia (N=1[24]), and stroke (N=1[25]). We also included meta-analyses and reviews of the effects of acute exercise on cognitive outcomes (N=4[26-29]), the effects of sedentary behavior on cognitive outcomes (N=1[30]), and the effects of physical activity on biomarkers of brain health (N=4[31-34]). Included in these systematic reviews and meta-analyses were more than 350 empirical studies with more than 40,000 individuals.

Evidence on the Overall Relationship

The Subcommittee concluded that there is moderate evidence for an association between greater amounts of physical activity and improvements in cognition, including performance on academic achievement tests; performance on neuropsychological tests, such as those involving processing speed, memory, and executive function; and risk of dementia. Such evidence has been demonstrated across numerous populations and individuals representing a gradient of normal to impaired cognitive health status. These effects are found across a variety of forms of physical activity, including aerobic activity (e.g., brisk walking), muscle-strengthening activity, yoga, and play activities (e.g., tag or other low organizational games). The findings regarding the relationship between levels of physical activity and cognition show considerable consistency across a variety of experimental designs and cognitive outcomes used to assess this relationship. The effect sizes of physical activity on cognition ranged from 0.10 to 0.67 standard deviations (SD), depending on the population, cognitive outcome, experimental design, and physical activity exposure. To place this effect size in perspective, a diagnosis of vascular cognitive impairment, non-dementia (a prevalent sub-category of mild cognitive impairment), is considered when dementia is absent with cerebrovascular involvement, and impairment is evident in at least one cognitive domain that is at least 1 and typically 1.5 SD outside of age- and education-adjusted norms. These impairments occur most commonly in the domain(s) of executive function. Thus, these effect sizes for cognitive and brain health outcomes are generally considered small to moderate in magnitude, and consistently positive. Although the studies reviewed indicate that the effects of physical activity influence numerous cognitive domains, the positive effects have been demonstrated most consistently, and are most frequently studied, in the executive function domain. The improvements in executive function are temporary following acute bouts of physical activity, and become more sustained following participation in an ongoing physical activity routine. As is described below, the Subcommittee indicated a moderate, rather than strong, conclusion because the relationship between physical activity and cognition varied based on specific factors.

Evidence on Specific Factors

Lifespan: The effect of physical activity on cognition has been observed at different stages of the lifespan. However, the quantity of evidence is not uniform across the lifespan, and the preponderance of data come from research in preadolescent children, young adults, and older adults.

Across childhood, effects ranged from non-significant,[12] to unable to be determined in children younger than age 5 years because of a small number of studies with poor quality experimental designs and a high risk of bias,[10] to significant during school-age years.[9, 11] Cognitive domains with the largest effects included executive function, attention, and academic achievement,[9, 11] but absolute measures of effect sizes were unable to be determined from these studies. In studies examining effects of engaging in physical activity on ADHD, the effect sizes ranged from 0.18 to 0.77 in favor of physical activity improving cognitive performance.[15-17] Cognitive domains most commonly affected in ADHD included executive function (e.g., attention, inhibition, impulsivity).[15, 17]

In adolescents, there were few rigorous experimental studies with control groups, few studies with well-described parameters and definitions of physical activity, and few studies with measures of cognitive function or academic achievement. Despite these limitations, the several reviews reported effect sizes in favor of physical activity ranging up to 0.37,[14] while a systematic review indicated that 75 percent of studies in adolescents reported an association between physical activity and better cognitive function.[13] However, as stated above, given that there were few rigorous experimental studies with randomized designs included in the reviews, the size and quality of the evidence is insufficient to provide a reliable grade.

In young and mid-life adults, effect sizes ranged from 0.12 to 0.15[4, 5] for physical activity improving cognition. Effects were largest for the cognitive domains of executive function, attention, processing speed,[5] and short-term memory.[4] In cognitively normal older adults, effect sizes ranged from non-significant[7] to .20 [8] to 0.48[6] in favor of physical activity interventions positively influencing cognitive outcomes. Effect sizes were greatest for measures of executive function,[6] global cognition,[8] and attention.[7]

Impaired cognitive function: Strong evidence demonstrates that greater amounts of physical activity are associated with a reduced risk of cognitive decline[20] and risk of dementia, including Alzheimer's disease (AD).[18] For example, a meta-analysis of 15 prospective studies of 1 to 12 years in duration with more than 33,000 participants found that greater amounts of physical activity were associated with a 38 percent reduced risk of cognitive decline.[20] Another meta-analysis of 10 prospective studies with more than 20,000 participants reported that greater amounts of physical activity were associated with a 40 percent reduced risk of developing AD.[18] Moderate evidence indicates that physical activity interventions can improve cognition in individuals with dementia, including AD.[19, 21] For example, one meta-analysis of 18 RCTs from 802 dementia patients reported an overall effect size of 0.42 and that this effect was also significant for individuals with AD or non-AD dementias.[19] These positive effects were found for interventions that were both high-frequency physical activity and low-frequency physical activity. However, given the heterogeneity in the assessment methods, insufficiently detailed description of the physical activity interventions, and moderate risks for bias, the strength of the evidence is rated as moderate. Moderate evidence also indicates that physical activity improves cognitive function in individuals with other diseases or disorders that impair cognitive function, including ADHD, schizophrenia, multiple sclerosis (MS), Parkinson's disease, and stroke.

Results regarding the efficacy of interventions to improve cognitive function in individuals with MS are conflicting.[22] However, interventions show the largest effects on executive function, learning, memory, and processing speed. (For more details on the effects of physical activity in individuals with MS, see *Part F. Chapter 10. Individuals with Chronic Conditions*.) Studies of Parkinson's disease show significant improvements in cognition following exercise interventions,[23] with the largest effect sizes in domains of general cognitive function and executive function. In schizophrenia, moderate-to-vigorous physical activity interventions have shown improvements in measures of global cognition, working memory, and attention, with effect sizes of 0.43.[24] In stroke populations, engaging in physical activity interventions shows significant improvements in domains of global cognition, attention, memory, and visuospatial abilities.[25]

Transient benefits have been observed resulting from acute bouts of physical activity in children with ADHD, but such benefits have not been frequently measured in individuals with other conditions. Despite consistency in effect sizes across conditions, the manner in which the studies were conducted and the quality of the cognitive outcomes and measures are variable. Thus, evidence on the effects of acute bouts of exercise on cognition in populations with cognitive deficits is insufficient.

Biomarkers: Effects also have been reported on biomarkers of brain health, including neurotrophic factors[32] and task-evoked brain activity, volume, and connectivity[31, 33, 34] across the lifespan, but the preponderance of data comes from work in children and adults over the age of 60. For example, effects of physical activity on volumetric and brain activity patterns are more frequently reported, and studied, in older adults and children than middle-aged adults.[31] Similarly, effects of physical activity on measures of white matter might be less understood across the lifespan compared to functional and volumetric data, but research on the effects of physical activity on white matter in mid-life is especially scarce.[34] A number of approaches have been used to assess biomarkers of brain health and cognition, including grey matter morphology (i.e., volume, density, and thickness), white matter integrity, and cortical electrophysiology. Other approaches include assessing neural networks, including evoked responses from cognitively demanding tasks; circulating neurotrophic factors linked to cognitive function and neuroplasticity; cerebral blood flow; task-evoked functional activity; resting state functional connectivity; magnetic resonance spectroscopy; and positron emission tomography. Most of the work in this area has emerged in the last 5-10 years and has used functional or volumetric approaches to assess the health and integrity of the brain.[31, 34] The majority of studies in this rather small but growing area report small-to-moderate positive effect sizes ranging from 0.1 to 0.7 of physical activity on brain outcomes.

Demographic factors, weight status, and physical activity type: The included reviews rarely reported whether effects of physical activity on cognitive outcomes were modified by age, sex,[6] race/ethnicity, socioeconomic status, presence of obesity, baseline fitness levels,[3] sedentary behavior[30] or physical activity intensity, frequency, or duration. However, one of the more consistent effects is that females show larger effect sizes than males.[6]

Dose-response: The included reviews rarely report whether a dose-response relationship was observed for the effects of physical activity on cognitive outcomes. However, one meta-analysis[6] reported that among older adults, larger effects on cognition were observed in randomized controlled trials in which physical activity bouts lasted 46-60 minutes in duration (compared to bout durations lasting 15-30 minutes and 31-45 minutes) and the interventions occurred for at least 6 months compared to interventions lasting 1-3 and 4-6 months. In addition, physical activity has a general effect across the aspects of cognition that were studied (i.e., executive, controlled, spatial, and speed), but the effect was selectively and disproportionately larger for tasks requiring greater amounts of executive control.[6]

Acute bouts of physical activity: Studies demonstrate a small, transient improvement in cognition following the cessation of a single, acute bout of physical activity, with effect sizes ranging from 0.014 to 0.67.[26-29] Reported effects were most consistent for domains of executive function,[26-29] but significant benefits were also realized for processing speed, attention, memory, and crystalized intelligence, the latter of which is a measure of general and verbal knowledge (e.g., what is the name of the first president of the United States).[26, 27, 29] Larger effects were also realized for preadolescent children and older adults relative to adolescents and young adults.[28]

Exercise intensity of an acute bout of activity had an effect on changes in cognition, with some findings suggesting an inverted-U shaped curve, as moderate-intensity exercise demonstrated a larger effect than light- and vigorous-intensity exercise,[27, 29] and other studies indicating that very light-, light-, and moderate-intensity exercise benefited cognition, but hard-, very hard-, and maximal-intensity exercise intensity demonstrated no benefit.[26] The timing of the assessment of cognition relative to the cessation of the acute bout of exercise also demonstrated differences in the magnitude of the effect, with negative effects in cognition observed during the first 10 minutes following the exercise bout and the largest positive effect observed from 11 to 20 minutes and a smaller effect observed after 20 minutes following the acute physical activity bout.[26] Physical activity bouts lasting 11 to 20 minutes demonstrated the greatest benefits, with bouts lasting less than 11 minutes or more than 20 minutes having smaller effects on cognition.[26]

Overall, this line of research warrants a moderate grade because studies reported significant variability in the quality of study design, including a lack of appropriate analytical approaches (e.g., intent-to-treat analyses), poor reporting of adherence and compliance, variability in how active participants were before assignment to the intervention, unknown reliability and validity of the cognitive assessments, inadequate blinding, and variability in control group conditions. As such, the studies included in these meta-analyses and systematic reviews generally have a high risk of bias and low precision. However, despite these limitations, these studies appear to have high applicability, generalizability, and consistency. The effects are also detectable using acute exercise paradigms, where preadolescent children and older adults demonstrate large and consistent positive effects of moderate-intensity physical activity,[26-29] with some evidence to support 11 to 20 minutes in duration as being optimal for cognitive outcomes.[26]

For additional details on this body of evidence, visit: https://health.gov/paguidelines/second-edition/report/supplementary-material.aspx for the Evidence Portfolio.

Comparing 2018 Findings with the 2008 Scientific Report

The 2008 Scientific Report[1] concluded that strong evidence demonstrated that physical activity delays the incidence of dementia and the onset of cognitive decline associated with aging. It also indicated that physical activity improves cognitive symptoms associated with dementia. Thus, the evidence described here considerably expands that described in 2008 by including significantly more observational studies and RCTs. This research finds that physical activity influences cognitive function across the lifespan, including both cognitively normal and impaired populations (e.g., schizophrenia). The effects are consistent across a variety of methods for assessing cognition (e.g., academic achievement and dementia diagnoses). The 2018 Scientific Report also demonstrates, for the first time, the positive effects of physical activity on biomarkers of brain health obtained from neuroimaging techniques (e.g., brain volume). Finally, the 2018 Scientific Report describes evidence on acute bouts of activity for improving cognitive function.

Public Health Impact

In 2017, the annual direct costs of Alzheimer's disease to American society was estimated to be $259 billion. In 2010, it was estimated that in the last 5 years of life, the cost of dementia per person was $287,000. Most of these costs are spent by the federal government under Medicare.[35] Given the expected increase in the number of Americans older than age 65 years, the costs associated with Alzheimer's disease or other dementias may increase to about $758 billion by the year 2050.[35] Physical activity may be a highly effective approach for improving function and mitigating costs associated with Alzheimer's disease and other cognitive impairments. In an analysis by,[36] about 13 percent (nearly 4.3 million) of Alzheimer's disease cases worldwide and about 21 percent of Alzheimer's disease cases in the United States are attributable to physical inactivity. According to these results, a 25 percent reduction in physical inactivity in the United States could potentially prevent 230,000 cases. The results from the 2018 Scientific Report provide support for the argument that physical activity reduces the risk of Alzheimer's disease and other dementias and that increasing physical activity in individuals with Alzheimer's disease could improve cognitive function.

The public health impact of the results summarized in the 2018 Scientific Report goes beyond Alzheimer's disease and dementia by demonstrating that physical activity influences cognitive function in children and healthy older adults. For example, academic achievement is a predictor of future job opportunities[37] and adult health outcomes.[38, 39] Thus, these findings, which indicate that increasing physical activity during childhood may positively influence cognition and academic achievement, may have further downstream effects on many features of adult health and quality of life.

Healthy older adults, even in the absence of a dementia, often show evidence for cognitive losses and decline, especially on measures of processing speed, memory, and executive function. It is estimated that by the year 2050, the population of adults older than 65 years in the United States will reach 83.7 million, which is nearly double the 2012 level of 43.1 million. An increase in the prevalence of cognitive decline is expected given this increase in the number of adults over the age of 65. This report suggests that physical activity may be an effective approach for improving cognitive function in this population.

Finally, we conclude that moderate evidence indicates that physical activity is an effective approach for improving cognitive function in populations that often experience cognitive deficits including ADHD, Parkinson's disease, multiple sclerosis, and schizophrenia. Evidence of such widespread benefits for physical activity across the lifespan and in individuals with a range of cognitive deficits, suggest that physical activity could be used as both an important first-line approach for managing cognitive symptoms and for improving cognitive function in all individuals living in the United States.

In summary, we provide compelling evidence that physical activity is related to a number of positive cognitive outcomes. This evidence comes from a variety of assessments that measure changes in brain structure and function, cognition, and applied academic outcomes. Further, a positive effect of physical activity on cognition is observed in children and adults, as well as in several special populations, suggesting that increasing physical activity may improve cognition in most, if not all, populations in the United States. Accordingly, such findings may serve to promote better cognitive function in healthy individuals, and serve to improve cognitive function in those suffering from certain cognitive and brain disorders. However, available scientific evidence is limited in certain populations (e.g., middle-aged adults, those with autism spectrum disorder), and thus more research is needed to better understand the relation of physical activity to cognitive function in these individuals. Additionally, the modifying effects of sedentary behavior and other health outcomes (e.g., adiposity) on cognitive function are not well understood at this time. (For more details on the effects of sedentary behavior on other health outcomes, see *Part F. Chapter 2. Sedentary Behavior*.) However, as noted here, the evidence linking physical activity to positive cognitive outcomes is moderate, and a substantial portion of the population benefits from physical activity participation.

Question 2. What is the relationship between physical activity and quality of life?

a) Does this relationship vary by population subgroup?
b) Is there a dose-response relationship? If yes, what is the shape of the relationship?
c) Does the relationship vary by age, sex, race/ethnicity, socioeconomic status, or weight status?

Data Sources: Systematic reviews, meta-analyses, pooled analysis

Conclusion Statements

Strong evidence demonstrates that, for the general population, greater amounts of physical activity are associated with a positive perception of quality of life. **PAGAC Grade: Strong.**

Strong evidence demonstrates that, for older adults (older than age 50 years; primarily 65 years and older), physical activity improves health-related quality of life when compared with minimal or no-treatment controls. **PAGAC Grade: Strong.**

Strong evidence demonstrates that, for adults ages 18 to 65 years, physical activity improves health-related quality of life when compared with minimal or no-treatment controls. **PAGAC Grade: Strong**.

Limited evidence suggests that among youth ages 5 to 18 years, lower levels of sedentary time are associated with higher perceptions of global quality of life. **PAGAC Grade: Limited**

Moderate evidence indicates that physical activity improves quality of life in individuals with schizophrenia. **PAGAC Grade: Moderate.**

Limited evidence suggests that physical activity improves quality of life for adults with major clinical depression. **PAGAC Grade: Limited.**

Insufficient evidence is available because of a small number of controlled studies with mixed results to determine the relationship between physical activity and quality of life in individuals with dementia. **Grade: Not assignable.**

Insufficient evidence is available to determine whether a dose-response relationship exists between physical activity and quality of life across populations. **PAGAC Grade: Not assignable.**

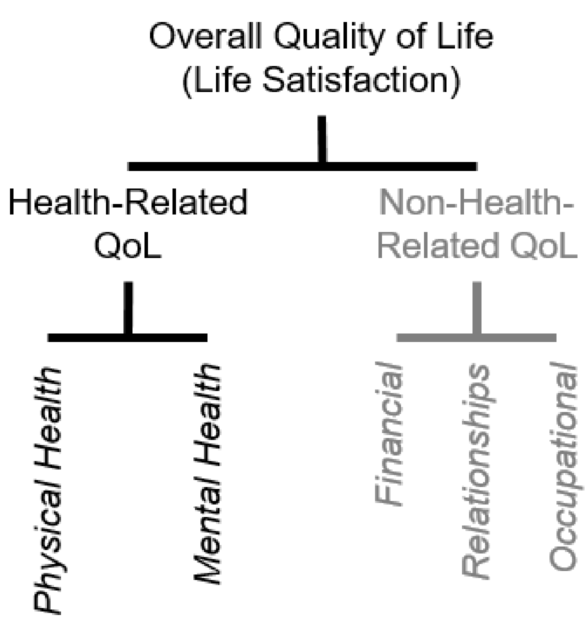
Insufficient evidence is available to determine whether the association between physical activity and quality of life varies as a function of race/ethnicity, socioeconomic status, or body mass index. **PAGAC Grade: Not assignable.**

Review of the Evidence

Introduction

Quality of life (QoL) "is a reflection of the way that individuals perceive and react to their health status and to other, nonmedical aspects of their lives.".[2] In its broadest form, QoL is sometimes referred to as satisfaction with life.[40] QoL has a hierarchical structure, with domain-specific components under the umbrella of overall QoL (Figure 3-1). One domain typically represents health-related QoL (HRQoL)[41]; this domain is often split further into sub-domains/subscales of physical health-related QoL (e.g., evaluations of physical function) and mental health-related QoL (e.g., emotional health).

Figure 3-1. Hierarchical Structure of Quality of Life



Maintaining or improving QoL is a universal goal. Being physically active has been suggested as one way to enhance perceptions of, and feelings of, QoL. This question focuses on the scientific literature that describes QoL as experienced by the general population across the lifespan. It also includes an assessment of the effects of physical activity on QoL in individuals with mental health issues. QoL among individuals who have a chronic physical condition, such as diabetes or osteoarthritis, is considered in *Part F. Chapter 10. Individuals with Chronic Conditions.*

The literature reviewed here focused on QoL and HRQoL, specifically. Searches were not conducted on "well-being" or its derivatives, such as subjective well-being, positive well-being, or psychological well-being. Those well-being concepts typically blend cognitive/evaluative and affective components[40] and this question is limited to the cognitive/evaluative aspects widely known as quality of life.

Literature Reviewed

To answer this question, the Subcommittee reviewed 18 systematic reviews across the following populations: older adults (general),[42-51] older adults (with dementia),[52] adults,[53-58] youth,[59] individuals with schizophrenia,[60, 61] individuals with depression,[52] and 14 meta-analyses across the following populations: adults,[62-64] older adults (general),[65-70] older adults (with dementia),[71, 72] schizophrenia,[73] and depression[74, 75] We also included one pooled analysis on older adults.[76]

General Population - Older Adults

The number of studies per review ranged from 6[46] to 53.[42] However, many reviews included outcomes other than QoL, such as body composition and muscle strength. Thus, the number of studies reviewed that included both physical activity and QoL was smaller, ranging from 1[46] to 42,[43] with many reviews including fewer than 10 studies: (N=2[65]), (N=3[42]), (N=4[45]), (N=4[50]), (N=5[44]), (N=6[49]).

The definition of "older adult" varied by study and primarily included individuals ages 65 years and older, but all studies included individuals of at least age 50 years and older. The systematic reviews covered the following timeframes: inception (of the database) to January 2016,[42] 2000-November 2012,[43] 2000 to April 2015,[44] 1966 to December 2006,[45] inception to February 2010,[46] 2006 - December 2013,[47] 1955 – 2008,[48] 1998 to July 2011,[49] inception to December 2013,[50] 1993 - December, 2007.[51]

The meta-analyses covered an extensive timeframe: 2001 to June 2010,[65] inception to September 2010,[66] 1973 to August 2007,[67] 1950 to November 2010,[69] inception to July 2012,[70] inception to May 2013.[68]

QoL was most often conceptualized as HRQoL, and assessed using the 36-item Short Form Health Survey (SF-36), a widely-used self-report measure of perceived physical and mental health and functioning.[42-45, 49, 65-70, 76] Other QoL measures that were used across studies included: MacNew global score,[42] WHOQoL-Bref,[43] EuroQoL Group 5 - Dimension Self-Report Questionnaire,[46, 68] Mental health-related quality of life,[47] World Health Organization (WHO) QoL for Elderly Scale,[50] Satisfaction with Life Scale and Life Satisfaction Index-A,[66] PGCMS and DQoL,[68] and QoL operationalized as depression, vitality, and perceived health.[48]

General Population - Adults

The number of studies reviewed ranged from 14[53, 55] to 56.[62] The number of studies reviewed that included both physical activity and QoL was 179.

The definition of adult varied from study to study. However, studies typically reported a mean age older than 18 years and younger than 65 years.[53-55, 57, 58, 63, 64] The systematic reviews covered the following timeframes: 1806 to 2006,[53] inception to November 2009,[54] 1985 to December 2014,[55] 1980 to August 2010,[57] 2001 to January 2016,[63] inception to May 2015,[58] and inception to February 2013.[56] The meta-analyses covered: inception to September 2007,[62] and inception to 2011.[64]

QoL was most often conceptualized as HRQoL, and assessed with the SF-36.[54, 57, 58, 62, 64] Other QoL measures included Satisfaction with Life Scale,[62] and WHOQoL.[54, 58, 62]

General Population - Youth

One systematic review was included, and covered inception to October 2013. A total of 91 studies were included, but only 14 addressed a QoL outcome. The mean age of those 14 studies ranged from approximately 10 years of age to approximately 17 years of age.[59]

Individuals with Schizophrenia

Systematic reviews that included a search for both physical activity and QoL ranged from 10 studies including 332 participants in a qualitative analysis,[60] an update to this review that included 13 studies involving 549 participants, [61] and a meta-analysis with 29 studies including 1,109 individuals with schizophrenia.[73] Although the earlier reviews,[60, 61] included numerous outcomes, the most recent systematic review and meta-analyses included 770 participants in controlled or non-controlled studies in which QoL was systematically measured.[73]

The reviews covered the following timeframe: inception to July 2011,[60] July 2011 to October 2014,[61] and inception to 2015.[73]

QoL was most often conceptualized as HRQoL, and assessed with the SF-36 or SF-12, the WHOQoL-Bref, and the EuroQoL Group 5- Dimension Self-Report Questionnaire.[73]

Individuals with Depression

The reviews covered the following timeframes: inception to June 2013,[52] inception to May 2013,[74] and inception to January 2013.[75] Two of these reviews included 7 studies, and another that examined the effects of yoga included 12 RCTs.

The number of studies reviewed that included both physical activity and QoL (N=10 studies) is much smaller than the total number of studies in the systematic reviews, ranging from one study[75] that included only the Mental Component of the SF-36, four studies in older adults with depression,[52] and a meta-analysis including four studies comparing physical activity to non-active controls, one study comparing physical activity to antidepressant medication, and one with comparison to cognitive therapy for depression.[74]

QoL was conceptualized as HRQoL, and assessed in most cases with the SF-36.[52, 74, 75]

Individuals with Dementia

The number of studies ranged from 2 studies[52, 71] to 13 studies.[72] The reviews covered the following timeframes: inception to February 2016,[72] inception to June 2013,[52] and inception to February 2009.[71] Notably, these reviews included numerous other outcomes. QoL was most often conceptualized as HRQoL, and assessed with the SF-36 or disease-specific scales for patients with dementia,[71, 72] such as the Alzheimer's Disease Related Quality of Life (ADQRL).[52] The total number of studies with both physical activity interventions and QoL was 14. These included approximately 920 individuals for qualitative analyses, within which 6 studies with 385 individuals underwent quantitative meta-analyses. The latter provided little evidence for physical activity to improve QoL in individuals with dementia.[72]

Physical Activity Exposures

Types of physical activity varied across studies and included multicomponent exercise interventions,[44-46, 48, 49, 52, 54, 55, 62, 65-67, 71, 72] aerobic training,[42, 43, 54, 56, 62, 72, 73] resistance training,[43, 52, 56, 62, 70, 72, 73] pilates,[50] Zumba dance,[58] active video games,[47] qigong and tai chi,[51, 52, 64] gardening,[63] walking,[56, 71] and yoga.[69, 73, 75] Some studies focused on physical activity volume, typically during leisure time, and did not differentiate type of activity.[53, 57] Of the studies reviewed, only one presented specific information on the frequency, intensity, time, and type (FITT) principles for exercise prescription,[70] however, the FITT principles were not reported in relation to QoL outcomes.

Evidence on the Overall Relationship

General Population - Older Adults

Overall, results showed that physical activity consistently resulted in improvements in QoL in older adults. One meta-analysis reported that collectively, exercise programs (1,317 participants) improved the QoL (overall and health-related combined) of older adult participants (Z=2.23, P=0.03), and the pooled standardized mean difference (SMD) was 0.86 (95% confidence interval (CI): 0.11-1.62).[68] In another meta-analysis, statistically significant improvements were found for the physical function subscale of the physical function component summary score of the SF-36 as a result of physical activity (Hedges' g=0.41, 95% CI: 0.19-0.64, P<0.001).[67] In that review, no differences were found for the other health-related quality of life (HRQoL) subscales, though the subscales of vitality (energy/fatigue), social functioning, role limitations due to emotional problems, and mental health (emotional well-being) were in the positive direction.[67] Some reviews showed a wide range in QoL score improvement, from 17.1 percent to 178 percent, and SF-36 subscales that improved were physical function, role limitations due to physical health or emotional problems, pain, general health, and vitality (energy/fatigue).[42]

A systematic review of 10 studies on Pilates in the elderly included 4 studies showing improvement in domains of HRQoL including World Health Organization's Quality of Life domains of sensorial abilities, activities, social participation, intimacy, while a meta-analysis pooling effects of HRQoL, depression, and activities of daily living showed a large composite positive effect size (Hedges' g=0.93; 95% CI: 0.631-1.25, P<0.001).[50] The Raymond et al[70] systematic review found improved HRQoL in six sub-scales of the SF-36, including physical functioning, role limitations due to physical health, vitality (energy/fatigue), social functioning, role limitations due to emotional problems, and mental health (emotional well-being) (P range <0.001-0.04); and a study in the Stevens et al[49] systematic review showed significant improvements in vitality (energy/fatigue; odds ratio (OR)=4.43; 95% CI: 0.31-8.54) and general health (OR=5.46; 95% CI: 1.69-9.24) scores in intervention groups vs. controls. A review of yoga studies reported that for the composite physical health subdomain of the SF-36, the estimated standardized mean difference (0.65; 95% CI: 0.02-1.28) favored the yoga intervention. On the composite mental health subdomain scale of the SF-36, the estimated standardized mean difference again favored yoga (SMD = 0.66; 95% CI: 0.10–1.22).[69]

Physical activity as part of other activities that involve mental and physical components, such as qigong and tai chi, hold great potential for improving QoL in both healthy and chronically ill individuals.[51] However, effect sizes were not included, it was not reported which of the subdomains of QoL were improved, and results and conclusions were not separated by healthy and chronically ill participants. Moreover, given the mind-body nature of these modes of physical activity, it is not clear whether changes in QoL would be the result of changes in physical activity or other components of the activity (e.g., breathing, meditation).

In a pooled analysis,[76] participants who were active for more than 150 minutes per week of physical activity but then dropped to fewer than 150 minutes per week from baseline to 6 months showed a 11.8 point drop (P<0.001) in SF-36 physical function scores. In contrast, those who were active for fewer than 150 minutes per week of physical activity but then increased to more than 150 minutes per week from baseline to 6 months showed an increase of 5.1 points in SF-36 physical function scores.[76] These results indicate the importance of maintaining physical activity for maintaining HRQoL in late adulthood.

The effects of physical activity on non-HRQoL domains are more equivocal. Studies examining non-HRQoL domains show consistent and positive associations between physical activity and the domains of functional capacity, general QoL, and autonomy. These domains have been related to QoL in the elderly. However, few studies were methodologically rigorous. Effect sizes were generally small or moderate and varied widely between studies and across QoL domains.[43]

Among frail older adults, one review found no significant differences in QoL among studies that used water exercises, flexibility exercises, tai chi, and resistance exercises[65] and others had too few studies to make a conclusion.[46-48] These studies of QoL were not intended to capture objective measures of physical function (e.g., balance, gait speed), as the measures of QoL were developed to assess perceptions of functioning. Thus, in the context of frail older adults, beneficial effects of physical activity on measures of physical function may not be immediately apparent on perceptions of functioning that are captured by common instruments assessing QoL.

In summary, the evidence points to a positive effect of physical activity on both overall and health-related QoL in older adults. Physical health-related QoL has been investigated more consistently than mental health-related QoL. The limited available literature suggests that the physical activity effects on physical and mental health composite scores appear to be similar in both direction and magnitude. There were insufficient studies and sample sizes to adequately analyze effects of different exercise training modalities on QoL, few studies with extended follow-up, and few studies that differentiated the effects as a function of functional ability or frailty status.

General Population - Adults

Of nine studies,[53-58, 62-64] seven (78%) concluded that a positive association existed between physical activity and overall QoL.[53, 54, 56-58, 63, 64] Of six that studied physical function, all (100%) concluded that a positive association existed between physical activity and the physical subdomain of QoL.[53-55, 57, 58, 62] All nine studies examined psychological QoL, and eight out of the nine (89%) concluded that a positive association existed between physical activity and QoL.[53, 54, 56-58, 62-64]

Of the nine studies, the exposure variable was primarily aerobic physical activity, mostly leisure-time physical activity in four,[53, 54, 57, 62] walking in one,[56] gardening in one,[63] Zumba dancing in one,[58] qigong and related alternative or complementary types of physical activity in one,[64] and a mixture of aerobic, strength training, and alternative or complementary types in one.[55]

The one meta-analysis reporting average effect sizes yielded a positive but not statistically significant trend for physical activity on overall QoL (N=7; SMD=0.11; 95% CI: -0.03 to 0.24) and statistically significant positive effect sizes for physical health QoL (N=6; SMD=0.22; 95% CI: 0.07-0.37) and psychological well-being (N=6; SMD=0.21; 95% CI: 0.06-0.36).[62]

Another review included 15 studies, of which 4 RCTs, 3 cohort studies, and 5 cross-sectional studies provided sufficient information about the physical activity exposure and measurement of QoL.[53] Three of the four RCTs reported significant improvements in reported QoL for the exposure group compared with the control group. All three of the cohort studies reported significantly higher QoL among those who were more physically active. All five of the cross-sectional studies reported a positive association between more physical activity and higher assessed QoL.

Pucci et al[57] included 58 individual studies, 18 of which assessed QoL with the SF-36. Three of the 18 were cohort studies and 15 were cross-sectional. Of the three cohort studies, all reported positive associations for mental health and two of the three for physical health and vitality. Of the 15 cross-sectional studies, 13 reported positive associations between physical activity and the physical health domain and 9 reported positive associations for the mental health domain, with positive associations for subdomains related to vitality (9 studies) and pain (8 studies).

The other six reviews reported similarly positive associations between greater amounts of physical activity and higher assessments of QoL.[54-56, 58, 63, 64]

General Population - Youth

There was no evidence available on the relationship between physical activity and QoL among youth. The evidence pertaining to the relationship between sedentary behavior and QoL among youth comes from one systematic review.[59] Of the 91 studies included in the review, 12 cross-sectional studies and 3 longitudinal studies provided information about the relationship between sedentary behavior and QoL among youth ages approximately 9 to 17 years. Nine of the 12 cross-sectional studies and 2 of the 3 longitudinal studies reported a negative association between sedentary behavior time and QoL.

Individuals with Dementia

Overall, little evidence supports a relationship between physical activity and QoL for individuals with dementia. A qualitative analysis of 14 studies reveals only 5 out of 13 studies reporting a positive relationship between physical activity interventions and improvements in QoL in this population.[52, 71, 72] Meta-analyses showed no significant differences in five out of six studies for QoL outcomes for individuals in physical activity intervention groups compared with controls.[72] The average effect was small and non-significant (SMD=0.33; 95% CI: -0.21 to 0.87) although this effect was inflated by a single outlier. Without that outlier, the effect was near zero (SMD=0.06; 95% CI: -0.10 to 0.22). These reviews examined a diversity of physical activity modalities, including aerobic training, strength training, combined aerobic and resistance training, flexibility, balance, yoga, and tai chi.[72]

Two studies of dementia patients found positive effects on selected domains of QoL, including physical role functioning,[71] while a more recent review with six studies had conflicting results for the association between physical activity and QoL in dementia.[52]

In summary, the evidence for a relationship between physical activity and QoL is conflicting, in part due to the small number of studies that systematically evaluated QoL, and inconsistency in outcome measures of QoL. In addition, the number of studies and sample sizes were insufficient to adequately analyze effects of different exercise training modalities on QoL, and no studies differentiated their effects based upon the categorical type of dementia (AD, Alzheimer's Disease and related dementias) or the stage(s) of dementia in the participants.

Individuals with Schizophrenia

Moderate evidence supports the positive effects of physical activity on QoL for individuals with schizophrenia. These results come from consistent findings from systematic reviews from inception to 2014 for inpatients and outpatients across the adult age span.[60, 61] The positive effects of physical activity are shown in a meta-analysis that examined 11 controlled and uncontrolled intervention studies, with moderate standardized effect sizes for overall QoL (Hedges' g=0.55, *P*<0.01), as well as for domains of physical (Hedges' g=0.50), social (Hedges' g=0.67), and environmental QoL (Hedges' g=0.62[73]). Mental QoL did not change in this population (Hedges' g=0.38). Both aerobic exercise (Hedges' g=0.58) and yoga interventions (Hedges' g=0.58) were found to be effective, consistent with reports from other systematic reviews. In addition to these effects of physical activity on QoL, the meta-analyses show that physical activity is associated with improvements on several other important outcomes that are related to QoL, including total symptom severity (Hedges' g=0.39, *P*<0.001); positive symptoms (Hedges' g=0.32, *P*<0.01), negative symptoms (Hedges' g=0.49, *P*<0.001) and general symptoms (Hedges' g=0.27, *P* <0.05); and global functioning (Hedges' g=0.32, *P*<0.01). Collectively, these consistently small to moderate effects indicate that individuals with schizophrenia and schizophrenia spectrum disorders may show improvements in QoL with physical activity.

Individuals with Depression

Limited evidence from 11 controlled studies suggests that physical activity improves selected domains of QoL for adults with major clinical depression, while the evidence for bipolar disorder is insufficient and understudied.[52, 74, 75]

Meta-analyses of four RCTs in adults with clinical depression comparing physical activity to either placebo or no physical activity found no statistically significant differences for the mental (SMD=-0.24; 95% CI: -0.76 to 0.29), psychological (SMD=0.28; 95% CI: -0.29 to 0.86), and social domains (SMD=0.19; 95% CI: -0.35 to 0.74).[74] However, two studies reported a moderate effect size for improved environment domain (SMD=0.62; 95% CI: 0.06-1.18), and four out of four studies reported a moderate effect size for improved physical domain (SMD=0.45; 95% CI: 0.06-0.83) in favor of the group assigned to structured physical activity. By contrast, controlled studies comparing physical activity to other therapeutic modalities for the treatment of depression, including cognitive therapy, as well as antidepressant medication, showed no between-group differences in the QoL mental or physical domains.[74] A review of four RCTs in older adults with depression found that physical activity improved

QoL in most reports.[52] One RCT comparing yoga to a relaxation control group showed improvement of 50 percent or greater on the mental QoL domain.[75]

Collectively, these studies provide limited evidence for a moderate effect size of physical activity on physical and mental domains, but not overall QoL outcomes for adults with depression, when compared to placebo or inactive controls. In older adults with clinical depression, limited evidence from a small number of controlled studies suggests that physical activity is associated with improved QoL outcomes.[52] Thus, advancing age may serve as a response modifier for the effects of physical activity on QoL, consistent with our report that physical activity has a strong positive effect on HRQoL in the non-depressed older population.

Evidence on Specific Factors

Dose-response: Meta-analyses did not report on the effect of different doses of physical activity on QoL outcomes.

Demographic factors, weight status, and physical activity type: Meta-analyses of older adults rarely reported whether effects of physical activity on QoL outcomes were modified by age, sex, socioeconomic status, race/ethnicity, presence of obesity, or baseline fitness levels, exercise intensity, frequency, or duration. One study that examined these associations found no significant differences when HRQoL outcomes were stratified according to country in which the study was conducted, sex, type of physical activity program, and whether the physical activity sessions were supervised.[67]

In adults, systematic reviews and the meta-analysis rarely examined whether the effect of physical activity on QoL outcomes were modified by age, sex, baseline fitness levels, socioeconomic status, presence of obesity, or exercise intensity, frequency, or duration.

For additional details on this body of evidence, visit: https://health.gov/paguidelines/second-edition/report/supplementary-material.aspx for the Evidence Portfolio.

Comparing 2018 Findings with the 2008 Scientific Report

The 2008 Scientific Report[1] included a section on well-being, which was broadly defined as the absence of distress. The conclusions from that report were that "evidence from prospective cohort studies indicates a small-to-moderate association that favors people that are physically active." The results that we describe here as a part of the 2018 Scientific Report significantly expand on these results by focusing on QoL instead of a more limited definition of well-being. In addition, the 2018 Scientific Report extends the 2008 findings by examining the effects of physical activity on physical and mental domains of HRQoL from RCTs that were conducted across the lifespan and in populations that often show significant losses in QoL (e.g., schizophrenia).

Public Health Impact

Improved perceptions of quality of life can be expected to decrease the use of health-care delivery services and help to limit the rising costs of medical care in the United States. Reductions and low levels of quality of life have been linked with mortality risk in older adults[77] and are associated with greater use of health-care services. Perceptions of quality of life can also serve as a barometer of healthy aging.[78] For individuals with schizophrenia and schizophreniform disorders, improved perceptions of quality of life, along with related outcomes of improved positive and negative symptoms, general symptoms, and global functioning, indicate that greater physical activity can be a useful adjunct for management of such conditions. Given the large proportion of the population with chronic conditions and the growing number of older Americans, an improved sense of quality of life from regular physical activity can be expected to influence feelings of suffering and resultant demands on the health care system.

Improved perceptions of quality of life also can be expected to reduce feelings of stress among individuals without chronic conditions. Americans report increasing levels of stress in their lives due to work, money, and the future of the nation.[79] This stress interferes with many aspects of health that can be mitigated by a higher sense of quality of life induced by regular physical activity. Thus, even in the absence of manifest disease, the benefits of physical activity are important for enabling Americans to live productive and rewarding lives.

Question 3. What is the relationship between physical activity and (1) affect, (2) anxiety, and (3) depressed mood and depression?

a) Is there a dose-response relationship? If yes, what is the shape of the relationship?
b) Does the relationship vary by age, sex, race/ethnicity, socioeconomic status, or weight status?
c) Does the relationship exist across a continuum of mood and affective disorders (i.e., depression)?
d) What is the relationship between physical activity and brain structure and function?

Sources of Evidence: Systematic reviews, meta-analyses, review of reviews

Conclusion Statements

Strong evidence demonstrates from studies of acute bouts of exercise that negative affect increases as experimentally imposed exercise intensity increases, and that negative affect is greatest when the intensity exceeds the lactate or ventilatory threshold. Such evidence has been demonstrated in acute bouts of exercise in adolescents and in adults up through middle-age. **PAGAC Grade: Strong.**

Strong evidence demonstrates that acute bouts of exercise can reduce state anxiety and that regular participation as well as longer durations of moderate-to-vigorous physical activity can reduce trait anxiety in adults and older adults. **PAGAC Grade: Strong**.

Insufficient evidence is available to determine the relationship between physical activity and anxiety among youth. **PAGAC Grade: Not assignable**.

Insufficient evidence is available to determine whether a relationship exists between physical activity and anxiety among individuals with dementia or intellectual disability. **PAGAC Grade: Not assignable.**

Strong evidence demonstrates that physical activity reduces the risk of experiencing depression. **PAGAC Grade: Strong.**

Strong evidence demonstrates that physical activity interventions reduce depressive symptoms in individuals with and without major depression across the lifespan. **PAGAG Grade: Strong**.

Insufficient evidence is available to determine whether a relationship between physical activity and depression exists among individuals with dementia, stroke, or intellectual disability. **PAGAC Grade: Not assignable.**

In adults, limited evidence suggests a dose-response of effect of physical activity on depression. **PAGAC Grade: Limited.**

In youth, insufficient evidence is available to determine the dose-response of physical activity on depression. **PAGAC Grade: Not assignable.**

Strong evidence demonstrates that experimentally imposed high-intensity physical activity reduces pleasure while exercising. **PAGAC Grade: Strong.**

Insufficient evidence is available on the dose-response of exercise on anxiety. **PAGAC Grade: Not assignable.**

Moderate evidence indicates that depressive symptoms can be reduced by even limited volumes and intensities of physical activity and that greater frequencies and volumes of activity have a larger effect on reducing depressive symptoms. **PAGAC Grade: Moderate.**

Insufficient evidence is available to determine whether sex, race/ethnicity, socioeconomic status, or weight status modify the associations between exercise and affect. **PAGAC Grade: Not assignable.**

Moderate evidence indicates that exercise reduces state anxiety more for females, adults older than age 25 years, and sedentary individuals than for other population subgroups. **PAGAG Grade: Moderate.**

Insufficient evidence is available to determine whether age, sex, race/ethnicity, socioeconomic status, or weight status modify the associations between exercise and trait anxiety. **PAGAC Grade: Not assignable.**

Limited evidence is available that females show greater reduction in depressive symptoms with physical activity than do males. **PAGAG Grade: Moderate.**

Strong evidence demonstrates that physical activity reduces anxiety symptoms in individuals with anxiety disorders and reduces depressive symptoms in individuals with major depression. **PAGAC Grade: Strong**.

Insufficient evidence is available to determine whether physical activity influences markers of brain structure and function in the context of affect, anxiety, or depressed mood and depression. **PAGAC Grade: Not assignable**.

Review of the Evidence

Elevating one’s mood, and reducing anxiety and depression are ubiquitous goals and are essential for maintaining a healthy and productive life. In this question, measurement of affect, anxiety, and depression includes subjective experiences of feeling states based on pleasure and arousal, feelings of apprehension and worry, depressive symptoms, as well as clinical diagnoses of anxiety or depression disorders. To address this question, the Subcommittee used 53 meta-analyses and systematic reviews of the literature that examined whether results from RCTs and prospective longitudinal studies are associated with affect (N=3; 1 meta-analysis and 2 systematic reviews), anxiety (N=13; 5 meta-analyses; 8 systematic reviews), or depressed mood or clinical depression (N=41; 27 meta-analyses; 14 systematic reviews). These reviews included results from healthy young and older adults, children, and adolescents as well as populations such as adults with dementia, schizophrenia, and stroke. We also included meta-analyses and reviews of the effects of acute exercise on affect and state anxiety outcomes.

Affect

Evidence on the Overall Relationship

For this question, the term "affect" is defined as the transient and subjective experience of feeling states based on independent dimensions of valence (pleasure/displeasure) and activation (arousal).[80] Results from 10 experimental studies of affective responses during exercise (N=241 participants) were examined in one high-quality meta-analysis.[81] Samples included in this review ranged from adolescents through middle adulthood. Most samples had poor to average fitness levels (VO_{2peak} range = 23.3-48.7). Exercise bouts involved using a treadmill or cycle ergometer for 15 to 40 minutes, although most tests were limited to 15- to 20-minute bouts. All studies used the single-item Feeling Scale.[82] The lactate threshold and ventilatory threshold are physiological markers that typically serve as reference points for intensity when marking these changes. Effects were estimated as the difference in affective valence (as defined by the scales used in the study, such as the Feeling Scale) at a given intensity when that intensity was imposed compared to when it was self-selected. When the imposed and self-selected exercise bouts were performed at equal intensities, no difference in affective valence was seen. When the imposed exercise intensity was varied experimentally, a clear dose-response pattern emerged. At exercise intensities below the lactate/ventilatory threshold, a small effect occurred (d = -0.36; 95% CI: -0.67 to -0.04), and imposed exercise intensity was slightly less pleasant than self-selected exercise. At the lactate/ventilatory threshold, a medium-sized effect occurred (d = -0.57; 95% CI: -0.99 to -0.15), and imposed exercise intensity was moderately less pleasant than self-selected exercise. Above the lactate/ventilatory threshold, a large effect occurred (d = -1.36; 95% CI: -1.86 to -0.87), and imposed exercise intensity was much less pleasant than self-selected exercise.

Findings regarding the effects of interval versus continuous exercise were mixed across nine experimental studies in which the type and intensity of exercise along with the timing of rest periods were carefully controlled and manipulated by the investigative teams.[83] Four studies documented a more unpleasant affective response during interval versus continuous exercise; four studies documented no difference in affective responses during interval and continuous exercise. Only one study reported more pleasure during interval versus continuous exercise. Six studies found no differences in post-exercise affect between interval and continuous exercise.

Non-experimental evidence from ecological momentary assessments provides insight into relations between physical activity and subsequent affective responses over a 3-hour interval.[84] In 8 out of 11 studies, physical activity was associated with more pleasant and activated subsequent affective states following the activity bout. Results were mixed with regard to physical activity and unpleasant feelings. Two studies found no association between physical activity and subsequent unpleasant feelings and two studies found that physical activity was associated with reduced unpleasant feelings. A fifth study found that physical activity did not lead to acute reductions in unpleasant feelings but that people who were typically more active reported fewer unpleasant feelings in general.

Dose-response: Strong evidence shows an effect of physical activity on immediate affective responses and that this effect is moderated by the imposed dose of activity.

Evidence on Specific Factors

Demographic factors and other moderators: Little is known about the persistence of the effects of physical activity on affective states across time or how they might be moderated by individual variability in demographic or other biological or environmental factors.

Biomarkers: Insufficient evidence was available from the reviewed literature to determine whether physical activity modifies biomarkers of brain structure and function in the context of affect. There were no studies reviewed that examined brain measures or other biomarkers.

Anxiety

Here, the Subcommittee defines anxiety as a noticeable, psychophysiological emotional state, which is most often characterized by feelings of apprehension, fear or expectations of fear, worry, nervousness, and physical sensations arising from activation of the autonomic nervous system (e.g., increased muscle tension, elevated heart rate, sweating). This normal human emotion becomes pathological (i.e., clinical anxiety or an anxiety disorder) when it results in changes in thoughts and actions, occurs even in the absence of an eliciting event, and when the response is disproportionate and unmanageable.[85] Anxiety and anxiety disorders are the most prevalent of mental disorders. With increasing levels of stress in the modern world, symptoms of anxiety are often elevated in those without clinical manifestations of anxiety. To date, hundreds of studies have examined the effects of exercise on anxiety reduction, both following single bouts of exercise (state anxiety: how anxious an individual feels at the moment) and as a result of regular exercise training (trait anxiety: how anxious an individual feels most of the time). The majority of this work has examined the effects of exercise in individuals without elevated symptoms of anxiety and/or not diagnosed with any clinical anxiety disorders.

Evidence on the Overall Relationship

To examine the effects of acute exercise bouts on measures of state anxiety, the Subcommittee reviewed evidence from a meta-analysis of 36 RCTs (involving 1,233 individuals [726 females]) examining the effects of acute exercise on state anxiety published since 1990.[86] Samples varied from adolescence through middle-aged adults, with an average age of 25.3 years. Of these samples, 17 were reportedly active, 6 were sedentary, 2 had a mixture of active and inactive participants, and 11 did not report baseline activity levels. Exercise bouts included continuous exercise on a treadmill or cycle ergometer or resistance exercise, lasting 20 to 30 minutes (1 study used 45 minutes and another used 50 minutes). The vast majority of the studies (75%) used either the 10- or 20-item State Anxiety Inventory[87] to assess anxiety before and after the exercise (or control) bouts. Study designs were either within-subject (64%) or between-subject (36%) randomizing, counterbalancing, or both the exercise treatment with a control (most often a quiet rest control – 64%).

The results from this analysis found that physical activity led to a small, but significant reduction in state anxiety symptoms following acute exercise compared with control (Hedges' g=0.16). Several moderator variables indicated that anxiety reduction was greater if: participants were female (Point Estimate=0.23), aged older than 25 years (Point Estimate=0.42), or sedentary (Point Estimate=0.39); the exercise intensity was high (compared to light or moderate; Point Estimate=0.36 vs 0.08, 0.03); the exercise modality involved a treadmill (Point Estimate=0.24); the control condition was quiet rest (Point Estimate=0.23); randomization and counterbalancing were used (Point Estimate=0.25); and overall study quality was high (PEDro score >6; Point Estimate=0.19).

To examine the effects of long durations (i.e., weeks or months of regular activity) of physical activity on measures of trait anxiety, the Subcommittee extracted evidence from studies reviewed in meta-analyses,[88-90] systematic reviews,[91-93] and a quantitative review of 18 meta-analyses[94]; 4 of these meta-analyses were conducted using only RCTs and 1 of these used clinically and non-clinically anxious adults.[95] Samples ranged from children to older adults, with the majority ranging from age 18 to 65 years. Four of the reviews[88, 89, 92, 93] focused on participants with either elevated anxiety symptoms or a clinical anxiety disorder. Exercise training involved aerobic and resistance exercise, with average duration of sessions and exercise intensity not well specified. Intervention lengths ranged from 2 weeks to 6 months, with a range of 1 to 7 training sessions per week. Outcome measures varied considerably, from assessments of anxiety symptoms to clinical assessments of anxiety; all were used to assess anxiety before and after the exercise (or control) interventions. Control comparisons involved standard care (most often pharmacotherapy or cognitive behavioral therapy), a waitlist group that is tested several times before beginning the intervention, a placebo group, or another exercise intervention.

Physical activity had a significant effect on the reduction of trait anxiety. One review[94] reported a moderate effect (Cohen d (d)=0.31 for non-RCT studies; d=0.45 from RCTs) and another review[90] reported a small-to-moderate effect for resistance exercise training (d=0.42). Reviews comparing the effects of exercise to other treatments[88, 89, 93, 94] consistently reported that exercise interventions were at least as effective as standard care treatment for anxiety and sometimes even better.[94] To use one example, a meta-analysis[88] of exercise compared to various control groups (including active treatments) on trait anxiety in patient populations showed that exercise was as efficacious as, and not inferior to, established treatments. Although most of the evidence is based on patient samples, evidence also supports the anxiolytic effects of exercise in healthy older adult samples.[91, 92] Finally, a meta-analysis of 16 studies examining resistance exercise training[90] revealed that it significantly reduced trait anxiety symptoms (d=0.42), more so in healthy individuals (d=0.50) compared to participants with a physical (d=0.15) or mental illness (d=0.37). In addition, there is not strong evidence for a dose-response effect and it appears based on effect sizes that resistance exercise training is comparable to the positive effects of aerobic exercise training for reducing trait anxiety.

In youth*,* two of the five studies reported information about the relationship between physical activity and anxiety. The review of reviews reported that vigorous exercise interventions compared with no intervention was not associated with a reduction in anxiety (SMD=-0.48; 95% CI: -0.97 to 0.01).[96]

There was insufficient evidence from reviews to determine if physical activity reduces state or trait anxiety in individuals with dementia or intellectual disabilities.

For individuals with post-traumatic stress disorder (PTSD), limited evidence suggests that physical activity is an effective treatment for anxiety symptoms. The Subcommittee examined evidence from four reviews, two of which were systematic reviews,[97, 98] one of which was a systematic review and meta-analysis,[99] and one of which examined PTSD and physical activity studies more descriptively, thus not allowing any conclusions regarding magnitude of effect.[100] This literature suffers from a lack of experimental studies, with only two RCTs examining exercise and seven RCTs examining yoga. Overall, the evidence indicates that exercise may have beneficial effects on PTSD symptoms and that regular physical activity may reduce risk of developing PTSD. The evidence also suggests that yoga may be useful (d=0.48) in alleviating PTSD symptoms, but the studies show little consistency regarding the type of yoga and the length of treatment.

Dose-response: Limited evidence suggests a dose-response effect of physical activity on either state or trait anxiety symptoms.

Evidence on Specific Factors

Demographic factors: Moderate evidence indicates that state anxiety reduction is moderated by sex and age such that females and those older than age 25 years show greater reductions in state anxiety after participating in physical activity.[86] Insufficient evidence was available from the examined literature on whether other demographic factors (race/ethnicity, socioeconomic status) moderate the effect of physical activity on anxiety symptoms (e.g., race).

Biomarkers: Insufficient evidence was available from the reviewed literature to determine whether physical activity modifies biomarkers of brain structure and function in the context of anxiety or anxiety disorders. Despite hypotheses from rodent and animal research,[94] were no studies reviewed that examined brain measures or other biomarkers in humans in relation to physical activity and anxiety.

Depression

For this question, depression is defined as an unpleasant, low activation feeling state characterized by sadness, or feelings of hopelessness or guilt. In the extreme, these feelings can manifest as the clinical disorder of major depression. In this section, we have separated the results for depression based on studies focusing on physical activity as a prevention for depression from those studies focusing on its effects as a treatment. We included 14 systematic reviews and 27 meta-analyses of this literature.

Evidence on the Overall Relationship

Adults

In the context of preventing depressive symptoms and major depression across the lifespan in both children and adults, the reviews and meta-analyses showed that greater amounts of physical activity are strongly associated with a reduced risk of developing depression. For one systematic review, 83 percent (25 of 30) of prospective observational studies found that greater amounts of physical activity were associated with a reduced risk of experiencing depression at follow-up.[101] Even low amounts of activity (less than 150 minutes per week) were associated with significantly reduced risk of depression, although more activity was associated with larger effects. Engaging in more than 30 minutes per day of activity reduced the odds of experiencing depression by 48 percent. Similarly, another meta-analysis found that increased sedentary behavior across 11 prospective studies was associated with an increased risk of depression (relative risk [RR]=1.14; 95% CI: 1.06 to 1.21).[102] Limitations of this literature are that most studies used self-reported assessments of physical activity and multiple metrics of depression and depressive symptoms. Otherwise, these studies were generally of high methodologic quality.

In the context of treatment, many studies have examined whether engaging in physical activity (through physical activity interventions) is an effective approach for reducing depressive symptoms or features of major depression. Most of these studies last approximately 12 weeks in duration. All of the meta-analyses and systematic reviews examined showed consistent and moderate-to-large effect sizes for the effect of physical activity on depressive symptoms across the adult lifespan,[68, 74, 103-110] including in non-demented elderly.[111-113] For example, Josefsson et al[108] reported a moderate-sized effect of physical activity interventions on depressive symptoms (Hedges' g = -0.77). Several reports found that the average effect sizes for physical activity treatment ranged from -0.53 to -1.39 across studies. Effect sizes tend to be larger for individuals with major depression (-1.03) and of more moderate size for individuals without clinical depression but with depressive symptoms (-0.59). When physical activity is compared to either cognitive behavioral therapy or anti-depressant pharmaceutical treatments, the groups show no significant differences, indicating that physical activity is as effective for treating depression as these other common approaches for treatment. The effects cannot be explained solely by placebo effects.[114]

Limited evidence also suggests beneficial effects on depressive symptoms from yoga,[75, 115, 116] tai chi and qigong,[117-120] or dance.[121] Unfortunately, this literature is plagued by low methodological rigor and analysis, which limit the conclusions that can be drawn.

Insufficient evidence is available to determine whether physical activity is an effective treatment for depression and depressive symptoms for caregivers,[122] people with dementia,[123, 124] PTSD,[99, 100] schizophrenia, intellectual disabilities, or other individuals with other neurologic/psychiatric conditions.[71, 125, 126]

Youth

For the effects of physical activity in youth, the evidence base comprised two meta-analyses,[54, 127, 128] two systematic reviews,[129, 130] and one review of reviews.[96] The meta-analyses included a total of 15 unique studies, with 2 studies included in both reviews[54, 127, 128]; all studies were experimental in design. Each of the systematic reviews included six longitudinal studies.[129, 130] The review of reviews[96] included four systematic reviews that had appropriate exposures and outcomes for this question; the sum of RCTs included in each of the 4 reviews totaled 93. In all of the reviews, parameters of physical activity were obtained from a variety of self-report instruments. Similarly, symptoms of depression were assessed with a wide variety of tools, standard and non-standard.[131]

All five studies reported statistically significant reductions in depressive symptoms in the more physically active groups. One meta-analysis reported a Hedges' g=-0.26 (95% CI: -0.43 to -0.08)[54, 128]; another a standardized mean difference of -0.61 (95% CI: -1.06 to -0.16).[127] The review of reviews reported a statistically significant reduction in the standardized mean difference among the more physically active groups compared with inactive controls (SMD = -0.62; 95% CI: -0.81 to -0.42).[96] The review of reviews also reported that physical activity interventions were comparable with psychologic and pharmaceutical therapies in terms of the reduction in depressive symptoms. One systematic review reported statistically significant reductions in depressive symptoms among the physically active groups in five of the six pertinent studies, and a nearly significant reduction ($P < 0.10$) in the sixth.[129] The other systematic review reported significantly higher levels of depressive symptoms among the more sedentary groups in all five of the pertinent studies.[130] One meta-analysis of adolescents that summarized results from eight RCTs reported that physical activity reduced depressive symptoms (SMD= -0.48), although this effect did not reach significance when only the higher quality studies were examined.[132] In studies limited to samples with clinical depression, physical activity had a significant effect on reducing depressive symptoms (SMD= -0.43).

Dose-response: In adults, modest evidence suggests a dose-response effect of physical activity on depression. Even brief amounts (20 minutes per day) of activity is sufficient to show a reduction in depressive symptoms, but longer durations of activity have a larger effect. In youth, although the physical activity exposure was aerobic in nature and presumably approximated current guidelines in volume and intensity, none of the reviews provided outcome information at more than two levels of exposure, which prevented an assessment of dose-response.

Evidence on Specific Factors

Demographic factors and weight status: Several reports indicate that the effects might be moderated by the sex of the individual, with studies including more females showing larger effect sizes.[74] Despite this effect modification, there are other reports showing similar effects across males and females.[94] In any case, potential sex differences (or lack thereof) should be interpreted with caution because of the higher prevalence of depression and depressive symptoms in females. In contrast, little to no information was provided about the influence, if any, of age, race/ethnicity, socioeconomic status, or weight status on the relationship between physical activity and measures of depressive symptoms or major depression.

In youth, little to no information was provided about the influence, if any, of age (within the ages 5 to 18 years),[132] sex, race/ethnicity, socioeconomic status, or weight status on the relationship between physical activity and the outcomes of interest.

Biomarkers: In both adults and youth, insufficient evidence was available from the meta-analyses and reviews to determine whether physical activity modifies biomarkers of brain structure and function in the context of depression or depressive symptoms.[133] Research using animal models of depression have described several mechanisms by which physical activity is likely leading to reductions in depressive symptoms,[133] but research in humans have not verified these mechanisms with a sufficient number of high-quality studies.

For additional details on this body of evidence, visit: https://health.gov/paguidelines/second-edition/report/supplementary-material.aspx for the Evidence Portfolio.

Comparing 2018 Findings with the 2008 Scientific Report

The 2008 Scientific Report[1] concluded that "population-based, prospective cohort studies provide substantial evidence that regular physical activity protects against the onset of depression symptoms and major depressive disorder." In addition, it concluded that RCTs showed that physical activity "reduces depression symptoms in people diagnosed as depressed, healthy adults, and medical patients without psychiatric disorders." In the context of anxiety, the 2008 Scientific Report[1] concluded that "a small number of nationally representative and population-based cross-sectional and prospective cohort studies supports that regular physical activity protects against the onset of anxiety disorders and anxiety symptoms." The 2008 Scientific Report[1] also concluded that "participation in physical activity programs reduces anxiety symptoms." The findings from the 2018 Scientific Report are consistent with those reported in 2008 but significantly extend them to include more information from prospective observational studies in the context of depression and from RCTs that now definitely demonstrate that physical activity is an effective treatment for reducing anxiety and depressive symptoms. In addition, the

2018 Scientific Report includes an assessment of acute bouts of physical activity on measures of affect and state anxiety. Finally, the 2018 Scientific Report also provides an examination of physical activity on reducing depression and state and trait anxiety across multiple age groups and populations (e.g., youth).

Public Health Impact

In the United States, fewer than half of children and adults engage in regular physical activity.[134] Affective responses during, but not following, exercise predict adherence at 6- and 12-month follow-ups.[135] Adherence and health benefits can be optimized by regulating the intensity of exercise. A tradeoff should be expected between exercise intensity (and expected health benefits) and adherence. When vigorous-intensity exercise training is imposed, affective responses are likely to undermine adherence and additional interventions should be considered for improving affective responses and supporting adherence (see *Part F. Chapter 11. Promoting Regular Physical Activity*).

Major depression is one of the most common mental disorders in the United States. According to the National Survey on Drug Use and Health in 2015,[136] an estimated 16.1 million adults ages 18 years or older, or approximately 6.7 percent of all US adults, had experienced at least one major depressive episode in the past year. These estimates were highest in adult females (8.5%) compared to males (4.7%) and in those between the ages of 18 to 25 years (10.3%). Children and adolescents also experience episodes of major depression with an estimate of 3 million, or 12.5 percent, of adolescents ages 12 to 17 years in the United States experiencing at least one episode in the past year. Similar to adults, female adolescents had higher prevalence (19.5%) compared to males (5.8%). These high prevalence rates have staggering costs associated with them. For example, in 2010, it was reported that annual costs related to major depression were $210.5 billion in the United States. Furthermore, major depression was the leading cause of disability for individuals ages 15 to 44 years, with almost 400 million disability days per year.[137]

Anxiety disorders are similarly prevalent and debilitating. For example, the 12-month prevalence of any anxiety disorder is 18.1 percent in the United States with females being 60 percent more likely than males to experience an anxiety disorder. Although healthcare costs associated with anxiety disorders have not been studied as frequently as in depression, a 1990 study found that annual costs associated with anxiety disorders exceeded $46 billion.

Despite these startling statistics, long-term adherence to many pharmaceutical treatments remains poor, and a better understanding of the impact of non-pharmaceutical interventions, such as physical activity, is needed. The results reported in this chapter clearly indicate that physical activity is an effective and robust approach for reducing the risk of depression that would clearly have downstream consequences for quality of life, health care costs, and job productivity. Furthermore, these results also demonstrate that physical activity is an effective approach for improving both anxiety and depressive symptoms (symptoms that often co-occur), with effect sizes that are similar to that of the most effective pharmaceutical approaches.

In sum, physical activity holds great promise as a means for preventing and treating common mood disorders that are a significant source of disability, lower quality of life, and increased health care burden.

Question 4: What is the relationship between physical activity and sleep?

a) Is there a dose-response relationship for either acute bouts of physical activity, or regular physical activity? If yes, what is the shape of the relationship?
b) Does the relationship vary by age, sex, race/ethnicity, socioeconomic status, or weight status?
c) Does the relationship exist for individuals with impaired sleep behaviors or disorders? If yes, for which sleep disorders?

Sources of evidence: Systematic reviews, meta-analyses

Conclusion Statements

Strong evidence demonstrates that both acute bouts of physical activity and regular physical activity improve sleep outcomes in adults. **PAGAC Grade: Strong.**

Moderate evidence indicates that longer duration acute bouts of physical activity and regular physical activity improve sleep outcomes. These positive effects are independent of exercise intensity. **PAGAC Grade: Moderate.**

Moderate evidence indicates that the effects of physical activity on sleep outcomes in adults are preserved across age and sex, with the exception of sleep onset latency, which declines with age. **PAGAC Grade: Moderate.**

Insufficient evidence is available to examine relationships between physical activity and sleep in children and adolescents and whether the relationships vary according to race/ethnicity, socioeconomic status, or weight status. **PAGAC Grade: Not assignable.**

Moderate evidence indicates that greater amounts of moderate-to-vigorous physical activity improves sleep in adults who report sleep problems, primarily symptoms of insomnia, and for obstructive sleep apnea. **PAGAC Grade: Moderate.**

Review of the Evidence

Introduction

Sleep is a reversible behavioral state of perceptual disengagement characterized by unresponsiveness to the environment.[138] It is an important determinant of health and well-being across the lifespan.[139] It is an essential biological function important for neural development, learning, memory, emotional regulation, and cardiovascular and metabolic health.[140] Sleep consists of four formally recognized stages and has several features that comprise the totality of sleep (Table F3-1). These stages and features are used by researchers to study sleep and, in a less formal manner, are used by everyone to recognize the quality and value of sleep.[138, 141-143] Insomnia and obstructive sleep apnea, two common disorders of sleep, are also defined in Table F3-1.[85, 137, 144, 145]

Table F3-1. Components of Sleep and Common Sleep Disorders

Sleep Outcomes and Behaviors	Definitions
Sleep (onset) latency	Length of time between going to bed and falling asleep.
Total sleep time (TST)	Total time of actual sleep, which is the sum of all time spent in each of the components (see Stages of sleep, below).
Wake-time after sleep onset (WASO)	Amount of time spent awake after sleep onset and before the final awakening, usually in the morning.
Sleep efficiency	The percentage of time of actual sleep out of all the time sleeping and trying to sleep. 100*(TST/(Sleep latency + TST + WASO)[143]
Stages of sleep	Sleep normally progresses through a series of four stages in repeated cycles of about 90 minutes.
Non-Rapid Eye Movement (NREM) Light Sleep	The two earliest phases of sleep (except in infants), stages N1 and N2, characterized by progressively deepening sleep as determined by brain wave activity and arousal thresholds.
NREM Slow Wave Sleep (Deep Sleep)	Stage N3, deep sleep, is characterized by slow brain wave activity. Slow wave sleep is associated with memory consolidation. Slow wave (deep) sleep is maximal in children and declines with age.
Rapid Eye Movement Sleep (REM)	REM sleep is characterized by episodes of rapid eye movements, brain wave activation, lack of tone in skeletal muscles, and dreaming.

Sleep Outcomes and Behaviors	Definitions
Sleep Quality and its measurement	Subjective perception of whole sleep experience. The most common scale used in this report and in the field of sleep medicine is the Pittsburgh Sleep Quality Index that scores subjective sleep quality, latency, duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication, and daytime dysfunction.[146]
Daytime Sleepiness and its measurement	Subjective perception of daytime sleepiness. The most common scale used in this report and in the field of sleep medicine is the Epworth Sleepiness Scale, in which subjects estimate how likely they are to doze off during 8 daytime conditions ranging from TV watching to driving.[147]
Prevalent Sleep Disorders	**Diagnostic Criterion, Symptom Profile, Prevalence**
Insomnia disorder; Chronic Insomnia Disorder	Difficulty falling asleep, staying asleep, or early awakening associated with distress or impairment (e.g., fatigue, poor concentration) ≥3 times per week for ≥3 months.[144, 145, 148]
Insomnia symptoms	Difficulty falling asleep, staying asleep, or early awakening associated with distress or impairment (e.g., fatigue, poor concentration) less often or less prolonged than for insomnia disorder.[144]
Obstructive Sleep Apnea (OSA)	15 or more apnea or hypopnea events ≥ 10 seconds in duration per hour based on monitoring, or 5 events per hour plus one or more signs or symptoms: 1) sleepiness, non-restorative sleep, fatigue, insomnia, 2) awakening with breath holding, gasping, choking, 3) bed partner notes snoring or breathing interruptions, 4) diagnosis of hypertension, mood disorder, cognitive dysfunction, coronary heart disease, heart failure, atrial fibrillation, type 2 diabetes mellitus (all linked to OSA).[141, 149, 150]

Literature Reviewed

The evidence base comprised nine meta-analyses[142, 151-158] and six systematic reviews.[55, 159-163] Ten of the reviews included only experimental studies,[55, 142, 151, 153, 154, 156, 157, 159, 161, 162] two of the reviews included only longitudinal studies,[158, 163] and three included only cross-sectional studies.[152, 155, 160] The 15 reviews included a total of 166 unique studies, 5 of which were cited in three different reviews, and 9 of which were cited in two reviews.

Sleep - General Population

Four meta-analyses[142, 152, 155, 156] and four systematic reviews[55, 160, 161, 163] focused on sleep stages and features in the general population. Two of the reviews[152, 160] included only adolescents, and one of those[160] included only female adolescents. One meta-analysis included 11 cross-sectional studies each with questionnaire-reported physical activity, presumably of moderate-to-vigorous intensity.[152] The systematic review[160] included two studies in which sedentary behavior was the exposure. The remaining six reviews,[55, 142, 155, 156, 161, 163] all of which focused on adults, included information from 122 unique studies. Of the 3 meta-analyses,[142, 155, 156] 2 included only experimental studies[142, 156]; the third included 12 cross-sectional studies and 1 experimental study.[155] Two of the three systematic reviews included only experimental studies[55, 161]; the third included only longitudinal studies.[163] The studies within these six reviews that focused primarily on adults included exposures that were mostly aerobic activities but were highly diverse, including activities such as walking, bowling, and yoga. One review included studies on the effects of a single acute bout of moderate-to-vigorous physical activity as well as assessing habitual moderate-to-vigorous intensity physical activity.[142]

Obstructive Sleep Apnea

Three meta-analyses[151, 153, 154] focused on obstructive sleep apnea. All of the 18 studies included in the three reviews were experimental trials; the physical activity interventions were mostly supervised exercise programs in which the subjects accumulated around 150 minutes per week of mostly moderate-intensity physical activity.

Insomnia

Three meta-analyses[156-158] and three systematic reviews[159, 162, 163] focused on adults with insomnia. One meta-analysis[158] included 4 longitudinal and 12 cross-sectional studies; sedentary behavior was the exposure of interest. The other meta-analysis[157] included 6 experimental studies; the exposure was either moderate-intensity physical activity or high-intensity strength training. The two systematic reviews[159, 162] included seven experimental studies of adults, one of which included only women. The exposure was mostly moderate-intensity aerobic activity. Collectively, the four reviews[157-159, 162] included 25 unique studies, 9 experimental, 4 longitudinal, and 16 cohort.

Evidence on the Overall Relationship

The three meta-analyses[142, 155, 156] and the three systematic reviews[55, 161, 163] all reported beneficial effects of greater amounts of physical activity on one or more aspect of sleep. The strongest evidence comes from analyses of 66 controlled intervention studies involving 2,863 community dwelling adults ranging from age 18 to 88 years, including a majority without sleep problems (89%).[142] The findings consistently show small-to-moderate size benefits of both regular physical activity and acute bouts of physical activity on multiple sleep outcomes, including total sleep time (both habitual and acute), sleep efficiency (both habitual and acute), sleep onset latency (both habitual and acute), sleep quality (habitual, insufficient information regarding acute), and rapid eye movement sleep (acute, insufficient information regarding habitual) (Table F3-2). Acute bouts of moderate-to-vigorous physical activity also shorten the time awake after falling asleep and reduce the time in Stage 1 sleep. Acute bouts further improve deep sleep; this effect is stronger among individuals who are habitually active.[142]

Table F3-2. Effect on Sleep Outcomes in Adults of Habitual Moderate-to-Vigorous Physical Activity Compared to Controls and Acute Bouts of Moderate-to-Vigorous Physical Activity Compared to Controls

Sleep Outcome	Regular Physical Activity Cohen d effect size, 95% CI, and P value	Acute Bouts of Physical Activity Cohen d effect size, 95% CI, and P value
Sleep Onset Latency	d=0.35 (95% CI: 0.00-0.70) *P*<0.05	d=0.17 (95% CI: -0.02-0.32) *P*=0.03
Total Sleep Time	d=0.25 (95% CI: 0.07- 0.43) *P*=0.005	d=0.22 (95% CI: 0.10-0.34) *P*<0.001
Wake-time after sleep onset	Insufficient data	d=0.38 (95% CI: 0.21-0.55) *P*<0.001
Sleep Efficiency	d=0.30 (95% CI: 0.06-0.55) *P*=0.02	d=0.25(95% CI: 0.12-0.39) *P*<0.001
Shorter Time in Stage 1 Sleep	Insufficient data	d=0.35 (95% CI: 0.18-0.52) *P*<0.001
Longer time in Slow Wave Sleep	The effects of an acute bout are greater among individuals with higher baseline physical activity	d=0.19 (95% CI: 0.02-0.35) *P*=0.03
Rapid Eye Movement Sleep	Insufficient data	d=-0.27 (95% CI: -0.45 to -0.08) *P*=0.005
Sleep Quality	d=0.74 (95% CI: 0.48-1.00)	Insufficient data

Note: Effect size using Cohen d defines the strength of the relationship, with d=0.01 very small, d=0.20 small, d=0.50 medium, and d=0.80 a large magnitude effect
Source: Adapted from data found in Kredlow et al., 2015.[142]

The time of day at which an acute bout of moderate-to-vigorous physical activity is performed appears unrelated to most aspects of sleep. A comparison of the effect of acute bouts of moderate-to-vigorous physical activity performed more than 8 hours before bedtime, 3 to 8 hours before bedtime, and less than 3 hours before bedtime, showed no detectable difference on sleep onset latency, total sleep time, sleep efficiency, slow wave sleep, stage 2 sleep, or rapid eye movement sleep latency.[142] Physical activity bouts performed less than 3 hours before bedtime were associated with significantly reduced wake time after sleep onset, and reduced stage 1 sleep, indicating less time spent in light sleep and fewer awakenings. In contrast, physical activity bouts performed 3 to 8 hours before bedtime were associated with reduced REM sleep.[142]

Dose-response: Moderate evidence indicates a dose-response relationship between the length in minutes but not the intensity or modality of moderate-to-vigorous physical activity and sleep outcomes. In adults, this evidence is supported by analyses from 59 controlled studies (N=2,863 participants) in which the length in minutes of acute physical activity bouts was found to moderate the beneficial effects on sleep onset latency (less), total sleep time (more), slow wave sleep (more), and rapid eye movement sleep (less).[142] In terms of regular physical activity, limited but concordant evidence suggests that more minutes of moderate-to-vigorous physical activity in each individual session is also associated with greater beneficial effects on reducing sleep onset latency. Taken together, these findings provide consistent evidence for a relationship between greater length in minutes of moderate-to–vigorous physical activity bouts associated with benefits to multiple objective and physiological sleep outcomes. In contrast to the length of each physical activity session, the number of weeks of the exercise intervention had a small but statistically significant effect on total sleep time, but no effect on sleep quality, latency, or efficiency.[142]

Regular physical activity levels influence the response to an acute bout of physical activity on slow wave sleep. Among individuals with high baseline physical activity, acute bouts of physical activity are associated with significantly greater time in slow wave sleep, whereas those with low baseline physical activity levels have non-significant differences. However, the amount of regular or baseline physical activity does not alter the effect of an acute bout on sleep onset latency, sleep efficiency, and total sleep time.[142] Thus, most of the beneficial effects of acute bouts of physical activity on sleep are similar for individuals with both low and high baseline physical activity levels.

The effect of moderate-to-vigorous physical activity on sleep outcomes is not known to vary for different types of physical activity. Although few of the included studies provided sufficient details of the intervention to inform the analyses, no differences were noted for the effects of light-, moderate-, or vigorous-intensity physical activity.[142] Similarly, no differences were noted in a comparison of aerobic with anaerobic physical activity. Mind-body exercises, such as tai chi or yoga, provided benefits equivalent to standard aerobic exercise. The effect on deep sleep was significantly better for biking than running, but their effects did not differ on other parameters of sleep.

Evidence on Specific Factors

Age: In adults, moderate evidence indicates that relationships between physical activity and sleep outcomes are consistent in their effects across young, middle-aged, and older men and women.[142, 155-158, 162, 163] Consistent evidence indicates a reduced beneficial effect of greater physical activity amount on sleep latency with aging, consisting of a 0.15 standard deviation decrease in the beneficial effects of regular physical activity for every decile increase in mean age.[142] In contrast, age does not moderate the relationship between greater amounts of regular physical activity and its beneficial effects on total sleep time, sleep efficiency, and sleep quality.

In contrast to systematic reviews in adults that include many controlled intervention studies, in children and adolescents, studies examining the relationship between physical activity and sleep are mostly cross-sectional, with a few cohort studies.[152, 155, 159] A meta-analysis of 15 studies of 12,604 individuals ages 14 to 24 years, reported a beneficial effect of physical activity on sleep with an overall standard mean difference of 0.77 (95% CI: 0.41-1.13).[155] Another meta-analysis of 11 cross-sectional studies reported a relationship between greater physical activity and earlier bedtime, but not sleep onset latency or total sleep time.[152] Similarly, analyses of epidemiological studies including adolescent females reported a relationship between increased screen-based sedentary time and greater sleep problems.[160]

Other demographic factors and weight status: Limited evidence suggests that greater physical activity volume provides a slightly greater benefit for men than women on a few sleep outcomes (stage 1 sleep and wake time after sleep onset), but the strong relationship between greater physical activity and the majority of reported and device-measured sleep outcomes is not significantly different for men and women.[142] Data were insufficient to determine whether the relationship between physical activity varied by race/ethnicity, socioeconomic factors, or body weight.

Obstructive sleep apnea: Moderate evidence indicates that physical activity is associated with significant improvements (reduction) in apnea hypopnea index (AHI), reduced daytime sleepiness, and improved sleep efficiency for individuals with obstructive sleep apnea. The AHI, the most widely used metric for grading the severity of obstructive sleep apnea, is the mean number of apneic plus hypopneic events per hour.

A meta-analysis of five RCTs of supervised aerobic, muscle-strengthening, or combined aerobic and resistive training including 129 participants showed a significant reduction in AHI index of -6.27 (95% CI: -8.54 to -3.99), and a small-to-moderate effect size improvement in sleep efficiency, as well as reduced daytime sleepiness, compared to controls.[154] Another meta-analysis of 180 participants in 6 RCTs and 2 pre-post studies (the pre-post studies contributed 10 percent of the total number of participants) reported a decrease in AHI (unstandardized mean difference (USMD) =-0.536 (95% CI: -0.865 to -0.206) and reduced Epworth sleepiness scale (USMD=-1.246; 95% CI: -2.397 to -0.0953).[151] Finally, a network meta-analysis compared the effectiveness of supervised aerobic exercise training with continuous positive airway pressure (CPAP), mandibular advancement devices (MAD), and weight loss on AHI.[153] CPAP, MAD, and weight loss are accepted treatments with demonstrated effectiveness.[164, 165] The analysis included a total of 80 RCTs with 4,325 participants. The reduction in AHI for the supervised exercise programs (-17.23; 95% CI: -25.82 to -8.54) was not inferior to CPAP (-25.27; 95% CI: -28.52 to -22.03), MAD (-15.20; 95% CI: -19.50 to -10.91), or weight loss (-12.27; 95% CI: -18.79 to -5.75). Similar results were found for daytime sleepiness index. However, the supervised exercise programs included a total of only 72 participants. Collectively, these findings provide moderate strength evidence for a consistent relationship between greater physical activity and clinically significant improvements in sleep outcomes for adults with obstructive sleep apnea.

Insomnia: Moderate evidence indicates a similar beneficial relationship of physical activity on sleep parameters in insomnia. A meta-analysis of 12 cross-sectional and 4 cohort studies with sample sizes ranging from 300 to 7,880 adults per study reported that sedentary behavior was associated with an increased risk of insomnia (poole OR=1.18; 95% CI; 1.01-1.36) and sleep disturbance (pooled OR=1.38; 95% CI: 1.28-1.49).[158] A meta-analysis of 6 RCTs including 305 middle-aged and older adults indicates that physical activity interventions including aerobic or resistance training are associated with small-to-moderate effect sizes improving sleep quality (SMD=0.47; 95% CI: 0.08-0.86), sleep onset latency (SMD=0.58; 95% CI: 0.08-1.08), and reduced sleep medication use (SMD=0.44; 95% CI: 0.14-0.74).[157] Other systematic reviews of clinical trials in adults with chronic insomnia and sleep complaints report similar relationships between greater physical activity and sleep onset latency, sleep quality, and total wake time after sleep onset.[159, 162]

None of the reviews reported on sleep problems among children or adolescents. In addition, beyond obstructive sleep apnea and general sleep problems including insomnia, evidence from systematic reviews is insufficient to analyze relationships between physical activity and sleep for other sleep disorders.

For additional details on this body of evidence, visit: https://health.gov/paguidelines/second-edition/report/supplementary-material.aspx for the Evidence Portfolio.

Comparing 2018 Findings with the 2008 Scientific Report

The 2008 Scientific Report[1] concluded that "A small number of observational, population-based studies provides initial evidence supporting a positive association of regular participation in physical activity with lower odds of disrupted or insufficient sleep, including sleep apnea." The 2008 Scientific Report[1] also concluded that "a small number of RCTs supports the conclusion that regular participation in physical activity has favorable effects on sleep quality and is a useful component of good sleep hygiene." The 2018 Scientific Report considerably extends these findings by including a significantly larger body of evidence, the results of which indicate that strong evidence now shows positive effects of both regular and acute physical activity on many different sleep outcomes. The 2018 Scientific Report also extends the 2008 findings to include both the effects of physical activity on sleep apnea as well as insomnia and other sleep complaints.

Public Health Impact

Sleep is integral to health and well-being across the lifespan.[139, 166] The most common clinically recognized problems with sleep are insomnia and obstructive sleep apnea. Using strict diagnostic criteria, around 10 percent of adults suffer from clinically diagnosed insomnia.[144] An estimated 26 percent of adults ages 30 to 70 years suffer from obstructive sleep apnea,[167, 168] and the prevalence appears to be rising, in part because a major risk factor for obstructive sleep apnea is obesity. Beyond these specific disorders, one-quarter of the population reports getting insufficient sleep at least 15 out of every 30 days[139, 169] and one-third report getting less than the recommended amount of sleep.[170] Twenty-five percent to 48 percent of the population report a sleep problem of some kind.[142]

The health effects of sleep problems are significant. They are associated with increased risk of accidents, obesity, cardiovascular risk factors, heart disease, stroke, and all-cause mortality.[150] The National Highway Traffic Safety Administration estimates that 2.5 percent of all fatal vehicle crashes and 2 percent of nonfatal crashes involve drowsy driving; others have placed the estimate as high as 15 percent to 33 percent.[140] The United States sustains economic losses up to $411 billion per year and loses an equivalent of 1.23 million working days per year due to insufficient sleep.[171] Obstructive sleep apnea, in particular, has strong associations with hypertension, heart failure, obesity, type 2 diabetes, myocardial infarction, stroke, up to 5-fold higher incidence of traffic and industrial accidents, and 50 percent higher mortality.[150, 172, 173]

The strong evidence in this question demonstrating the beneficial effects on sleep of both acute bouts and habitual participation in moderate-to-vigorous physical activity demonstrates that substantial medical and economic costs would be favorably influenced by a more physically active society. Less easily measurable but as important are the reported benefits associated with feeling well rested and more energetic. Finally, the strong evidence that habitual moderate-to-vigorous physical activity reduces the risk of excessive weight gain (see *Part F. Chapter 5. Cardiometabolic Health and Prevention of Weight Gain*), an important risk factor for obstructive sleep apnea, indicates that physical activity could have a favorable impact on the incidence, as well as the treatment of, obstructive sleep apnea.

NEEDS FOR FUTURE RESEARCH

1. Conduct randomized controlled trials of moderate-to-vigorous physical activity across the lifespan, including in youth, to better understand its effects on cognitive development, quality of life and health-related quality of life, state and trait anxiety, and sleep outcomes.

   Rationale: Despite considerable research focused on the importance of physical activity on brain health in adults and older adults, the paucity of knowledge during other periods of the lifespan should be addressed to better understand physical activity effects on cognition, quality of life, affect, anxiety and depression, and sleep outcomes, and how they may change, across the entire lifespan. Physical activity may beneficially affect measures of brain health in common childhood disorders such as attention deficit hyperactivity disorder and autism spectrum disorder, but the impact on these conditions, or the long-term impact of physical activity during childhood on adult outcomes are largely unknown.

2. Conduct randomized controlled trials that manipulate the physical activity dose in a systematic fashion to improve the understanding of the dose-response relationship and durability of physical activity effects on brain health. Conduct these studies in healthy children and adults, and also in populations with conditions and impairments of brain health (e.g., dementia, sleep disorders, mood disorders).

   Rationale: To date, little evidence exists to draw strong conclusions about the optimal intensity, duration, and frequency of physical activity to enhance brain health (i.e., cognition, quality of life, anxiety, depression, sleep). This work is critically needed to better inform the public and practitioners about the amount of activity needed to observe changes in brain health outcomes in healthy individuals and in individuals with cognitive, sleep, or mood disorders. Although the current literature base does not allow for a firm understanding of a dose-response relationship between either acute or chronic physical activity on brain health, recommended doses of physical activity (e.g., moderate-to vigorous-intensity) have demonstrated positive effects on brain health across the lifespan.

3. Conduct randomized controlled trials of both light and moderate-to-vigorous physical activity in individuals with cognitive (e.g., dementia), mood (e.g., anxiety, depression), sleep (e.g., insomnia), and other mental health disorders (e.g., schizophrenia) to better understand its effects on brain health in these conditions, including aspects of quality of life and health-related quality of life. Further, conduct randomized controlled trials and observational studies in individuals at different stages or severity of impairment, including studies in individuals at risk of disease (e.g., genetic risk) as well as individual with comorbid conditions (e.g., anxiety and depression) to examine whether physical activity delays or prevents disease onset and progression, or interacts with common treatments used by individuals with disorders and diseases.

   Rationale: Knowledge of this area varies across impairments, with some diseases and disorders having significantly more research than others (e.g., depression). Yet, even in the context of some of these more common conditions, there is a paucity of research on some outcomes that are highly relevant for optimal functioning, such as the impact of physical activity on sleep, cognitive, and quality of life in individuals with depression. In addition, little is known about the effects of physical activity on conditions that often co-occur, like anxiety and depression. Other conditions that are also associated with impaired brain health (e.g., autism spectrum disorder, cancer, traumatic brain injury) have received little focus to date. Research in this area would contribute to a better understanding of etiologic subcategories of cognitive, sleep, mood, and other mental health conditions such as Alzheimer’s disease and related dementias, and Lewy Body, Vascular, and Mixed Dementias, which are increasingly recognized and diagnosed within the domains of impaired mental and neurological health in aging.

4. Conduct randomized controlled trials of physical activity that examine brain imaging and other biomarker metrics across the lifespan and in conditions characterized by cognitive, mood, and sleep impairments.

   Rationale: These studies could yield a better understanding of circulating biomarkers (e.g., neurotrophins) associated with brain health, and the relative roles of genetic (e.g., *ApoE4* gene) and environmental risk factors (e.g., stroke risk factors, traumatic brain injury) as covariates influencing the response to physical activity. To date, although candidate biomarkers and environmental risk factors have been identified, little systematic study in humans has emerged in the literature especially in relation to markers associated with affect, anxiety, depression, and sleep.

5. Conduct studies to monitor sedentary time and conduct randomized controlled trials that systematically reduce sedentary behaviors to improve the understanding of the impact of varying contexts, patterns, and durations of sedentary behavior on brain health outcomes (e.g., depression symptoms) throughout the lifespan and in populations with brain health disorders and diseases.

   Rationale: The understanding of the effects of sedentary behavior on brain health is in its infancy. Given that recent evidence indicates that sedentary behavior is distinct from physical inactivity, a greater understanding of the effect of sedentary behavior on brain health may inform and target interventions aimed at improving brain health across a variety of populations, including school-aged children, middle-aged adults, and older adults, as these populations spend considerable time during their day engaged in sitting and other sedentary behaviors. In addition, portable health technologies that continuously measure physical activity, estimate its intensity, and characterize sleep behavior, may offer inroads to better understand such relationships, and perhaps test novel interventions using connected health approaches.

6. Conduct appropriate analyses to examine effect modification by demographic factors. Such analytical approaches require studies that include large samples and substantial variation in sample characteristics (i.e., race/ethnicity, socioeconomic status).

   Rationale: Although some understanding of the effects of physical activity during the developing years and in aging has emerged, evidence for other demographic factors has not been demonstrated in a systematic fashion, affording little opportunity to form strong conclusions about any potential effect of these factors. Findings that incorporate other demographic factors stand to generalize the physical activity-brain health literature, improving understanding of this relationship more broadly across the U.S. population, deepening understanding of health disparities, and informing interventions aimed at improving brain health.

7. Conduct randomized controlled trials and prospective observational studies that will improve understanding of the latency and persistence of the improvements in brain health following both acute and regular physical activity. These studies should have larger sample sizes, longer follow-up

periods, and a broader range of instruments and outcomes relevant for brain health (e.g., mental subdomain of health-related quality of life, affect).

Rationale: To date, the temporal dynamics of the effects of physical activity on brain health are poorly understood. Yet, it is known that individuals start and stop exercise regimens on a regular basis and such variability in the consistency of physical activity may differentially influence the impact of physical activity on brain health outcomes. It is possible that the persistence of the effects might also depend on the dose of activity (frequency, intensity, time, type), the age of the individual, the presence of a disorder or disease, or other factors. Enrolling samples of sufficient size to support mediator analyses (i.e., exploration of putative mechanisms through which the interventions operate) will provide useful information for adapting the interventions to optimize uptake among different subgroups as well as to identify key elements that are essential to improving brain health.

8. Conduct randomized controlled trials and prospective observational research on the impact of muscle-strengthening exercises (often referred to in the literature as resistance training) and other forms of physical activity (e.g., yoga, tai chi), and other modes of activity on brain health outcomes.

   Rationale: Most research in this area has been conducted using aerobic exercise approaches (e.g., brisk walking). Given the effects of muscle-strengthening exercises and the increased popularity of many other forms of physical activity (e.g., yoga, tai chi) and the evolving evidence of their influence on multiple health outcomes, it will be important to understand how these different modalities differentially influence cognition, quality of life, affective, anxiety, depression, and sleep outcomes.

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PART F. CHAPTER 4. CANCER PREVENTION

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INTRODUCTION

In 2017, 1,688,780 new cancer cases and 600,920 cancer deaths are projected to occur in the United States.[1] On average, 38 percent of American women and 42 percent of American men will be diagnosed with an invasive cancer over their lifetimes.[2] Although several genetic causes of cancer have been identified, most cases of cancer are due to the environment or lifestyle.[3] In addition to lack of physical activity, other known lifestyle and preventable causes of cancer include tobacco use, alcohol intake, diet, obesity, and behaviors that increase exposure to oncogenic viruses. Therefore, there is great need and possibilities for cancer prevention through lifestyle change.

There are more than 100 types of cancer based on body site or cell of origin. Furthermore, most cancers include subtypes defined by anatomy, histology, or genomics. Cancer types and subtypes often differ in etiology or natural course. Therefore, studying the association of physical activity with cancer risk is tantamount to determining the effect of physical activity on scores of endpoints. In this report, subtypes of cancer sites are listed where etiologies, including physical activity exposure, are known to vary by subtype.

Decades of epidemiologic research have identified a physically active lifestyle as protective against the occurrence of some common cancers. The 2008 Physical Activity Guidelines Advisory Committee concluded that a moderate, inverse relationship existed between increased levels of physical activity and reduced risks of colon and breast cancers.[4] The 2008 Committee also found some evidence of reductions in risk of lung, endometrial, and ovarian cancers with increased physical activity, but no change in risk of prostate or rectal cancers.[4] Information was deemed too sparse to make conclusions for other cancers. The *Physical Activity Guidelines Advisory Committee Report, 2008*[4] provided probable risk reduction levels, based on reviews of individual reports; no meta-analyses were performed, and none were found from the literature at that time. Since that report was released, the epidemiologic literature has grown enough to allow the use of meta-analytic and pooled analysis techniques to provide robust estimates of the effect of physical activity on occurrence of both common and rarer cancers.

Interest in understanding the health effects associated with sedentary behavior (sitting) is also increasing. The 2008 Advisory Committee did not review the evidence on the association between sedentary behavior and cancer incidence. However, since 2008, an emerging literature has accumulated with respect to the association between sedentary time and cancer incidence and the Cancer Prevention Subcommittee included a question on this issue. (For additional information on the health effects associated with sedentary behavior, see *Part F. Chapter 2. Sedentary Behavior*.)

The 2008 Scientific Report also cited some mechanisms that may explain the associations between physical activity and cancer risk, but did not perform a systematic review.[4] Given the extremely large literature in this area,[5-8] including human experimental, observational, animal models, and other laboratory work, the Cancer Prevention Subcommittee was not able to perform a systematic review of the literature on mechanisms linking physical activity to cancer. However, the Subcommittee recognizes that this topic is a critical area of research that needs further attention and helps provide more understanding of how physical activity is related to cancer.

Finally, while many of the reviewed cancers occur in children as well as adults (e.g., leukemia, lymphoma), the etiology of these cancers often differs significantly in children versus adults. In addition, the usual long latency period for physical activity to protect against cancer development in adults will likely not be relevant to cancers occurring in children. For this reason, the literature review on physical activity and cancer risk has been limited to adults. Therefore, the Subcommittee limited its search to cancers in adults.

REVIEW OF THE SCIENCE

Overview of Questions Addressed

This chapter addresses two major questions and related subquestions:

1. What is the relationship between physical activity and specific cancer incidence?
    a) Is there a dose-response relationship? If yes, what is the shape of the relationship?
    b) Does the relationship vary by age, sex, race/ethnicity, socioeconomic status, or weight status?
    c) Does the relationship vary by specific cancer subtypes?
    d) Is the relationship present in individuals at high risk, such as those with familial predisposition to cancer?

2. What is the relationship between sedentary behavior and cancer incidence?
   a) Is there a dose-response relationship? If yes, what is the shape of the relationship?
   b) Does the relationship vary by age, sex, race/ethnicity, socioeconomic status, or weight status?
   c) Is the relationship independent of levels of light, moderate, or vigorous physical activity?
   d) Is there any evidence that bouts or breaks in sedentary behavior are important factors?

Data Sources and Process Used to Answer Questions

Systematic literature searches were conducted to answer Questions 1 and 2. The databases searched included PubMed, Cochrane, and CINAHL. The literature search to address Question 1 was limited to systematic reviews, meta-analyses, and pooled analyses. The literature search strategy to address Question 2 was expanded to also include original research articles, and was conducted in two steps. Step 1 involved a search for existing systematic reviews and meta-analyses that could address the question. Step 2 involved a de novo literature search of more recent original research studies published after the systematic reviews and meta-analyses. Question 2 is the same as the cancer component of Question 4 in the sedentary behavior chapter (for details, see *Part F. Chapter 2. Sedentary Behavior*.)

In the studies included in the meta-analyses, systematic reviews, and pooled analyses, physical activity was measured by self-report, with different types of physical activity questionnaires. In many studies, participants were presented with a list of typical activities (e.g., walking, running, biking), and asked to indicate the frequency and duration of each activity. Other studies used more general questions about time spent in moderate- or vigorous-intensity activities. Most collected information on recreational activities, several also included occupational activities, and only a few included household activities. Some estimated total physical activity, adding up all of these activities; most limited estimation of amount of activity to leisure time activity. Most of the meta-analyses estimated MET-hours per week of moderate and vigorous physical activities where data were available, but the cut-points for “highest” versus “lowest” activity levels varied across studies. Although most studies assigned a MET value of 6 for vigorous activities, some assigned a value of 8.

Most of the meta-analyses, as well as the large pooled study,[9] were restricted to prospective cohort studies in order to minimize error from reporting that might occur because of recall of past physical activity levels that is required in case-control studies. However, for some more rare cancers, meta-analyses or pooled analyses did include case-control studies. For this reason, the Subcommittee did not exclude results from systematic reviews, meta-analyses, or pooled analyses in making conclusions about the associations between physical activity and risk for specific cancers.

Question 1: What is the relationship between physical activity and specific cancer incidence?

a) Is there a dose-response relationship? If yes, what is the shape of the relationship?
b) Does the relationship vary by age, sex, race/ethnicity, socioeconomic status, or weight status?
c) Does the relationship vary by specific cancer subtypes?
d) Is the relationship present in individuals at high risk, such as those with familial predisposition to cancer?

Sources of evidence: Meta-analyses, systematic reviews, pooled analyses

Cancers for Which Physical Activity Shows Strong Evidence of a Protective Effect

Bladder Cancer

Conclusion Statements

Strong evidence demonstrates that greater amounts of physical activity are associated with reduced risk of developing bladder cancer. **PAGAC Grade: Strong.**

Moderate evidence indicates a dose-response relationship between increasing physical activity levels and decreasing risk of bladder cancer. **PAGAC Grade: Moderate.**

Limited evidence suggests that the effects of physical activity on bladder cancer risk are lower for men than for women. **PAGAC Grade: Limited.** Insufficient evidence is available to determine whether the effects of physical activity on risk of bladder cancer differ by specific age, race/ethnicity, socioeconomic groups, or weight status. **PAGAC Grade: Not assignable.**

Insufficient evidence is available to determine whether the effects of physical activity are similar for all types of bladder cancer. **PAGAC Grade: Not assignable**

Insufficient evidence is available to determine whether the effects of physical activity on bladder cancer risk differ in individuals at elevated risk of bladder cancer. **PAGAC Grade: Not assignable.**

Review of the Evidence

Based on data from 2010 to 2014, the incidence rate of bladder cancer was 19.8 per 100,000 men and women per year.[10] The number of deaths was 4.4 per 100,000 men and women per year. Several factors increase risk of bladder cancer, including smoking, exposure to certain occupational toxins, and arsenic in drinking water.[11] Bladder cancer is more common in individuals older than age 55 years than in younger individuals, in men than in women, and in individuals with a personal or family history of cancer of the urinary tract.

To examine the association between physical activity and risk of bladder cancer, the Subcommittee reviewed one published meta-analysis.[12] The meta-analysis contained data from 11 cohort and 4 case-control studies. The Subcommittee also reviewed one pooled analysis of 12 large prospective cohort studies[9] and meta-analysis data from the World Cancer Research Fund, which included data from 12 cohort studies.[13]

Evidence on the Overall Relationship

A considerable body of epidemiologic data exists on the association between physical activity and risk of developing bladder cancer. The meta-analysis reported that risk of bladder cancer was significantly lower for individuals engaging in the highest versus lowest categories of recreational or occupational physical activity level (relative risk (RR)=0.85; 95% confidence interval (CI): 0.74-0.98).[12] Most studies adjusted for multiple potential confounding factors, including age, body mass index (BMI), and other bladder cancer risk factors. Similar to these findings, the pooled analysis of 12 cohort studies found a statistically significant relationship between the 90th versus 10th percentile level for leisure time physical activity and decreased risk of bladder cancer (RR=0.87; 95% CI: 0.82-0.92).[9] In contrast, the World Cancer Research Fund meta-analysis summary result for highest versus lowest physical activity, which did not include studies focused on occupational physical activity, showed a non-statistically significant effect (RR=0.94, 95% CI: 0.83-1.06).[13]

Dose-response: The meta-analysis examined the dose-response relationship by quartiles of physical activity in each study. Compared with the least active quartile, those in quartiles 2, 3, and 4 had RR (95% CIs) of 0.90 (0.83-0.97), 0.86 (0.77-0.96), and 0.83 (0.72-0.95), respectively.[12] The pooled analysis of 12 cohort studies found a significant linear relationship between increasing leisure time physical activity percentile and decreasing risk of bladder cancer ($P_{overall}$<0.0001; $P_{non\text{-}linear}$=0.59).[9]

Evidence on Specific Factors

Sex: The meta-analysis found some differences in physical activity effect on bladder cancer risk between men (RR=0.92, 95% CI: 0.82-1.05) and women (RR=0.83; 95% CI: 0.73-0.94).[12] Although the pooled analysis found that the effect size of physical activity on risk of bladder cancer was similar in men and women, the association was statistically significant only in women ($P_{heterogeneity}$=0.81).[9]

Age: None of the analyses provided data within specific age groups.

Race/ethnicity: All but one study in the meta-analysis were conducted in the United States and Europe; the one study in Asia (men only) showed a non-statistically significant association of physical activity with bladder cancer risk (RR=0.94; 95% CI: 0.77-1.15).[12]

Socioeconomic status: None of the analyses presented data on the effect of socioeconomic status on the association between physical activity and bladder cancer incidence. Hence, no conclusions can be made on this factor.

Weight status: The pooled analysis examined associations between the 90th percentile versus 10th percentile of physical activity level by BMI. Risk of bladder cancer associated with physical activity level did not differ for those with BMI <25.0 kg/m^2 versus BMI $\geq$25 kg/m^2 ($P_{interaction}$ = 0.80).[9]

Cancer subtype: Neither the meta-analysis nor the pooled analysis provided data by subtype of bladder cancer.

Individuals at high risk: No information was provided in the meta-analysis or in the pooled analysis about the effects of physical activity in individuals at elevated risk of bladder cancer.

For additional details on this body of evidence, visit: https://health.gov/paguidelines/second-edition/report/supplementary-material.aspx for the Evidence Portfolio.

Breast Cancer

Conclusion Statements

Strong evidence demonstrates that greater amounts of physical activity are associated with a lower risk of breast cancer. **PAGAC Grade: Strong.**

Strong evidence demonstrates that a dose-response relationship exists between greater amounts of physical activity and lower breast cancer risk. **PAGAC Grade: Strong.**

Moderate evidence indicates that greater amounts of physical activity are associated with a greater risk reduction in all women regardless of body mass index. **PAGAC Grade: Moderate.** Insufficient evidence is available to determine whether the amount of physical activity and risk of breast cancer incidence varies by age. **PAGAC Grade: Not assignable.** Limited evidence suggests that the relationship between physical activity and breast cancer does not vary by race/ethnicity. **PAGAC Grade: Limited.** Insufficient evidence is available to determine whether the relationship between physical activity and breast cancer varies by socioeconomic status. **PAGAC Grade: Not assignable.**

Limited, but inconsistent, evidence suggests that the relationship between physical activity and breast cancer varies by specific histologic types of breast cancers. **PAGAC Grade: Limited**.

Limited evidence suggests that the relationship between physical activity and breast cancer is apparent in women at increased breast cancer risk, as an enhanced effect of physical activity was associated with premenopausal breast cancer in women with a positive family history of breast cancer. **PAGAC Grade: Limited.**

Review of the Evidence

Based on data from 2010 to 2014, the incidence rate of female breast cancer was 124.9 per 100,000 women per year. The number of deaths was 21.2 per 100,000 women per year.[14] Most commonly, breast cancer occurs in ducts of the breast (ductal carcinoma); lobular carcinoma and inflammatory breast cancer are less common. Breast cancers are typically categorized by estrogen receptor (ER) and progesterone receptor (PR) status (positive (+)/negative (-)), as well as by presence of human epidermal growth factor type 2 receptor (HER2/neu positive (+)/negative (-)). Breast tumors can be further characterized by grade, which is the degree of cellular abnormality seen microscopically. Stage of breast cancer is determined by both pathological and clinical diagnosis. In situ (or Stage 0) breast cancer is that which has not invaded based the lining of the duct or lobule. By definition, Stages 1-4 is invasive breast cancer that has spread to local or distant tissues

The major risk factors for breast cancer, besides increasing age and physical inactivity, are: inherited changes in genetic factors, a first degree family history of breast cancer, increased mammographic density, atypical hyperplasia, radiation therapy, alcohol intake, early age at menarche and late age at menopause, first full-term pregnancy after age 30 years and nulliparity, long term use of menopausal hormone therapy, overweight or obesity after menopause, and White race.[15]

The Subcommittee used information from four meta-analyses[16-19] and two pooled analyses.[9, 20] The meta-analysis by Wu et al[16] included 31 prospective cohort studies published to November 2012. The meta-analysis by Neilson et al[17] included 80 reports from 67 different studies published to June 2015. The meta-analysis by Pizot et al[18] included 38 prospective cohort studies published between 1987 and 2014. The meta-analysis by Liu et al[19] included 126 cohort studies that examined a variety of cancers. Of these, nine studies were included in the breast cancer analysis and five of them were used in the dose-response analysis. The pooled analysis by Gong et al[20] included four studies combined in the African American Breast Cancer Consortium. The pooled analysis by Moore et al[9] included nine cohort studies with 35,178 breast cancer cases. All types of physical activity were included in the meta-analyses by Wu et al[16] and Pizot et al[18]; recreational physical activity only was included in the meta-analyses by Neilson et al[17] and Liu et al[19] and the pooled analysis by Moore et al.[9] The pooled analysis by Gong et al[20] included vigorous physical activity but did not specify what type of activity was specifically recorded and used as the exposure assessment. The meta-analysis by Neilson et al[17] was likewise restricted to moderate-to-vigorous recreational physical activity. The dose-response relationship was tested in all of these meta-analyses and pooled analyses,[9, 16-20] and evidence for a linear statistically significant association between greater amounts of physical activity and lower breast cancer risk was observed in four of these meta-analyses.[16-19]

Evidence on the Overall Relationship

The meta-analysis by Wu et al[16] estimated that the highest versus the lowest categories of all types of physical activity in the 38 cohort studies they included was associated with a decreased risk of breast cancer (RR=0.88; 95% CI: 0.85-0.90). Wu et al[16] also presented the results stratified by menopausal status. For premenopausal women, the random effects model estimates were 0.77 (95% CI: 0.69-0.86) and for postmenopausal women the effect estimates were 0.88 (95% CI: 0.87-0.92).[16] These authors also presented the results for the association between breast cancer incidence and physical activity by type of activity. For occupational activity, the relative risk was 0.84 (95% CI: 0.73-0.96); for non-occupational activity, it was 0.87 (95% CI: 0.82-0.91); for recreational activity, it was 0.87 (95% CI: 0.83-0.91); for household activity, it was 0.89 (95% CI: 0.83-0.95), and for walking, it was 0.87 (95% CI: 0.79-0.96).[16]

Neilson et al[17] reported all results for the association between physical activity and breast cancer risk stratified by menopausal status. Data from 36 case-control and 13 cohort studies were combined to estimate the relative risk of premenopausal breast cancer associated with moderate-to-vigorous recreational activity; for postmenopausal women, data from 38 case-control and 26 cohort studies were combined. For premenopausal women, the estimated odds ratio (OR) was 0.80 (95% CI: 0.74-0.87) and for postmenopausal women, the odds ratio was 0.79 (95% CI: 0.74-0.84).

Pizot et al[18] presented the results for all types of physical activity combined. These authors found a statistically significant reduction for breast cancer incidence when comparing the highest versus the lowest amounts of all types of physical activity combined (OR: 0.88; 95% CI: 0.85-0.91). When examining the associations by type of activity, they reported risk reductions for non-occupational physical activity (OR=0.88; 95% CI: 0.85-0.92 from 30 studies) and occupational physical activity (OR=0.87; 95% CI: 0.83-0.90) based on 11 studies). Pizot et al[18] also reported the results for the association between all types of physical activity combined and breast cancer risk by menopausal status. Premenopausal and postmenopausal women had very similar risk reductions for highest versus lowest levels of physical activity (RR=0.87; 95% CI: 0.78-0.96 and RR=0.88; 95% CI: 0.85-0.91, respectively). Pizot et al[18] also provided risk estimates for studies that used comparable methods for assessing physical activity. Risk reductions were greater in studies that measured physical activity in hours per week (RR=0.81; 95% CI: 0.76-0.87) than in MET-hours per week (RR=0.87; 95% CI: 0.83-0.91) or in other units (RR=0.89; 95% CI: 0.85-0.92).[18]

Liu et al[19] reported decreased risk of overall breast cancer incidence when they compared participants with the highest to the lowest amounts of leisure time physical activity (RR=0.88; 95% CI: 0.84-0.91).

In their pooled analysis from the African American Breast Cancer Epidemiology and Risk Consortium, Gong et al[20] reported that any vigorous activity versus none was associated with a reduction in odds of breast cancer incidence of 0.88 (95% CI: 0.81-0.96).

Moore et al[9] compared participants in the 90th percentile to those in the 10th percentile of physical activity in their pooled analysis and found a statistically significant association with breast cancer incidence (hazard ratio (HR)=0.90; 95% CI: 0.87-0.93).

Dose-response: Evidence for a linear statistically significant association between greater amounts of physical activity and lower breast cancer risk was observed in four of the meta-analyses.[16-19] Using data from three studies, Wu et al[16] observed a statistically significant linear relationship between higher amounts of non-occupational physical activity and lower breast cancer risk. The risk of breast cancer was 2 percent lower (RR=0.98; 95% CI: 0.97-0.99) for every 25 MET-hours per week increment in non-occupational activity (roughly equivalent to 10 hours per week of light household activity). Using data on recreational activity from seven studies, Wu et al[16] estimated that the risk of breast cancer was 3 percent lower (RR=0.97; 95% CI: 0.95-0.98) for every 10 MET-hours per week increment in recreational activity (roughly equivalent to 4 hours per week of walking at 2 miles per hour). Wu et al[16] also found a linear relationship between breast cancer risk and moderate plus vigorous recreational activity using data from eight studies. The risk of breast cancer was 5 percent lower (RR=0.95; 95% CI: 0.93-0.97) for every 2 hours per week increment in moderate plus vigorous activity.[16] When examining vigorous recreational activity only with data from eight studies, Wu et al[16] found that the risk of breast cancer was 5 percent lower (RR=0.95; 95% CI: 0.92-0.97) for every 2 hours per week spent in this level of recreational activity.

Neilson et al[17] plotted dose-response curves across levels of moderate-to-vigorous recreational activity by menopausal status and found a statistically significant, curvilinear dose-response relationship for both menopausal groups. The authors speculated that this curvilinear dose-response association suggested a point of diminishing returns when moderate-to-vigorous recreational activity went beyond 20 to 30 MET-hours per week. However, the 95% confidence intervals were wide at the upper levels of activity, which precluded any definitive conclusions about the nature of this dose-response relationship at very high levels of activity. Neilson et al[17] also plotted dose-response curves with respect to activity duration (hours per week) using data from 13 studies and they found a clear inverse linear association with postmenopausal breast cancer risk. For premenopausal breast cancer risk, using data from 10 studies they observed a J-shaped, statistically significant non-linear trend with an inflection point around 3 hours per week. These studies were distinct from those in the MET-hours per week analysis. The authors investigated the possible reasons for this J-shaped association and suggested that measurement error, covariate adjustment, and heterogeneity across these studies might partially explain these unexpected findings. The study by Neilson et al[17] is the only meta-analysis to examine the dose-response relationships separately for premenopausal and postmenopausal breast cancer.

Pizot et al[18] performed dose-response analyses with 11 studies that reported physical activity in MET-hours per week and with 11 studies that reported duration of physical activity in hours per week and noted statistically significant dose-response relationships between amounts of physical activity and breast cancer risk without evidence for a threshold.

Liu et al[19] also found a statistically significant decreasing risk for breast cancer across categories of leisure time physical activity estimated in MET-hours per week.

Gong et al[20] tested for a linear trend across categories of hours per week of vigorous physical activity and found evidence for a statistically significant trend, although the dose-response association was not very evident with the highest category of physical activity (7 hours per week), which was associated with a risk of 0.86 (95% CI: 0.68-1.10) compared with the lowest category (<2 hours per week), which had a risk of 0.90 (95% CI: 0.81-1.01).

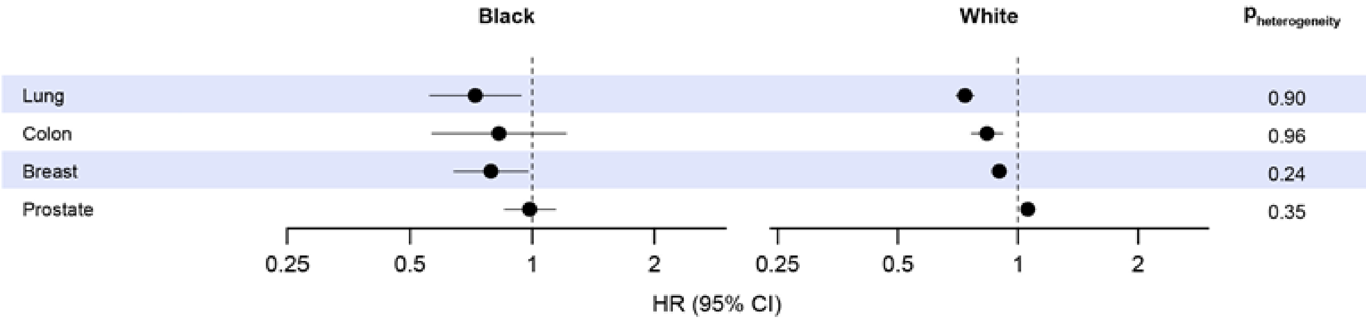
Finally, Moore et al[9] also found a linear dose-response relationship between increasing levels of leisure time physical activity and decreased breast cancer risk (*P*<0.0001).

Evidence on Specific Factors

Age: Only the pooled analysis by Gong et al[20] reported results by age (<50 years versus ≥50 years) and found comparable risk reductions for both age groups of 15 and 12 percent that were borderline statistically significant. Several of these meta-analyses and pooled analyses did examine the effects of physical activity on breast cancer risk by menopausal status, which could be a proxy for age. Overall, there appears to be a somewhat greater breast cancer risk reduction associated with higher amounts of physical activity among postmenopausal women than premenopausal women.

Race/ethnicity: The pooled analysis by Gong et al[20], which included only American women of African ancestry, reported a statistically significant 12 percent decreased risk associated with vigorous physical activity. Neilson et al[17] presented the results for studies by racial groups and found statistically significant reductions in premenopausal breast cancer risk for White, White-Hispanic, and Asian women. For postmenopausal women, statistically significant reductions in breast cancer risk also were evident for White-Hispanic and Asian women. No statistically significant risk reductions were found for Hispanic or Black women in either menopausal category.[17] The Moore et al[9] pooled analysis found similar associations between highest versus lowest physical activity level and breast cancer risk in black and white women (*P* heterogeneity = 0.24) (Figure F4-1). No other studies presented their results by race/ethnic groups.

Figure F4-1. Summary Multivariable Hazard Ratios and 95% Confidence Intervals (CI) for a Higher (90th percentile) versus Lower (10th percentile) Level of Leisure-Time Physical Activity, by Cancer Type, Stratified by Race/Ethnicity



Source: Reproduced with permission from [Moore et al[9], Association of leisure-time physical activity with risk of 26 types of cancer in 1.44 million adults. 2016. 176(6):816–825]. Copyright©(2016) American Medical Association. All rights reserved.

Socioeconomic status: None of the analyses presented data on the effect of socioeconomic status on the association between physical activity and breast cancer incidence. Hence, no conclusions can be made on this factor.

Weight status: A statistically significant effect modification of the association between breast cancer incidence and physical activity by BMI was found in the meta-analysis by Neilson et al,[17] with greater risk reductions found in both premenopausal and postmenopausal women with a BMI <25 kg/m^2 (RR=0.85; 95% CI: 0.73-0.99 and RR=0.84; 95% CI: 0.77-0.92, respectively) than in women with a BMI ≥25 kg/m^2 (RR=0.99; 95% CI: 0.98-1.00 and RR=0.88; 95% CI: 0.82-0.95, respectively). Pizot et al[18] reported risk reductions in breast cancer incidence for both women with low and high BMI (RR=0.84; 95% CI: 0.78-0.90 and RR=0.87; 95% CI: 0.81-0.93). In contrast, in the Moore et al[9] pooled analysis no effect modification by BMI was observed for the association between leisure time physical activity and breast cancer incidence.

Cancer subtype: The association between physical activity and different breast cancer subtypes was considered in four of these meta-analyses and pooled analyses but the findings were inconsistent.[16, 17, 19, 20] Wu et al[16] found stronger risk reductions for invasive breast cancers than in situ tumor stage cancers (RR=0.81; 95% CI: 0.73-0.91 versus RR=0.86; 95% CI: 0.74-0.99). These results also were found in the meta-analysis by Liu et al,[19] in which greater risk reductions for invasive cancers compared with in situ breast cancers were found. Wu et al[16] also reported that women with estrogen receptor negative/progesterone receptor negative breast cancer tumors had a greater reduction in risk compared with estrogen receptor positive/progesterone receptor positive breast cancer cases (RR=0.77; 95% CI: 0.65-0.90 and RR=0.93; 95% CI: 0.87-0.98). Gong et al[20] reported a statistically significant inverse association with vigorous physical activity for estrogen receptor positive breast cancer (OR=0.88; 95% CI: 0.80-0.98) but not for estrogen receptor negative breast cancer (OR=0.93; 95% CI: 0.82-1.06). Pizot et al[18] observed stronger risk reductions for women with estrogen receptor negative breast cancer (OR=0.80; 95% CI: 0.83-0.90) than for estrogen receptor positive breast cancers (OR=0.89; 95% CI: 0.83-0.95) associated with physical activity. Neilson et al[17] found statistically significant associations between moderate-to-vigorous recreational activity and ductal and lobular tumor histology in postmenopausal women but observed no inverse associations for mucinous or tubular breast cancers. They also stratified their study results by hormone receptor status and found inverse and statistically significant associations for estrogen receptor positive/progesterone receptor positive premenopausal and postmenopausal breast cancers. In addition, they found that tumors with several combinations of hormone receptor and HER2/neu status were also protected with high levels of physical activity including: 1) estrogen receptor positive, 2) progesterone receptor positive, 3) estrogen receptor positive/progesterone receptor negative, 4) HER2 positive, or 5) HER2 negative/estrogen receptor positive/progesterone receptor positive postmenopausal breast cancer. In addition, physical activity protected against: 1) estrogen receptor negative/progesterone receptor negative, HER2 negative, or p53 premenopausal breast cancers. No clear pattern of greater risk reductions by tumor grade was seen.[17]

Other factors: No effect modification by geographic location (i.e., America, Europe, Asia) was observed in the meta-analysis by Wu et al.[16] No other analyses examined effect modification of the association between physical activity and breast cancer incidence by geographic location. The pooled analysis by Gong et al[20] of African Americans suggested that having no family history of breast cancer conferred greater risk reduction associated with physical activity than having a positive family history. Neilson et al[17] found limited evidence that a positive family history of breast cancer was associated with a greater risk reduction than no family history in premenopausal women (RR=0.28; 95% CI: 0.14-0.58 versus RR=0.72; 95%CI: 0.58-0.88). For postmenopausal women, the effect of physical activity on reducing breast cancer risk in women with and without a family history of breast cancer was nearly equal (RR=0.85; 95% CI: 0.70-1.02 versus RR=0.83; 95% CI: 0.75-0.92). The stratified analyses in the meta-analysis by Neilson et al[17] for premenopausal women with a family history of breast cancer were based on only three studies and must be interpreted with caution.

In the analyses by Gong et al[20] and Neilson et al,[17] physical activity conferred a greater benefit for breast cancer risk reduction among parous women as compared to nulliparous women. In the Neilson et al[17] meta-analysis, premenopausal parous women had a 36 percent risk reduction (OR=0.64; 95% CI: 0.46-0.90) associated with higher amounts of moderate-to-vigorous recreational activity.

The meta-analysis by Pizot et al,[18] showed a statistically significant effect modification between hormone replacement therapy use and breast cancer risk. A beneficial effect of physical activity was observed only in those women who never used hormone replacement therapy while ever users had no risk reductions associated with physical activity. Neilson et al[17] found that not using hormone replacement therapy and ever use were both associated with statistically significant reduced breast cancer risks but that the effects were stronger in non-users than ever users.

For additional details on this body of evidence, visit: https://health.gov/paguidelines/second-edition/report/supplementary-material.aspx for the Evidence Portfolio.

Colon Cancer

Conclusion Statements

Strong evidence demonstrates that greater amounts of recreational, occupational, or total physical activity are associated with a lower risk of developing colon cancer. **PAGAC Grade: Strong.**

Strong evidence demonstrates a dose-response relationship between increasing physical activity levels and decreasing risk of colon cancer. **PAGAC Grade: Strong.**

Strong evidence demonstrates that the effects of physical activity on colon cancer risk are evident in both men and women. **PAGAC Grade: Strong.** Insufficient evidence is available to determine whether the effects of physical activity on risk of colon cancer differ by specific age, race/ethnic, or socioeconomic groups in the United States. **PAGAC Grade: Not assignable.** Moderate evidence indicates that weight status does not affect the associations between physical activity and colon cancer risk. **PAGAC Grade: Moderate.**

Strong evidence demonstrates that greater amounts of physical activity are associated with a lower risk of developing both proximal and distal colon cancer. **PAGAC Grade: Strong.**

Insufficient evidence is available to determine whether the effects of physical activity on colon cancer risk differ in individuals at elevated risk of colon cancer. **PAGAC Grade: Not assignable.**

Review of the Evidence

Colon cancer is the third most commonly diagnosed cancer in the United States in both men and women.[21] Based on data from 2010-2014, the incidence rate of colon cancer in the United States was 28.2 per 100,000 men and women per year. Risk factors for colon cancer include: increased age, African-American race or Jewish ethnicity, family history of colorectal cancer, personal history of adenomatous colorectal polyps, history of certain inflammatory bowel conditions, a known family history of a hereditary colorectal cancer syndrome, diabetes mellitus, smoking, obesity, alcohol intake, and eating red and processed meats.[22]

To examine the association between physical activity and risk of colon cancer, 8 systematic reviews were reviewed[19, 23-29] of which 7[19, 23-28] included meta-analyses, as well as one pooled analysis of 12 large prospective cohort studies.[9] The Subcommittee also reviewed meta-analysis data from the World Cancer Research Fund.[30, 31] Because the association of physical activity with colon and rectal cancer differs by site (see the section on rectal cancer, below), the Subcommittee did not include studies where colorectal cancer was the outcome of interest because the relationship between physical activity and colon cancer likely would be obscured. The reviews contained data from between 8 and 21 epidemiologic studies.

Evidence on the Overall Relationship

A large body of epidemiologic data exists on the association between physical activity and risk of developing colon cancer. The most recent meta-analysis reported that risk of colon cancer is significantly reduced for individuals engaging in the highest versus lowest categories of physical activity level (RR=0.81, 95% CI: 0.83-0.93).[19] Other meta-analyses found similar effect sizes showing inverse associations between highest versus lowest levels of physical activity and risk of developing colon cancer.[23-27, 30, 31] Most studies adjusted for multiple potential confounding factors, including age, BMI, and colon cancer risk factors, although adjustment for colon cancer screening (which could be related to physical activity level) was not typically done. To address this issue, one meta-analysis examined the associations between physical activity and colon cancer risk before 1993 (before testing fecal occult blood was widely used), between 1993 and 1999, and after 1999 when colon cancer screening (by endoscopy) became widely available.[28] The risk estimates for physical activity and colon cancer risk did not differ between the time periods. Studies published before 1993 (RR=0.74; 95% CI: 0.67-0.82); those published between 1993 and 1999 (RR=0.78, 95% CI: 0.70-0.86); and those published after 1999 (RR=0.78; 95% CI: 0.73-0.83) demonstrated similar risk reductions for this association.

Dose-response: A dose-response relationship is apparent, with risk decreasing at higher levels of physical activity. A dose-response meta-analysis of three cohort studies found that per 30 minutes per day of recreational physical activity, the relative risk of colon cancer was 0.88 (95% CI: 0.80-0.96).[31] In contrast, dose-response estimates per 5 MET-hours per week of total physical activity were significant only for distal colon cancer, with a relative risk of 0.92 (5 studies, 95% CI: 0.89-0.96).[31] One meta-analysis estimated dose-response by percentile of physical activity, and found a linear reduction in risk across the 20th to 95th percentiles and estimated risk reductions between these two percentiles of 0.13 in men and 0.14 in women.[23] This same meta-analysis plotted risk for colon cancer by leisure time physical activity in those studies with MET-hours per week or MET-minutes per week data, and found dose-response risk reductions in both men and women. The pooled analysis of 12 cohort studies found a significant relationship between increasing leisure time physical activity percentile and decreased risk of colon cancer ($P_{overall}$<0.0001; $P_{non\text{-}linear}$=0.4).[9]

Evidence on Specific Factors

Sex: Meta-analyses found that physical activity reduced colon cancer risk in both men and women, and there were no statistically significant differences in this effect by sex overall,[23] or for proximal or distal colon cancer.[24, 26]

Age: None of the analyses or the systematic review provided data within specific age groups.

Race/ethnicity: Studies in the United States and Europe were primarily in Caucasians. One systematic review of Japanese studies reported on data from two cohort and six case-control studies, and found that the association of increased physical activity with reduced risk for colon cancer was stronger in men than women, and stronger in proximal than distal cancer.[29] The pooled analysis of 12 cohort studies examined the association between the 90th percentile versus 10th percentile of physical activity level in Black and White individuals (Figure F4-1).[9] The hazard ratio was similar in the two groups ($P_{heterogeneity}$= 0.96).

Socioeconomic status: None of the analyses or the systematic review presented data on the effect of socioeconomic status on the association between physical activity and colon cancer incidence. Hence, no conclusions can be made on this factor.

Weight status: The pooled analysis examined associations between the 90th percentile versus 10th percentile of physical activity level by BMI. Risk of colon cancer for those with BMI <25.0 kg/m² did not differ from that of individuals with BMI ≥25 kg/m² (*P*-value for effect modification=0.81).[9]

Cancer subtype: Two meta-analyses were conducted on studies that included data by anatomic subsite.[24, 26] Comparing most to least active individuals, the relative risks for proximal colon cancer were almost identical in the two reports: 0.73 (95% CI: 0.66-0.81)[24] and 0.76 (95% CI: 0.70-0.83).[26] Similarly, the relative risks for distal colon cancer were almost identical in the two reports: 0.74 (95% CI: 0.68-0.80)[24] and 0.77 (95% CI: 0.71-0.83).[26] A dose-response meta-analysis of three cohort studies found that per 30 minutes per day of recreational physical activity, the relative risks of proximal and distal colon cancer were 0.89 (95% CI: 0.82-0.96), and 0.87 (95% CI: 0.77-0.98), respectively.[31]

Individuals at high risk: No information was provided in the systematic review or analyses about effects of physical activity in individuals at elevated risk of colon cancer.

For additional details on this body of evidence, visit: https://health.gov/paguidelines/second-edition/report/supplementary-material.aspx for the Evidence Portfolio.

Endometrial Cancer

Conclusion Statements

Strong evidence demonstrates that greater amounts of physical activity are associated with a lower risk of endometrial cancer. **PAGAC Grade: Strong.**

Moderate evidence indicates that a dose-response relationship exists between greater amounts of physical activity and lower endometrial cancer risk. **PAGAC Grade: Moderate.**

Moderate evidence indicates that greater amounts of physical activity are associated with a greater risk reduction in women with a body mass index of greater than 25 kg/m² compared to women with a body mass index of less than 25 kg/m². **PAGAC Grade: Moderate.** Insufficient evidence is available to determine whether the association between physical activity and risk of endometrial cancer varies by age, race/ethnicity, or socioeconomic status. **PAGAC Grade: Not assignable.**

Insufficient evidence is available to determine whether specific histologic types of endometrial cancers modify the relationships between amounts of physical activity and risk of endometrial cancer. **PAGAC Grade: Not assignable.**

Insufficient evidence is available to determine whether the effects of physical activity on endometrial cancer risk differ in individuals at elevated risk of endometrial cancer. **PAGAC Grade: Not assignable.**

Review of the Evidence

Based on data from 2010 to 2014, the incidence rate of endometrial cancer was 25.7 per 100,000 women per year.[32] The number of deaths was 4.6 per 100,000 women per year. Several factors increase risk of endometrial cancer, including obesity and having metabolic syndrome, hyperinsulinemia, nulliparity, early age at menarche, late age at menopause, polycystic ovarian syndrome, first degree relative with endometrial cancer, and Lynch syndrome.[32]

The Subcommittee used information from four meta-analyses[19, 33-35] and one pooled analysis.[9] The meta-analysis by Keum et al[33] included 20 studies (10 cohort and 10 case-control studies) published to September 2013. The meta-analysis by Moore et al[34] included nine prospective studies published to December 2009. The meta-analysis by Schmid et al[35] included 33 studies (15 prospective cohort studies, 3 retrospective cohort studies, 1 case-cohort study and 14 case-control studies). The meta-analysis by Liu et al[19] included 126 cohort studies. Of these, nine studies were a binary endometrial cancer analysis and five of them were used in the dose-response analysis. The pooled analysis[9] included 9 cohort studies with 5,346 endometrial cancer cases. Recreational physical activity was included in two of the meta-analyses[19, 33] and the pooled analysis.[9] Moore et al[34] included recreational and occupational activity in their review and Schmid et al[35] included recreational, occupational, and household activity and walking in their review. The dose-response relationship was examined in three of the meta-analyses[19, 33, 35] and in the pooled analysis.[9]

Evidence on the Overall Relationship

The meta-analysis by Keum et al[33] found that the highest versus lowest categories of leisure time physical activity in the 20 studies they included were associated with a decreased risk of endometrial cancer (RR=0.82; 95% CI: 0.75-0.90). The meta-analysis by Moore et al[34] reported that the highest versus lowest amounts of recreational physical activity were associated with a statistically significant reduction in endometrial cancer incidence (RR=0.73; 95% CI: 0.58-0.93). These authors also presented the results for highest versus lowest amounts of occupational physical activity and found similar risk reductions (OR=0.79; 95% CI: 0.71-0.88). Schmid et al[35] presented the results for all types of physical activity combined as well as by type of activity. These authors found a statistically significant reduction for endometrial cancer incidence when comparing the highest versus the lowest amounts of all types of physical activity combined (OR=0.80; 95% CI: 0.75-0.85). When examining the associations by type of activity, they reported risk reductions for recreational (OR=0.84; 95% CI: 0.78-0.91), occupational (OR=0.81; 95% CI: 0.75-0.87), and household (OR=0.70; 95% CI: 0.47-1.02) activities as well as for walking (OR=0.82; 95% CI: 0.69-0.97). Schmid et al[35] also presented their results by the intensity of physical activity and reported that endometrial cancer risk was decreased with all intensity levels of physical activity (light, moderate-to-vigorous, and vigorous) and these risk reductions were all statistically significant. The greatest reduction in endometrial cancer incidence was associated with light-intensity physical activity for which a relative risk of 0.65 was observed (95% CI: 0.49-0.86). Moderate-to-vigorous and vigorous-intensity physical activity had similar associations, with endometrial cancer risk of RR=0.83 (95% CI: 0.71-0.96) and 0.80 (95% CI: 0.72-0.90), respectively.[35] Liu et al[19] reported a null association for overall endometrial cancer incidence when they compared participants with the highest to the lowest amounts of leisure time physical activity (RR=0.94; 95% CI: 0.77-1.15). Moore et al[9] compared participants in the 90th percentile to those in the 10th percentile of physical activity and found a statistically significant decreased risk of endometrial cancer (HR=0.79; 95% CI: 0.68-0.92).

Dose-response: Keum et al[33] observed a non-linear statistically significant relationship between greater amounts of leisure time physical activity and lower endometrial cancer risk. They estimated that per 3 MET-hours per week, the relative risk was 0.98 (95% CI: 0.95-1.00) and per 1 hour per week, the RR was 0.95 (95% CI: 0.93-0.98). Schmid et al[35] restricted their assessment of dose-response to studies that reported their results in MET-hours per week and to account for variability in the range of MET-hour levels in the individual studies, they performed analyses summarizing studies that provided the risk estimates for 3-8, 9-20 and greater than 20 MET-hours as compared to less than 3 MET-hours of physical activity per week. They obtained relative risks of 0.94 (95% CI: 0.74-1.20), 0.79 (95% CI: 0.64-0.98), and 0.87 (95% CI: 0.71-1.06) for 3-8, 9-20 and greater than 20 MET-hours as compared to less than 3 MET-hours of physical activity per week. In addition, within the range of 0 to approximately 40 MET-hours per week of recreational physical activity, they observed a non-linear inverse dose-response relationship for recreational physical activity with endometrial cancer risk ($P_{non\text{-}linearity}$<0.05), which indicated a 5 percent reduced risk of endometrial cancer for those engaging in 12 MET-hours per week of recreational activity compared to those not engaging in regular physical activity (RR=0.95 (95% CI: 0.91-0.99). Liu et al[19] estimated the hazard ratios across categories of leisure time physical activity from 0 to 40 MET-hours per week in increments of between 10 and 20 MET-hours per week. They found no evidence for a linear dose-response trend (*P*-trend=0.46). However, Moore et al[9] did observe a statistically significant linear dose-response trend (P<0.0001) between greater amounts of physical activity and lower endometrial cancer risk.

Evidence on Specific Factors

Age: None of the analyses presented their results stratified by different age groups, hence, no conclusions can be made regarding the role of age on the association between physical activity and endometrial cancer.

Race/ethnicity: No conclusions can be made regarding the role of race/ethnicity in the association between physical activity and endometrial cancers because none of the analyses considered these factors.

Socioeconomic status: None of the analyses presented data on the effect of socioeconomic status on the association between physical activity and endometrial cancer incidence. Hence, no conclusions can be made on this factor.

Weight status: A statistically significant effect modification of the association between endometrial cancer incidence and physical activity by BMI was found in the meta-analysis by Schmid et al,[35] with a greater risk reduction found in women with a BMI ≥25 kg/m^2 (OR=0.69 (95% CI: 0.52-0.91) than in women with a BMI <25 kg/m^2 (OR=0.97; 95% CI: 0.84-1.13). In the Moore et al[9] pooled analysis, effect modification by BMI was observed for the association between leisure time physical activity and endometrial cancer incidence. This pooled analysis showed no effect of physical activity on endometrial cancer incidence for women with a BMI <25 kg/m^2 but stronger risk reductions were observed for those with a BMI ≥25 kg/m^2 (Note: no risk estimates were provided in the Moore et al[9] pooled analysis).

Cancer subtype: None of the analyses considered the association with physical activity for different endometrial cancer subtypes.

Other factors: No effect modification by geographic location (i.e., America, Europe, Asia) was observed in the meta-analyses by Keum et al[33] or Schmid et al.[35] Likewise, no effect modification was observed by use or hormone therapy, oral contraceptives, menopausal status, or parity.[33, 35] There was some indication that smokers who were more physically active as compared to the least active smokers had a greater reduction in endometrial cancer incidence (RR=0.79 (95% CI: 0.71-0.87) than non-smokers who were the most active compared to the least active (RR=0.87 (95% CI: 0.73-1.03).[33]

For additional details on this body of evidence, visit: https://health.gov/paguidelines/second-edition/report/supplementary-material.aspx for the Evidence Portfolio.

Esophageal Cancer

Conclusion Statements

Strong evidence demonstrates that greater amounts of recreational, occupational, or total physical activity are associated with a lower risk of developing adenocarcinoma of the esophagus. **PAGAC Grade: Strong.**

Limited evidence suggests that greater amounts of physical activity are not associated with a lower risk of developing squamous cell carcinoma of the esophagus. **PAGAC Grade: Limited.**

Limited evidence suggests a dose-response relationship between physical activity and risk of adenocarcinoma of the esophagus. **PAGAC Grade: Limited.**

Available evidence is insufficient to determine whether the effects of physical activity on esophageal cancer risk differ by age, sex, race/ethnicity, weight status, socioeconomic status, or in individuals at elevated risk of esophageal cancer. **PAGAC Grade: Not assignable.**

Review of the Evidence

Based on data from 2010-2014, the incidence rate of esophageal cancer in the United States was 4.2 per 100,000 men and women per year, and deaths from this cancer were 4.1 per 100,000.[36] Esophageal cancer is classified into two main types: adenocarcinoma, which occurs in the lower part of the esophagus, and squamous cell carcinoma, which develops in the upper part. Risk factors for esophageal adenocarcinoma include obesity, Barrett's esophagus, smoking, and gastro-esophageal reflux disease.[37] Risk factors for squamous cell carcinoma of the esophagus include smoking, alcohol use, and exposure to some forms of human papilloma virus.[38]

The Subcommittee reviewed evidence of associations between physical activity and esophageal cancer risk. Three meta-analyses were reviewed,[39-41] and one pooled analysis of six cohort studies.[9] Because the biology and etiology of the two types of esophageal cancers differ considerably, the Subcommittee focused on results that were separate for these types rather than for all esophageal cancer combined.

Two dozen epidemiologic studies on the association between physical activity and risk of developing esophageal cancer have been published. Some meta-analyses limited the evidence to studies with incidence outcomes only,[40] while others included studies with either incidence or mortality as the disease indicator.[39]

Evidence on the Overall Relationship

In the most comprehensive meta-analysis of physical activity and esophageal cancer risk,[39] 24 individual studies were available for the meta-analysis, of which 9 were cohort and 15 were case-control studies. This meta-analysis found that risk of esophageal adenocarcinoma was statistically significantly reduced for individuals engaging in highest versus lowest levels of activity (RR=0.79; 95% CI: 0.66-0.94). Conversely, physical activity was not related to risk of squamous cell carcinoma of the esophagus (RR=0.94; 95% CI: 0.41-2.16). Other meta-analyses found similar effect sizes showing inverse associations between highest versus lowest levels of physical activity and risk of developing adenocarcinoma of the esophagus, but not squamous cell esophageal cancer.[40, 41] When all types of esophageal cancer were combined, adjustment for smoking, adiposity, and alcohol intake did not substantially alter effect sizes. Similar trends were seen in the pooled analysis (adenocarcinoma HR=0.58, 95% CI: 0.37-0.89; squamous cell esophageal cancer HR=0.80, 95% CI: 0.61-1.06).[9]

Dose-response: One meta-analysis performed dose-response analyses for all esophageal cancers combined from five studies.[41] The meta-analysis reported that the middle and highest tertiles or quartiles of physical activity were associated with reductions of 12 percent (RR=0.88 95% CI: 0.7-1.1) and 24 percent (RR-0.76; 95% CI: 0.60-0.97), respectively.[41] However, given that these analyses were only for combined adenocarcinoma and squamous cell carcinoma, the dose-response relationship cannot be accurately defined. The pooled analysis estimated dose-response using within-study percentile; with increasing percentile of physical activity, incidence of esophageal adenocarcinoma was statistically significantly and linearly decreased (P<0.0001).[9] Because the percentiles were not defined for dose, the dose-response relationship cannot be accurately determined.

Evidence on Specific Factors

Age: None of the analyses reported effects of physical activity by specific age groups.

Sex: Analysis by sex was performed for all esophageal cancers combined in all reviewed meta-analyses; risk reduction was higher for women than men, but data were not presented for adenocarcinoma of the esophagus.[39-41] However, given that these analyses were only for adenocarcinoma and squamous cell carcinoma combined, the relationship within sex cannot be accurately defined. In the pooled analysis, similar effects of physical activity on reduced risk for adenocarcinoma of the esophagus were seen for both men and women ($P_{\text{effect modification}}$=0.75). Given the discrepancies between the meta-analysis and the pooled analysis, the Subcommittee could not determine whether physical activity reduces risk for esophageal cancer in both sexes.

Race/ethnicity: Studies included primarily Caucasian and Asian populations, with little difference observed between the two populations for combined adenocarcinoma and squamous cell carcinoma of the esophagus. No analyses were available for adenocarcinoma by race/ethnicity.

Socioeconomic status: None of the analyses presented data on the effect of socioeconomic status on the association between physical activity and esophageal cancer incidence. Hence, no conclusions can be made on this factor.

Weight status: The pooled analysis[9] examined the effect of highest versus lowest level of physical activity on esophageal adenocarcinoma in individuals with BMI <25 kg/m^2 versus $\geq$25 kg/m^2. The analysis found similar effect sizes in the two groups, although the statistically significant effect was limited to those in the overweight/obese group ($P_{\text{effect modification}}$=0.60). BMI did not change the effect of physical activity on squamous cell carcinoma of the esophagus ($P_{\text{effect modification}}$ =0.60). Because no information was available from a meta-analysis, the Subcommittee could not conclude that weight status was unrelated to physical activity effect.

Individuals at high risk: No information was provided in the analyses about effects of physical activity in individuals at elevated risk of esophageal cancer.

Cancer subtype: In the most comprehensive meta-analysis of physical activity and esophageal cancer risk,[39] 24 individual studies were available for the meta-analysis, of which 9 were cohort and 15 were case-control studies. This meta-analysis found that risk of esophageal adenocarcinoma was statistically significantly reduced for individuals engaging in highest versus lowest levels of activity (RR=0.79; 95% CI: 0.66-0.94). Conversely, physical activity was not related to risk for squamous cell carcinoma of the esophagus (RR=0.94; 95% CI 0.41-2.16).

For additional details on this body of evidence, visit: https://health.gov/paguidelines/second-edition/report/supplementary-material.aspx for the Evidence Portfolio.

Gastric Cancer

Conclusion Statements

Strong evidence demonstrates that greater amounts of physical activity are associated with a lower risk of developing gastric cancer. **PAGAC Grade: Strong.**

Moderate evidence indicates that as levels of physical activity increase, risk of gastric cancer decreases. **PAGAC Grade: Moderate.**

Insufficient evidence is available on whether the effects of physical activity on gastric cancer risk vary by sex, age, race/ethnicity, socioeconomic groups, or weight status. **PAGAC Grade: Not assignable.**

Moderate evidence indicates that as levels of physical activity increase, the risk of both subtypes of gastric cancer—cardia and non-cardia adenocarcinoma—decreases. **PAGAC Grade: Moderate.**

Insufficient evidence is available to determine whether the effects of physical activity on gastric cancer risk differ in individuals at elevated risk of gastric cancer. **PAGAC Grade: Not assignable.**

Review of the Evidence

In the United States, the incidence rate of gastric cancer is 7.3 per 100,000 men and women per year, based on data from 2010 to 2014.[42] The major risk factor for this cancer is infection with Helicobacter pylori. Other risk factors include smoking, genetics, some industrial chemicals, and regular intake of highly salted foods. Gastric cancer is classified into two main subtypes: cardia adenocarcinoma and noncardia adenocarcinoma. Biologically, cardia gastric cancer is similar to the adjacent esophageal adenocarcinoma.

Evidence on the Overall Relationship

The Subcommittee reviewed five meta-analyses on the associations between physical activity and gastric cancer[39, 40, 43-45] and one pooled analysis of seven cohort studies.[9] Because the biology and etiology of the two subtypes of gastric cancers may differ, results that were separate for these subtypes, as well as all gastric cancer combined, were reviewed.

Considerable evidence indicates that physical activity is associated with a reduced risk of gastric cancer. Some meta-analyses limited studies to those with incidence outcomes only,[40, 44] while one included studies with either incidence or mortality as the outcome.[39] This latter found no difference in effect size when studies with fatal cases as endpoints were removed.

In the most comprehensive meta-analysis of physical activity and incident gastric cancer risk,[44] 22 individual studies were available for the meta-analysis, of which 10 were cohort and 12 were case-control studies. This meta-analysis found that risk of gastric cancer was statistically significantly reduced for individuals engaging in highest versus lowest levels of activity (RR=0.81; 95% CI: 0.73-0.89). Similar results were found in the other meta-analyses and the pooled analysis.[9, 39, 40, 43, 45] Adjustment for smoking, adiposity, and alcohol intake did not substantially alter effect sizes.

Dose-response: One meta-analysis estimated dose-response analyses for all gastric cancers combined.[45] Compared with the least active individuals, those in the middle activity tertile had an adjusted odds ratio of 0.91 (95% CI: 0.82-1.02), and those in the highest tertile had an adjusted odds ratio of 0.78 (95% CI: 0.68-0.90) ($P_{\text{difference between groups}}$ = 0.08).[45] The pooled analysis estimated dose-response using within-study percentile.[9] With increasing percentile of physical activity, incidence of gastric cardia cancer was statistically significantly, but non-linearly, decreased (P_{overall} = 0.02, $P_{\text{non-linear}}$ = 0.0037). With increasing percentile of physical activity, incidence of gastric noncardia cancer was statistically significantly decreased (P_{overall} = 0.015, $P_{\text{non-linear}}$ = 0.58).

Evidence on Specific Factors

Age: None of the analyses reported the effects of physical activity on gastric cancer by age group.

Sex: Analysis by sex was performed for all gastric cancers combined. Risk reduction was statistically significant in men (RR=0.87; 95% CI: 0.77-0.99), but not women (RR=0.77; 95% CI: 0.53-1.12).[44]

Race/ethnicity: Studies included primarily Caucasian and Asian populations, with little difference between the two. In one meta-analysis,[44] 3 of 10 cohort studies and 6 of 12 case-control studies were of Asian populations. The relative risk of high versus low physical activity on all gastric cancer combined was 0.82 (95% CI: 0.74-0.90).

Socioeconomic status: None of the analyses presented data on the effect of socioeconomic status on the association between physical activity and gastric cancer incidence. Hence, no conclusions can be made on this factor.

Weight status: The pooled analysis examined the effect of 90th versus 10^{th} percentile of level of physical activity on gastric cancer in individuals with BMI <25 kg/m^2 versus ≥25 kg/m^2.[9] The study found that high physical activity level was associated with decreased gastric cardia cancer in individuals with BMI ≥25 kg/m^2, but not in those with BMI <25 kg/m^2 (*P* for effect modification: 0.02). In contrast, physical activity was not statistically significantly associated with risk for gastric noncardia cancer in either BMI category.

Cancer subtype: The analyses estimated overall associations by cancer subtype (gastric cardia versus noncardia). In the largest meta-analysis, high physical activity levels were associated with noncardia (RR=0.62; 95% CI: 0.52-0.75), but not gastric cardia cancer (RR=0.80; 95% CI: 0.64-1.01).[44] In contrast, pooled analysis found a significant association between 90th versus 10^{th} percentile of level of physical activity and risk of gastric cardia cancer (HR=0.80; 95% CI: 0.64-0.95), but no significant association with gastric noncardia cancer.[9]

Individuals at high risk: No information was provided in the analyses about effects of physical activity in individuals at elevated risk of gastric cancer.

For additional details on this body of evidence, visit: https://health.gov/paguidelines/second-edition/report/supplementary-material.aspx for the Evidence Portfolio.

Renal Cancer

Conclusion Statements

Strong evidence demonstrates that greater amounts of physical activity are associated with reduced risk of developing renal cancer. **PAGAC Grade: Strong.**

Limited evidence suggests that a dose-response relationship exists between increasing physical activity levels and decreasing risk of renal cancer. **PAGAC Grade: Limited.**

Limited evidence suggests that the effects of physical activity on renal cancer risk are similar for men and women. **PAGAC Grade: Limited.** Limited evidence suggests that the effects of physical activity on renal cancer risk do not vary by weight status. **PAGAC Grade: Limited.** Insufficient evidence is available to determine whether the effects of physical activity on risk of renal cancer differ by specific age, race/ethnic, or socioeconomic groups. **PAGAC Grade: Not assignable.**

Insufficient evidence is available to determine whether the effects of physical activity are similar for all subtypes of renal cancer. **PAGAC Grade: Not assignable.**

Insufficient evidence is available to determine whether the effects of physical activity on renal cancer risk differ in individuals at elevated risk of renal cancer. **PAGAC Grade: Not assignable.**

Review of the Evidence

Based on data from 2010 to 2014, the incidence rate of renal cancer was 15.6 per 100,000 men and women per year. The number of deaths was 3.9 per 100,000 men and women per year.[46] Several factors increase risk of renal cancer, including smoking, obesity, exposure to certain occupational toxins, hypertension, and history of some rare medical conditions.[47] Renal cancer is more common in men than in women and in individuals with a personal or family history of cancer of the urinary tract.

To examine the association between physical activity and risk of renal cancer, the Subcommittee reviewed one published meta-analysis.[48] The meta-analysis contained data from 11 cohort and 8 case-control studies. The Subcommittee also reviewed 1 pooled analysis of 11 large prospective cohort studies[9] and meta-analysis data from the World Cancer Research Fund, which included data from 12 cohort studies.[49]

Evidence on the Overall Relationship

A considerable body of epidemiologic data exists on the association between physical activity and risk of developing renal cancer. The meta-analysis (19 cohort studies, of which 2 used renal cancer mortality as the endpoint) reported that risk of renal cancer was significantly lower for individuals engaging in the highest versus lowest categories of physical activity level (RR=0.88; 95% CI: 0.79-0.97).[48] Most studies adjusted for multiple potential confounding factors, including age, BMI, and renal cancer risk factors. When the analysis was limited to the 17 cohort studies that did not use renal cancer mortality as the endpoint, risk estimates were similar (RR=0.88; 95% CI: 0.80-0.98). Similar to these findings, the pooled analysis of 11 cohort studies found a statistically significant relationship between the 90th versus 10th percentile level for leisure time physical activity and decreased risk of renal cancer (RR=0.77; 95% CI: 0.70-0.85).[9] The World Cancer Research Fund meta-analysis found similar results for highest versus lowest: 1) total physical activity (RR=0.89; 95% CI: 0.72-1.10); 2) occupational physical activity (RR=0.96; 95% CI: 0.76-1.23); and 3) recreational physical activity (RR=0.84; 95% CI: 0.70-1.01).[49]

Dose-response: The meta-analysis did not examine the dose-response relationship of physical activity with renal cancer risk. The pooled analysis of 11 cohort studies found a significant linear relationship between increasing leisure time physical activity percentile and decreasing risk of renal cancer ($P_{overall}$<0.0001; $P_{non\text{-}linear}$=0.624).[9]

Evidence on Specific Factors

Sex: The meta-analysis found some differences in the effects of physical activity on renal cancer risk between men (RR=0.91; 95% CI: 0.81-1.03) and women (RR=0.85; 95% CI: 0.57-1.29).[48] In that meta-analysis, studies that presented data for men and women combined had a combined relative risk of 0.85 (95% CI: 0.73-0.98). The pooled analysis found that the effect size of physical activity on risk for renal cancer was similar, and statistically significant, in both men and women.[9]

Age: None of the analyses provided data within specific age groups.

Race/ethnicity: All but three studies in the meta-analysis were conducted in the United States and Europe; a meta-analysis of the three studies in Asia showed no association of physical activity with renal cancer risk (RR=1.00; 95% CI: 0.83-1.20).[48]

Socioeconomic status: None of the analyses presented data on the effect of socioeconomic status on the association between physical activity and renal cancer incidence. Hence, no conclusions can be made on this factor.

Weight status: The pooled analysis examined associations between the 90th percentile versus 10th percentile of physical activity level by BMI. Risk of renal cancer associated with physical activity level did not differ for those with BMI <25.0 kg/m^2 versus BMI $\geq$25 ($P_{interaction}$ = 0.39).[9]

Cancer subtype: Neither the meta-analyses nor the pooled analysis provided data by subtype of renal cancer.

Individuals at high risk: No information was provided in the meta-analyses or pooled analysis about effects of physical activity in individuals at elevated risk of renal cancer.

For additional details on this body of evidence, visit: https://health.gov/paguidelines/second-edition/report/supplementary-material.aspx for the Evidence Portfolio.

Cancers for Which Physical Activity Shows Moderate Evidence of a Protective Effect

Lung Cancer

Conclusion Statements

Moderate evidence indicates that greater amounts of physical activity are associated with a lower risk of lung cancer. **PAGAC Grade: Moderate.**

Limited evidence suggests that a dose-response relationship exists between greater amounts of physical activity and lower lung cancer risk. **PAGAC Grade: Limited.**

Limited evidence suggests that the relationship between amount of physical activity and risk of lung cancer does not vary by age. **PAGAC Grade: Limited.** Limited evidence suggests that greater amounts of physical activity are associated with a greater risk reduction in females than in males. **PAGAC Grade: Limited.** Limited evidence suggests that greater amounts of physical activity are associated with a greater risk reduction in those with a body mass index of less than 25 kg/m^2 than in those with higher body mass index. **PAGAC Grade: Limited.** Insufficient evidence is available to determine whether this relationship varies by race/ethnicity or socioeconomic status because these factors have yet to be examined in the studies conducted to date. **PAGAC Grade: Not assignable.**

Limited evidence suggests that specific histologic types of lung cancers do not modify the relationships between amounts of physical activity and risk of lung cancer incidence. **PAGAC Grade: Limited.**

Moderate evidence indicates that greater amounts of physical activity are associated with a greater risk reduction in current and former smokers than in never smokers. **PAGAC Grade: Moderate.**

Review of the Evidence

Between 2010 and 2014, the incidence rate of lung and bronchus cancer was 55.8 per 100,000 men and women per year. The number of deaths was 44.7 per 100,000 men and women per year.[50] Lung cancer is the number one cause of cancer mortality in the U.S. The main risk factor for lung cancer is both active and passive tobacco use. Other risk factors include occupational exposures (including arsenic, radon, chloromethyl ethers, chromium, nickel, polycyclic aromatic hydrocarbons), outdoor air pollution (i.e., particulate matter) and dietary intake (i.e., low fruit and vegetable intake).

The Subcommittee used information from six meta-analyses[19, 51-55] and one pooled analysis.[9] The meta-analysis by Sun et al[51] included 14 prospective cohort studies published to May 2012 with 1,644,305 participants. The meta-analysis by Buffart et al[52] included seven prospective cohort studies published to November 2011. The meta-analysis by Schmid et al[53] included 25 studies (18 prospective cohort, 6 case-control, and 1 nested case-control) published to September 2015 that included 3,147,747 participants and 29,123 cases. The Brenner et al[55] meta-analysis included 28 studies (6 case-control and 22 cohort) published to May 2015. The Zhong et al[54] meta-analysis included 18 studies (12 cohort and 6 case-control) published to January 2014 that included 2,648,470 participants and 26,453 cases. The Liu et al[19] meta-analysis included 126 cohort studies, which included 15 studies in a lung cancer analysis and a pooled analysis[9] that included 12 cohort studies with 19,133 cases. All types of physical activity were included in two of the meta-analyses[51, 54] and leisure time/recreational physical activity was included in the four remaining meta-analyses.[19, 52, 53, 55] The pooled analysis[9] included only leisure time/recreational physical activity in their report. The dose-response relationship was tested in one of the reviews only[52] and no evidence for an association was found. The analyses in the Buffart et al[52] review were restricted to smokers only.

Evidence on the Overall Relationship

The first meta-analysis published by Sun et al[51] found risk reductions for both medium and high levels of physical activity compared to low levels with relative risks of 0.87 (95% CI: 0.83-0.90) and 0.77 (95% CI: 0.73-0.81), respectively. The meta-analysis by Buffart et al,[52] which was restricted to smokers only, reported reductions for moderate, moderate-to-vigorous, and vigorous physical activity amounts compared to low amounts that were all statistically significant decreases (moderate: RR=0.79; 95% CI: 0.70-0.90; moderate-to-vigorous physical activity: RR=0.87; 95% CI: 0.81-0.93; vigorous physical activity: RR=0.74; 95% CI: 0.67-0.82). Brenner et al[55] reported a 25 percent reduction in lung cancer risk when comparing the highest versus lowest amounts of physical activity in all studies combined (RR=0.75; 95% CI: 0.68-0.84). Schmid et al[53] similarly reported a 21 percent reduction in lung cancer risk when comparing the highest versus lowest amounts of physical activity (RR=0.79; 95% CI: 0.72-0.87). Zhong et al[54] reported reductions for both moderate amounts of physical activity (0.87; 95% CI: 0.84-0.90) and high amounts of physical activity (RR=0.75; 95% CI: 0.68-0.84). Liu et al[19] reported an analysis for overall lung cancer that compared the highest to the lowest amounts of leisure time physical activity that was a null association (RR=0.99; 95% CI: 0.97-1.01). Moore et al[9] compared the 90th percentile to the 10th percentile of physical activity and found a statistically significant risk reduction of about 26 percent (HR=0.74; 95% CI: 0.71-0.77).

Dose-response: The dose-response relationship was not examined in any of the studies with the exception of the Moore et al[9] pooled analysis that provided dose-response curves for the association between physical activity and lung cancer incidence. There was a statistically significant linear trend (P_{trend}<0.0001) between greater amounts of physical activity and lower lung cancer risk.

Evidence on Specific Factors

Age: Brenner et al[55] examined sub-group effects by age and found no statistically significant differences by age subgroups.

Sex: Buffart et al[52] examined the association by sex (this study examined smokers only) and found a stronger protective effect of higher levels of physical activity among women than among men (RR=0.68; 95% CI: 0.57-0.82 and RR=0.85; 95% CI: 0.77-0.93, respectively).

Race/ethnicity: No conclusions can be made regarding the role of race or ethnicity in the association between physical activity and lung cancers. None of the meta-analyses reported on these population subgroups, preventing any systematic conclusions related to these factors. The Moore et al[9] pooled analysis, however, found similar associations between highest versus lowest physical activity level and lung cancer risk in Black and White individuals ($P_{heterogeneity}$=0.90) (Figure F4-1).[9]

Socioeconomic status: None of the analyses presented data on the effect of socioeconomic status on the association between physical activity and lung cancer incidence. Hence, no conclusions can be made on this factor.

Weight status: A statistically significant effect modification by BMI was found in the Moore et al[9] pooled analysis, with stronger reductions for participants with BMI <25 kg/m^2 than for those ≥25 kg/m^2.

Cancer subtype: Schmid et al[53] examined the effects by different histologic type and no statistically significant differences by cancer subtype were found.

Other factors: Clear effect modification by smoking status was found by Moore et al,[9] with strong reductions for the association between physical activity and lung cancer observed for current and former smokers but not for never smokers ($P_{effect\ modification}$<0.001). Zhong et al[54] found similar magnitude risk reductions for former, current, and never smokers. These risk reductions ranged between 24 to 26 percent and were statistically significant. Schmid et al[53] also reported effect modification by smoking status, with substantial risk reductions for the association between physical activity and lung cancer for former smokers (RR=0.68; 95% CI: 0.51-0.90), current smokers (RR=0.80; 95% CI: 0.70-0.90) but not for never smokers (RR=1.05; 95% CI: 0.78-1.40). Likewise, Brenner et al[55] reported no association between physical activity and lung cancer for never smokers (RR=0.96; 95% CI: 0.79-1.18) whereas former smokers had a risk reduction between higher amounts of physical activity and lung cancer (RR=0.77; 95% CI: 0.69-0.85) as did current smokers (RR=0.77; 95% 0.72-0.83).

For additional details on this body of evidence, visit: https://health.gov/paguidelines/second-edition/report/supplementary-material.aspx for the Evidence Portfolio.

Cancers for Which Physical Activity Shows Limited Evidence for a Protective Effect

Hematologic Cancers

Conclusion Statements

Limited evidence suggests a null relationship between physical activity and leukemia incidence. Limited evidence suggests that physical activity has a protective effect on lymphoma and myeloma such that greater amounts of physical activity reduce the risk of lymphoma and myeloma. **PAGAC Grade: Limited.**

Insufficient evidence is available to determine whether a dose-response relationship exists between greater amounts of physical activity and reduced risk of hematologic cancers. **PAGAC Grade: Not assignable.**

Insufficient evidence is available to determine whether sex modifies the relationship between physical activity and Hodgkin lymphoma, with a risk reduction observed with physical activity for females only. **PAGAC Grade: Not assignable.** Insufficient evidence is available to determine whether body mass index, smoking, or alcohol affect the relationship between physical activity and risk of developing other hematologic cancers, or whether this relationship varies by sex, age, race/ethnicity, or socioeconomic status. **PAGAC Grade: Not assignable.**

Insufficient evidence is available to determine whether the relationship between physical activity varies by specific types of hematologic cancers. **PAGAC Grade: Not assignable**.

Insufficient evidence is available to determine whether the effects of physical activity on hematologic cancers differ in individuals at elevated risk of hematologic cancers. **PAGAC Grade: Not assignable**.

Review of the Evidence

Hematologic cancers, which include cancers that originate in the blood cells, have three main types: 1) leukemia (cancer of the blood and bone marrow, including chronic myeloid leukemia, chronic lymphocytic leukemia, acute myeloid leukemia, acute lymphocytic leukemia, and other subtypes); 2) lymphoma (cancer of the lymphatic system with Hodgkin lymphoma and non-Hodgkin lymphoma as the two main types); and 3) myeloma (cancer of the plasma cells). Between 2010 and 2014, the incidence rate of leukemia was 13.7 per 100,000 men and women per year. The number of deaths was 6.8 per 100,000 men and women per year.[56] For non-Hodgkin lymphoma, the incidence rate for this same time period was 19.5 per 100,000 men and women per year. The number of deaths was 5.9 per 100,000 men and women per year.[57] For Hodgkin lymphoma, the incidence rate was 2.6 per 100,000 men and women per year. The number of deaths was 0.3 per 100,000 men and women per year.[58] For myeloma, the incidence rate was 6.6 per 100,000 men and women per year. The number of deaths was 3.3 per 100,000 men and women per year.[59]

The main known risk factors for leukemia are: radiation, chemical exposures (e.g., benzene), chemotherapy, Down syndrome, and having a family history of leukemia. The main risk factors for lymphoma are: age older than 50 years, male sex, Caucasian race, having an autoimmune disease, HIV/AIDS, high fat and meat diet, and pesticide exposure. For myeloma, the main risk factors are: African American race, age older than 50 years, male sex, obesity, and exposure to radiation and the petroleum industry.

The Subcommittee used information from three meta-analyses[19, 60, 61] and two pooled analyses.[9, 62] The meta-analysis by Jochem et al[60] included 23 studies (15 cohort and 8 case-control studies) conducted up to 2013 with 19,334 hematologic cancers. The meta-analysis by Vermaete et al[61] included 12 studies (7 case-control and 5 cohort studies) also published by 2013 with 9,511 lymphomas. The third meta-analysis, by Liu et al,[19] included 126 cohort studies conducted to the end of 2014 that included 8 studies used in the lymphoid neoplasm analysis (number of cases not specified). The pooled analysis by Aschebrook-Kilfoy et al[62] was based on the InterLymph Non-Hodgkin Lymphoma Subtypes Project, which included 14 case-control studies published by the end of 2011, included 324 cases of Mycosis fungoides and Sézary syndrome (rare cutaneous T-cell lymphomas). The Moore et al[9] pooled analysis included 12 U.S. and European cohort studies of which 10 cohorts reported on myeloid leukemia with 1,692 cases, 9 cohorts on myeloma with 2,161 cases, 11 cohorts for non-Hodgkin lymphoma with 6,953 cases, and 10 cohorts for lymphocytic leukemia with 2,160 cases. All types of physical activity were included in two of the meta-analyses[60, 61] and leisure-type physical activity was included in the third meta-analysis.[19] The first pooled analysis[62] included all types of physical activity combined, and the second pooled analysis[9] included only recreational and leisure time physical activity in their report.

Evidence on the Overall Relationship

None of the analyses that were identified combined all types of hematologic cancers to provide an overall estimate of the association with physical activity. Rather, separate estimates were provided in each review given the different etiologies of these cancers.

A null association between physical activity and leukemia was reported in two analyses (RR=0.97; 95% CI: 0.84-1.13[60]; HR=0.98; 95% CI: 0.87-1.11[9]), with the latter study reporting on lymphocytic leukemia.

For non-Hodgkin lymphoma, a non-statistically significant risk reduction of about 8 to 9 percent was found in 3 of the reviews that considered this hematologic cancer when comparing the highest versus the lowest levels of physical activity (RR=0.91; 95% CI: 0.82-1.00[60]; 0.92; 95% CI: 0.81-1.04[61]; HR=0.91; 95% CI: 0.83-1.00[9]).

For Hodgkin lymphoma, a non-statistically significant risk reduction of about 16 to 18 percent was reported in 2 reviews that included this hematologic cancer (RR=0.86; 95% CI: 0.58-1.26[60]; OR=0.82; 95% CI: 0.47-1.42[61]).

Two studies reported on all types of lymphoma combined in association with physical activity and reported a 10 percent reduction in all types of lymphoma with greater amounts of physical activity (pooled RR=0.90; 95% CI: 0.81-0.99[60] and pooled OR=0.90; 95% CI: 0.79-1.02[61]). Another meta-analysis reported on lymphoid neoplasms combined and reported a null association between greater amounts of physical activity and lymphoid neoplasms (RR=0.97; 95% CI: 0.86-1.10).[19]

Two studies reported separate results for multiple myeloma/myeloma, with risk reductions ranging from 14 to 17 percent (RR=0.86; 95% CI: 0.68-1.09[60]; HR=0.83; 95% CI: 0.72-0.95[9]) when comparing the highest to lowest levels of physical activity in these studies.

Other rare types of hematologic cancers also were reported separately in the meta-analysis by Jochem et al[60] and no associations between physical activity and risk of follicular lymphoma and large B-cell lymphoma (RR=0.98; 95% CI: 0.85-1.11) and chronic lymphocytic lymphoma/small lymphocytic lymphoma (RR=0.99; 95% CI: 0.75-1.29) were observed. Finally, the InterLymph NHL subtypes project reported on the associations between moderate and vigorous physical activity and mycosis fungoides and Sezary syndrome as well. For moderate physical activity, the fully adjusted odds ratio was 0.46 (95% CI: 0.22-0.97) and for vigorous physical activity, the odds ratio was 0.58 (95% CI: 0.32-1.08).[62]

Dose-response: Moore et al[9] observed a statistically significant trend between increasing percentiles of physical activity and decreasing risk of myeloid leukemia (P_{trend}=0.0035), myeloma (P_{trend}=0.007) and non-Hodgkin lymphoma (P_{trend}=0.007). Two other analyses that also examined the dose-response trends did not find any evidence of an association between increasing physical activity levels and all hematologic cancers combined[60] or for mycosis fungoides and Sezary syndrome.[62]

Evidence on Specific Factors

Age: None of the analyses reported on the effects of physical activity for different age groups for any specific hematologic cancers.

Sex: Only one meta-analysis examined effect modification by sex[60] and no statistically significant effect modification was observed. Different risk estimates were found, however, for Hodgkin lymphoma for which a statistically significant risk reduction was observed for women but not for men (RR=0.56; 95% CI: 0.37-0.86 and RR=1.04; 95% CI: 0.58-1.87), respectively.

Race/ethnicity: No conclusions can be made regarding the role of race or ethnicity in the association between physical activity and hematologic cancers. None of these analyses reported on these population subgroups, preventing any systematic conclusions related to these factors.

Socioeconomic status: None of the analyses presented data on the effect of socioeconomic status on the association between physical activity and hematologic cancer incidence. Hence, no conclusions can be made on this factor.

Weight status: No effect modification by BMI was found in the Moore et al[9] pooled analysis or adiposity in the Jochem et al[60] meta-analysis.

Cancer subtype: As described above, hematologic cancers are comprised of several different cancer sites and the results are described above. No studies to date have provided results on specific subtypes within each of these hematologic cancers.

Other factors: No effect modification by alcohol or smoking status was found for any of the hematologic cancers in the meta-analysis by Jochem et al.[60] Moore et al[9] reported an effect modification by smoking status for myeloma but none for the other hematologic cancers.

For additional details on this body of evidence, visit: https://health.gov/paguidelines/second-edition/report/supplementary-material.aspx for the Evidence Portfolio.

Head and Neck Cancers

Conclusion Statements

Limited evidence suggests that greater amounts of physical activity are associated with a lower risk of head and neck cancer incidence. **PAGAC Grade: Limited.**

Insufficient evidence is available to determine whether a dose-response relationship exists between physical activity and head and neck cancer incidence. **PAGAC Grade: Not assignable.**

Limited evidence suggests that the relationship between physical activity and head and neck cancer incidence does not vary by age, sex, BMI, or smoking. **PAGAC Grade: Limited.** Insufficient evidence is available to determine whether this relationship varies by race/ethnicity or socioeconomic status because these factors have yet to be examined in the studies conducted to date. **PAGAC Grade: Not assignable.**

Limited evidence suggests that this relationship varies by specific types of head and neck cancers. **PAGAC Grade: Limited.**

Insufficient evidence is available to determine whether the effects of physical activity on head and neck cancers differ in individuals at elevated risk of head and neck cancers. **PAGAC Grade: Not assignable.**

Review of the Evidence

In 2014, an estimated 346,902 people were living with head and neck cancers in the United States.[63] These cancers include cancers that originate in the oral cavity, pharynx, larynx, paranasal sinuses and nasal cavity, and salivary glands. The main known risk factors for head and neck cancers are tobacco and alcohol use and infection with human papillomavirus.[64]

The Subcommittee used information from two pooled analyses.[9, 65] The pooled analysis by Nicolotti et al[65] combined 4 case-control studies from the International Head and Neck Consortium (INHANCE) that included 2,289 cases and 5,580 controls, and the Moore et al[9] pooled analysis included 12 U.S. and European cohort studies; of these, 11 cohorts reported on head and neck cancers with 3,985 cases. Both of these pooled analyses included only recreational and leisure time physical activity in their reports.

Evidence on the Overall Relationship

The INHANCE pooled analysis observed a risk reduction for all head and neck cancers combined for both moderate recreational physical activity (OR=0.78; 95% CI: 0.66-0.91) and high recreational physical activity (OR=0.72; 95% CI: 0.46-1.16). The pooled analysis by Moore et al[9] reported a risk reduction for all head and neck cancers when comparing the 90th to 10th percentile of study participants' physical activity levels (HR=0.85; 95% CI: 0.78-0.93).

Dose-response: No dose-response analyses were conducted in either of these pooled analyses.

Evidence on Specific Factors

Age: The INHANCE pooled analysis[65] examined results stratified by age and reported a decreased risk for study participants ages 45 years or older (OR=0.66; 95% CI: 0.48-0.91) but not for participants younger than age 45 years (OR=0.76; 95% CI: 0.17-3.52). No stratification on age was reported in the Moore et al[9] pooled analysis.

Sex: No effect modification by sex was observed in the INHANCE consortium analysis. For all head and neck cancers combined, the risk reductions for both females (OR=0.64; 95% CI: 0.27-1.54) and males (OR=0.75; 95% CI: 0.38-1.46) were similar in magnitude and non-statistically significant. No consideration of effect modification by sex was made in the pooled analysis by Moore et al.[9]

Race/ethnicity: No conclusions can be made regarding whether or not the inverse relationship between physical activity and head and neck cancer varies by race or ethnicity. The studies did not report on these population subgroups, preventing any systematic conclusions related to these factors.

Socioeconomic status: Neither pooled analysis presented data on the effect of socioeconomic status on the association between physical activity and head and neck cancer incidence. Hence, no conclusions can be made on this factor.

Weight status: No effect modification by BMI was found in the Moore et al[9] pooled analysis.

Cancer subtype: Only the INHANCE consortium[65] considered specific subtypes of head and neck cancer and reported risk reductions for oral cavity and pharyngeal cancers but not for laryngeal cancers. For oral cavity cancers, moderate amounts of physical activity (OR=0.74; 95% CI: 0.56-0.97) and high amounts of physical activity (OR=0.53; 95% CI: 0.32-0.88) were both associated with around a 25 percent and nearly 50 percent risk reductions, respectively, compared to the least active study participants. For pharyngeal cancers, both moderate and high amounts of physical activity were also associated with risk reductions of about 30 percent to 40 percent (OR=0.67; 95% CI: 0.53-0.85) and OR=0.58; 95% CI: 0.38-0.89). The associations for laryngeal cancer and physical activity were inconsistent with other head and neck cancers. For moderate amounts of physical activity, a non-statistically significant reduction was observed, and for high amounts of physical activity, an increased risk was reported (OR=0.81; 95% CI: 0.60-1.11) and OR=1.73; 95% CI: 1.04-2.88), respectively. The Moore et al[9] pooled analysis did not report on specific types of head and neck cancers separately.

Other factors: No effect modification by smoking status was found in either pooled analysis and no evidence exists regarding the relationship among individuals at high risk of head and neck cancers.

For additional details on this body of evidence, visit: https://health.gov/paguidelines/second-edition/report/supplementary-material.aspx for the Evidence Portfolio.

Ovarian Cancer

Conclusion Statements

Limited evidence suggests a weak relationship between greater levels of physical activity and lower risk of ovarian cancer. **PAGAC Grade: Limited.**

Limited evidence suggests that no dose-response relationship exists between greater amounts of physical activity and lower ovarian cancer risk. **PAGAC Grade: Limited.**

Insufficient evidence is available to determine whether the relationship between physical activity and ovarian cancer is modified by age, race/ethnicity, socioeconomic status, or weight status. **PAGAC Grade: Not assignable.**

Insufficient evidence is available to determine whether the relationship between physical activity and ovarian cancer is modified by specific histologic types of ovarian cancers. **PAGAC Grade: Not assignable**

Insufficient evidence is available to determine whether the effects of physical activity on ovarian cancer risk differ in individuals at elevated risk of ovarian cancer. **PAGAC Grade: Not assignable**

Review of the Evidence

Based on data from 2010 to 2014, the incidence rate of ovarian cancer was 11.7 per 100,000 women per year. The number of deaths was 7.4 per 100,000 women per year.[66] The risk factors for ovarian cancer include obesity; nulliparity; first degree family history of ovarian, breast or colorectal cancer; family cancer syndromes (e.g., hereditary breast and ovarian cancer syndrome, hereditary nonpolyposis colon cancer); personal history of breast cancer; and estrogen-only therapy after menopause. Ovarian cancer risk is decreased with oral contraceptive use of at least 3 to 6 months and some forms of injectable hormonal contraceptive.[67]

The Subcommittee used information from two meta-analyses[19, 68] and two pooled analyses.[9, 69] The meta-analysis by Zhong et al[68] included 19 studies (9 prospective cohort and 10 case-control studies) published between 1984 and June 2014. The meta-analysis by Liu et al[19] included 126 cohort studies, which included 9 studies in an ovarian cancer analysis. The pooled analysis from the Ovarian Cancer Association Consortium (OCAC) by Cannioto et al[69] included 9 case-control studies published to September 2016 with 8,309 cases and 12,612 controls. The pooled analysis[9] included 9 cohort studies with 2,880 ovarian cancer cases. Recreational physical activity was included in one meta-analysis[19] and in both the pooled analyses,[9, 69] and non-occupational physical activity was included in the meta-analysis by Zhong et al.[68] The dose-response relationship was tested in two of the meta-analyses[19, 68] and in the pooled analysis.[9]

Evidence on the Overall Relationship

The pooled-analysis published by Cannioto et al[69] found chronic physical inactivity compared to some physical activity was associated with an increased risk of ovarian cancer (OR=1.34; 95% CI: 1.14-1.57). The meta-analysis by Zhong et al[68] reported that any non-occupational physical activity versus none was associated with a borderline statistically significant reduction in ovarian cancer incidence (RR=0.92; 95% CI: 0.84-1.00). These authors also presented the results for moderate and high amounts of non-occupational physical activity compared to low amounts and found similar risk reductions (OR=0.91; 95% CI: 0.85-0.99 and OR=0.89; 95% CI: 0.79-1.01, respectively). Liu et al[19] reported a null association for overall ovarian cancer when they compared participants with the highest to the lowest amounts of leisure time physical activity (RR=0.96; 95% CI: 0.74-1.26). Moore et al[9] compared participants in the 90th

percentile to those in the 10th percentile of physical activity and found no association with ovarian cancer incidence (HR=1.01; 95% CI: 0.91-1.13).

Dose-response: Zhong et al[68] observed a non-statistically significant relationship between increasing amounts of non-occupational physical activity and decreasing ovarian cancer risk. In addition, Zhong et al[68] reported that a 2 MET-hours per week or 2 hours per week increment in non-occupational activity conferred a relative risk of ovarian cancer risk of 0.98 (95% CI: 0.96-1.01) and 0.97 (95% CI: 0.94-1.01), respectively. Liu et al[19] estimated the hazard ratios across categories of leisure time physical activity, from 0 to 80 MET-hours per week in increments of between 10 and 20 MET-hours per week. They found no evidence for a linear dose-response trend (P_{trend}=0.28). Moore et al[9] also found no evidence for a linear dose-response trend (P_{trend}=0.77).

Evidence on Specific Factors

Age: None of the analyses presented their results stratified by different age groups. As a result, no conclusions about the role of age on the association between physical activity and ovarian cancer can be made.

Race/ethnicity: No effect modification by race on the association between recreational physical activity and ovarian cancer incidence was observed in the pooled analysis by Cannioto et al.[69] No other analyses considered the effect of race/ethnicity on this association.

Socioeconomic status: None of the analyses presented data on the effect of socioeconomic status on the association between physical activity and ovarian cancer incidence. Hence, no conclusions can be made on this factor.

Weight status: A statistically significant effect modification by BMI was found by Cannioto et al,[69] with a greater increased risk associated with physical inactivity in women with a BMI <25 kg/m^2 (OR=1.33; 95% CI: 1.19-1.49) than in women with a BMI ≥25 kg/m^2 (OR=1.21; 95% CI: 1.09-1.34). In the Moore et al[9] pooled analysis, no effect modification by BMI was observed for the association between leisure time physical activity and ovarian cancer incidence.

Cancer subtype: Zhong et al[54] examined the effects by different ovarian cancer subtype (borderline and invasive tumors) and no statistically significant differences by cancer subtype were found. No other analyses considered the association with physical activity for different ovarian cancer subtypes.

Other factors: No effect modification by menopausal status was observed in the pooled analysis by Cannioto et al.[69] No other analyses considered menopausal status or any other factors as potential effect modifiers of the association between physical activity and ovarian cancer incidence.

For additional details on this body of evidence, visit: https://health.gov/paguidelines/second-edition/report/supplementary-material.aspx for the Evidence Portfolio.

Pancreatic Cancer

Conclusion Statements

Limited evidence suggests that greater amounts of physical activity are associated with a lower risk of developing pancreatic cancer. **PAGAC Grade: Limited.**

Limited evidence suggests that a dose-response association does not exist between physical activity and pancreatic cancer. **PAGAC Grade: Limited.**

Limited evidence suggests that the effects of physical activity on pancreatic cancer risk do not vary by sex. **PAGAC Grade: Limited.** Insufficient evidence is available to determine whether the effects of physical activity on pancreatic cancer risk vary by age, race/ethnicity, socioeconomic groups, or weight status. **PAGAC Grade: Not assignable.**

Insufficient evidence is available to determine whether the effects of physical activity on pancreatic cancer risk differ by cancer subtypes. **PAGAC Grade: Not assignable.**

Insufficient evidence is available to determine whether the effects of physical activity on pancreatic cancer risk differ in individuals at elevated risk for pancreatic cancer. **PAGAC Grade: Not assignable.**

Review of the Evidence

Pancreatic cancer is the third leading cause of cancer mortality in the United States, and its incidence is rising,[70] possibly due to increasing prevalence of obesity and diabetes, two risk factors for the disease.[71,72] Based on data from 2010 to 2014, the incidence rate of pancreatic cancer in the United States was 12.5 per 100,000 men and women per year and the number of deaths was 10.9 per 100,000 men and women per year.[73]

Evidence on the Overall Relationship

The Subcommittee reviewed five systematic reviews on the association between physical activity and risk of pancreatic cancer,[19, 74-77] of which four,[19, 75-77] included meta-analyses. The Subcommittee also reviewed one pooled analysis of 10 cohort studies.[9] In the most recent of the 4 meta-analyses of physical activity and pancreatic cancer risk,[75] 26 individual studies were available for the meta-analysis, of which three quarters represented cohort studies. Some studies included in the meta-analyses and systematic review used mortality as a proxy for incidence. Because the five-year survival rate for pancreatic cancer is only seven percent, mortality provides a reasonable estimate for incidence. The Farris et al[75] meta-analysis suggests that risk of pancreatic cancer is statistically significantly reduced for individuals engaging in highest versus lowest levels of activity (RR=0.89; 95% CI: 0.82-0.96), but the effect was stronger in case-control studies.[75] Similar results were seen in the systematic review and other meta-analyses.[19, 74, 76, 77] The pooled analysis found no association between high levels of physical activity and risk of pancreatic cancer (HR=0.93; 95% CI: 0.83-1.08).[9]

Dose-response: Dose-response relationships were assessed in three meta-analyses.[19, 75, 76] However, the analyses found no statistically significant associations between increased dose of physical activity and risk of pancreatic cancer, including assessments of duration, frequency, and energy expenditure.[19, 76] Similarly, the pooled analysis did not find evidence of a dose-response relationship between physical activity level and risk of pancreatic cancer ($P_{overall}$ = 0.08, $P_{non\text{-}linear}$ = 0.36).

Evidence on Specific Factors

Age: One meta-analysis[75] examined the association of physical activity with pancreatic cancer by age, and found that only in studies with median age younger than 50 years was physical activity associated with reduced risk (RR=0.61; 95% CI: 0.50-0.75). In comparison, the estimates for studies with median ages 50 to 60 years and older than 60 years were RR=0.93 (95% CI: 0.87-1.01) and RR=1.00 (95% CI: 0.89-1.12), respectively.

Sex: Meta-analyses found similar effects of physical activity on pancreatic cancer risk in males and females, although neither subgroup analysis was statistically significant. In contrast, those studies that combined sexes showed significant effects (RR=0.79; 95% CI: 0.68-0.91).[75]

Race/ethnicity: Studies included primarily Caucasian individuals. One meta-analysis reported results by geographic area of included studies (United States, Canada, Europe, Asia), and found that effect size was similar across areas but was of marginal statistical significance within areas.[75]

Socioeconomic status: None of the analyses or the systematic review presented data on the effect of socioeconomic status on the association between physical activity and pancreatic cancer incidence. Hence, no conclusions can be made on this factor.

Weight status: One meta-analysis reported that adjustment for adiposity somewhat attenuated the association between physical activity and pancreatic cancer risk in cohort studies.[76] In the pooled analysis, BMI status did not change the lack of association between physical activity and risk of pancreatic cancer development.[9]

Cancer subtype: None of the analyses or the systematic review reported on effects of physical activity on subtypes of pancreatic cancer (adenocarcinoma vs. neuroendocrine tumors). However, 95 percent of pancreatic cancers are adenocarcinomas.

Individuals at high risk: No information was provided in the systematic review or analyses about effects of physical activity in individuals at elevated risk of pancreatic cancer.

For additional details on this body of evidence, visit: https://health.gov/paguidelines/second-edition/report/supplementary-material.aspx for the Evidence Portfolio.

Prostate Cancer

Conclusion Statements

Limited evidence suggests a weak relationship between greater levels of physical activity and lower prostate cancer risk. **PAGAC Grade: Limited.**

Insufficient evidence is available to determine whether a dose-response relationship exists between higher levels of physical activity and lower prostate cancer risk. **PAGAC Grade: Not assignable.**

Insufficient evidence is available to determine whether the association between physical activity and prostate cancer varies by age, race/ethnicity, weight status, socioeconomic status, or smoking status. **PAGAC Grade: Not assignable.**

Insufficient evidence is available to determine whether the relationship between physical activity and prostate cancer varies by tumor sub-type, as risk reductions were observed with increased levels of physical activity in both men with aggressive versus non-aggressive prostate cancer. **PAGAC Grade: Not assignable.**

Review of the Evidence

Between 2010 and 2014, the incidence rate of prostate cancer was 119.8 per 100,000 men per year. The number of deaths was 20.1 per 100,000 men per year.[78] The main risk factors for prostate cancer are: older age, family history of prostate cancer, elevated endogenous androgen exposure, high dietary fat and dairy products intake, and possibly some occupational exposures.[79]

The Subcommittee used information from two meta-analyses[19, 80] and one pooled analysis.[9] The first meta-analysis by Liu et al[80] included 43 studies (19 prospective cohort studies and 24 case-control studies) published to May 2011 with 88,294 cases. The second meta-analysis by Liu et al[19] included 126 cohort studies; of these, 18 were included in a prostate cancer analysis. The Moore et al[9] pooled analysis included 12 cohort studies; of these, 7 were included in the prostate cancer analysis with 46,890 cases. All types of physical activity were included in the first meta-analysis by Liu et al[80] and leisure time physical activity was included in second meta-analysis by Liu et al[19] and the pooled analysis by Moore et al.[9]

Evidence on the Overall Relationship

The first meta-analysis published by Liu et al[80] found risk reductions for all types of physical activity. For total physical activity, when comparing the highest versus lowest amounts of physical activity, a 10 percent risk reduction was observed that was statistically significant (RR=0.90; 95% CI: 0.84-0.95). Occupational physical activity showed larger reductions than did total physical activity, with a relative risk of 0.81 (95% CI: 0.73-0.91), while recreational physical activity showed smaller risk reductions, with a relative risk of 0.95 (95% CI: 0.80-1.00), respectively. In the Liu et al[19] meta-analysis, when the association between the highest to the lowest amounts of leisure time physical activity was assessed as a binary analysis, the relative risk was 0.93 (95% CI: 0.85-1.01) for overall prostate cancers. Moore et al[9] compared the 90th percentile to the 10th percentile of physical activity and found a moderate risk increase of about 5 percent for higher amounts of physical activity (HR=1.05; 95% CI: 1.03-1.08).

Dose-response: Evidence for a dose-response relationship between increasing percentiles of physical activity and slightly increased prostate cancer risk was found in the Moore et al[9] pooled analysis (P_{trend}<0.0048). No other meta-analyses examined the dose-response relationship between physical activity and prostate cancer risk.

Evidence on Specific Factors

Age: Liu et al[80] examined sub-group effects by age and found stronger risk reductions for men ages 20 to 65 years versus men older than age 65 years.

Race/ethnicity: Liu et al[80] examined the associations between physical activity and population source. For total physical activity, they found stronger risk reductions for European and American populations than for Canadian and Asia-Pacific study populations. In addition, they examined race as an effect modifier and found larger risk reductions for Blacks (RR=0.74; 95% CI: 0.57-0.95) than for Whites (RR=0.86; 95% CI: 0.77-0.97). The Moore et al[9] pooled analysis found similar lack of associations between highest versus lowest physical activity level and prostate cancer risk in Black and White men ($P_{heterogeneity}$=0.35) (Figure F4-1).[9] No studies examined effect modification by socioeconomic status.

Socioeconomic status: None of the analyses presented data on the effect of socioeconomic status on the association between physical activity and prostate cancer incidence. Hence, no conclusions can be made on this factor.

Weight status: No evidence for effect modification by BMI was found in either the meta-analysis by Liu et al[80] or the Moore et al[9] pooled analysis for participants with BMI <25 kg/m^2 compared to those with BMI ≥25 kg/m^2.

Cancer stage and subtype: Liu et al[80] examined the associations between physical activity and prostate cancer risk by cancer stage. They found no effect modification for localized versus advanced prostate cancer stage. Liu et al[19] examined the effects of physical activity within subgroups of prostate cancer defined by tumor aggressiveness. For non-aggressive prostate cancer, the relative risk was 0.98 (95% CI: 0.79-1.21) and for aggressive prostate cancer, the relative risk was 0.89 (95% CI: 0.71-1.12).

Other factors: No effect modification by smoking status was found by Moore et al.[9] Liu et al[80] considered the associations between physical activity and prostate cancer stage by history of prostate specific antigen (PSA) testing and found that men with a previous history of a test had no benefit from physical activity (RR=1.05; 95% CI: 0.92-1.20) while those with no previous PSA test did have a non-statistically significant reduction in risk of prostate cancer (RR=0.83; 95% CI: 0.63-1.11).

For additional details on this body of evidence, visit: https://health.gov/paguidelines/second-edition/report/supplementary-material.aspx for the Evidence Portfolio.

Brain Cancer

Conclusion Statements

Insufficient evidence is available to determine whether a relationship between physical activity and overall brain cancer incidence exists. **PACAC Grade: Not assignable.** Limited evidence suggests that physical activity decreases the risk of certain types of brain cancer. Specifically, a reduced risk is observed for glioma and meningioma. **PAGAC Grade: Limited.**

Insufficient evidence is available to determine whether a dose-response relationship exists between physical activity and brain cancer incidence. **PAGAC Grade: Not assignable.**

Insufficient evidence is available to determine whether the relationship between physical activity and brain cancer incidence varies by age, sex, race/ethnicity or socioeconomic status because these factors have yet to be examined in the studies conducted to date. **PAGAC Grade: Not assignable.** Insufficient evidence is available to determine whether the relationship between physical activity and brain cancer incidence varies by body mass index. **PAGAC Grade: Not assignable.**

Insufficient evidence is available to determine whether the relationship between physical activity and brain cancer incidence differs in individuals at high risk of brain cancer. **PAGAC Grade: Not assignable.**

Review of the Evidence

In 2014, an estimated 162,341 people were living with brain and other nervous system cancers in the United States.[81] Brain cancer has many different types and the causes of brain cancer remain unknown.

The Subcommittee used information from one meta-analysis[82] and one pooled analysis.[9] The meta-analysis included four studies of meningioma (three cohort and one case-control study) and five studies of glioma (three cohort and two case-control studies).[82] The pooled analysis by Moore et al[9] included 12 U.S. and European cohort studies; of these, 10 cohorts were included in the brain cancer analysis, with 2,110 cases. The Niedermaier et al[82] meta-analysis included 2,982 meningioma cases from 9 studies and 3,057 glioma cases from 7 studies. The type of physical activity assessed in the studies included in the meta-analysis[82] was not specified and the pooled analysis by Moore et al[9] was restricted to leisure time physical activity.

Evidence on the Overall Relationship

Some evidence of an inverse relationship between physical activity and certain types of brain cancer was found. For meningioma, a reduced risk was reported when comparing study participants with the highest versus the lowest levels of physical activity (RR=0.73; 95% CI: 0.61-0.88).[82] Similarly, a reduced risk of glioma was reported with higher levels of physical activity (RR=0.86; 95% CI: 0.76-0.97).[82] This risk reduction for brain cancer (no brain cancer sub-type specified) was not observed in the pooled analysis.[9] In that study, when comparing the 90th to 10th percentile of study participants' physical activity levels, the hazard ratio was 1.06 (95% CI: 0.93-1.20).

Dose-response: No dose-response analysis was conducted in the meta-analysis because of the heterogeneous physical activity assessments done in the studies that were assessed.[82] The pooled analysis[9] found no evidence for a dose-response relationship between increasing percentiles of physical activity and brain cancer risk.

Evidence on Specific Factors

Age: The two analyses adjusted for age but did not stratify their results by age group, therefore providing no evidence for effect modification by age.

Sex: No effect modification by sex was observed in the meta-analysis by Niedermaier et al[82] and no consideration of sex was made in the pooled analysis by Moore et al.[9]

Race/ethnicity: No conclusions can be made regarding whether or not the inverse relationship between physical activity and brain cancer varies by race or ethnicity. The studies did not report on these population subgroups, preventing any systematic conclusions related to these factors.

Socioeconomic status: None of the analyses presented data on the effect of socioeconomic status on the association between physical activity and brain cancer incidence. Hence, no conclusions can be made on this factor.

Weight status: No effect modification by BMI was found in either of the two analyses.[9, 82]

Cancer subtype: Only the meta-analysis by Niedermaier et al[82] considered specific subtypes of brain cancer and found risk reductions for both meningioma and glioma.

Other factors: No effect modification by smoking status was found in the pooled analysis.[9] No studies considered the effect of physical activity among individuals at high risk of brain cancer.

For additional details on this body of evidence, visit: https://health.gov/paguidelines/second-edition/report/supplementary-material.aspx for the Evidence Portfolio.

Cancers for Which Physical Activity Shows Evidence for No Effect

Thyroid Cancer

Conclusion Statements

Moderate evidence indicates that greater amounts of physical activity are not associated with risk of developing thyroid cancer. **PAGAC Grade: Moderate.**

Insufficient evidence is available to determine whether physical activity levels and risk of thyroid cancer have a dose-response relationship. **PAGAC Grade: Not assignable.**

Insufficient evidence is available to determine whether the effects of physical activity on thyroid cancer differ by specific sex, age, race/ethnicity, or socioeconomic groups. **PAGAC Grade: Not assignable.** Insufficient evidence is available to determine whether weight status affects the association between physical activity and thyroid cancer risk. **PAGAC Grade: Not assignable.**

Insufficient evidence is available to determine whether the association of physical activity with thyroid cancer risk differs by subtype of thyroid cancer. **PAGAC Grade: Not assignable.**

Insufficient evidence is available to determine whether the association of physical activity with thyroid cancer risk differs in individuals at elevated risk of thyroid cancer. **PAGAC Grade: Not assignable.**

Review of the Evidence

The incidence and mortality of thyroid cancer are increasing in the United States.[83] Based on data from 2010 to 2014, the incidence rate of thyroid cancer was 14.2 per 100,000 men and women per year. The number of deaths was 0.5 per 100,000 men and women per year. Although the increase in incidence is in part due to increased screening, the increased mortality suggests that part of the increase in incidence is real. Risk factors for thyroid cancer include being female, radiation exposure, some hereditary conditions, low iodine intake, and obesity.[84, 85]

The Subcommittee reviewed evidence of associations between physical activity and thyroid cancer risk. One meta-analysis was reviewed,[86] as well as one pooled analysis of 5 cohorts,[87] and one pooled analysis of 11 cohort studies.[9]

Evidence on the Overall Relationship

A small number of epidemiologic studies have examined the association between physical activity and risk of developing thyroid cancer. In the meta-analysis of physical activity and thyroid cancer risk, data from eight cohort and three case-control studies were included.[86] The meta-analysis suggests that risk for thyroid cancer is not associated with high versus low levels of activity (RR=1.06; 95% CI: 0.79-1.42). When the meta-analysis was limited to cohort studies, physical activity was associated with increased risk of thyroid cancer (RR=1.28; 95% CI: 1.01-1.63).[86] The five-cohort pooled analysis found no significant association between physical activity and thyroid cancer risk (RR=1.18; 95% CI: 1.00-1.39).[87] The pooled analysis of 11 cohorts similarly found no statistically significant association between high levels of physical activity and thyroid cancer risk (RR=0.92; 95% CI: 0.81-1.06).[9]

Dose-response: The larger pooled analysis[9] showed no statistically significant associations between increased dose of physical activity and risk of thyroid cancer.

Evidence on Specific Factors

Age: Risk estimates by age were presented only in the pooled analysis of five cohorts.[87] They observed statistically significant differences according to age at diagnosis ($P_{\text{-interaction}}$=0.03), whereby the association was strongest for thyroid cancers diagnosed before age 50 years (80 cases, HR=2.58; 95% CI: 1.41-4.74, P_{trend}=0.002) compared to thyroid cancers diagnosed at ages 50 to 59 years (127 cases, HR=1.09; 95% CI: 0.72-1.66, P_{trend}=0.68) or at ages 60 years or older (611 cases, HR=1.11; 95% CI: 0.92-1.34, P_{trend}=0.28).[87] Given that this subgroup association was evident only in a subset[87] of all of the studies that have addressed thyroid cancer and physical activity,[9, 86] the Subcommittee could not determine that high levels of physical activity increases risk of thyroid cancer in young individuals.

Sex: The relative risk estimates for women in the individual studies stratified by sex (approximately half) reflect the overall risk estimate. The pooled analysis found similar risk estimates between men and women (both showing no statistically significant associations). In the smaller pooled analysis, association was non-statistically significantly stronger in men (HR=1.40; 95% CI: 1.06-1.86) compared to women (HR=1.07; 95% CI: 0.87-1.32; $P_{interaction}$=0.21).[87]

Race/ethnicity: The studies included in these analyses were primarily from Caucasian individuals. Studies in the meta-analysis[86] that showed data for Asians had similar relative risks to those from the U.S. and European studies.

Socioeconomic status: None of the analyses presented data on the effect of socioeconomic status on the association between physical activity and thyroid cancer incidence. Hence, no conclusions can be made on this factor.

Weight status: The pooled analysis of five cohorts found the association for high versus low physical activity was statistically significantly stronger among participants with BMI ≥25 kg/m^2 (HR=1.34; 95% CI: 1.09-1.64) compared to those with BMI <25 kg/m^2 (HR=0.92; 95% CI: 0.69-1.22; $P_{interaction}$=0.03).[87] The pooled analysis of 11 cohorts, in contrast, found no difference in effect by BMI <25 kg/m^2 versus >25 kg/m^2 ($P_{effect\ modification}$ = 0.37).[9]

Cancer subtype: Neither the meta-analysis nor the larger pooled analysis reported on the effects of physical activity by subtypes of thyroid cancer (papillary, follicular, medullary, anaplastic). In the pooled analysis of five cohorts, the association was non-statistically significantly stronger for follicular thyroid cancer (HR=1.55; 95% CI: 1.03-2.35) compared to papillary thyroid cancer (HR=1.18; 95% CI: 0.97-1.44; $P_{interaction}$= 0.24).[87]

Individuals at high risk: No information was provided in the meta-analysis or pooled analyses about effects of physical activity in individuals at elevated risk of thyroid cancer.

For additional details on this body of evidence, visit: https://health.gov/paguidelines/second-edition/report/supplementary-material.aspx for the Evidence Portfolio.

Rectal Cancer

Conclusion Statements

Limited evidence suggests that greater amounts of physical activity are not associated with risk of developing rectal cancer. **PAGAC Grade: Limited.**

Insufficient evidence is available to determine whether a dose-response relationship between increasing physical activity levels and decreasing risk of rectal cancer exists. **PAGAC Grade: Not assignable.**

Insufficient evidence is available to determine whether the effects of physical activity on rectal cancer risk differ by sex, age, race/ethnicity, weight status, or socioeconomic groups in the United States. **PAGAC Grade: Not assignable.**

Insufficient evidence is available to determine whether the effects of physical activity on rectal cancer risk differ by subtype of rectal cancer. **PAGAC Grade: Not assignable.**

Insufficient evidence is available to determine whether the effects of physical activity on rectal cancer risk differ in individuals at elevated risk for rectal cancer. **PAGAC Grade: Not assignable.**

Review of the Evidence

Based on data from 2010-2014, the incidence rate of rectal cancer in the United States was 11.8 per 100,000 men and women per year.[21] Risk factors for rectal cancer include: increased age, obesity, personal history of adenomatous colorectal polyps, family history of colorectal cancer, certain genetic polymorphisms, inflammatory bowel disease, alcohol use, and cigarette smoking.[30, 88, 89]

To examine the association between physical activity and risk of rectal cancer, the Subcommittee reviewed four systematic reviews[19, 23, 26, 29] of which three[19, 23, 26] included meta-analyses. The Subcommittee also reviewed one pooled analysis of 12 large prospective cohort studies[9] and meta-analysis data from the World Cancer Research Fund.[30, 31] The reviews contained data from between 5 and 14 epidemiologic studies.

Evidence on the Overall Relationship

A considerable body of epidemiologic data exists on the association between physical activity and risk of developing rectal cancer. The most recent published meta-analysis (nine cohort studies) reported that risk of rectal cancer did not differ for individuals engaging in the highest versus lowest categories of physical activity level (RR=1.07; 95% CI: 0.93-1.24).[19] Other meta-analyses similarly found no associations between highest versus lowest levels of physical activity and risk of developing rectal cancer.[23, 26, 30, 31] Most studies adjusted for multiple potential confounding factors, including age, BMI, and rectal cancer risk factors, although adjustment for colorectal cancer screening (which could be related to physical activity level) was not typically done. In contrast to these findings, the pooled analysis of 12 cohort studies found a statistically significant relationship between the 90th versus 10th percentile level for leisure time physical activity and decreased risk of rectal cancer (RR=0.87; 95% CI: 0.80-0.95).[9] It is not clear why the results of the pooled analysis differ from those of the meta-analyses. The pooled analysis included only a subset of studies contained in the meta-analyses. In addition, the pooled analysis compared the top versus bottom decile of physical activity, while the meta-analyses used whatever the source studies reported as high or low activity levels, typically top and bottom quartiles.

Dose-response: Given the lack of overall associations between physical activity and risk of rectal cancer, none of the meta-analyses examined dose-response relationships. The pooled analysis of 12 cohort studies found a significant U-shaped relationship between increasing leisure time physical activity percentile and risk of rectal cancer ($P_{overall}$=0.0002; $P_{non\text{-}linear}$=0.0008).[9]

Evidence on Specific Factors

Sex: The pooled analysis found that the effect of physical activity on risk of rectal cancer was statistically significant in men, but not women ($P_{heterogeneity}$=0.09).[9]

Age: None of the analyses or the systematic review provided data within specific age groups.

Race/ethnicity: Studies in the United States and Europe were primarily in Caucasians. A systematic review of Japanese studies reported on data from two cohort and six case-control studies, and found no association of higher physical activity with risk of rectal cancer.[29]

Socioeconomic status: None of the analyses or the systematic review presented data on the effect of socioeconomic status on the association between physical activity and rectal cancer incidence. Hence, no conclusions can be made on this factor.

Weight status: The pooled analysis examined associations between the 90th percentile versus 10th percentile of physical activity level by BMI. Risk of rectal cancer for those with BMI <25.0 kg/m^2 did not differ from that of individuals with BMI $\geq$25 kg/m^2 ($P_{effect\ modification}$=0.50).[9]

Cancer subtype: None of the analyses or the systematic review considered the association with physical activity for different rectal cancer subtypes.

Individuals at high risk: No information was provided in the systematic review or analyses about effects of physical activity in individuals at elevated risk of rectal cancer.

For additional details on this body of evidence, visit: https://health.gov/paguidelines/second-edition/report/supplementary-material.aspx for the Evidence Portfolio.

Other Cancers

No systematic reviews or meta-analyses included sufficient information to make conclusions about the associations between physical activity and occurrence of other cancers, including liver, gallbladder, small intestine, soft tissue, or melanoma. However, the pooled analysis by Moore et al,[9] provided some data on these cancers that are useful to note. Statistically significantly reduced risks were observed for the 90th versus 10th percentile of physical activity level for liver cancer (HR=0.73; 95% CI: 0.55-0.98). Statistically significantly increased risks were seen for malignant melanoma (HR=1.27; 95% CI: 1.16-1.40). No statistically significant associations were observed for cancers of the small intestine (HR=0.78; 95% CI: 0.60-1.00), soft tissue (HR=0.94; 95% CI: 0.67-1.31), and gallbladder (HR=0.72; 95% CI: 0.51-1.01).

Question 2: What is the relationship between sedentary behavior and cancer incidence?

a) Is there a dose-response relationship? If yes, what is the shape of the relationship?
b) Does the relationship vary by age, sex, race/ethnicity, socioeconomic status, or weight status?
c) Is the relationship independent of levels of light, moderate, or vigorous physical activity?
d) Is there any evidence that bouts or breaks in sedentary behavior are important factors?

Sources of evidence: Meta-analyses, systematic reviews, original research articles

Conclusion Statements

Moderate evidence indicates a significant relationship between greater time spent in sedentary behavior and higher risk of incident cancer, particularly for endometrial, colon, and lung cancer. **PAGAC Grade: Moderate.**

Limited evidence suggests the existence of a direct dose-response relationship between sedentary behavior and incident endometrial, colon, and lung cancers. **PAGAC Grade: Limited.**

Insufficient evidence is available to determine whether the relationship between sedentary behavior and incident cancer varies by age, sex, race/ethnicity, socioeconomic status, or weight status. **PAGAC Grade: Not assignable.**

Insufficient evidence is available to determine whether the relationship between sedentary behavior and incident cancer varies by amount of moderate-to-vigorous physical activity. **PAGAC Grade: Not assignable.**

Insufficient evidence is available to determine whether bouts or breaks in sedentary behavior are important factors in the relationship between sedentary behavior and incident cancer. **PAGAC Grade: Not assignable.**

Review of the Evidence

Sources of evidence included systematic reviews and meta-analyses published from January 2000 to February 21, 2017, and recent original research articles published between January 2014 and April 25, 2017. The sources of evidence were identified through the same search that was used to provide evidence for Question 4 in *Part F. Chapter 2. Sedentary Behavior*. Further details about the search strategy are provided in that chapter.

For details on the review of the evidence to address Question 2, the reader is referred to *Part F. Chapter 2: Sedentary Behavio*r. Briefly, two meta-analyses examined the association between sedentary behavior and total cancer incidence,[90, 91] and reported summary relative risk estimates of 1.20 (95% CI: 1.12-1.28)[90] and 1.13 (95% CI: 1.05-1.21)[91] for highest versus lowest levels of sedentary behavior.

Two meta-analyses examined the association between sedentary behavior and endometrial cancer, and both reported a significant association when comparing the highest versus lowest levels of sedentary time: a relative risk of 1.36 (95% CI: 1.15-1.60) was reported by Schmid and Leitzmann,[92] and a relative risk of 1.28 (95% CI: 1.08-1.53) was reported by Shen et al.[90] The meta-analysis by Shen et al[90] reported a statistically significant association between sedentary behavior and combined colorectal cancer (RR= .30; 95% CI: 1.12-1.49); whereas Schmid and Leitzmann[92] reported a statistically significant association for colon cancer (RR=1.28; 95% CI: 1.13-1.45) but not for rectal cancer (RR=1.03; 95% CI: 0.89-1.19). These two meta-analyses also examined the association between sedentary behavior and lung cancer, and both reported a statistically significant association when comparing the highest versus lowest levels of sedentary time: a relative risk of 1.21 (95% CI: 1.03-1.43) was reported by Schmid and Leitzmann,[92] and a relative risk of 1.27 (95% CI: 1.06-1.52) was reported by Shen et al.[90] It is important to note that many studies reported significant associations between sedentary behavior and incident cancer risk using statistical models that included an estimate of moderate-to-vigorous physical activity as a covariate.

OVERALL SUMMARY AND CONCLUSIONS

In reviewing 45 systematic reviews, meta-analyses, and pooled analyses comprising hundreds of epidemiologic studies with several million study participants, the Subcommittee determined that strong evidence linked highest versus lowest physical activity levels to reduced risks of bladder, breast, colon, endometrial, esophageal adenocarcinoma, renal, and gastric cancers, with risk reductions ranging from approximately 10 percent to 20 percent. The Subcommittee found evidence of a 25 percent reduction in lung cancer risk with highest versus lowest levels of physical activity, but could not rule out confounding by tobacco use and therefore considered the association to be a lower grade of strength. The Subcommittee determined that limited evidence suggested an association between increased physical activity and decreased risks of hematologic, head and neck, ovary, pancreas, and prostate cancers. No grade could be assigned for brain cancer. The Subcommittee found limited evidence of no effect of physical activity on risk of thyroid or rectal cancer. Finally, due to lack of evidence, the Subcommittee did not review several other cancer sites.

A dose-response relationship between physical activity and specific cancer risk was evident, but given the inconsistent methods of measuring and categorizing physical activity levels in the various studies, meta-analyses, and pooled analyses, it was not possible to determine exact levels of physical activity that provide given levels of effect.

Investigation by cancer subtype showed that increased physical activity is associated with reduced risk of breast cancer regardless of hormone receptor status, and of colon cancer originating both proximally and distally. Conversely, although high levels of physical activity were associated with reduced adenocarcinoma of the esophagus, no statistically significant effect was observed for squamous cell cancer of the esophagus. Little information was available for other subtypes of cancer.

Effects of physical activity on specific cancer risk were clearly seen for both women and men for colon and renal cancers, while for other cancers such as bladder, esophagus, gastric, lung, and pancreas, differences by sex could not be ruled out. Little information was available on differences in physical activity effect on cancer risk by age or socioeconomic status. Few estimates were available for specific race/ethnic groups other than Whites. For several cancers, individuals of Asian race appeared to have similar protection from physical activity as do non-Asian individuals. The pooled analysis suggested that, similar to Whites, physical activity reduces risks of lung, colon, and breast cancers in African Americans, but is not related to prostate cancer risk in African Americans. For some particular U.S. populations (Latino, Native American, Pacific Islander), data are so sparse that systematic reviews, meta-analyses, and pooled analyses have not presented data on these race/ethnic populations. Weight status affected the association between physical activity and risk of several cancers, including breast, endometrium, lung, ovary, and thyroid, and possibly for esophageal adenocarcinoma and gastric cardia cancers.

The Subcommittee's review of the literature on sedentary behavior and risk of endometrial, colon, and lung cancers found that highest versus lowest levels of sedentary time increased risks of these cancers by a statistically significant range of 20 percent to 35 percent, with an evidence grade of strong. Conclusions could not be drawn for associations between sedentary time and other specific cancers.

In summary, the Subcommittee's review of the extensive epidemiologic literature resulted in convincing evidence linking increased physical activity to lower risk of several commonly occurring cancers in adults, as well as possible lower risk of several other cancers in adults. These effects appear to apply broadly across sex, most cancer subtypes, and, for most cancers, regardless of weight status. Most of the existing data on physical activity and cancer risk come from studies of Whites. The existing data on other racial and ethnic groups, including African Americans and Asians, suggest that physical activity confers similar benefits. Although data on diverse racial and ethnic groups are insufficient, there are no data to say that physical activity will not help individuals of all races and ethnicities.

Table F4-1. Summary of Associations of Physical Activity and Sedentary Behavior with Specific Cancers, with Subcommittee-assigned Evidence Grade

Cancer	Evidence Grade*
Physical activity protects:	
Bladder, breast, colon, endometrium, esophagus (adenocarcinoma), renal, gastric	Strong
Lung	Moderate
Hematologic, head & neck, ovary, pancreas, prostate	Limited
Brain	Not assignable
No effect of physical activity:	

Cancer	Evidence Grade*
Thyroid	Limited
Rectal	Limited
Sedentary behavior increases risk:	
Endometrium, colon, lung	Moderate

Note: *Evidence grade refers to strength of evidence in the literature regarding associations between physical activity and cancer risk. For effect sizes and directions of these associations, see reviews of evidence with specific cancers.

Comparing 2018 Findings with the 2008 Scientific Report

The *Physical Activity Guidelines Advisory Committee Report, 2008*[4] concluded that evidence supported a moderate, inverse relation between physical activity and the development of colon and breast cancer. In that report, few studies detailed the associations by subgroups (age, sex, weight status, cancer site) or by particular types of physical activity. It further concluded that there was no association between physical activity and the development of prostate or rectal cancer.

The 2008 Scientific Report[4] did not comment on the associations between physical activity and risk of bladder, gastric, endometrial, renal, hematological, head and neck, pancreatic, ovarian, brain, or thyroid cancers because few studies in these cancers were available at that time. Further, given that the evidence of associations between sedentary behavior and cancer incidence has largely been published since 2008, the prior report did not include information on this exposure.

The 2008 Scientific Report[4] reviewed some mechanisms that may explain the associations between physical activity and cancer risk, but the review was not systematic.

Public Health Impact

In 2017, an estimated 1,688,780 Americans will be diagnosed with a new cancer and 600,920 individuals will die of cancer.[1] From our review, regular aerobic physical activity likely confers substantial beneficial effects on reducing risks for occurrence of several cancers, notably some of the most commonly occurring cancers (e.g., breast, colon, and lung cancers), as well as several obesity-related cancers (e.g., postmenopausal breast, colon, esophageal adenocarcinoma, and renal). Given the significant impact of cancer on quality of life, financial stability, and mortality, the reduction in risk of common cancers from high levels of physical activity could have a large public health impact. Substantial reductions in the incidence of cancer, mortality from cancer, and cancer-related costs would be expected if currently inactive individuals became more physically active. Therefore, the Subcommittee believes that all individuals should be encouraged to engage in recommended levels of physical activity in order to reduce risk for developing cancer.

NEEDS FOR FUTURE RESEARCH

1. Conduct epidemiologic studies of effects of physical activity on risk of cancer for specific cancer sites that have not been adequately studied, preferably large prospective cohort studies.

   Rationale: Very little evidence exists on the relationship between physical activity and the risk of cancer at several sites, particularly the rare cancers. Therefore additional pooled datasets and meta-analyses may be needed. Additional studies would provide the data necessary for the useful insights that would be possible through analyses of pooled datasets and meta-analyses.

2. Conduct epidemiologic studies of effects of physical activity on risk of cancer in specific race, ethnic, and socioeconomic groups.

   Rationale: Few studies have had sufficiently large numbers of participants from specific racial, ethnic, or socioeconomic subgroups to assess the effects of physical activity on risk of developing cancer. This additional research is particularly important, as many groups are at high risk of cancer (i.e., African Americans are at increased risk for colon, prostate, and breast cancers), are typically diagnosed with more advanced disease (i.e. individuals from low socioeconomic groups or others without access to medical care), and are often insufficiently active.

3. Conduct studies to test effect modification by age on the associations between physical activity and cancer risk.

   Rationale: Some evidence suggests that risk for some cancers such as colon and breast is increasing in younger age groups, who are also less active today than in previous generations. It would be important to know whether physical activity can be protective in this younger age group.

4. Conduct epidemiologic studies, preferably prospective cohort studies, to determine effects of specific types of physical activity on cancer risk.

Rationale: Few data are available on the associations of specific activities on cancer risk. It would be useful to know whether moderate-intensity activities such as walking are sufficient to provide protection. Also, insufficient data exist on associations of other activities such as muscle-strengthening activity on cancer risk.

5. Conduct epidemiologic studies, preferably prospective cohort studies, to more precisely determine dose-response effect of physical activity on cancer risk.

Rationale: All data in available studies have been from self-reported recall of usual activities. Collecting data with device-based measures of activity will be important, as will determining precise measures of dose of activity.

6. Conduct randomized controlled clinical trials testing exercise effects on cancer incidence.

Rationale: All available data are from observational studies, which could suffer from confounding effects of other variables. Randomized trials in high risk individuals could be more cost-effective, as trials with smaller sample sizes or shorter follow-up durations might be feasible.

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PART F. CHAPTER 5. CARDIOMETABOLIC HEALTH AND PREVENTION OF WEIGHT GAIN

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INTRODUCTION

The Committee identified cardiometabolic health and weight management as key areas to include in this report, with a focus on preventing the onset of specific outcomes. The Committee considered the broad areas of cardiometabolic health and weight management when determining the specific areas to be examined in this *2018 Physical Activity Guidelines Advisory Committee Scientific Report*, and also considered how this report could expand the conclusions provided in the *Physical Activity Guidelines Advisory Committee Report, 2008*.[1] Within this context, the Cardiometabolic Health and Prevention of Weight Gain Subcommittee prioritized three areas for this chapter that included the association between physical activity and prevention of weight gain, incidence of hypertension, and incidence of type 2 diabetes mellitus. The rationale for inclusion of these areas within this report follows.

Excessive body weight has been shown to be associated with numerous negative health outcomes that include, but are not limited to cardiovascular disease (CVD), diabetes, some forms of cancer, and musculoskeletal disorders.[2,3] Recent estimates indicate that prevalence of overweight (body mass index (BMI) 25 to ≤30 kg/m^2) in the United States for adult men is approximately 40 percent and for women is 30 percent,[4] with estimates of obesity (BMI ≥30 kg/m^2) for men being approximately 35 percent and for women being 40 percent.[5] Thus, an ongoing need for effective treatments for both overweight and obesity is recognized. From a public health perspective, however, the strategies that prevent or minimize weight gain, which may result in a lower prevalence of overweight and obesity, are important to lower the health consequences of excessive body weight. This chapter focuses on physical activity and its potential influence on body weight, with a particular focus on minimizing weight gain, maintaining body weight, and preventing overweight and obesity in adults. The potential influence of physical activity on body weight in youth is addressed in *Part F. Chapter 7. Youth* and during pregnancy is addressed in *Part F. Chapter 8. Women Who are Pregnant or Postpartum*, and the potential influence of sedentary behavior on body weight is addressed in *Part F. Chapter 2. Sedentary Behavior*.

CVD is the leading cause of death in the United States and the world, accounting for approximately 1 in 3 deaths (807,775, or 30.8%) in the United States and 17.3 million (31%) worldwide.[6,7] Hypertension is the most common, costly, and preventable CVD risk factor. According to the *Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure* (JNC 7)[8] blood pressure classification scheme, hypertension affects 86 million (34%) adults in the United States and 1.4 billion (31%) adults globally.[6,7] Hypertension also is the most common primary diagnosis in the United States, and the leading cause for medication prescriptions among adults older than age 50 years.[9] Another 36 percent of adults in the United States have prehypertension, and one in five adults with prehypertension is estimated to develop hypertension in 4 years.[6,10] By 2030, it is estimated that 41 percent of adults in the United States will have hypertension, and almost an equal amount will have prehypertension. From 2010 to 2030, the total direct costs attributed to hypertension are projected to triple ($130.7 to $389.9 billion), while the indirect costs due to lost productivity will double ($25.4 to $42.8 billion).[6] Curbing this growing and expensive public health crisis is a national and global priority.[7,11] This chapter focuses on physical activity and its potential influence to prevention hypertension. The influence of physical activity on resting blood pressure in adults with hypertension is addressed in *Part F. Chapter 10. Individuals with Chronic Conditions*.

Diabetes mellitus, more commonly referred to as diabetes, is a chronic disease characterized by a deficiency and/or defect in the action of insulin. Type 2 diabetes is characterized by a relative resistance to insulin usually accompanied by resistance to the effect of insulin and comprises 90 to 95 percent of all cases of diabetes. The risk of developing type 2 diabetes is reduced by regular participation in moderate-to-vigorous physical activity. An estimated 23 million people (9.4% of the U.S. population) are known to have type 2 diabetes.[12] The prevalence rises from about 3 percent among people ages 18 to 44 years to 13 percent of people ages 45 to 64 years, and 21 percent of people ages 65 years and older.[12] Common complications of diabetes affect the eyes, kidneys, nerves, and blood vessels, leading to, among other problems, loss of vision, kidney failure, and lower limb amputations. Risk factors for these conditions are common among people with diabetes: 88 percent have overweight or obesity, 41 percent report no moderate-to-vigorous physical activity, 74 percent have high blood pressure, 16 percent have a hemoglobin A1c (HbA1c) value greater than 9 percent. In 2012, the total estimated cost of diabetes in the United States was $176 billion in direct medical costs and $69 billion in reduced productivity.[13] People with type 2 diabetes have medical expenditures about 2.3 times higher than they would if they did not have the disease. This chapter focuses on type 2 diabetes prevention because the risk of developing the condition is reduced by regular participation in moderate-to-vigorous physical activity. Gestational diabetes is addressed in *Part F. Chapter 8. Women Who are Pregnant or Postpartum*. The relationship between sedentary behavior and the incidence of type 2 diabetes is described in *Part F. Chapter 2. Sedentary Behavior*. Among individuals who already have type 2 diabetes, the effect of habitual moderate-to-vigorous physical activity on the development of other chronic diseases, quality of life, physical function, and the prevention of disease progression is described in *Part F. Chapter 10. Individuals with Chronic Conditions.*

REVIEW OF THE SCIENCE

Overview of Questions Addressed

This chapter addresses 3 major questions and related subquestions:

1. What is the relationship between physical activity and prevention of weight gain?
    a) Is there a dose-response relationship? If yes, what is the shape of the relationship?
    b) Does the relationship vary by age, sex, race/ethnicity, socioeconomic status, or weight status?
    c) Does the relationship vary based on levels of light, moderate, or vigorous physical activity?

2. In people with normal blood pressure or prehypertension, what is the relationship between physical activity and blood pressure?
    a) Is there a dose-response relationship? If yes, what is the shape of the relationship?
    b) Does the relationship vary by age, sex, race/ethnicity, socioeconomic status, weight status, or resting blood pressure level?

c) Does the relationship vary based on frequency, duration, intensity, type (mode), or how physical activity is measured?

3. In adults without diabetes, what is the relationship between physical activity and type 2 diabetes?
   a) Is there a dose-response relationship? If yes, what is the shape of the relationship?
   b) Does the relationship vary by age, sex, race/ethnicity, socioeconomic status, or weight status?
   c) Does the relationship vary based on: frequency, duration, intensity, type (mode), and how physical activity is measured?

Data Sources and Process Used to Answer Questions

For Question 1 (prevention of weight gain) the Subcommittee determined that existing reviews (systematic reviews, meta-analyses, pooled analyses, and reports) identified from an initial search did not answer the research question. A complete de novo search of original research was conducted.

The Subcommittee determined that systematic reviews, meta-analyses, pooled analyses, and reports provided sufficient literature to answer research Questions 2 and 3. In an effort to reduce duplication of efforts, the searches for existing reviews and title triage for Question 2 (blood pressure) and Question 3 (incidence of type 2 diabetes) were done concurrently with the Chronic Conditions Subcommittee's Question 3 (individuals with hypertension) and Question 4 (individuals with type 2 diabetes). The search strategies for each of these questions were developed to address the needs of both Subcommittees. Title triage addressed the inclusion criteria of both Subcommittees. Abstract and full-text triage were done separately for each Subcommittee. For complete details on the systematic literature review process, see *Part E. Systematic Review Literature Search Methodology.*

Question 1. What is the relationship between physical activity and prevention of weight gain?

a) Is there a dose-response relationship? If yes, what is the shape of the relationship?
b) Does the relationship vary by age, sex, race/ethnicity, socioeconomic status, or weight status?
c) Does the relationship vary based on levels of light, moderate, or vigorous physical activity?

Sources of evidence: Original research articles

Conclusion Statements

Strong evidence demonstrates a relationship between greater amounts of physical activity and attenuated weight gain in adults, with some evidence to support that this relationship is most pronounced when physical activity exposure is above 150 minutes per week. **PAGAC Grade: Strong.**

Limited evidence suggests a dose-response relationship between physical activity and the risk of weight gain in adults, with greater amounts of physical activity associated with lower risk of weight gain. **PAGAC Grade: Limited.**

Limited evidence suggests that the relationship between greater amounts of physical activity and attenuated weight gain in adults varies by age, with the effect diminishing with increasing age. The evidence from studies of older adults, however, is inconsistent. **PAGAC Grade: Limited.**

Moderate evidence indicates that the relationship between greater amounts of physical activity and attenuated weight gain in adults does not appear to vary by sex. **PAGAC Grade: Moderate.**

Insufficient evidence is available to determine whether the relationship between greater amounts of physical activity and attenuated weight gain in adults varies by race/ethnicity. **PAGAC Grade: Not assignable.**

Insufficient evidence is available to determine whether the relationship between greater amounts of physical activity and attenuated weight gain in adults varies by socioeconomic status. **PAGAC Grade: Not assignable.**

Insufficient evidence is available to determine whether the relationship between greater amounts of physical activity and attenuated weight gain in adults varies by initial weight status. **PAGAC Grade: Not assignable.**

Strong evidence demonstrates that the significant relationship between greater time spent in physical activity and attenuated weight gain in adults is observed with moderate-to-vigorous physical activity. **PAGAC Grade: Strong.**

Insufficient evidence is available to determine an association between light-intensity activity and attenuated weight gain in adults. **PAGAC Grade: Not assignable.**

Review of the Evidence

To answer this question, the Subcommittee reviewed evidence from 33 original research studies.[14-46] Most of the studies showing an association between greater physical activity and attenuated weight gain (N=26) were prospective cohort studies,[14-18, 20, 22-24, 27-31, 34-36, 38-46] with follow-up periods ranging from 1 to 22 years and one study involving 6-year follow-up after a block randomized controlled trial (RCT). For the seven studies not showing an effect, six were cohort studies with the follow-up period ranging from 1 to 20 years.[19, 21, 25, 32, 33, 37] Three of these studies had follow-up periods of 2 or fewer years,[21, 24, 33] and one was a secondary analysis of data from a randomized study.[26]

Of studies showing an inverse association with weight gain, 7 studies assessed physical activity at one time point to examine the association with weight gain,[17, 22, 27, 28, 31, 35, 41] whereas 19 studies assessed physical activity at two or more time points to assess this association with weight gain.[14-16, 18, 20, 23, 24, 29, 30, 34, 36, 38-40, 42-46] For the seven studies that examined the association with weight gain but did not show an effect, three studies measured physical activity at one time point[21, 32, 33] and four studies measured physical activity at multiple time points.[19, 25, 26, 37]

The studies reviewed provided substantial information to allow for evaluation of an overall association between physical activity and either weight gain, increase in BMI, or development of obesity. Although data were available to examine whether these associations were influenced by sex and age, very limited information was provided within the studies reviewed to examine the influence of race/ethnicity, socioeconomic status, initial weight status, or dietary intake and eating behaviors, on the relationship between physical activity and weight gain. Moreover, although substantial information was provided for moderate-to-vigorous physical activity, few studies provided data for light-intensity physical activity.

Evidence on the Overall Relationship

Twenty-six of 33 studies demonstrate a significant relationship between greater amounts of physical activity and attenuated weight gain in adults.[14-18, 20, 22-24, 27-31, 34-36, 38-46] Eleven of the 26 studies that demonstrated a relationship reported data for the volume of physical activity where the effect is observed.[17, 20, 27, 29, 30, 34, 36, 40, 41, 43, 45] The evidence for a specific volume threshold of physical activity that is associated with prevention of weight gain in adults is inconsistent. Studies find that at least 1 hour per week of moderate intensity reduces the risk of developing obesity in both normal weight women (incidence rate ratio (IRR)=0.81; 95% confidence interval (CI): 0.71-0.93) and overweight women (IRR=0.88; 95% CI: 0.81-0.95)[39]; however, a similar result may be observed with less than 1 hour per week if the activity is of vigorous intensity, rather than moderate intensity. Williams and Wood[45] have reported that running equivalent to 4.4 km per week (~2.8 miles per week (~28 minutes per week at a 10-minute per mile pace) in men and 6.2 km per week (~3.8 miles per week (~38 minutes per week at a 10-minute per mile pace) in women may be sufficient to prevent weight gain associated with aging. Some evidence also supports the need to achieve at least 150 minutes per week of moderate intensity physical activity to minimize weight gain or to prevent increases in BMI.[29, 30, 43] Studies also support greater amounts of physical activity to prevent or minimize weight gain, with some studies reporting this effect with greater than 150 minutes per week at a moderate intensity,[36] 500 or more MET-minutes per week (≥167 minutes per week at a 3-MET intensity),[20, 41] or more than 300 minutes per week.[17, 27, 34]

Dose-Response: Some of the reviewed studies provided data on the dose-response relationship of physical activity and weight gain,[17, 27, 36, 41] maintenance of a healthy weight,[20] and development of obesity.[39]

Sims et al[41] reported a trend (*P*<0.08) for minimized weight gain in women engaging in more than 8.3–20 MET-hours per week (>167-400 minutes per week at a 3-MET intensity) or more than 20 MET-hours per week (>400 minutes per week at a 3-MET intensity) of physical activity, compared with those engaged in less than 1.7 MET-hours per week (<33 minutes per week at a 3-MET intensity). A physical activity volume of 1.7-8.3 MET-hours per week was not protective against weight gain, however.

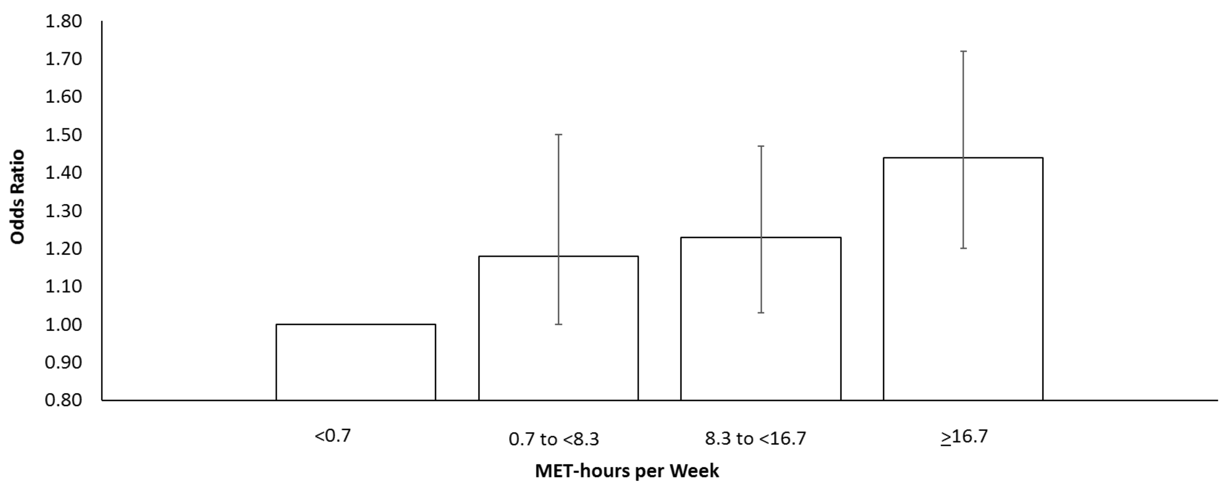
Two studies provide evidence of a dose-response to prevent weight gain of approximately 2 kg. Moholdt et al[36] identified four groups based on physical activity ("Inactive": no leisure-time physical activity; "Below Recommended": active <150 minutes per week in moderate intensity or <60 minutes per week in vigorous intensity leisure-time physical activity; "Recommended": active at 150 minutes per week in moderate intensity or 60 minutes per week in vigorous intensity leisure-time physical activity; "Above Recommended": active >150 minutes per week in moderate intensity or >60 minutes per week minutes per week in vigorous intensity leisure-time physical activity). For men, compared with those in the "Inactive" category, the risk of gaining ≥2.3 kg was 0.97 (95% CI: 0.87-1.08) for those in the "Recommended" category and 0.79 (95% CI: 0.69-0.91) for those in the "Above Recommended" category. A similar pattern was observed in women, with the risk of 0.97 (95% CI: 0.88-1.07) for those in the "Recommended" category and 0.69 (95% CI: 0.59-0.82) for those in the "Above Recommended" category. Gebel et al[27] reported a 10 percent reduction in the odds of ≥2kg weight gain with 300 or more minutes per week of moderate-to-vigorous physical activity compared with less than 150 minutes per week of moderate-to-vigorous physical activity; however, 150-249 minutes per week was not predictive of weight change.

Blanck et al[17] reported that the odds of gaining 10 or more pounds (≥4.5 kg) was significantly lower with 18 or more MET-hours per week (0.88; 95% CI: 0.77-0.99) in women with normal weight compared with the reference of more than 0 but less than 4 MET-hours per week (1.0). Compared to the reference, the odds of gaining this magnitude of weight did not differ with 0 MET-hours per week (1.01; 95% CI: 0.82-

1.01), 4 to less than 10 MET-hours per week (0.93; 95% CI: 0.80-1.08), and 10 to less than 18 MET-hours per week (0.99; 95% CI: 0.87-1.14).

Brown et al[20] report on a dose-response relationship for physical activity and the odds of maintaining a healthy weight (i.e., BMI of ≥18.5 to <25 kg/m^2). Compared with less than 0.7 MET-hours per week, the odds ratio (OR) for maintaining a normal BMI was 1.18 (95% CI: 1.00-1.40) for 0.7 to less than 8.3 MET-hours per week, 1.23 (95% CI: 1.03-1.47) for 8.3 to less than 16.7 MET-hours per week, and 1.44 (95% CI: 1.20-1.72) for 16.7 or more MET-hours per week (Figure F5-1).[20]

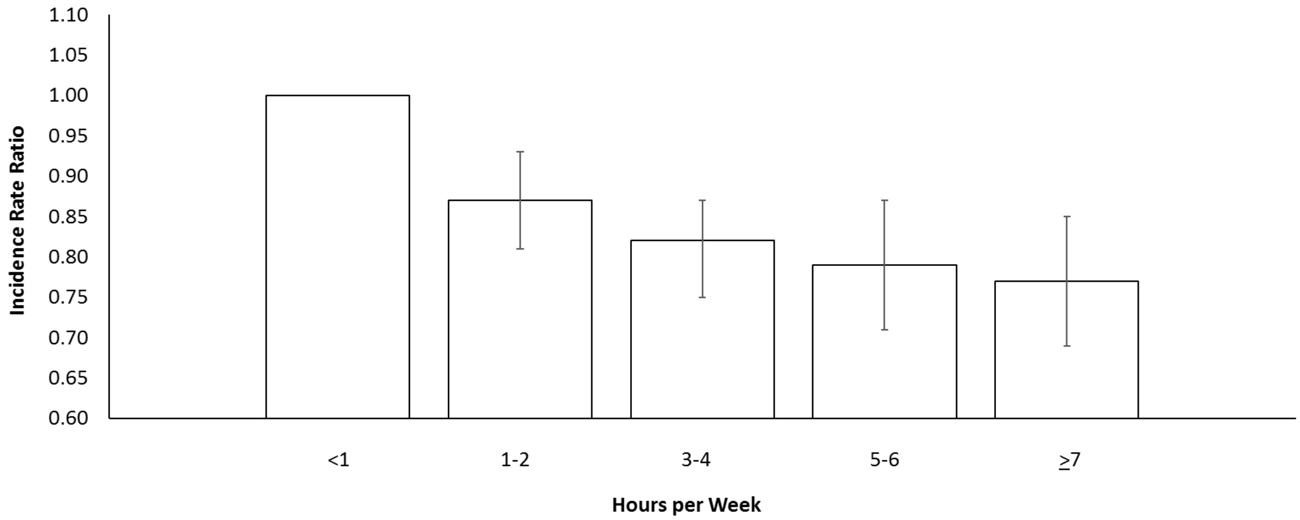
Figure F5-1. Odds of Maintaining a Healthy Weight by Level of Physical Activity



Source: Adapted from data found in Brown et al., 2016.[20]

Rosenberg et al[39] reported on the dose-response relationship for vigorous intensity physical activity and the likelihood of developing obesity. In women with normal weight and overweight, when compared to less than 1 hour per week, the incidence of developing obesity was significantly reduced in a graded manner, with vigorous intensity activity of 1 to 2 hours per week (0.87; 95% CI: 0.81-0.93), 3 to 4 hours per week (0.82; 95% CI: 0.75-0.88), 5 to 6 hours per week (0.79; 95% CI: 0.71-0.87), and 7 or more hours per week (0.77; 95% CI: 0.69-0.85) (Figure F5-2).[39]

Figure F5-2. Incidence Rate Ratio of Developing Obesity at Various Levels of Vigorous Physical Activity



Source: Adapted from data found in Rosenberg et al., 2013.[39]

Evidence on Specific Factors

Age: In general, the 26 studies in which a significant inverse association between physical activity and weight gain was observed encompassed a broad age range that included young, middle-aged, and older adults. Six studies analyzed the data specifically by age, with the evidence suggesting attenuation of this association with increasing age in both men and women.[34-36, 41, 44, 46] This pattern of results was inconsistent in the studies that included both men and women, however. MacInnis et al[35] reported a significant inverse association between physical activity and magnitude of weight gain across a mean follow-up of approximately 12 years in adults ages 40 to 49 years, with this association not observed in adults ages 50 to 59 years or 60 to 69 years. Williams[46] reported that running attenuated weight gain in men younger than 55 years of age and in women younger than 50 years of age.

These results are not consistent with the finding of Moholdt et al,[36] who reported that physical activity was significantly associated with reduced odds of gaining 2.3 or more kg in both men and women. Additional analyses, however, showed a significant interaction with age with a lower odds of a 2.3 or more kg weight gain in physically active adult men ages 40 years or older but not in those younger. In contrast, the inverse association between physical activity and odds of a 2.3 or more kg weight gain was observed across the age spectrum (younger than age 40 years, age 40 to 59 years, and age 60 years and older) in women. Moreover, Williams and Thompson[44] reported that the weight gain associated with the cessation of running was consistent between men less than 45 years of age and 45 years or older.

However, among women, weight gain was greater in women ages 45 years or older compared with their younger counterparts.

Two studies examined the association between physical activity and weight gain only in women. Lee et al[34] examined data from the Women's Health Initiative study and reported a trend for greater weight gain with lower levels of activity in women younger than age 64 years, but not in women ages 65 years and older. Similar findings were reported by Sims et al[41] in a study of post-menopausal women ages 50 to 79 years, which showed attenuated weight gain with greater amounts of physical activity in women ages 50 to 59 years, but not in those of ages 60 to 69 years or 70 to 79 years.

Sex: The 26 studies in which a significant inverse association between physical activity and weight gain was observed included either women (N=10)[14, 16, 17, 20, 22, 28, 31, 34, 39, 41] or both men and women (N=16).[15, 18, 23, 24, 27, 29, 40, 43-46] Of the 16 studies that included both men and women, 6 did not analyze the data separately by sex.[18, 24, 27, 29, 40, 43] Of the 10 studies that presented findings separately by sex, 8 reported that the association between physical activity and weight gain was consistent for both men and women.[15, 23, 30, 35, 36, 38, 42, 44-46]

Race/ethnicity: In general, the 26 studies in which a significant inverse association between physical activity and weight gain was observed encompassed diverse races and ethnicities. When specified, for studies conducted based on adults residing in the United States, a broad range of races and ethnicities appeared to be represented in the study samples[18, 24, 30, 31, 41] or the sample included only black/African Americans.[39] Some of the studies were conducted in countries outside of the United States, including Australia,[20, 27, 35, 43] France,[42] Great Britain,[38] Norway,[36] South Africa,[28] Spain,[15] Sweden,[23] and the Philippines.[14, 22] Although some studies included race or ethnicity as a covariate in the analyses, none of them presented data separately by race or ethnicity to allow for comparisons.

Socioeconomic status: Of those studies showing an inverse association between physical activity and weight gain, some studies provided a measure of socioeconomic status as a descriptive variable or as a covariate in analyses. Only one study isolated the effect of socioeconomic status on the association between physical activity and weight gain, and it was reported that socioeconomic status attenuated this association even though it remained statistically significant.[18]

Weight status: The 26 studies in which a significant inverse association between physical activity and weight gain was observed included adults of normal, overweight, and obese weight status. However, 19 of these studies did not report on whether the association between physical activity and weight gain varied by initial weight status. Of the remaining seven studies, two reported that the association did not differ by weight status,[39, 41] three reported the association to be more favorable in adults who had normal weight versus overweight or obesity,[17, 31, 34] and two studies reported results showing a more favorable pattern in adults with overweight compared to those with normal weight.[15, 36]

Light, moderate, or vigorous physical activity: In the 26 studies in which a significant inverse association between physical activity and weight gain was observed, investigators examined a variety of domains of physical activity. These included leisure-time/recreational activity, occupational activity, household activity, walking, and total steps of physical activity. Moreover, various intensities of physical activity (light, moderate, vigorous, moderate-to-vigorous) were assessed across these studies.

Total leisure-time physical activity was consistently inversely associated with weight change across the studies reviewed.[17, 23, 34, 35, 38, 41, 42] Studies reporting on moderate intensity,[15, 24] vigorous intensity,[18, 28, 29, 35, 39, 44-46] and moderate-to-vigorous intensity[20, 27-31, 36, 40] physical activity showed consistent patterns of inverse associations with weight gain. Light-intensity physical activity, however, was either not associated with weight change[29] or was associated with weight gain.[24]

Walking was not consistently associated with change in weight or BMI[28, 35] or with the incidence of developing obesity.[39] In contrast, however, Smith et al[43] reported that achieving 10,000 steps or more per day attenuated weight gain compared with not achieving 10,000 steps per day.

Studies also examined occupational and household activity. Occupational activity was inversely associated with weight gain,[14, 22, 35] with this association being observed with moderate- and vigorous intensity occupational activity,[14, 35] but not with light-intensity occupational activity.[14] Household activity does not appear to minimize weight gain.[22, 35]

For additional details on this body of evidence, visit: https://health.gov/paguidelines/second-edition/report/supplementary-material.aspx for the Evidence Portfolio.

Comparing 2018 Findings with the 2008 Scientific Report

The *Physical Activity Guidelines Advisory Committee Report, 2008*[1] concluded physical activity was associated with modest weight loss,[1] prevention of weight gain following weight loss,[1] and reductions in total and regional adiposity.[1] This evidence review expands these previous findings by providing evidence from prospective studies for an inverse association between physical activity and both weight gain and incidence of obesity, and a positive association between physical activity and maintenance of a BMI within a range of ≥18.5 to <25 kg/m^2. Evidence also exists to support that attenuation of weight gain is most pronounced when physical activity exposure is more than 150 minutes per week.

Public Health Impact

Weight gain that results in overweight or obesity is associated with increased risk for numerous chronic conditions. This is a significant health concern in the United States due to the high prevalence of both overweight and obesity. Thus, while it is important to focus on effective treatments for overweight and obesity, there is also a need to implement effective public health strategies to prevent weight gain and the onset of both overweight and obesity. The scientific evidence supports that physical activity can be an effective lifestyle behavior to prevent or minimize weight gain in adults. Therefore, public health initiatives to prevent weight gain, overweight, and obesity should include physical activity as an important lifestyle behavior.

Question 2. In people with normal blood pressure or prehypertension, what is the relationship between physical activity and blood pressure?

a) Is there a dose-response relationship? If yes, what is the shape of the relationship?
b) Does the relationship vary by age, sex, race/ethnicity, socioeconomic status, weight status, or resting blood pressure level?
c) Does the relationship vary based on frequency, duration, intensity, type (mode), or how physical activity is measured?

Source of evidence: Systematic reviews, meta-analyses

Conclusion Statements

Strong evidence demonstrates that physical activity reduces blood pressure among adults with prehypertension and normal blood pressure. **PAGAC Grade: Strong.**

Strong evidence demonstrates an inverse dose-response relationship between physical activity and incident hypertension among adults with normal blood pressure. **PAGAC Grade: Strong.**

Insufficient evidence is available to determine whether a dose-response relationship exists between physical activity and incident hypertension among adults with prehypertension. **PAGAC Grade: Not assignable.**

Insufficient evidence is available to determine whether the relationship between physical activity and blood pressure varies by age, sex, race/ethnicity, socioeconomic status, or weight status among adults with normal blood pressure and prehypertension. **PAGAC Grade: Not assignable.**

Strong evidence demonstrates the magnitude of the blood pressure response to physical activity varies by resting blood pressure level, with greater benefits occurring among adults with prehypertension than normal blood pressure. **PAGAC Grade: Strong.**

Insufficient evidence is available to determine whether the relationship between blood pressure and physical activity varies by the frequency, intensity, time, and duration of physical activity, or how physical activity is measured among adults with normal blood pressure and prehypertension. **PAGAC Grade: Not assignable.**

Moderate evidence indicates the relationship between resting blood pressure level and the magnitude of benefit does not vary by type (mode, i.e., aerobic, dynamic resistance, combined) of physical activity among adults with normal blood pressure and prehypertension. **PAGAC Grade: Moderate.**

Review of the Evidence

To answer this question, the Subcommittee reviewed 10 meta-analyses (Supplemental Table 5-1).[47-56] The coverage dates ranged from earliest coverage to 2016, the total number of included studies ranged from 9 to 93, and the total included study sample size consisted of 485,747 adults ranging from 233 to 330,222 participants. Two meta-analyses examined longitudinal prospective cohort studies,[55, 56] and eight meta-analyses examined randomized controlled trials.[47-54] The 10 meta-analyses[47-56] included adults with hypertension and normal blood pressure, while five included adults with prehypertension.[47, 48, 50, 51, 53] Because the literature reviewed for this question was based upon the JNC 7 blood pressure classification scheme, the Subcommittee used the JNC 7 blood pressure classification scheme[8] for data extraction purposes. The JNC 7 defines these blood pressure classifications as follows: Hypertension is defined as having a resting systolic blood pressure of 140 mmHg or greater and/or a resting diastolic blood pressure 90 mmHg or greater, or taking antihypertensive medication, regardless of the resting blood pressure level. Prehypertension is defined as a systolic blood pressure from 120 to 139 mmHg and /or diastolic blood pressure from 80 to 89 mmHg. Normal blood pressure is defined as having a systolic blood pressure less than 120 mmHg and diastolic blood pressure less than 80 mmHg. However, it should be noted that during the preparation of the 2018 Scientific Report, the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines released the 2017

Guideline for the Prevention, Detection, Evaluation and Management of High Blood Pressure in Adults.[57] The new guidelines define hypertension as a resting systolic blood pressure of 130 mmHg or greater and/or a resting diastolic blood pressure 80 mmHg or greater, or taking antihypertensive medication, regardless of the resting blood pressure level. Furthermore, the term prehypertension was eliminated and elevated blood pressure was added indicating a resting systolic blood pressure between 120 to 129 mmHg and a diastolic blood pressure < 80 mmHg. However, the new guidelines did not alter the conclusion statements made in this report.

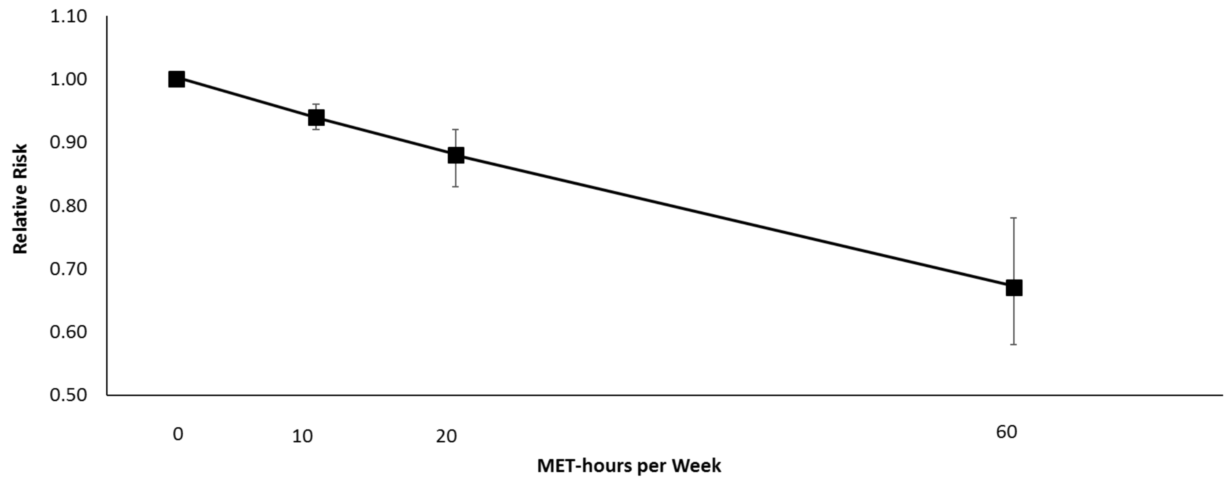
Evidence on the Overall Relationship

Strong evidence demonstrates that physical activity reduces blood pressure among adults with prehypertension and normal blood pressure. Eight meta-analyses of RCTs examined the blood pressure response to physical activity among initially sedentary adults with prehypertension[47, 48, 50, 51, 53] and/or normal blood pressure.[47-49, 51-54] Of the five meta-analyses involving adults with prehypertension, five reported a statistically significant reduction in systolic blood pressure and four reported a statistically significant reduction in diastolic blood pressure (see Supplementary Table S-F5-2). Of the seven meta-analyses involving adults with normal blood pressure, three reported a statistically significant reduction and one reported a statistically significant rise in systolic blood pressure, and six reported a statistically significant reduction in diastolic blood pressure (see Supplementary Table S-F5-2). Blood pressure reductions of the magnitude observed in these meta-analyses of about 2 to 5 mmHg for systolic blood pressure and 1 to 4 mmHg for diastolic blood pressure may be sufficient to reduce the risk of coronary heart disease by 4 to 5 percent and stroke by 6 to 8 percent among adults with prehypertension and normal blood pressure.[8, 58, 59] Furthermore, they may be of sufficient magnitude to lower the resting blood pressure of some samples with prehypertension into normotensive ranges. When studies disclosed the information, the frequency of physical activity ranged from 1 to 7 days per week, with 3 days per week most common; the intensity ranged from low to vigorous, with low to moderate most common; the time ranged from 8 to 63 minutes per session, with 30 to 60 minutes per session most common; and the study duration ranged from 4 to 52 weeks, with 16 to 20 weeks most common.

The Subcommittee also regarded the association between physical activity and the risk of developing hypertension (referred to as incident hypertension) as an indicator of the blood pressure response to physical activity. Huai et al[55] examined this association among 136,846 adults with normal blood pressure at baseline. After an average of 10 years (2 to 45 years) of follow up, 15,607 adults developed hypertension (11.4% of the sample). In this meta-analysis, high amounts (i.e., volume and/or intensity) of leisure-time physical activity were associated with a 19 percent decreased risk of incident hypertension compared to the referent group engaging in low amounts of leisure-time physical activity (relative risk (RR)=0.81; 95% CI: 0.76-0.85). Moderate amounts of leisure-time physical activity were associated with an 11 percent decreased risk of hypertension compared to the referent group engaging in low amounts of leisure-time physical activity (RR=0.89; 95% CI: 0.85-0.94). However, Huai et al[55] found no significant associations with occupational and commuting physical activity and incident hypertension.

Dose-response: Strong evidence demonstrates an inverse dose-response relationship between physical activity and incident hypertension among adults with normal blood pressure. Two meta-analyses investigated the relationship of physical activity and incident hypertension among adults with normal blood pressure.[55, 56] Of these, Liu et al[56] quantified the dose-response relationship between physical activity and incident hypertension among adults with normal blood pressure (Figure F5-3). Among 330,222 adults with normal blood pressure, after 2 to 20 years of follow up, 67,698 incident cases of hypertension occurred (20.5% of the sample). The risk of hypertension was reduced by 6 percent (RR=0.94; 95% CI: 0.92-0.96) at 10 MET-hours per week of leisure-time light, moderate, and vigorous physical activity (LMVPA) among adults with normal blood pressure. The protective effect increased by about 6 percent for each further increase of 10 MET-hours per week. For adults with 20 MET hours per week of leisure-time LMVPA, the risk of hypertension was reduced by 12 percent (RR=0.88; 95% CI: 0.83-0.92); and for those for 60 MET-hours per week of leisure-time LMVPA, the risk of hypertension was reduced by 33 percent (RR=0.67; 95% CI: 0.58-0.78). The relationship between leisure-time physical activity and incident hypertension was linear, with no cutoff of benefit, and slightly weaker with (RR=0.94; 95% CI: 0.92-0.96) than without (RR=0.91; 95% CI: 0.89-0.93) BMI adjustment. These same dose-response trends were seen for total physical activity such that for each 50 MET-hours per week increase in total physical activity, the risk of hypertension was reduced by 7 percent (RR=0.93; 95% CI: 0.88-0.98); and for 64.5 MET-hours per week of total physical activity, the risk of hypertension was reduced by 10 percent. The relationship between total physical activity and incident hypertension was linear, with no cutoff of benefit, and slightly stronger with than without BMI adjustment. The authors acknowledged their meta-analysis was limited by the considerable variety of physical activity self-report questionnaires used in the primary level studies.

Figure F5-3. Inverse Relationship Between Incident Hypertension and Leisure-Time Physical Activity, by MET-Hours per Week Among Adults with Normal Blood Pressure



Source: Adapted from data found in Liu et al., 2017.[56]

The available evidence is insufficient to determine whether a dose-response relationship exists between physical activity and incident hypertension among adults with prehypertension, as the magnitude and precision of the effect cannot be ascertained from findings that are too scarce to synthesize.

Evidence on Specific Factors

Demographic characteristics and weight status: The available evidence is insufficient to determine whether the relationship between physical activity and blood pressure varies by age, sex, race/ethnicity, socioeconomic status, or weight status among adults with prehypertension and normal blood pressure. In the few instances where age, sex, race/ethnicity, socioeconomic status, and weight status were examined as moderators of the blood pressure response to physical activity, the findings were too disparate to synthesize because they were often not reported separately by blood pressure classification but were reported for the overall sample that included adults with hypertension, prehypertension, and normal blood pressure.

Three meta-analyses found age not to be a significant moderator of the blood pressure response to physical activity,[47, 48, 56] but two of these contained samples with mixed blood pressure levels, and the other did not stratify analyses by age. One meta-analysis reported that men exhibited blood pressure reductions twice as large as did women following aerobic exercise training among samples with mixed blood pressure levels,[48] and another found no difference by sex.[56] Race/ethnicity was poorly reported, and when reported in three of the meta-analyses,[53, 55, 56] the samples primarily included White and some

Asian participants. Three meta-analyses reported the weight status of their samples, which ranged from normal weight to overweight.[47, 51, 53] Among a large sample of 330,222 adults with normal blood pressure who were followed for 2 to 20 years, Liu et al[56] found that the inverse dose-response relationship between leisure-time physical activity and incident hypertension was slightly weaker with (RR=0.94; 95% CI: 0.92-0.96) than without BMI adjustment (RR=0.91; 95% CI: 0.89-0.93), but these analyses were not stratified by BMI. These authors also found that the relationship between total physical activity and incident hypertension was slightly stronger with than without BMI adjustment, but these analyses were also not stratified by BMI. Cornelissen and Smart[48] found the systolic blood pressure reductions resulting from aerobic exercise training tended to be larger with greater ($\beta 1$=0.49, *P*=0.08) than less ($\beta 1$=0.45, *P*=0.06) weight loss among a sample of 5,223 adults with mixed blood pressure levels. Therefore, no conclusions can be made regarding the influence of age, sex, race/ethnicity, socioeconomic status, or weight status on the relationship between physical activity and blood pressure.

African Americans have the highest prevalence of hypertension of any ethnic group in the world.[60] The progression from prehypertension to hypertension is also faster among African Americans than Whites.[11] African Americans are more likely to have their hypertension identified and treated, but less likely to have their hypertension controlled than are Whites, despite using more antihypertensive medications.[61-63] As verified by this review, surprisingly little published research in the form of meta-analyses and systematic reviews exists on the association between physical activity and incident hypertension among African Americans. There are findings, however, from recent original studies, such as the Jackson Heart Study, that may also inform the association between physical activity and incident hypertension in African Americans.[64]

Resting blood pressure level: Strong evidence demonstrates the magnitude of the blood pressure response to physical activity varies by resting blood pressure level, with greater benefits occurring among adults with prehypertension than with normal blood pressure. Of the six meta-analyses examining blood pressure classification as a moderator of the blood pressure response to physical activity,[47-49, 51, 53, 54] four[48, 49, 51, 53] found that the greatest blood pressure reductions occurred among samples with hypertension (5 to 8 mmHg, 4 to 6 percent of resting blood pressure level) followed by samples with prehypertension (2 to 4 mmHg, 2 to 4 percent of resting blood pressure level), and normal blood pressure (1 to 2 mmHg, 1 to 2 percent of resting blood pressure level) (see online Supplemental Table 2). Consistent with the law of initial values,[65, 66] adults with prehypertension experience blood pressure reductions from exercise training that are about 2 to 4 times greater than the blood pressure reductions that occur among adults with normal blood pressure. Blood pressure reductions of this magnitude may be sufficient to reduce the resting blood pressure of some of the samples with prehypertension into normotensive ranges. They also may be sufficient to reduce the risk of coronary heart disease by 4 to 5 percent and stroke by 6 to 8 percent among adults with normal blood pressure and prehypertension.[8, 58, 59]

Frequency: The frequency of physical activity was reported in seven meta-analyses,[47-51, 53, 56] and ranged from 0 to 7 days per week. However, no conclusions can be made about the influence of frequency on the blood pressure response to physical activity because the findings were too scarce and too disparate to synthesize.

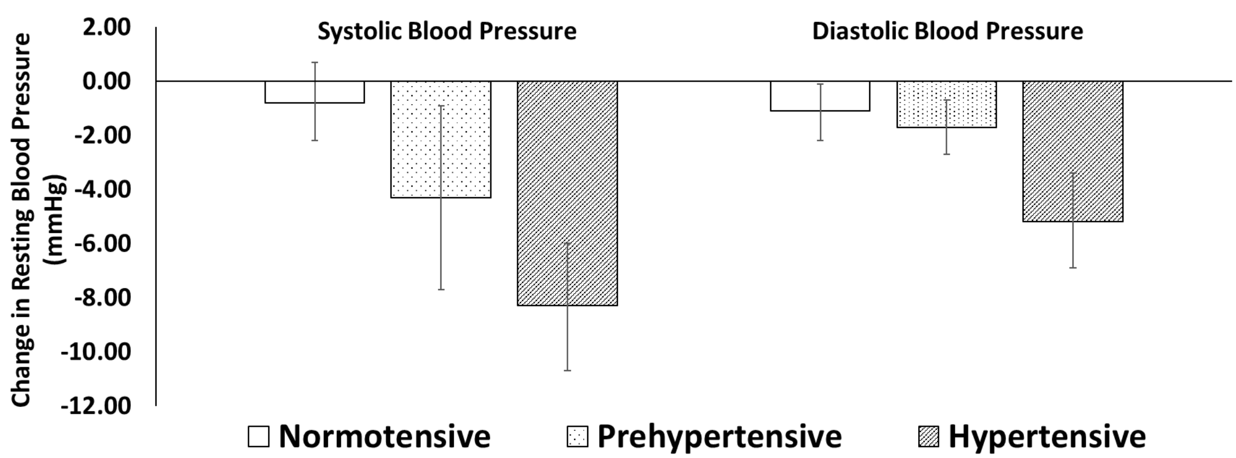
Intensity: The intensity of physical activity was reported in all meta-analyses,[47-56] and ranged from low to vigorous intensity. However, no conclusions can be made regarding the influence of intensity on the blood pressure response to physical activity as the magnitude and precision of the effect could not be determined from findings that were too scarce to synthesize.

Time: The time of the exercise session was reported in six meta-analyses,[48-51, 54, 56] and ranged from 12 to 63 minutes. Time was not disclosed in three meta-analyses.[47, 52, 53] However, no conclusions can be made regarding the influence of time on the blood pressure response to physical activity, as the magnitude and precision of the effect could not be determined from a lack of findings on the time of the exercise session.

Duration: All chronic (i.e., training) meta-analyses reported the duration of the physical activity intervention, and they ranged from 4 to 52 weeks.[47-51, 53, 54] However, no conclusions can be made regarding the influence of duration on the blood pressure response to physical activity as the magnitude and precision of the effect could not be determined from findings that were too scarce to synthesize.

Type (Mode): Moderate evidence indicates the relationship between resting blood pressure level and the blood pressure response to physical activity does not vary by type (i.e., aerobic, dynamic resistance, combined) of physical activity. Three meta-analyses examined the blood pressure response to aerobic exercise training,[48-50] three meta-analyses examined the blood pressure response to resistance exercise training (one acute[52] and two chronic),[47, 53] one meta-analysis examined the blood pressure response to combined aerobic and resistance exercise training (also referred to as concurrent exercise training),[51] and one meta-analysis examined the blood pressure response to isometric resistance training.[54] Cornelissen and Smart[48] examined aerobic exercise training performed, on average, at moderate to vigorous intensity for 40 minutes per session 3 days per week for 16 weeks and reported systolic/diastolic blood pressure reductions of -8.3 (95% CI: -10.7 to -6.0)/-5.2 (95% CI: -6.9 to -3.4), -4.3 (95% CI: -7.7 to -0.9)/-1.7 (95% CI: -2.7 to -0.7), and -0.8 (95% CI: -2.2 to +0.7)/-1.1 (95% CI: -2.2 to -0.1) mmHg among adults with hypertension, prehypertension, and normal blood pressure, respectively (Figure F5-4). MacDonald et al[53] examined dynamic resistance training performed, on average, at moderate intensity for 32 minutes per session 3 days per week for 14 weeks, which approximates 90 minutes of moderate intensity or 45 minutes of vigorous intensity physical activity per week, and reported systolic/diastolic blood pressure changes of -5.7 (95% CI: -9.0 to -2.7)/-5.2 (95% CI -8.4, -1.9), -3.0 (95% CI: -5.1 to -1.0)/-3.3 (95% CI: -5.3 to -1.4), and 0.0 (95% CI: -2.5 to 2.5)/-0.9 (95% CI: -2.1 to 2.2) mmHg among adults with hypertension, prehypertension, and normal blood pressure, respectively. Corso et al[51] examined combined aerobic and dynamic resistance exercise training performed, on average, at moderate intensity for 58 minutes per session 3 days per week for 20 weeks and reported systolic/diastolic blood pressure changes of -5.3 (95% CI -6.4 to -4.2)/-5.6 (95% CI -6.9 to -3.8), -2.9 (95% CI -3.9 to -1.9)/-3.6 (95% CI -5.0 to -0.2), and +0.9 (95% CI 0.2 to 1.6)/-1.5 (95% CI -2.5 to -0.4) mmHg among adults with hypertension, prehypertension, and normal blood pressure, respectively.

Figure F5-4. Blood Pressure Response to 16 Weeks of Aerobic Exercise Training



Source: Adapted from data found in Cornelissen and Smart, 2013.[48]

Carlson et al[54] investigated the blood pressure response to 4 or more weeks of isometric resistance training at 30 percent to 50 percent maximal voluntary contraction with 4 contractions held for 2 minutes with 1 to 3 minutes of rest between contractions among adults with hypertension (N=61) and normal blood pressure (N=162). Systolic, diastolic, and mean arterial blood pressure were reduced among the adults with hypertension, all of whom were on medication, by -4.3 (95% CI: -6.6 to -2.2)/-5.5 (95% CI: -7.9 to -3.3)/-6.1 (95% CI: -8.0 to -4.0) mmHg, and by -7.8 (95% CI: -9.2 to -6.4)/-3.1 (95% CI: -3.9 to -2.3)/-3.6 (95% CI: -4.4 to -2.7) mmHg among adults with normal blood pressure, respectively. Carlson et al[54] were unable to explain the larger reductions in systolic blood pressure among the adults with normal blood pressure compared to adults with hypertension, and the reverse pattern of blood pressure response for diastolic blood pressure and mean arterial pressure. The sample size of the meta-analysis by Carlson et al[54] investigating isometric resistance training was much smaller than the sample size of the meta-analyses investigating aerobic,[48] dynamic resistance,[53] and combined[51] exercise training. For these reasons, any conclusions made about the blood pressure benefits of isometric resistance training should be made with caution. It also should be noted that the existing literature included in this report on physical activity and blood pressure has examined aerobic, resistance, and combined types of physical activity.

Collectively, these findings indicate the blood pressure response to aerobic, dynamic resistance, and combined types of physical activity elicit blood pressure reductions of 2 to 4 mmHg (2 to 4 percent of resting blood pressure level) among adults with prehypertension and 1 to 2 mmHg (1 to 2 percent of resting blood pressure level) among adults with normal blood pressure, independent of type (mode). These blood pressure reductions are about 2 to 4 times greater among adults with prehypertension than normal blood pressure. These blood pressure benefits occurred at about 6 MET hours per week of moderate-to-vigorous physical activity.

How physical activity was measured: All meta-analyses that examined the blood pressure response to physical activity included interventions that were structured by the frequency, intensity, time, duration, and type (mode) of physical activity, but the details of these features of the physical activity interventions were not well disclosed. None of these meta-analyses reported any physical activity measure outside of the structured physical activity intervention. No conclusions can be made regarding how physical activity was measured, as the magnitude and precision of the effect could not be determined from findings that were too scarce to synthesize.

For additional details on this body of evidence, visit: online Supplementary Tables S-F5-1 and S-F5-2 and https://health.gov/paguidelines/second-edition/report/supplementary-material.aspx for the Evidence Portfolio.

Comparing 2018 Findings with the 2008 Scientific Report

The 2008 Scientific Report concluded that both aerobic and dynamic resistance exercise training of moderate-to-vigorous intensity produced small but clinically important reductions in systolic and diastolic blood pressure in adults, with the evidence more convincing for aerobic than dynamic resistance exercise.[1] The 2018 Scientific Report extends these findings in four ways. First, the 2018 Scientific Report provides strong evidence that physical activity reduces blood pressure among adults with prehypertension and normal blood pressure. Second, it provides strong evidence of an inverse dose-response relationship between leisure-time physical activity and incident hypertension among adults with normal blood pressure. Third, due to an accumulating amount of highly consistent evidence over the past decade, the 2018 Scientific Report provides strong evidence demonstrating the magnitude of the blood pressure response to physical activity is greater among adults with prehypertension than with normal blood pressure. Fourth, reflecting on the accumulating evidence over the past decade, the 2018 Scientific Report indicates aerobic and dynamic resistance exercise may be equally effective in reducing blood pressure at a lower volume of physical activity.

Public Health Impact

Hypertension is the most common, costly, and preventable cardiovascular disease risk factor. According to the JNC 7 blood pressure classification scheme, by 2030 it is estimated that nearly 40 percent of adults in the United States will have hypertension and almost an equal amount will have prehypertension. Due to the clinically important role of physical activity in the prevention of hypertension, adults with normal blood pressure and prehypertension are encouraged to engage in at least 90 minutes per week or more of moderate intensity or at least 45 minutes per week or more of vigorous intensity aerobic and/or dynamic resistance physical activity, or some combination of these. Because there appears to be no cut off to the amount of physical activity that confers benefit, even greater amounts of physical activity should be encouraged. These recommendations are particularly important for African Americans to reduce the high disease burden of hypertension among this population group.

Question 3: In adults without diabetes, what is the relationship between physical activity and type 2 diabetes?

a) Is there a dose-response relationship? If yes, what is the shape of the relationship?
b) Does the relationship vary by age, sex, race/ethnicity, socioeconomic status, or weight status?
c) Does the relationship vary based on: frequency, duration, intensity, type (mode), and how physical activity is measured?

Sources of evidence: Systematic reviews, meta-analyses, pooled analysis

Conclusion Statements

Strong evidence demonstrates a significant relationship between a higher volume of physical activity and lower incidence of type 2 diabetes. **PAGAC Grade: Strong.**

Strong evidence demonstrates that an inverse curvilinear dose-response relationship exists between the volume of physical activity and incidence of type 2 diabetes, with a decreasing slope at higher levels of physical activity. **PAGAC Grade: Strong.**

Moderate evidence indicates no effect modification by weight status. An inverse relationship exists between a higher volume of physical activity and lower incidence of type 2 diabetes for people who have normal weight, overweight, or obesity. **PAGAC Grade: Moderate.**

Limited evidence suggests that the relationship between a higher volume of physical activity and lower incidence of type 2 diabetes is not influenced by age, sex, or race/ethnicity. **PAGAC Grade: Limited.**

Insufficient evidence is available to determine whether the relationship between physical activity and the incidence of type 2 diabetes varies by socioeconomic status. **PAGAC Grade: Not assignable.**

Insufficient evidence is available to determine whether the relationship between physical activity and the incidence of type 2 diabetes varies by the frequency, intensity, duration, or type of physical activity, or how physical activity is measured. **PAGAC Grade: Not assignable.**

Review of the Evidence

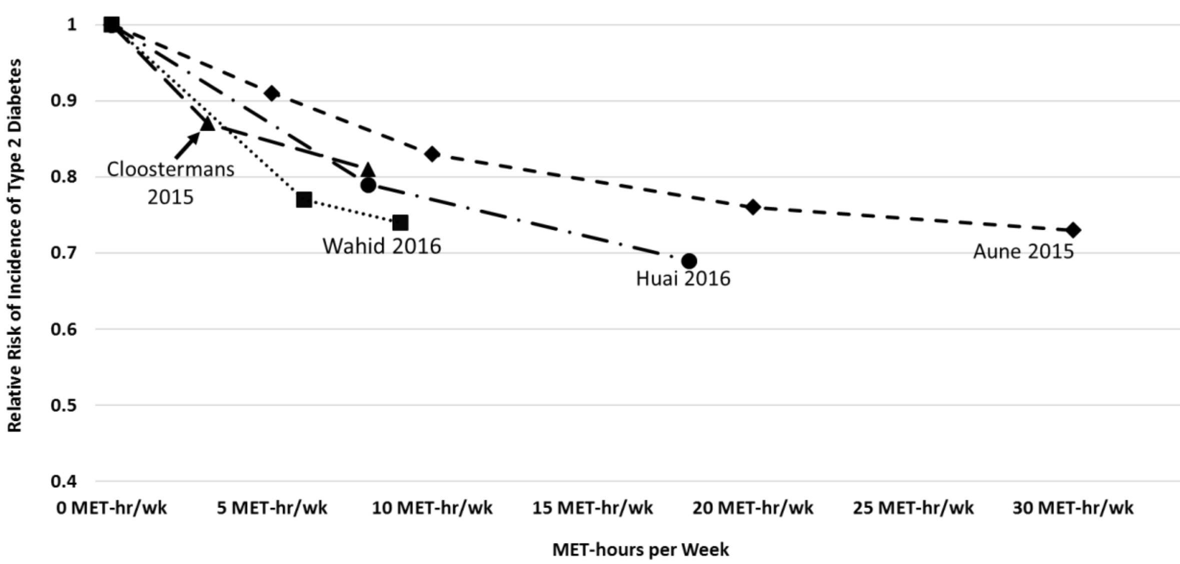
The evidence base comprised seven meta-analyses,[67-73] four systematic reviews,[74-77] and one pooled analysis.[78] Ten[68-71, 73-78] of the articles included only cohort studies, one included cohort and experimental studies,[72] and one included cohort, experimental, and case-control studies.[67] The number of studies included in each review ranged from 2 to 81, with a median of 8.5. For the eight reviews for which data on number of participants were provided, the total number ranged from 4,550 to about 300,000, with a median of 140,000. All reviews except one, which had no age restrictions,[67] included only adults. Mean age was not commonly provided; the three studies for which it was provided reported a mean age of 50[68, 72] and 52[78] years. Almost all physical activity behavior was self-reported leisure-time moderate-to-vigorous, though a few studies included other domains (i.e., occupational, transportation, household).[67, 68, 71, 77] Seven reviews provided risk estimates for at least three doses of physical activity, enabling an assessment of dose-response.[67-69, 71, 73, 74, 76]

Evidence on the Overall Relationship

All meta-analyses,[67-73] systematic reviews,[74-77] and the pooled analysis[78] reported an inverse relationship between volume of physical activity and the incidence of type 2 diabetes. Three meta-analyses,[67, 70, 72] one systematic review,[77] and the pooled analysis[78] provided quantitative estimates of the reduction in risk comparing participants engaging in "high" volume of physical activity with participants engaging in "low" volume of physical activity. The volume of physical activity represented by "high" and "low" was not provided. It is expected that "high" is at or near the target zone recommended in the 2008 Scientific Report for moderate-to-vigorous physical activity (i.e., 150 to 300 minutes per week of moderate intensity physical activity, 75 to 150 minutes per week of vigorous intensity physical activity, or an equivalent combination)[1] and "low" is at or near zero reported moderate-to-vigorous physical activity. The estimated relative risks and 95% confidence interval for these four studies were: 0.65 (95% CI: 0.59-0.71) for total physical activity and 0.74 (95% CI: 0.70-0.79) for leisure-time physical activity[67]; 0.69 (95% CI: 0.58-0.83) without adjustment for BMI and 0.83 (95% CI: 0.76-0.90) with adjustment for BMI[70]; odds ratios of 0.53 (95% CI: 0.40-0.70)[72]; and 0.45 (95% CI: 0.31-0.77).[78] Warburton et al,[77] a systematic review including 20 pertinent cohort studies, reported that all 20 studies found an inverse relationship between volume of moderate-to-vigorous physical activity and risk of type 2 diabetes, and that comparing the highest with the least active participants, the average risk reduction was 42 percent. These findings suggest that a reasonable estimate of the reduction in type 2 diabetes associated with 150 to 300 minutes per week of moderate to vigorous physical activity would be about 25 to 35 percent.

Dose-response: Five of the meta-analyses provided estimates for at least three levels of moderate-to-vigorous physical activity (Figure F5-5). Aune et al[67] reported that "there was evidence of a nonlinear association between MET-hours per week of leisure-time physical activity and type 2 diabetes ($P_{\text{nonlinearity}}$ <0.0001), with a slightly more pronounced reduction in risk at low levels of activity than at high levels." Cloostermans et al[68] calculated OR of 1.0 for 150 or more minutes per week of moderate-to-vigorous physical activity, OR of 1.08 (95% CI: 1.04-1.13) for more than 0 to less than150 minutes per week of moderate-to-vigorous physical activity, and OR of 1.23 (95% CI: 1.04-1.39) for 0 minutes per week of moderate-to-vigorous physical activity. All the Cloostermans et al[68] values have been divided by 1.23 in Figure F5-5, below, to match the orientation of the other meta-analyses (i.e., lowest activity group is the referent group with relative risk of 1.0). Huai et al[69] calculated hazard ratios for participants grouped into those with low (HR=1.0), moderate (HR=0.79; 95% CI: 0.70-0.89), and high (HR=0.69; 95% CI: 0.61-0.78) volumes of physical activity. Wahid et al[73] provided relative risk estimates of 0.77 (95% CI: 0.71-0.84) at 6 MET-hours per week and 0.74 (95% CIs not provided) at 11.25 MET-hours per week. The dose-response curves from these four reviews are shown in Figure F5-5. The shape of the dose-response curve for the fifth review that provided estimates for at least three levels of physical activity is similar to the curves from the four studies shown in Figure F5-5.[71] The curve is not included because the units for volume of physical activity are incompatible with the other studies. Kyu et al[71] combined and extrapolated domain-specific moderate-to-vigorous physical activity into total MET-minutes per week of MVPA and, using <600 MET-minutes per week as the referent value, reported risk reductions of 14 percent for 600 to 3,999 MET-minutes per week, 25 percent for 4,000 to 7,999 MET-minutes per week, and 28 percent for 8,000 or more MET-minutes per week. In a systematic review, Warburton et al[77] reported that the majority (84%) of the 20 included studies revealed incremental reductions in the risk for type 2 diabetes with increasing activity/fitness levels.

Figure F5-5. Dose-response Curves for Moderate-to-Vigorous Physical Activity and Relative Risk of Type 2 Diabetes



Source: Adapted from data found in Cloostermans et al., 2015,[68] Wahid et al., 2016,[73] Huai et al., 2016,[69] Aune et al., 2015.[67]

These findings indicate an inverse curvilinear relationship between volume of moderate-to-vigorous physical activity and the reduction in risk of type 2 diabetes, with a decreasing slope at higher levels of physical activity. This indicates that less active individuals who add a certain amount of physical activity to their daily routine reduce their risk of developing type 2 diabetes to a larger extent than more physically active individuals who add the same amount of physical activity to their daily routine. The absolute risk of the more physically active individuals remains below that of the less active individuals; their relative reduction in risk per unit of added physical activity is merely lower. Two of the articles included statistically significant risk reduction estimates for volumes of physical activity below the current target of 150 to 300 minutes per week of moderate-to-vigorous,[68, 73] confirming that benefit accrues below the target zone.

Evidence on Specific Factors

Physical activity, weight status, and risk of type 2 diabetes: The relationship between physical activity, weight status, and risk of type 2 diabetes is complicated because weight status affects risk of type 2 diabetes and physical activity affects risk of type 2 diabetes and weight status (for more details on this relationship see Question 1 in this chapter). When populations are stratified by BMI, higher levels of physical activity are associated with reduced risk of type 2 diabetes at all strata of BMI. For example, in a joint analysis of three physical activity behavior groups (low = 0 minutes per week of self-reported moderate-to-vigorous, middle = >0 to <150 minutes per week, high = ≥150 minutes per week) and BMI strata, among individuals with overweight (25 to <30 kg/m^2), the hazard ratio for the high active group was 2.26 (95% CI: 1.74–2.93), the middle active group was 2.45 (95% CI: 1.87–3.20), and the low active group was 2.86 (95% CI: 1.93–4.22). Among individuals with obesity (≥30 kg/m^2), the hazard ratio for the high active group was 6.13 (95% CI: 4.25–8.84), the middle active group was 6.93 (95% CI: 4.20–11.43), and the low active group was 7.43 (95% CI: 3.47–15.89).[68] Similar findings are reported in the systematic review by Fogelholm.[74]

Evidence also suggests that the combination of low levels of physical activity and high levels of adiposity, usually assessed as BMI, is a stronger risk factor for type 2 diabetes than one would expect if they were acting independently of each other. Qin et al[75] identified five articles that provided enough information for them to calculate estimates of the "biological interaction." The "attributable portion(s) due to biological interaction" were 46 percent,[79] 42 percent,[80] 29 percent,[81] 22 percent,[82] and 5 percent.[83] The analyses indicate that a substantial portion of the reduction in risk for type 2 diabetes (median value 29% of the five studies) is due to the combined effect of physical activity and adiposity.

Given this interaction and the known contribution of obesity to the risk of developing type 2 diabetes, it is not surprising that adjusting for BMI reduces the magnitude of the risk reduction attributable to physical activity.[67, 68, 70, 76, 77] For example, Jeon et al[70] in a high versus low comparison, reported a relative risk of 0.69 (95% CI: 0.58-0.83) without adjustment for BMI and a relative risk of 0.83 (95% CI: 0.76-0.90) with adjustment for BMI.

Age, sex, race/ethnicity, socioeconomic status: Although the importance of weight status as a risk factor for type 2 diabetes was uniformly acknowledged in these reports, the studies provide little information about demographic factors such as age, sex, or race/ethnicity. Information in a few suggest age, sex, and race/ethnicity have little or no impact on the relationship between physical activity and type 2 diabetes.[67, 68, 78] No conclusion could be made about the impact of socioeconomic status because none of the studies provided information about this variable.

Type of physical activity: The physical activity of interest in these papers was largely restricted to moderate-to-vigorous aerobic physical activity. The Subcommittee was unable to draw a conclusion because the studies provided no information about whether frequency, duration, intensity, type of physical activity, or the way physical activity was measured had any influence on the relationship between physical activity and the incidence of type 2 diabetes.

For additional details on this body of evidence, visit: https://health.gov/paguidelines/second-edition/report/supplementary-material.aspx for the Evidence Portfolio.

Comparing 2018 Findings with the 2008 Scientific Report

The 2008 Scientific Report[1] concluded that "approximately 30 minutes of moderate intensity exercise at least 5 days per week provides a substantial (25% to 36%) reduction in the risk of type 2 diabetes".[1] This evidence review confirms that estimate and expands on the previous findings by providing evidence for an inverse curvilinear dose-response association, demonstrating that risk reductions accrue at levels below the target range of 150 to 300 minutes per week of moderate-to-vigorous physical activity, and providing evidence of an interaction, but no effect modification, between physical activity and weight status.

Public Health Impact

Currently about 9.4 percent of the U.S. adult population has type 2 diabetes, with associated annual direct medical costs and lost productivity of about $245 billion per year.[12, 13] The evidence presented here confirms that about 150 to 300 minutes per week of moderate-to-vigorous physical activity reduces the risk of developing type 2 diabetes by 25 to 35 percent. This applies to people with normal weight, overweight, or obesity. Given that less than half of the U.S. population currently participates in 150 minutes or more per week of moderate-to-vigorous physical activity, the potential reduction in incidence and costs of type 2 diabetes is substantial.[84] Moreover, the fact that physical activity reduces the risk of excessive weight gain means that the reduction in risk could be even greater because excessive weight is an independent risk factor for type 2 diabetes.

NEEDS FOR FUTURE RESEARCH

1. Conduct longitudinal research on lower exposure levels of physical activity to allow for an enhanced understanding of the dose-response associations between physical activity and weight gain, hypertension, and type 2 diabetes across a wider spectrum of exposure.

   Rationale: Only limited evidence is currently available on the effect of physical activity less than 150 minutes per week on prevention of weight gain, hypertension, and type 2 diabetes. Thus, limited data are currently available to inform whether lower amounts of physical activity can be effective for preventing these conditions. Having this knowledge is important and will inform public health recommendations regarding the minimum physical activity exposure that can be effective for preventing weight gain or the development of obesity, hypertension, and type 2 diabetes.

2. Conduct large research trials with ample sample sizes to allow for stratum-specific analyses to determine whether the influence of physical activity on the prevention of weight gain, hypertension, and type 2 diabetes varies by age, sex, race/ethnicity, socioeconomic status, or initial weight status.

   Rationale: Only limited evidence is currently available on whether the influence of physical activity on weight gain or risk of hypertension or type 2 diabetes varies by age, sex, race/ethnicity, socioeconomic status, weight status. Moreover, little is known about whether the influence of physical activity varies when the exposure to physical activity is consistent across individuals with different demographic characteristics. Having this information will inform public health recommendations regarding whether physical activity exposure to prevent weight gain needs to vary by age, sex, race/ethnicity, socioeconomic status, weight status, and other demographic characteristics, and may allow for more precise individual-level physical activity recommendations. Thus, adequately designed and statistically powered studies are needed to allow for comparisons across the various strata of demographic characteristics to examine whether the influence of physical activity varies by these factors.

3. Conduct experimental research on varying intensities (light, moderate, and vigorous) of physical activity, while holding energy expenditure constant, to determine the independent effects of physical activity intensity on weight gain, hypertension, and type 2 diabetes.

   Rationale: Limited evidence is available on whether the influence of physical activity on weight gain, hypertension, or type 2 diabetes is consistent across intensities (light, moderate, vigorous) when total energy expenditure is held constant, and only limited evidence is available on the influence of light-intensity physical activity on weight gain. This information will inform public health recommendations regarding whether the emphasis to prevent weight gain, hypertension, or type 2 diabetes should be on total volume of physical activity regardless of intensity, or whether the emphasis needs to be on volume of physical activity that is performed at a specific intensity.

4. Conduct observational and experimental research that quantifies energy intake and eating behavior to determine whether these factors influence the association between physical activity and weight gain.

   Rationale: The majority of the studies examined regarding weight gain either did not report that diet and eating behavior were measured or considered in the analysis. Given that both dietary factors, primarily energy intake, and energy expenditure from physical activity can influence body weight regulation, it is important to understand whether the physical activity exposure necessary to limit weight gain will vary based on diet or eating behavior patterns.

5. Within research that is conducted, disclose the standard criteria and methods that were used to determine the blood pressure status of the study sample to better isolate samples with hypertension from those with normal blood pressure and prehypertension, and report results separately by blood pressure classification.

   Rationale: Strong evidence demonstrates the magnitude of the blood pressure response to physical activity varies by resting blood pressure, with greater benefits occurring among adults with prehypertension than normal blood pressure. However, study samples often include mixed samples of adults with hypertension, prehypertension, and normal blood pressure, and findings are frequently not reported separately by blood pressure classification. Consistent with the law of initial values, this practice underestimates the blood pressure benefits of physical activity. In addition, samples with prehypertension are underrepresented as they are often mixed with samples with hypertension. Reporting findings by blood pressure classification will inform public health recommendations on the magnitude and precision of the blood pressure reductions that result from physical activity among adults with normal blood pressure and prehypertension.

6. Conduct randomized controlled trials to examine the influence of types of physical activity other than aerobic, dynamic resistance, or combined aerobic and dynamic resistance physical activity on blood pressure and other health outcomes among adults with normal blood pressure and prehypertension.

   Rationale: Limited evidence on these topics is available among adults with normal blood pressure and prehypertension. Gaining this information will inform the public health recommendations on the types of physical activity that optimize blood pressure benefit.

7. Conduct experimental research that examines both the acute (i.e., short-term or immediate, referred to as postexercise hypotension) and the chronic (i.e., long-term or training) blood pressure response to physical activity among adults with prehypertension and normal blood pressure.

   Rationale: Insufficient evidence exists on the acute blood pressure response to physical activity despite primary-level reports suggesting a close relationship between the blood pressure response to acute and chronic exercise. Developing a better understanding of acute blood pressure responses will inform public health recommendations on possible behavioral strategies to increase adherence to physical activity for blood pressure benefit.

8. Conduct observational and experimental research examining the relationship between physical activity and blood pressure using the 2017 *Guideline for the Prevention, Detection, Evaluation and Management of High Blood Pressure in Adults*[57] new blood pressure classification scheme.

   Rationale: The literature that was reviewed to answer this question was based upon The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) blood pressure classification scheme.[8] The new guideline increases the number of people with hypertension, eliminates the category of prehypertension, and adds the category of elevated blood pressure. The relationship between physical activity and blood pressure according to this new blood pressure classification scheme remains to be determined.

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PART F. CHAPTER 6. ALL-CAUSE MORTALITY, CARDIOVASCULAR MORTALITY, AND INCIDENT CARDIOVASCULAR DISEASE

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INTRODUCTION

The *Physical Activity Guidelines Advisory Committee Report, 2008*[1] concluded that the amount of moderate-to-vigorous physical activity is inversely associated with all-cause mortality, cardiovascular disease (CVD) mortality, and incident CVD. All of the dose-response data used to develop the physical activity targets for the *2008 Physical Activity Guidelines*[2] were developed using epidemiologic data from longitudinal cohort studies with moderate-to-vigorous physical activity as the lone physical activity exposure.

In 2008, the Advisory Committee[1] relied mostly on the primary literature to perform its work on all-cause mortality, CVD mortality, and CVD. Since then, studies on the relationship of moderate-to-vigorous physical activity to these outcomes have continued to be published. In 2008, the assessment of CVD as an outcome was principally limited to coronary artery disease.[1] Since then, studies have been published on incident cerebrovascular disease—primarily ischemic stroke—and incident heart failure. In addition, due to the volume of conducted studies, reviews, pooled analyses, and meta-analyses with many component studies and large sample sizes now are available on the relationship of moderate-to-vigorous physical activity to all-cause mortality, CVD mortality, and CVD. The abundance of reviews permitted the Subcommittee to rely on systematic reviews, meta-analyses, and pooled analyses to perform our review.

In 2008, the Advisory Committee[1] began to define a dose-response relationship among moderate-to-vigorous physical activity and both all-cause and CVD mortality as a curvilinear one, with an early decrease in risk with greater amounts of moderate-to-vigorous physical activity, and with continuing benefit with still greater physical activity amounts. While undertaking the current review, the Subcommittee believed it important to confirm whether this relationship still holds with new data, and to examine whether it extends to the various CVD outcomes of incident CVD, cerebrovascular disease (ischemic stroke), and incident heart failure.

REVIEW OF THE SCIENCE

Overview of Questions Addressed

This chapter addresses three major questions and related subquestions:

1. What is the relationship between physical activity and all-cause mortality?
   a) Is there a dose-response relationship? If yes, what is the shape of the relationship?
   b) Does the relationship vary by age, sex, race/ethnicity, socioeconomic status, or weight status?
2. What is the relationship between physical activity and cardiovascular disease mortality?
   a) Is there a dose-response relationship? If yes, what is the shape of the relationship?
   b) Does the relationship vary by age, sex, race/ethnicity, socioeconomic status, or weight status?
3. What is the relationship between physical activity and cardiovascular disease incidence?
   a) Is there a dose-response relationship? If yes, what is the shape of the relationship?
   b) Does the relationship vary by age, sex, race/ethnicity, socioeconomic status, or weight status?

Data Sources and Process Used to Answer Questions

The Exposure Subcommittee determined that systematic reviews, meta-analyses, and pooled analyses provided sufficient literature to answer all three research questions. One search and triage process was conducted for Questions 1 through 3, which covered all-cause mortality, cardiovascular disease mortality, and cardiovascular disease incidence. For complete details on the systematic literature review process, see *Part E. Scientific Literature Search Methodology*.

Question 1. What is the relationship between physical activity and all-cause mortality?

a) Is there a dose-response relationship? If yes, what is the shape of the relationship?
b) Does the relationship vary by age, sex, race/ethnicity, or socioeconomic status, and weight status?

Source of Evidence: Systematic reviews, meta-analyses, pooled analyses

Conclusion Statements

Strong evidence demonstrates a clear inverse dose-response relationship between the amount of moderate-to-vigorous physical activity and all-cause mortality. The strength of the evidence is very unlikely to be modified by more studies of these outcomes. **PAGAC Grade: Strong.**

Strong evidence demonstrates a dose-response relationship between physical activity and all-cause mortality. The shape of the curve is nonlinear, with the greatest benefit seen early in the dose-response relationship. The relationship of moderate-to-vigorous physical activity and risk reduction has no lower limit. Risk appears to continue to decrease with increased exposure up to at least three to five times the amounts of the lower bound of moderate-to-vigorous physical activity recommended in the 2008 Guidelines (i.e., 150 minutes per week). The new data are consistent with those used to develop the 2008 Guidelines. **PAGAC Grade: Strong.**

Strong evidence demonstrates that the dose-response relationships between moderate-to-vigorous physical activity and all-cause mortality do not vary by age, sex, race, or weight status. **PAGAC Grade: Strong.**

Insufficient evidence is available to determine whether these relationships vary by ethnicity or socioeconomic status. **PAGAC Grade: Not assignable.**

Review of the Evidence

An initial search for systematic reviews, meta-analyses, pooled analyses, and reports identified sufficient literature to answer the research question as determined by the Subcommittee. Additional searches for original research were not needed.

In data collected from 2006 to 2017, the outcomes of all-cause mortality, CVD mortality, and incident CVD were often considered in the same systematic reviews and meta-analyses. Therefore, the systematic reviews and meta-analyses contributing to the understanding of the relation of physical activity to these three outcomes had significant overlap. Similarly, many of the same studies appeared in the systematic reviews and meta-analyses identified in our searches. In this section, we deal only with all-cause mortality.

A total of 12 existing reviews were included in the analysis of the relation of physical activity to all-cause mortality: 2 systematic reviews,[3, 4] 7 meta-analyses,[5-11] and 3 pooled analyses.[12-14] Of these 12 reviews, 5 also addressed CVD mortality and are reported later in the chapter. Follow-up for these studies ranged from 3.8 to longer than 20 years, and up to 3.4 million participants in total were studied across these reviews and meta-analyses.

The two systematic reviews included a large number of contributing studies: 121[3] and 254.[4] However, in Milton et al,[3] only seven addressed all-cause mortality, nine addressed CVD, and three addressed stroke. For Warburton et al,[4] 70 component studies addressed all-cause mortality, 49 addressed CVD, and 25 addressed stroke. The total numbers for each outcome were not reported. The studies covered extensive timeframes: from 1990 to 2013 and from 1950 to 2008, respectively.

The meta-analyses ranged from 9 to 80 studies. Most meta-analyses covered an extensive timeframe: from inception of the database to 1 year before publication,[5, 7, 10, 11] from 1945 to 2013,[8] and from 1970s and 1990s to 2007 and 2006.[6, 9] The pooled analyses include data from six prospective cohort studies Arem et al[12] and Moore et al,[13] (used the same six cohorts) and from 11 cohorts O'Donovan et al.[14]

The majority of the included reviews examined self-reported leisure time moderate-to-vigorous physical activity. Most reviews also established specific physical activity dose categories in metabolic equivalents of task (MET) for minutes or hours per week using quartiles or a variety of categories such as inactive and low, medium, and high levels of physical activity, or high versus low levels of physical activity.

Three reviews addressed specific types of physical activity. Kelly et al[8] studied cycling and walking. Samitz et al[10] studied domain-specific physical activity defined into leisure-time physical activity, activities of daily living, and occupational physical activity. Hamer and Chida[6] studied habitual walking only.

One pooled analysis[14] separately examined individuals who meet the physical activity guidelines in one or two sessions in addition to the usual physical activity categories (inactive, insufficiently active, and regularly active). Merom et al[15] examined dancing versus walking.

Evidence on the Overall Relationship

All the included reviews addressed all-cause mortality as an outcome and five of them also examined CVD mortality.

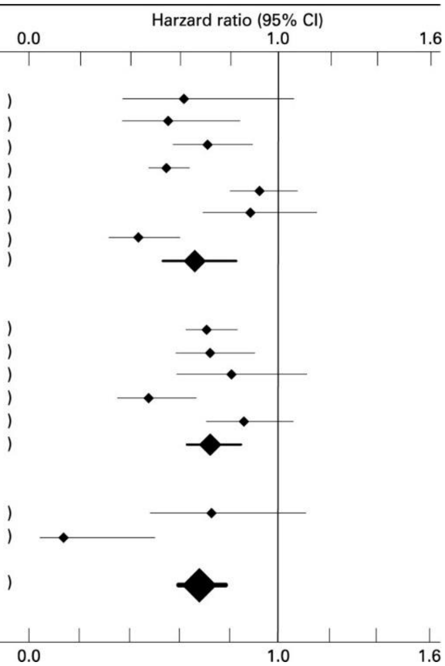
All studies reported an inverse relationship between moderate-to-vigorous physical activity and all-cause mortality in a dose-response fashion as described below. There were no null studies. The pooled analysis, in which individuals meeting guidelines in one or two sessions per week and individuals meeting guidelines with three or more sessions per week were compared to an inactive group, showed no differences in the effect sizes for all-cause mortality between individuals meeting guidelines in 1 to 2 sessions per week (hazard ratio (HR)= 0.60; confidence interval (CI): 0.45-0.82) and individuals meeting guidelines in 3 or more sessions per week (HR=0.59; CI: 0.48-0.73), compared to the inactive group.[14]

In the analysis by Kelly et al,[8] the effect sizes for cycling and walking were similar. For exercise of 11.25 MET-hours per week (675 MET-minutes per week), the reduction in risk for all-cause mortality was 11 percent (95% CI: 4%-17%) for walking and 10 percent (95% CI: 6%-13%) for cycling. The shape of the dose-response relationship was modeled through meta-analysis of pooled relative risks within three exposure intervals. Consistent with other studies, the dose-response analysis showed that for walking or cycling, the greatest reduction in risk for all-cause mortality occurred within the lowest exposure categories of physical activity.

Hamer and Chida[6] studied the effect of walking only on both all-cause mortality and CVD mortality. The analysis included 18 prospective studies with 459,833 total participants. The Forest plots, displayed in Figure F6-1, show a dose-response for amount (volume of walking) and walking pace. Hamer and Chida[6] found walking pace to be a stronger independent predictor of all-cause mortality than volume: 48 percent versus 26 percent risk reductions, respectively. However, within the exposure categories the studies had considerable heterogeneity. The greatest walking exposure groups averaged more than 5.2 hours per week or more than 10.7 miles per week, and the groups ranged from more than 1 hour per week to more than 2 hours per day and more than 6.0 miles per week to more than 12.4 miles per week. Walking pace was generally assessed as a relative rather than an absolute measure, although several studies defined ‘‘brisk’’ as more than 3.0 miles per hour and ‘‘moderate’’ as 2.0 to 2.9 miles per hour. Minimal walking categories averaged approximately 3 hours per week (ranging from approximately 30 minutes per week to approximately 5 hours per week) or 6.1 miles per week (ranging from approximately 3.1 miles per week to approximately 9.3 miles per week), which equated to a casual or moderate walking pace of approximately 2 miles per hour.

Figure F6-1. The Association Between Walking and All-Cause Mortality in Men and Women

	Authors (year)	Exposure	Sample size	Hazard ratio (95% CI)	
Male					
1	Wannamethee *et al* (1998)[11]	Walking > 1 hour/day	4311	0.62	(0.37 to 1.05)
2	Hakim *et al* (1998)[12]	Walking > 3.2 km/day	707	0.55	(0.37 to 0.83)
3	Bijnen *et al* (1998)[13]	Walking > 1 hour/week	802	0.71	(0.58 to 0.88)
4	Davey Smith *et al* (2000)[19]	Brisk walking	6702	0.55	(0.48 to 0.63)
5	Fujita *et al* (2004)[24]	Walking > 1 hour/day	20 004	0.92	(0.80 to 1.06)
66a	Schnohr *et al* (2007)[26]	Walking > 2 hours/day	3204	0.89	(0.69 to 1.14)
66b	Schnohr *et al* (2007)[26]	Brisk walking	3204	0.43	(0.32 to 0.59)
	Subtotal		38 934	0.66	(0.53 to 0.83)
Female					
1	Gregg *et al* (2003)[23]	Walking > 898 kcal/week	9518	0.71	(0.62 to 0.82)
2	Fujita *et al* (2004)[24]	Walking > 1 hour/day	21 159	0.72	(0.59 to 0.89)
3a	Schnohr *et al* (2007)[26]	Walking > 2 hours/day	4104	0.81	(0.59 to 1.10)
3b	Schnohr *et al* (2007)[26]	Brisk walking	4104	0.48	(0.35 to 0.66)
4	Matthew *et al* (2007)[27]	Walking > 10 MET-hours/day	67 143	0.86	(0.71 to 1.05)
	Subtotal		106 028	0.72	(0.62 to 0.84)
Male and female					
1	LaCroix *et al* (1996)[10]	Walking > 4 hours/week	1645	0.73	(0.48 to 1.10)
2	Stessman *et al* (2000)[18]	Walking > 4 hours/week	456	0.14	(0.04 to 0.50)
	Total		147 063	0.68	(0.59 to 0.78)
	Test for heterogeneity			$\chi^2(13) = 31.35, p < 0.001$	
	Test for overall effect			$\chi^2(1) = 57.86, p < 0.001$	



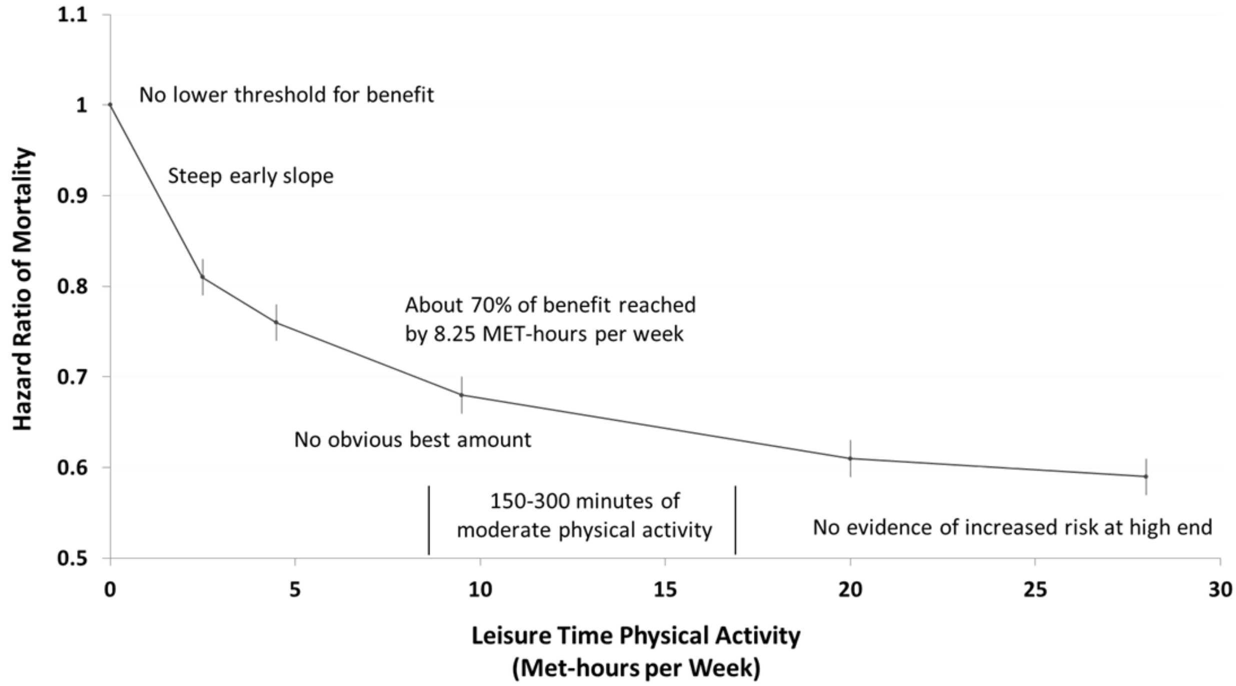
Note: Walking is favored, with a shift of the estimate to the left. These estimates are similar to the effects on cardiovascular disease mortality in Question 2, Figure F6-4.
Source: Reproduced from [Walking and primary prevention: A meta-analysis of prospective cohort studies, Hamer and Chida[6], 42, 2008] with permission from BMJ Publishing Group Ltd.

Dose-response: Every one of the 12 studies within our analysis demonstrated a significant inverse dose-response relationship with all-cause mortality across physical activity exposure groups. The uniformity and strength of these relationships led to the strength of association finding for this subquestion. The uniformity of findings prompted us to highlight the two pooled analyses of Arem et al[12] and Moore et al.[13] In these pooled analyses of six studies, combining data at the individual level allowed an examination of the strength of effects and confidence boundaries across large populations with great precision.

Moore et al[13] reported a pooled analysis of the association of leisure-time physical activity with mortality during follow-up in pooled data from six prospective cohort studies in the National Cancer Institute Cohort Consortium. The combined pooled cohort included 654,827 individuals, ages 21 to 90 years. Moderate-to-vigorous physical activity in MET-hours per week was used to generate adjusted survival curves (for participants ages 40 years and older), with 95% confidence intervals derived by bootstrap. The study included a median 10 years of follow-up and 82,465 deaths. Figure F6-2 shows the survival curves against several characteristics of the relationship common among the studies reporting on dose-response on all-cause mortality. The survival curve from this analysis demonstrates several important points:

1. The beneficial effect has no lowest threshold.
2. The slope is steepest at the lowest amounts of moderate-to-vigorous physical activity.
3. At least 70 percent of the potential benefit on all-cause mortality is reached by achieving 8.25 MET-hours (150 minutes) per week of moderate-to-vigorous physical activity.
4. There is no obvious best amount.
5. There is no apparent upper threshold.
6. Benefits continue to accrue as more physical activity is accrued.
7. Activity volumes (amounts) up to four times the 2008 Guidelines[2] (150-300 minutes moderate-intensity physical activity) show no evidence of increased mortality risk.

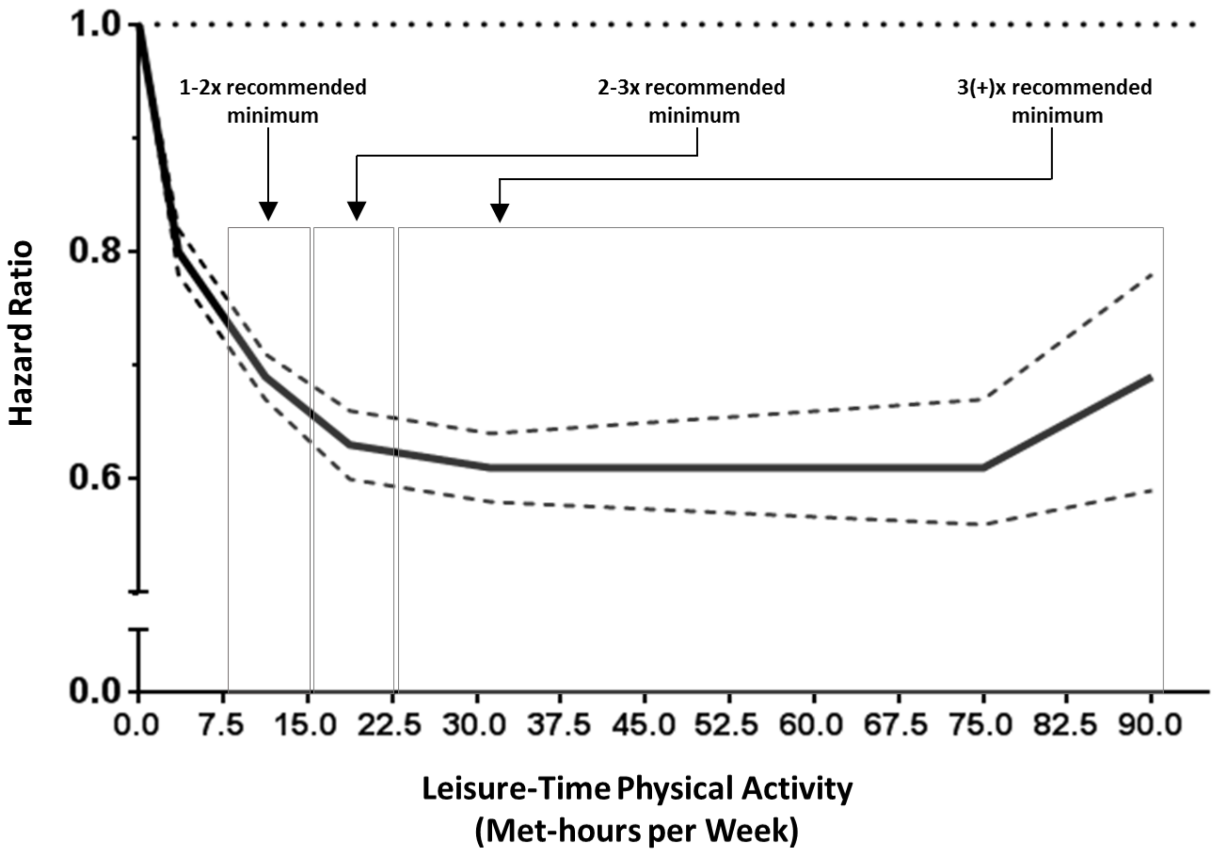
Figure F6-2. Relationships of Moderate-to-Vigorous Physical Activity to All-Cause Mortality, with Highlighted Characteristics Common to Studies of This Type



Source: Adapted from data found in Moore et al., 2012.[13]

Similarly, Arem et al[12] reported a pooled analysis of six studies in the National Cancer Institute Cohort Consortium (baseline collection in 1992-2003; the same studies reported in Moore et al.[13] These were population-based prospective cohorts in the United States and Europe, with self-reported physical activity analyzed in 2014. A total of 661,137 men and women (median age, 62 years; range 21 to 98 years) and 116,686 deaths were included. Cox proportional hazards regression with cohort stratification was used to generate multivariable-adjusted hazard ratios and 95% confidence intervals. Median follow-up time was 14.2 years. The dose response-relationship from this report is shown in Figure F6-3. Several characteristics of this dose-response relationship are reminiscent of that of Moore et al[13] (Figure F6-2). However, several differences in results are described below.

Figure F6-3. Relationships of Moderate-to-Vigorous Physical Activity to All-Cause Mortality, with Highlighted Characteristics Common to Studies of this Type



Source: Adapted from data found in Arem et al., 2015.[12]

Here the relationship is carried out to a category (greater than 75 MET-hours per week) representing approximately ten times the exposure of the lower end of the 2008 Guidelines[2] (i.e., 150 minutes per week). At this greater exposure, an apparent uptick in mortality risk occurs. This possible uptick is not apparent in the Moore et al[13] study that went only to about four times the Guidelines exposure. In the Arem et al[12] pooled study of 661,137 individuals only 18,831 participants (2.8% of the total) were included in the 40 to 75 MET-hours per week category, and only 4,077 (0.62%) in the more than 75 MET-hours per week category.[12] These accounted for only 1,390 (1.2%) and 212 (0.18%) of 116,686 deaths in the combined analysis, respectively, and the error bars are large. Figure F6-3 indicates that the point estimate of risk for the greatest exposure group is the same as the estimate for those meeting the 2008 Guidelines (7.5 to 15 MET-hours per week, or 150 to 300 minutes per week). This apparent uptick in risk at extreme volumes of exercise has been observed before. Paffenbarger et al[16, 17] reported it in the Harvard Alumni Heart study for CVD (heart attack) risk, in 1978 and 1993. However, as in these previous reports, the apparent rise in risk at very high amounts of moderate-to-vigorous physical activity did not reach the level of statistical significance.[12]

In a seminal paper in 2016, Ekelund et al[5] examined the associations of sedentary behavior (sitting and television watching) and physical activity (moderate-to-vigorous physical activity) with all-cause mortality. See *Part D. Integrating the Evidence* and *Part F. Chapter 2. Sedentary Behavior* for more details on these interactions. Using 16 contributing studies, combining data across all studies to analyse the association of daily sitting time and physical activity with all-cause mortality, estimating summary hazard ratios using Cox regression, and expressing physical activity in terms of MET-hours per week of moderate-to-vigorous physical activity, Ekelund et al[5] found the same curvilinear relationships among physical activity and all-cause mortality as observed Arem et al[12] and Moore et al.[13]

Evidence on Specific Factors

Demographic factors and weight status: Most studies reported overall distributions of demographic factors (race, sex, weight status) across exposure groups within individual studies in their reviews and meta-analyses. Given the nature of meta-analyses—conducted at the study level versus the individual level—it is difficult to detect differential effects by demographic factors and weight status unless the specific component studies performed them within their analysis. Some studies examined subgroup effects directly in their review or meta-analysis; one focused on adults older than 60 years.[7] In such studies, no subgroup effects were detected. The O'Donovan et al[14] analysis of "weekend warrior" physical activity behavior on all-cause mortality, showed no differential responses by sex.

However, the pooled analyses[12, 13] permit a direct examination of the relative effects across demographic categories. In these studies, effects are reported for strata across sex, race, and body mass index (BMI) and the aggregate event data reported according to strata. Although not directly tested in these reports, no differential effects across sex, race, or BMI strata are readily apparent. Strata for socioeconomic status and ethnicity were not reported.

For additional details on this body of evidence, visit: https://health.gov/paguidelines/second-edition/report/supplementary-material.aspx for the Evidence Portfolio.

Comparing 2018 Findings with the 2008 Scientific Report

Compared with the 2008 Advisory Committee, this Subcommittee's review of systematic reviews, meta-analyses, and pooled studies exploited the analysis of larger cohorts and provided more precision around the effect size estimates. Our review identified the same dose-effect estimates relating moderate-to-vigorous physical activity with all-cause mortality as was described in 2008. Given the large population sizes and heterogeneity studied, we have more confidence in the precision of these numbers as well as their generalizability to U.S. adult men and women, and populations of all races, ages, and body sizes.

Question 2. What is the relationship between physical activity and cardiovascular disease mortality?

a) Is there a dose-response relationship? If yes, what is the shape of the relationship?
b) Does the relationship vary by age, sex, race/ethnicity, or socioeconomic status, and weight status?

Source of Evidence: Systematic reviews, meta-analyses, pooled analyses

Conclusion Statements

Strong evidence demonstrates that a strong inverse dose-response relation exists between amount of moderate-to-vigorous physical activity and cardiovascular disease mortality. The strength of the evidence is very unlikely to be modified by more studies of this outcome. **PAGAC Grade: Strong.**

Strong evidence demonstrates that the shape of the curve is nonlinear, with the greatest benefit seen early in the dose-response relationship. The relationship of moderate-to-vigorous physical activity and risk reduction has no lower limit. Risk appears to continue to decrease with increased exposure up to at least three to five times the amounts of moderate-to-vigorous physical activity recommended in the 2008 Guidelines (i.e., 150 minutes per week). The new data are consistent with those used to develop the 2008 Guidelines. **PAGAC Grade: Strong.**

Strong evidence demonstrates that these relationships do not vary by age, sex, race, or weight status. **PAGAC Grade: Strong.**

Insufficient evidence is available to determine whether these relationships vary by ethnicity or socioeconomic status. **PAGAC Grade: Not assignable.**

Review of the Evidence

An initial search for systematic reviews, meta-analyses, pooled analyses, and reports identified sufficient literature to answer the research question as determined by the Subcommittee. Additional searches for original research were not needed.

In data collected from 2006 to 2017, the outcomes of all-cause mortality, CVD mortality, and incident CVD were often considered in the same systematic reviews and meta-analyses. Therefore, the systematic reviews and meta-analyses contributing to the understanding of the relation of physical activity to these three outcomes had significant overlap. Similarly, many of the same studies appeared in the systematic reviews and meta-analyses identified in our searches. In this section, we address only CVD mortality; however, the format and conclusions differ little from those made for all-cause mortality.

A note on nomenclature is necessary here. For this discussion, CVD mortality refers to mortality attributable to CVD in its broadest sense. CVD refers to diseases beyond coronary artery disease, but does not include:

- non-atheromatous or infectious valvular disease and others, such as diseases due to coronary heart disease secondary to coronary artery disease,
- cerebrovascular disease secondary to a cerebrovascular accident or stroke,
- heart failure of ischemic (coronary) or non-ischemic etiology.

A total of six existing reviews were included: one systematic review,[3] three meta-analyses,[5, 6, 18] and two pooled analyses.[14, 15] The reviews were published from 2008 to 2017. The systematic review[3] included 121 studies and a timeframe from 1983 to 2013. The meta-analyses included a range of 16 to 36 studies and covered an extensive timeframe: Ekelund et al,[5] from inception of the database to 2015; Hamer and Chida,[6] and Wahid et al,[18] from 1970s and 1980s to 2007 and 2014 respectively. The pooled analyses included data from 11 cohorts, each from different population surveys.[14, 15]

The majority of the included reviews examined self-reported leisure time moderate-to-vigorous physical activity. Most reviews also established specific physical activity dose categories in MET-minutes or MET-hours per week using quartiles or a variety of categories such as inactive and low, medium, and high levels of physical activity, or high versus low levels of physical activity.

One pooled analysis[14] examined a “weekend warrior” category (meeting the physical activity guidelines in one or two sessions per seek) in addition to the usual physical activity categories (insufficiently active and regularly active) compared to an inactive group. Two reviews addressed specific types of physical activity: dancing[15] and habitual walking.[6]

Evidence on the Overall Relationship

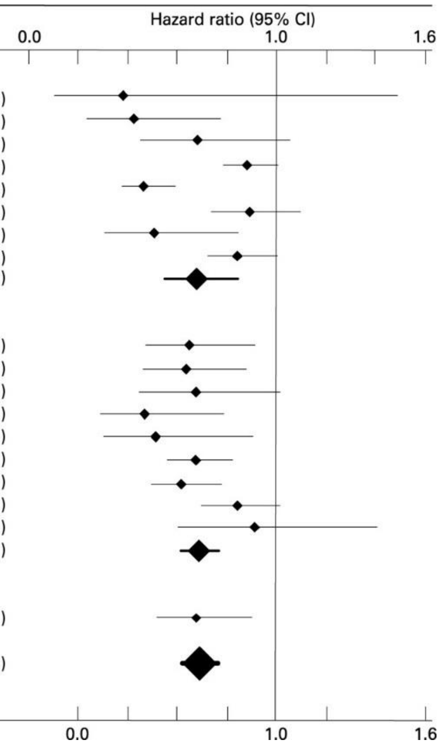
All of the included reviews addressed CVD mortality and four of them also assessed all-cause mortality in addition to other outcomes.

As it was for all-cause mortality, all reviews reported an inverse relationship between moderate-to-vigorous physical activity and all-cause mortality in a dose-response fashion, as described below. The reviews included no null studies. The pooled analysis in which individuals meeting guidelines in one or two sessions per week and individuals meeting guidelines with three or more sessions per week were compared to an inactive group, showed no differences (overlapping hazard ratios) in the effect sizes for CVD mortality (HR=0.59 to 0.60).

As noted above, Hamer and Chida[6] studied walking only on both all-cause mortality and CVD mortality. The analysis included 18 prospective studies with 459,833 total participants. The Forest plots for CVD mortality are shown in in Figure F6-4. The effect sizes and confidence intervals for all categories of walking pace and amount are reminiscent of those determined for all-cause mortality (Figure F6-1). This is an example of how closely aligned the moderate-to-vigorous physical activity relationship is for both CVD mortality and all-cause mortality within and across studies.

Figure F6-4. The Association Between Walking and Cardiovascular Mortality Risk in Men and Women

	Authors (year)	Exposure	Sample size	Hazard ratio (95% CI)
Male				
1	Hakim *et al* (1998)[12]	Walking > 3.2 km/day	707	0.39 (0.10 to 1.49)
2	Hakim *et al* (1999)[14]	Walking > 2.5 km/day	2678	0.43 (0.24 to 0.77)
3	Bijnen *et al* (1998)[13]	Walking > 1 hour/week	802	0.69 (0.45 to 1.05)
4	Sesso *et al* (2000)[17]	Walking > 10 km/week	12 516	0.88 (0.78 to 1.00)
5	Davey Smith *et al* (2000)[19]	Brisk walking	6702	0.47 (0.37 to 0.59)
6a	Tanasescu *et al* (2002)[22]	Walking > 3.5 hours/week	44 452	0.90 (0.73 to 1.10)
6b	Tanasescu *et al* (2002)[22]	Brisk walking	44 452	0.51 (0.31 to 0.84)
7	Noda *et al* (2005)[25]	Walking > 1 hour/day	31 023	0.85 (0.72 to 1.00)
	Subtotal		143 332	0.68 (0.55 to 0.85)
Female				
1a	Manson *et al* (1999)[15]	Walking > 3 hours/week	72 488	0.65 (0.47 to 0.91)
1b	Manson *et al* (1999)[15]	Brisk walking	72 488	0.64 (0.47 to 0.88)
2	Sesso *et al* (1999)[16]	Walking > 10 km/week	1564	0.67 (0.45 to 1.01)
3a	Lee *et al* (2001)[20]	Walking > 2 hours/week	39 372	0.48 (0.29 to 0.78)
3b	Lee *et al* (2001)[20]	Brisk walking	39 372	0.52 (0.30 to 0.90)
4	Manson *et al* (2002)[21]	Walking > 3 hours/week	73 743	0.68 (0.56 to 0.82)
5	Gregg *et al* (2003)[23]	Walking > 898 kcal/week	9518	0.62 (0.49 to 0.78)
6	Noda *et al* (2005)[25]	Walking > 1 hour/day	42 242	0.84 (0.70 to 1.02)
7	Matthew *et al* (2007)[27]	Walking > 10 MET-hour/day	67 143	0.92 (0.60 to 1.40)
	Subtotal		417 930	0.69 (0.61 to 0.77)
Male and female				
1	LaCroix *et al* (1996)[10]	Walking > 4 hours/week	1645	0.68 (0.52 to 0.90)
	Total		562 907	0.69 (0.61 to 0.77)
	Test for heterogeneity			$\chi^2(17) = 42.91$, $p < 0.001$
	Test for overall effect			$\chi^2(1) = 47.68$, $p < 0.001$



Note: Walking is favored, with a shift of the estimate to the left. Notice the similarity of these estimates to the effects on all-cause mortality in Question 1, Figure F6-1.
Source: Reproduced from [Walking and primary prevention: A meta-analysis of prospective cohort studies, Hamer and Chida[6], 42, 2008] with permission from BMJ Publishing Group Ltd.

Dose-response: Here also, the findings for the dose-response relationships between moderate-to-vigorous physical activity and CVD mortality are basically identical to those found for the relationships between moderate-to-vigorous physical activity and all-cause mortality.

Every one of the 12 studies within our analysis demonstrated a significant inverse dose-response relationship with CVD mortality across physical activity exposure groups. The uniformity and strength of these relationships led to the strength of association finding for this subquestion.

Wahid et al[18] used 36 studies, 33 pertaining to CVD and 3 pertaining to type 2 diabetes mellitus to model the effects of three physical activity categories (low physical activity, 0.1-11.5 MET-hours per week; medium physical activity, 11.5-29.5 MET-hours per week; and high physical activity; ≥29.5 MET-hours per week) in a dose-response fashion on CVD incidence and mortality, coronary heart disease incidence and mortality, myocardial infarction incidence, heart failure incidence, and stroke incidence. For those conditions for which all three categories had entries (CVD incidence, CVD mortality, stroke incidence and

CHD incidence), all but CVD mortality demonstrated a strong curvilinear dose-response relationship across categories.

Evidence on Specific Factors

Demographic factors and weight status*:* Similar to all-cause mortality, the studies providing the strongest evidence regarding subgroup moderation effects on CVD mortality were the pooled analyses of Merom et al[15] and O'Donovan et al.[14] Again, as for all-cause mortality, no differential effects across sex, race, or BMI strata were readily apparent. Strata for socioeconomic status and ethnicity were not reported.

For additional details on this body of evidence, visit: https://health.gov/paguidelines/second-edition/report/supplementary-material.aspx for the Evidence Portfolio.

Question 3. What is the relationship between physical activity and cardiovascular disease incidence?

a) Is there a dose-response relationship? If yes, what is the shape of the relationship?
b) Does the relationship vary by age, sex, race/ethnicity, socioeconomic status, or weight status?

Source of evidence: Systematic reviews and meta-analyses

Conclusion Statements

Strong evidence demonstrates a significant relationship between greater amounts of physical activity and decreased incidence of cardiovascular disease, stroke, and heart failure. The strength of the evidence is unlikely to be modified by more studies of these outcomes. **PAGAC Grade: Strong.**

Strong evidence demonstrates a significant dose-response relationship between physical activity and cardiovascular disease, stroke, and heart failure. When exposures are expressed as energy expenditure (MET-hours per week), the shape of the curve for incident CVD appears to be nonlinear, with the greatest benefit seen early in the dose-response relationship. It is unclear whether the shapes of the relations for incident stroke and heart failure are linear or nonlinear. There is no lower limit for the relation of MPVA and risk reduction. Risk appears to continue to decrease with increased exposure up to at least five times the current recommended levels of moderate-to-vigorous physical activity. **PAGAC Grade: Strong.**

Insufficient evidence is available to determine whether these relationships vary by age, sex, race, ethnicity, socioeconomic status, or weight status. **PAGAC Grade: Not assignable.**

Review of the Evidence

An initial search for systematic reviews, meta-analyses, pooled analyses, and reports identified sufficient literature to answer the research question as determined by the Subcommittee. Additional searches for original research were not needed.

A total of 10 existing reviews were included: 1 systematic review[4] and 9 meta-analyses.[18-26] The reviews were published from 2008 to 2016. The systematic review[4] included 254 studies published between 1950 and 2008.

The meta-analyses included a range of 12 to 43 studies. Most meta-analyses covered an extensive timeframe: from database inception to 2013,[25] from 1954 and 1966 to 2007,[24, 26] and from the 1980s and 1990s to 2005–2016.[18-23]

The majority of included reviews examined self-reported physical activity. Different domains of physical activity were also assessed, including total[21]; occupational and leisure[20]; occupational, leisure, and transport[23]; and leisure physical activity only.[24] Some reviews also established specific dose categories in MET-minutes or MET-hours per week.[18, 21, 22, 26] Other reviews used minimal or low versus moderate or high physical activity levels as reported in individual studies.[4, 19, 24] Two meta-analyses specifically examined tai chi[25] and walking.[26]

Included reviews addressed the incidence of CVD in a variety of ways. Several addressed incident coronary heart disease,[21, 23, 24, 26] incident stroke,[19, 21, 25] and incident heart failure.[20, 22] Warburton et al[4] reviewed incident stroke and coronary (ischemic) heart disease. Wahid et al[18] used 33 studies to address CVD incidence and mortality, coronary heart disease incidence and mortality, myocardial infarction incidence, heart failure incidence, and stroke incidence. Thus, in all, six studies addressed incident coronary heart disease; five studies addressed incident stroke; and three studies addressed incident heart failure.

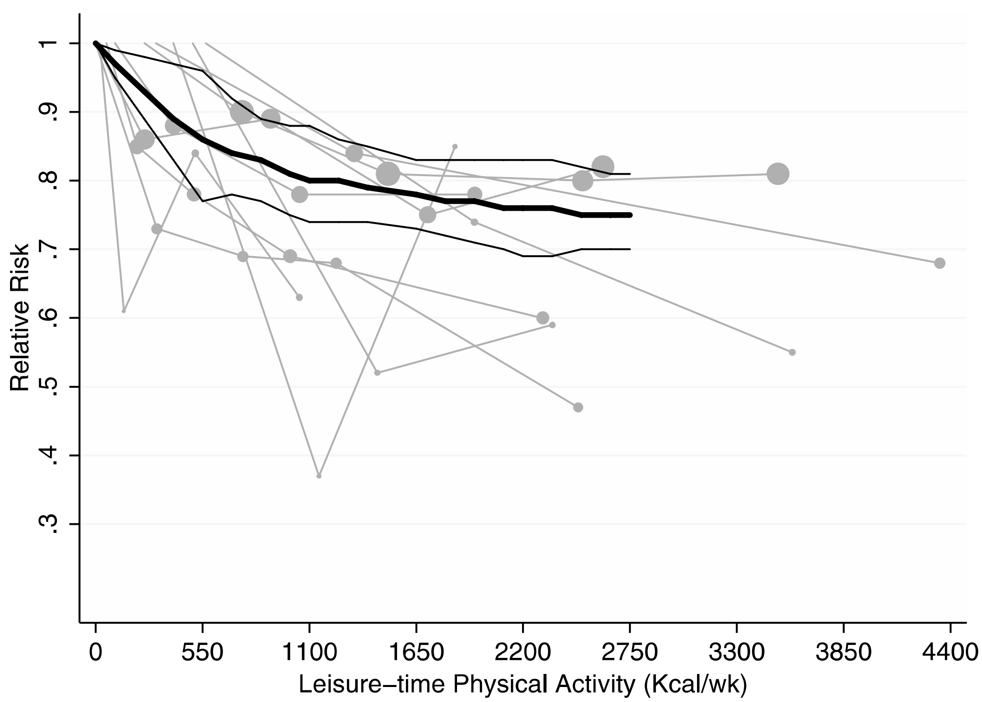
Evidence on the Overall Relationship

All six studies addressing incident coronary heart disease, the five studies addressing incident stroke, and the three studies addressing incident heart failure demonstrated significant dose-response inverse relationships with increased amounts of physical activity. There were no null studies. The shapes of the relationships are discussed below.

Coronary Heart Disease

Sattelmair et al[23] performed a pooled sample meta-analysis of epidemiologic studies to investigate the relationship of MPVA to incident coronary heart disease. Pooled dose-response estimates were derived from qualitative estimates describing low, moderate, and high physical activity. Of the 33 studies initially selected for analysis, 9 permitted quantitative estimates of kilocalories per week of moderate-to-vigorous physical activity. Those participating in leisure-time physical activity at the lower limit of the 2008 Guidelines[2] had a 14 percent reduced risk of developing coronary heart disease (Relative Risk (RR)=0.86 +/-0.09) compared with those reporting no leisure-time physical activity. They reported an inverse dose-response relationship similar to the curves for all-cause mortality and CVD mortality. These curves are characterized by an early decrease in risk, continued benefit with greater exposure, no lower threshold, and no upper limit (Figure F6-5). One MET-hour per week is approximately equal to 1.05 kilocalories per kilogram (kg) per week. Therefore, for a 70 kg individual, the lower boundary of the 2008 Guidelines[2] for moderate-to-vigorous physical activity is achieved at 600 kilocalories per week.

Figure F6-5. Plot with Spline and 95% Confidence Intervals of Relative Risk of Coronary Heart Disease by Kilocalories per Week of Leisure-time Physical Activity



Note: Individual study results are plotted with grey lines; the thick black line shows the trend line for both sexes combined from a random spline-fit model and the thinner black lines show the 95% CI for the trend.
Source: Sattelmair et al., 2011,[23] Dose response between physical Activity and Risk of Coronary Heart Disease, a Meta-Analysis, Circulation, 124: 789-795. https://doi.org/10.1161/CIRCULATIONAHA.110.010710

This analysis points to an important aspect of understanding how the interpretation of dose-response relationships may depend on the modeling parameters. When the dose-response relationships of the pooled studies are modeled using the qualitative exposures of low, moderate, and high physical activity, the dose-response relationship appears linear. When, however, the physical activity exposures are modeled according to MET-hours per week (Figure F6-5), the curvilinear relationship is revealed.

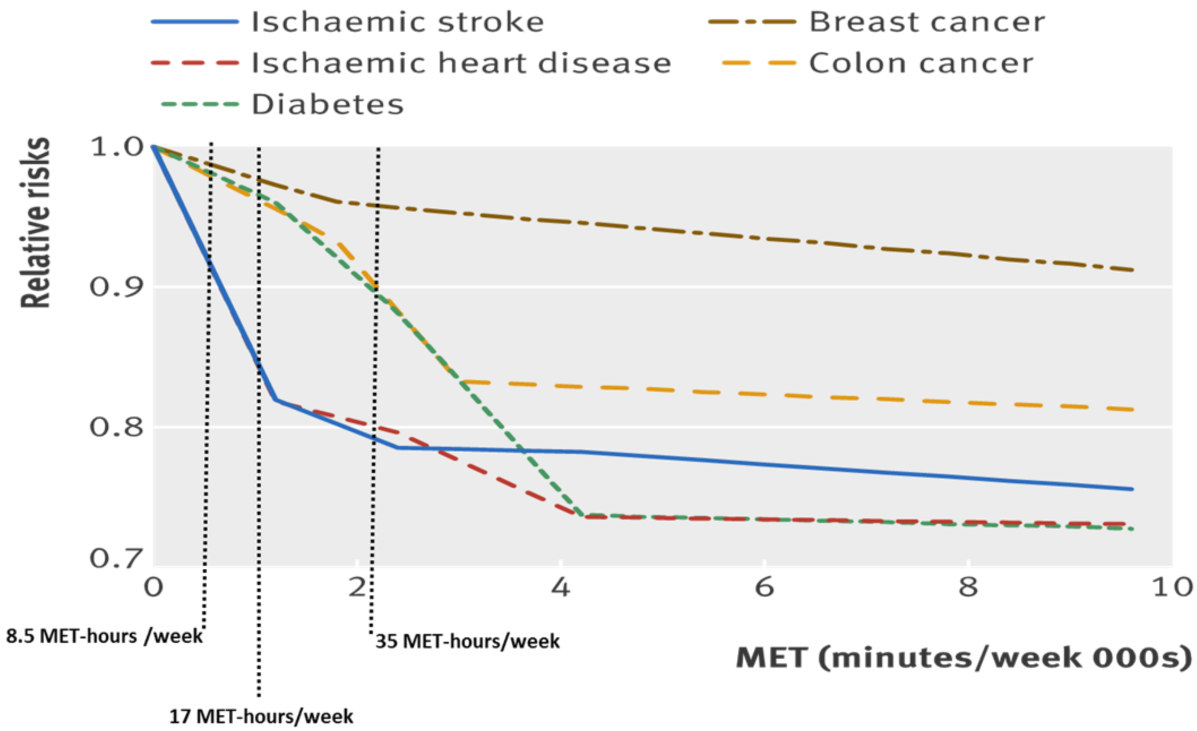
Evidence on Specific Factors

Demographic factors and weight status*:* As it was for previously studied outcomes in this chapter, the studies providing the strongest evidence regarding subgroup moderation effects on cardiovascular mortality were the pooled analyses; particularly that of Sattelmair et al.[23] Of the six studies dealing with incident CHD in our analysis, to the best of our knowledge, only Sattelmair et al[23] explicitly tested for disease modification by specific factors. Although no interactions were reported for effect modification by race or BMI strata, they observed a significant interaction by sex (*P*=0.03); the association was stronger among women than men.

Stroke and Coronary Heart Disease

Kyu et al[21] studied the dose-response associations between total physical activity and risk of breast cancer, colon cancer, diabetes, ischemic heart disease, and ischemic stroke events using 174 studies: 43 for ischemic heart disease, and 26 for ischemic stroke. Total physical activity in MET-minutes per week was estimated from all included studies. Continuous and categorical dose-responses between physical activity and outcomes were assessed. Categorical dose-response compared insufficiently active (less than10 MET hours per week), low active (10 to 66 MET-hours) moderately active (67 to 133 MET-hours) and highly active (greater than or equal to 134 MET-hours). Compared with insufficiently active individuals, the risk reduction for those in the highly active category was 25 percent (RR=0.754; 95% CI: 0.704-0.809) for ischemic heart disease and 26 percent (RR=0.736; 95% CI: 0.659-0.811) for ischemic stroke. Again, for ischemic stroke and ischemic heart disease (equivalent to coronary heart disease), the same typical curvilinear dose-response relationship is seen as for all-cause mortality and CVD mortality. However, the initial and maximal effect sizes are attenuated, so that achieving the lower bound of the 2008 Guidelines[2] achieves only 36 percent reduction in initial risk for incident ischemic stroke and heart failure (Figure F6-6).

Figure F6-6. Dose-Response Relationships Between Total Physical Activity and Risk of Breast Cancer, Colon Cancer, Diabetes, Ischemic Heart Disease, and Ischemic Stroke Events Using 174 Studies (43 For Ischemic Heart Disease, and 26 For Ischemic Stroke)



Note: For reference, shown are the lower end (8.5 MET-hours/week) and upper bounds (17 MET-hours/week) of the 2008 Guidelines for moderate-to-vigorous physical activity. Also indicated is the moderate-to-vigorous physical activity amount associated with normalization of the risk from greater than 8 hours per day of sedentary activity from Ekelund, 2016 (35 MET-hours/week).
Source: Reproduced from [Physical activity and risk of breast cancer, colon cancer, diabetes, ischemic heart disease, and ischemic stroke events: Systematic review and dose-response meta-analysis for the Global Burden of Disease Study 2013, Kyu et al[21], 354, 2016] with permission from BMJ Publishing Group Ltd. and Ekelund et al., 2016.[5]

Evidence on Specific Factors

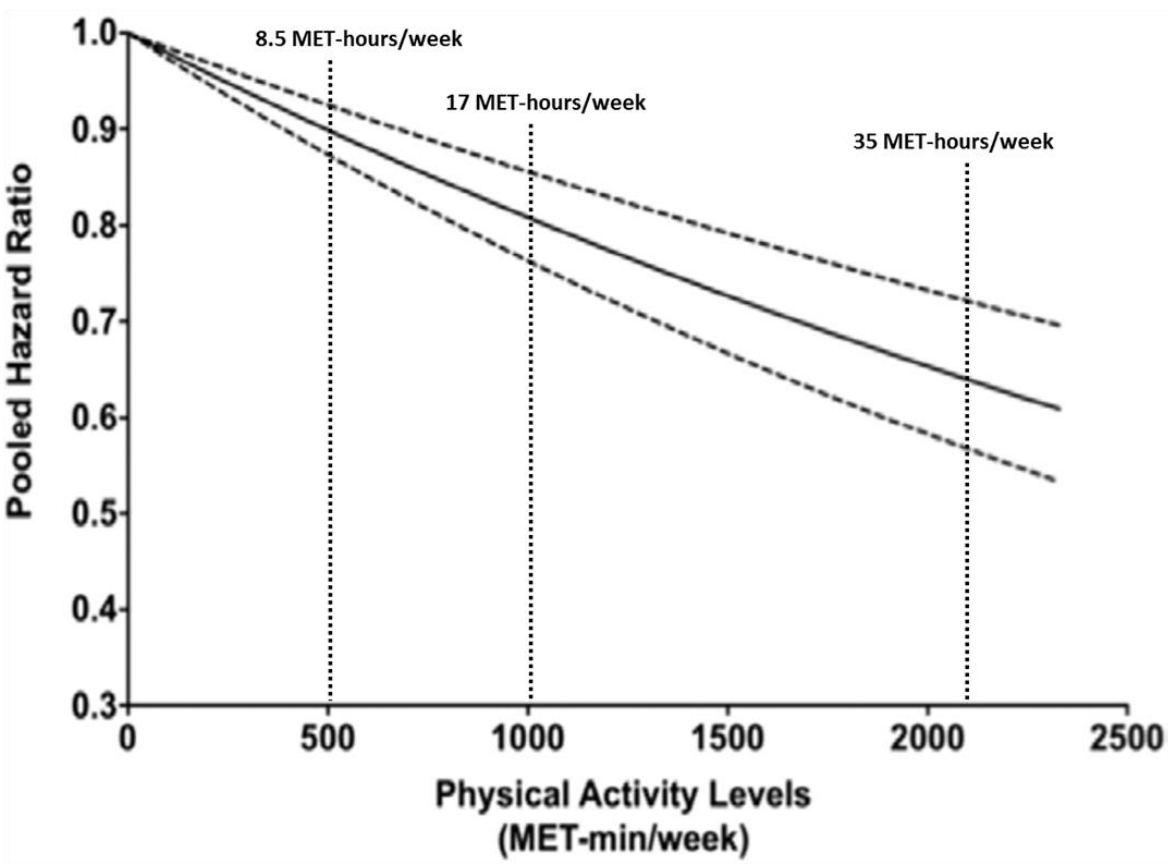
Demographic factors and weight status*:* No effect modifications by age, sex, or weight status were reported for the five reviews that studied incident ischemic stroke. Socioeconomic status and race/ethnicity were not reported in these studies.

Heart Failure

Pandey et al[22] studied the categorical dose-response relationships between physical activity and heart failure risk. As in the previously discussed analysis by Kyu et al,[21] these authors used generalized least-squares regression modeling to assess the quantitative relationship between physical activity (MET-minutes per week) and heart failure risk across studies reporting quantitative physical activity estimates.

Twelve prospective cohort studies with 20,203 heart failure events among 370,460 participants (53.5% women; median follow-up, 13 years) were included. As seen in Figure F6-7, the greatest levels of physical activity were associated with significantly reduced risk of heart failure (pooled HR for highest versus lowest physical activity=0.70; 95% CI: 0.67-0.73). Compared with participants reporting no leisure-time physical activity, those who engaged in 2008 Guidelines -recommended minimum levels of physical activity (500 MET-minutes per week[2] had modest reductions in heart failure risk (pooled HR=0.90; 95% CI: 0.87-0.92). Thus, only 33 percent of the maximal benefit was achieved at the 2008 Guidelines[2] amount. Thus, for heart failure, it appears that the dose-response relationship is linear, and not the curvilinear relationship observed for the other outcomes discussed in this chapter.

Figure F6-7. Dose-Response Relationships Between Moderate-to-Vigorous Physical Activity and Risk of Incident Heart Failure



Note: For reference, shown are the lower end (8.5 MET-hours/week) and upper bounds (17 MET-hours/week) of the 2008 Guidelines for moderate-to-vigorous physical activity. Also indicated is the moderate-to-vigorous physical activity amount associated with normalization of the risk from greater than 8 hours per day of sedentary activity from Ekelund et al., 2016 (17 MET-hours/week).

Source: Used with permission, Pandey et al., 2015[22] 2016, Dose–Response Relationship Between Physical Activity and Risk of Heart Failure, a Meta-Analysis, Circulation, 132: 1786-1794. https://doi.org/10.1161/CIRCULATIONAHA.115.015853. Lines added from Ekelund et al., 2016.[5]

Evidence on Specific Factors

Demographic factors and weight status: No effect modifications by age, sex, or weight status were reported for the two reviews that studied incident heart failure. Socioeconomic status and race/ethnicity were not reported in these studies.

For additional details on this body of evidence, visit: https://health.gov/paguidelines/second-edition/report/supplementary-material.aspx for the Evidence Portfolio.

OVERALL SUMMARY, CONCLUSIONS, AND PUBLIC HEALTH IMPACT

The effects of moderate-to-vigorous physical activity on atherosclerotic CVDs of coronary heart disease, ischemic stroke and heart failure are very similar to those of all-cause mortality and CVD mortality. The evidence continues to support the conclusion that increasing moderate-to-vigorous physical activity levels by even small amounts in the inactive U.S. population has the potential to have an important and substantial impact on these outcomes in the adult population. With respect to reductions in risk for these endpoints, the following points are clear:

- Any amount of physical activity has greater benefit than no physical activity at all;
- More moderate-to-vigorous physical activity is better than none;
- Meeting current moderate-to-vigorous physical activity guidelines will result in an all-cause mortality risk reduction that is about 75 percent of the maximal benefit;
- More physical activity results in greater benefit, although the incremental benefit is less; and
- There is no evidence of excess risk over the maximal effect observed at about three to five times the moderate-to-vigorous physical activity of the current guidelines.

When the activity is quantified by volume in terms of energy expenditure of task (MET-hours per week), these relationships seem to hold for several modes and intensities of physical activity, including walking, running, and biking.

NEEDS FOR FUTURE RESEARCH

Several advances in our understanding of the relationships among physical activity and these outcomes have occurred since the Physical Activity Guidelines Advisory Committee Report, 2008.[1] Most of the literature upon which the conclusions were based used survey data and questionnaire data; physical activity exposures were assessed using self-reported estimates of time spent in aerobic continuous moderate-to-vigorous physical activity accumulated in bouts of at least ten minutes. Therefore, all other components across the physical activity spectrum – sedentary behavior, light-intensity physical activity, and any moderate-to-vigorous physical activity in bouts less than 10 minutes – was considered "baseline" physical activity. Researchers have begun to incorporate device-based measures of physical activity into their measurement armamentarium. This has permitted assessments of the relationship of activity of less than moderate-to-vigorous intensity with health outcomes; it has permitted the assessment of the effects of episodes of moderate-to-vigorous physical activity of less than 10 minutes on health outcomes. These issues are addressed in *Part F. Chapter 1. Physical Activity Behaviors: Steps, Bouts, and High Intensity Training*.

More research is needed in these areas:

1. Conduct research on the role of light intensity physical activities in risk reduction for all-cause mortality, cardiovascular disease mortality, and incident cardiovascular disease (coronary heart disease, stroke and heart failure). This can most economically and efficiently be accomplished by incorporating devices (pedometers or wearables) to measure physical activity into all clinical drug trials with all-cause mortality, cardiovascular disease mortality, or incident cardiovascular disease as outcomes.

   Rationale: As reported in this chapter, the benefits of moderate-to-vigorous physical activity on all-cause mortality, cardiovascular disease mortality, and incident cardiovascular disease (coronary heart disease, stroke and heart failure) are well-documented and strong. However, these studies ignore the effects of physical activity that are not characterized as moderate-to-vigorous in intensity (i.e., light intensity). The development of device-based measures of physical activity (pedometers, accelerometers, and other wearables) provides the scientific imperative to begin to explore the relations of all intensities and amounts of physical activity—light- to vigorous-intensity; small to large total amounts. These studies are beginning to appear.[27-31] Unfortunately, there are not enough studies on the relation of light-intensity physical activity, total physical activity, or step counts per day to provide enough information for meta-analyses to be performed in these areas for the outcomes of interest here. Therefore, this is a major future research need in this area.

2. Conduct research on the possibility of increased risk associated with high amounts of physical activity.

   Rationale: Whether high amounts (volumes) of aerobic physical exercise lead to increased cardiac morbidity or mortality is an important, yet open question. As discussed in this chapter, there is a hint in some studies of an increase in cardiovascular risk in high-volume aerobic athletes. Recent reports document increased coronary calcium scores in masters athletes[32, 33]; however, there seems to be a U-shaped relationship with life-long volume of training.[33] These findings may explain the hint of an increased cardiovascular risk in long-term athletes. Clearly, this issue demands more study in athletic populations.

3. Conduct research on the relative importance of the various characteristics of physical activity exposure (total volume, intensity, frequency and mode) on all-cause mortality, cardiovascular disease mortality, and incident cardiovascular disease (coronary heart disease, stroke and heart failure).

   Rationale: The second edition of the Physical Activity Guidelines Advisory Committee Scientific Report, continues to rely on studies of aerobic ambulatory moderate-to-vigorous physical activity, primarily collected via survey, to understand the relationship of physical activity to all-cause mortality, cardiovascular disease mortality, and incident cardiovascular disease. Underexplored are the importance of frequency and intensity relative to volume of aerobic exercise; the importance of muscle strengthening to these clinical outcomes; whether swimming, biking, and rowing contribute to cardiovascular health equally to aerobic ambulatory exercise; and what the energy expenditures and programs are for these aerobic activities for equivalent clinical outcomes. If we are going to prescribe exercise of all modalities as options for individuals who want to exercise for health, we need better understanding of the relative contributions of a general range of options.

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Physical Activity Considerations for Selected Populations

- Part F. Chapter 7. Youth
- Part F. Chapter 8. Women Who are Pregnant or Postpartum
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PART F. CHAPTER 7. YOUTH

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INTRODUCTION

The *2008 Physical Activity Guidelines for Americans* included a physical activity recommendation for children and adolescents, ages 6 to 17 years.[1] That guideline was based on the conclusion in the *Physical Activity Guidelines Advisory Committee Report, 2008* that strong evidence demonstrated that, in children and adolescents, higher levels of physical activity are associated with multiple beneficial health outcomes, including cardiorespiratory and muscular fitness, bone health, and maintenance of healthy weight status.[2] The 2018 Physical Activity Guidelines Advisory Committee, in establishing the parameters of its work, opted to examine new evidence addressing the relationships between physical activity and health outcomes in school-aged youth. In addition, the Subcommittee considered two issues that were not examined by the 2008 Committee: 1) the association between physical activity and health outcomes in children younger than age 6 years, and 2) the association between sedentary behavior and health outcomes in children and adolescents.

REVIEW OF THE SCIENCE

Overview of Questions Addressed

This chapter addresses three major questions and related subquestions:

1. In children younger than age 6 years, is physical activity related to health outcomes?
   a) What is the relationship between physical activity and adiposity or weight status?
   b) What is the relationship between physical activity and bone health?
   c) What is the relationship between physical activity and cardiometabolic health?
   d) Are there dose-response relationships? If so, what are the shapes of those relationships?
   e) Do the relationships vary by age, sex, race/ethnicity, weight status, or socioeconomic status?

2. In children and adolescents, is physical activity related to health outcomes?
   a) What is the relationship between physical activity and cardiorespiratory and muscular fitness?
   b) What is the relationship between physical activity and adiposity or weight status? Does physical activity prevent or reduce the risk of excessive increases in adiposity or weight status?
   c) What is the relationship between physical activity and cardiometabolic health?
   d) What is the relationship between physical activity and bone health?
   e) Are there dose-response relationships? If so, what are the shapes of those relationships?
   f) Do the relationships vary by age, sex, race/ethnicity, weight status, or socioeconomic status?

3. In children and adolescents, is sedentary behavior related to health outcomes?
   a) What is the relationship between sedentary behavior and cardiometabolic health?
   b) What is the relationship between sedentary behavior and adiposity or weight status?
   c) What is the relationship between sedentary behavior and bone health?
   d) Are there dose-response relationships? If so, what are the shapes of those relationships?
   e) Do the relationships vary by age, sex, race/ethnicity, weight status, or socioeconomic status?

Data Sources and Process Used to Answer Questions

In considering the evidence linking physical activity to health outcomes in school-aged youth, the Subcommittee based its review on systematic reviews and meta-analyses that had examined longitudinal studies of the relationships between physical activity and the following health outcomes: cardiorespiratory and muscular fitness, adiposity or weight status, bone health, and cardiometabolic health. In most cases, the systematic reviews and meta-analyses included primary research articles published since 2006. Many of those studies had employed objective, device-based measures of physical activity.

In the past decade, a substantial volume of research has examined physical activity and its relationship to health factors in children younger than age 6 years. Accordingly, the Subcommittee opted to examine this relationship initially including only systematic reviews and meta-analyses. However, the reviews provided insufficient information, so the Subcommittee conducted a de novo search of the primary research literature. Only studies using longitudinal designs were included, and the following three indicators of health were considered: adiposity or weight status, bone health, and cardiometabolic health. Almost all of the relevant studies focused on children ages 3 to 5 years.

In addition, over the past decade researchers and professionals in multiple fields have expressed concern regarding the potential impact of high levels of sedentary behavior on children's health. Accordingly, the Subcommittee opted to examine the evidence regarding the relationship between sedentary behavior and selected health outcomes. That examination relied on systematic reviews and meta-analyses, several of which have summarized studies with longitudinal designs. For bone health, the review of evidence focused on the primary research literature.

Question 1. In children younger than age 6 years, is physical activity related to health outcomes?

a) What is the relationship between physical activity and adiposity or weight status?
b) What is the relationship between physical activity and bone health?
c) What is the relationship between physical activity and cardiometabolic health?
d) Are there dose-response relationships? If so, what are the shapes of those relationships?
e) Do the relationships vary by age, sex, race/ethnicity, weight status, or socioeconomic status?

Source of evidence: Original research studies

Conclusion Statements

Strong evidence demonstrates that higher amounts of physical activity are associated with more favorable indicators of bone health and with reduced risk for excessive increases in body weight and adiposity in children ages 3 to 6 years. **PAGAC Grade: Strong.**

Subquestions

Strong evidence demonstrates that higher amounts of physical activity are associated with a reduced risk of excessive increases in body weight and adiposity in children ages 3 to 6 years. **PAGAC Grade: Strong.**

Strong evidence demonstrates that higher amounts of physical activity are associated with favorable indicators of bone health in children ages 3 to 6 years. **PAGAC Grade: Strong.**

Insufficient evidence is available to determine the effects of physical activity on cardiometabolic risk factors in children under 6 years of age. **PAGAC Grade: Not assignable.**

Insufficient evidence is available to determine the dose-response relationship between physical activity and health effects in children younger than 6 years of age. **PAGAC Grade: Not assignable.**

insufficient evidence is available to determine whether the relationship between physical activity and health effects in children younger than 6 years of age is moderated by age, sex, race/ethnicity, weight status, or socioeconomic status. **PAGAC Grade: Not assignable.**

Review of the Evidence

Evidence on the Overall Relationship

The conclusion that higher amounts of physical activity are associated with beneficial health outcomes in children younger than 6 years of age was based on the conclusions for two subquestions. Specifically, it was concluded that strong evidence demonstrated that higher amounts of physical activity are associated with favorable indicators of bone health and reduced risk of excessive increases in body weight and adiposity in children ages 3 to 6 years. The evidence supporting these conclusions is summarized below.

Evidence on Specific Factors

Body weight and adiposity: The conclusion that higher levels of physical activity are associated with reduced risk for excessive increases in body weight and adiposity was based primarily on the findings of 14 studies.[3-16] All these studies used prospective observational study designs, and they employed device-based measures of physical activity. Twelve of the 14 studies found negative associations between physical activity and weight and/or adiposity measured at follow-up.[3-10, 12-15] Although the evidence indicated a benefit of greater amounts of physical activity, it was not sufficient to identify a particular dose of physical activity that was needed to provide benefits.

Bone health: The Subcommittee’s conclusion regarding the positive effects of physical activity on measures of bone health in children younger than age 6 years was supported by the findings of 10 research articles based on four separate studies.[17-26] These included a mix of randomized controlled trials and prospective observational studies. All the studies used state-of-the-art bone imaging procedures. Several types of physical activity were found to be associated with bone health, including gymnastics and other bone-strengthening activities, such as jumping and hopping. Total physical activity as assessed by accelerometry also was found to be positively associated with measures of bone health.

The evidence was not sufficient to identify a particular dose of physical activity that was needed to produce benefits, however.

Cardiometabolic health: Very few studies have examined the relationship between physical activity and indicators of cardiometabolic health in children younger than age 6 years.[9, 27, 28] Accordingly, this subquestion was graded as Not Assignable.

Dose-response: Few studies of physical activity and health in children younger than age 6 years have been designed in a manner that allows examination of dose-response relationships. Therefore, this subquestion was graded as Not Assignable.

Demographic factors and weight status: The studies on physical activity and health in children younger than age 6 years have rarely been designed in a manner that provided for examination of the potential modifying effects of demographic characteristics, such as sex, age, race/ethnicity, weight status, and socioeconomic status. Accordingly, this subquestion was graded as Not Assignable.

For additional details on this body of evidence, visit: https://health.gov/paguidelines/second-edition/report/supplementary-material.aspx for the Evidence Portfolio.

Comparing 2018 Findings with the 2008 Scientific Report

The 2008 Scientific Report included the overall conclusion that "physical activity provides important health benefits for children and adolescents".[2] The scientific literature that was cited as supporting that conclusion was limited to studies on children ages 5 to 19 years. This age range was selected because the scientific literature at that time included few studies on children younger than age 6 years. However, in the intervening decade, a substantial amount of research has focused on physical activity and its relationship with health in children younger than 6 years, particularly those ages 3 to 5 years. Accordingly, this literature was systematically reviewed, and it supports the conclusions presented above. These conclusions, by focusing on the early childhood developmental period, extend the scope of the 2018 Committee's work to an age range younger than that addressed by the 2008 Scientific Report.

Public Health Impact

Approximately 13 million children, representing more than 4 percent of the U.S. population, are younger than age 6 years. The evidence summarized above demonstrates that higher amounts of physical activity are associated with better health indicators in this age group. It is noteworthy that the beneficial effects were documented for adiposity and bone health, two health characteristics that are known to track into later life.[29, 30] Accordingly, efforts aimed at enabling and encouraging young children to be more physically active, especially activities facilitating bone health and avoidance of excessive weight gain, would be expected to have a positive impact on the future health of the nation. As noted above, the existing literature demonstrates that higher doses of physical activity, as compared with lower doses, provide important health benefits in children ages 3 to 5 years. However, that literature does not provide extensive information on dose-response relationships, nor does it suggest a dose range that would serve as a suitable public health target. In lieu of more direct evidence on dose-response relationships, the Subcommittee concluded that important public health benefits would result if children, who fall below the median level for device-based measured total physical activity, increased their activity to at least that median. Descriptive epidemiologic studies, using device-based measures of physical activity, have observed that the median time spent in light-, moderate-, or vigorous-intensity physical activity approximates three hours per day in children ages three to five years.[31] Further, because bone-strengthening and muscle-strengthening activities provide important benefits to bone health, the Subcommittee concludes that these young children would benefit from regular participation in activities like gymnastics that involve jumping, leaping, and landing.

Question 2. In children and adolescents, is physical activity related to health outcomes?

a) What is the relationship between physical activity and cardiorespiratory and muscular fitness?
b) What is the relationship between physical activity and adiposity or weight status? Does physical activity prevent or reduce the risk of excessive increases in adiposity or weight?
c) What is the relationship between physical activity and cardiometabolic health?
d) What is the relationship between physical activity and bone health?
e) Are there dose-response relationships? If so, what are the shapes of those relationships?
f) Do the relationships vary by age, sex, race/ethnicity, weight status, or socioeconomic status?

Sources of evidence: Systematic reviews, meta-analyses

Conclusion Statements

Strong evidence demonstrates that, in children and adolescents, higher amounts of physical activity are associated with more favorable status for multiple health indicators, including cardiorespiratory and muscular fitness, bone health, and weight status or adiposity. **PAGAC Grade: Strong.**

Moderate evidence indicates that physical activity is positively associated with cardiometabolic health in children and adolescents. **PAGAC Grade: Moderate.**

Subquestions

Strong evidence demonstrates that increased moderate-to-vigorous physical activity increases cardiorespiratory fitness and that increased resistance exercise increases muscular fitness in children and adolescents. **PAGAC Grade: Strong.**

Strong evidence demonstrates that higher levels of physical activity are associated with smaller increases in weight and adiposity during childhood and adolescence. **PAGAC Grade: Strong.**

Moderate evidence indicates that physical activity is positively associated with cardiometabolic health in children and adolescents in general; the evidence is strong for plasma triglycerides and insulin. **PAGAC Grade: Moderate.**

Strong evidence demonstrates that children and youth who are more physically active than their peers have higher bone mass, improved bone structure, and greater bone strength. **PAGAC Grade: Strong**.

Insufficient evidence is available to determine the dose-response relationship between physical activity and health effects during childhood and adolescence. **PAGAC Grade: Not assignable.**

Insufficient evidence is available to determine whether the relationship between physical activity and health effects in youth is moderated by age, sex, race/ethnicity, weight status or socioeconomic status. **PAGAC Grade: Not assignable.**

Review of the Evidence

The conclusion that higher amounts of physical activity are associated with beneficial health outcomes in youth was based on the conclusions for four subquestions. Specifically, the Subcommittee concluded that strong evidence demonstrates that higher amounts of physical activity are associated with increased cardiorespiratory and muscular fitness, smaller age-related increases in body weight and adiposity, and higher bone mass, improved bone structure, and greater bone strength. Moderate evidence indicated that physical activity is positively associated with indicators of cardiometabolic health. The evidence supporting these conclusions is summarized below. It is important to note that, in most cases, the evidence available to address this question was based on a review of research on children ages 6 years and above. However, relevant research on children younger than 6 years, when available, was also considered.

Cardiorespiratory and Muscular Fitness

Six meta-analyses,[32-37] and nine systematic reviews[38-46] were identified that examined the association between physical activity and cardiorespiratory fitness. Two reviews[40, 45] included muscular fitness outcomes.

Overall, the reviews included publications from inception of the database through 2016. Reviews were focused on the impact of a variety of physical activity intervention or program types on cardiorespiratory fitness outcomes, including afterschool programs,[32] school-based interventions,[41-43] exercise training or aerobic exercise programs,[33-37, 40, 45] active transportation,[39] and exergaming[38, 44, 46]; two reviews[37, 40] included interventions from any setting. Reviews focused on interventions among children and adolescents ages 2 to 18 years; most studies focused on children and adolescents between the ages of 6 and 18 years.

Evidence on the Overall Relationship

All identified reviews concluded that physical activity positively affects measures of cardiorespiratory fitness. The strongest evidence for the impact of physical activity on cardiorespiratory fitness was for organized group-based programs that included specific exercise prescriptions among youth. A meta-analysis of afterschool interventions that included a component designed to promote physical activity identified a pooled effect size from six relevant studies of 0.16 (range -0.23 to 0.86; 95% confidence interval (CI): 0.01-0.30).[32] Systematic reviews did not provide effect sizes but were consistent with findings that school-based interventions were effective for increasing fitness.[41-43] Organized exercise training programs were more effective for improving fitness levels than were general physical activity programs; effect size 4.19 (95% CI: 3.68-4.70) vs. 3.34 (95% CI: 2.08-4.60).[33] Supervised exercise training studies yielded 7 percent to 8 percent increases in VO_2max.[34-36]

A single review identified associations between active transportation and health outcomes across 68 studies, 10 of which included fitness outcomes.[39] Active transportation through cycling was clearly linked with improvements in cardiorespiratory fitness. The association between walking and fitness was less apparent, perhaps because of the lower intensity level of walking compared with cycling.

Three reviews evaluated the impact of exergaming on fitness levels.[38, 44, 46] Findings were mixed, with about half of included studies finding a positive impact of exergaming on some measure of fitness and the other half finding non-significant or null effects; no studies identified a negative impact of exergaming on fitness. Importantly, exergaming appears to be a feasible and acceptable strategy for increasing light-intensity physical activity. Exergaming also appears to be feasible for increasing participation in physical activity at the lower limit of the moderate-intensity range. However, the included reviews did not provide sufficient evidence that the level of energy expended during exergaming is sufficient for increasing measures of cardiorespiratory fitness.

Two systematic reviews specifically looked at musculoskeletal fitness, both of which generally concluded that studies including a muscle strengthening component had a positive impact on muscular fitness.[40, 45] Although effect sizes were not provided within the systematic reviews, results of positive outcomes for muscle-strengthening activity on at least one measure of muscular fitness were consistent.

All identified reviews concluded that physical activity positively affected at least one measure of cardiorespiratory fitness. Organized group-based programs were typically implemented on 3 or more days per week for 30 to 60 minutes, at 50 percent to 90 percent VO_2max or heart rate (HR) max. The evidence for the impact of active transportation and exergaming is less clear.

Two identified reviews concluded that two or more sessions of muscle-strengthening activity weekly was effective for improving measures of muscular fitness. Specific detail on session duration, intensity, and types of exercise was not readily apparent in the information provided.

Dose-response: The studies reviewed were not able to establish dose-response relationships for these modes of exercise and physical activity.

Evidence on Specific Factors

Demographic factors and weight status: The reviews typically focused solely on the impact of physical activity on cardiorespiratory fitness and did not specifically explore subgroup analyses or effect modifiers. Several of the studies included in the reviews focused on children with overweight or obesity. These studies generally concluded that physical activity positively affects cardiorespiratory and muscular fitness outcomes, regardless of weight status. The reviews did not provide comparisons between children with normal weight and those with overweight or obesity.

Cardiometabolic Health

Nine articles including one systematic review[47] and eight meta-analyses[33-36, 48-51] were identified that examined the association between physical activity and cardiometabolic health in children and adolescents. Three of the meta-analyses were exclusively concerned with the effects of physical activity among children and adolescents with overweight or obesity.[36, 49, 50]

Five out of five meta-analyses that analyzed the association between physical activity and plasma triglycerides reported a significant, beneficial effect.[33, 34, 36, 48, 49] Three[33, 36, 51] out of four meta-analyses[33, 36, 48, 51] that analyzed the association between physical activity and plasma insulin reported a significant, beneficial effect. The results for high density lipoprotein (HDL)-cholesterol and blood pressure were not as strong, but were suggestive of a potential benefit from physical activity. Three[33, 48, 49] out of six[33-36, 48, 49] meta-analyses reported a significant, beneficial effect of physical activity on HDL-cholesterol, two[48, 50] out of three[36, 48, 50] meta-analyses reported a significant benefit for systolic blood pressure, while one[50] out of three[36, 48, 50] meta-analyses reported a significant benefit for diastolic blood pressure.

Dose-response: Although the individual studies reviewed in the meta-analyses varied with respect to intervention duration and exercise intensity, they provided insufficient evidence to make any conclusions about dose-response associations. In general, most studies on the effects of physical activity on cardiometabolic risk factors in children were not designed to test a specific risk factor. Rather, specific risk factors were measured as one of the outcomes among many others. Thus, the children may not have had elevated levels of each risk factor at baseline, making it difficult to determine the true effects of physical activity among high-risk children (e.g., those with high blood pressure, insulin resistance).

Demographic factors and weight status: Given that only systematic reviews and meta-analyses were included in this review, limited information is available on the effects of age, sex race/ethnicity, or socioeconomic status on the association between physical activity and cardiometabolic risk factors in children. Two meta-analyses reported that the effects in children with overweight and obesity were greater than in normal weight children for reductions in triglycerides[34] and markers of insulin resistance.[51]

Body Weight and/or Adiposity

The Subcommittee identified a substantial number of systematic reviews and meta-analyses summarizing the scientific literature on the relationship between physical activity and weight status and/or adiposity. However, most of those articles focused on studies in which multiple exposures, often both physical activity and diet, were considered in ways that did not allow determining the independent association of physical activity with weight-related outcomes. Ten articles did focus on studies that considered the independent association of physical activity with weight-related outcomes, and these included systematic reviews[52-56] and meta-analyses[35, 48, 57-59] examining studies with both experimental and prospective, observational study designs. When the conclusions of those articles were considered, the collective findings were deemed to be inconsistent and the evidence linking physical activity to better weight status and/or adiposity was considered to be of moderate strength. However, the consideration of evidence progressed to a third stage that involved considering only the five reviews that focused on studies using prospective, observational study designs.[53-56, 59] The decision to focus on those reviews was based on the belief that prospective, observational study designs are particularly appropriate for an outcome such as adiposity. Observation of differential effects of physical activity doses (e.g., higher vs. lower) may require exposure for periods that are practical in observational studies but longer than feasible in experimental trials. When that subset of five reviews was considered, consistent evidence of an inverse association between physical activity and indicators of weight status and/or adiposity was found.

Dose-response: The aforementioned five reviews, while concluding that higher amounts of physical activity provided beneficial body weight and adiposity outcomes, did not describe dose-response relationships.[53-55, 59] One review concluded that higher intensity physical activity provided greater benefit than less intense physical activity.[54]

Demographic factors and weight status: The five systematic reviews focusing on prospective observational studies gave limited attention to demographic effect modifiers. One review concluded that the protective effect of physical activity on weight-related outcomes was evident in both sexes.[54] This protective effect was reported in reviews focusing on both children of preschool age[55, 56] as well as older children and adolescents.[53, 54]

Bone Health

The Subcommittee identified five meta-analyses[48, 57, 60-62] and five systematic reviews.[41, 63-66] Reviews included all publications through 2016 and focused on studies among children and adolescents ages 3 to 18 years; most studies focused on children and adolescents ages 8 to 15 years, i.e., the peri-pubertal years. Intervention studies were primarily school-based. The volume of the exercise within interventions varied among the studies. However, almost all interventions included high-impact, dynamic, short duration exercise, such as hopping, skipping, jumping, and tumbling. Only two reviews considered observational studies.[65, 66] Results from the observational studies were consistent with results from the intervention studies. All reviews (systematic and meta-analyses) concluded that in youth, physical activity is positively associated with bone mass accrual and/or bone structure.

The greatest amount of evidence for the effect of physical activity on bone strength was for bone mass outcomes. In their meta-analysis, Specker et al[60] examined 22 trials (15 were randomized) and noted that the difference in annual increase in bone mass between intervention and control groups was 0.8 percent (95% CI: 0.3-1.3) for total body; 1.5 percent (95% CI: 0.5-2.5) for femoral neck; and 1.7 percent (95% CI: 0.4-3.1) for spine. Weaver et al[66] identified 38 reports of randomized controlled trials or clinical trials where exercise was used as an intervention to increase bone mass outcomes. Thirty of these reports (84%) reported statistically significant differences between exercise and control groups, ranging from approximately 1 percent to 6 percent over 6 months for total body, femoral neck, and spine. Nineteen prospective longitudinal reports were also examined in the Weaver et al[66] review. Of these, 17 reports (89%) indicated that the most active youth had significantly more bone mass when compared to less active peers.

In addition to its association with bone mass, physical activity is associated with bone structure. This is important because the skeleton needs to be strong to bear loads, but at the same time light for energy-efficient movement. Of the systematic reviews, Tan et al[65] and Weaver et al[66] included specific critiques of studies addressing bone structure. In Tan et al,[65] 14 intervention studies and 23 observational studies (cross-sectional and longitudinal) were examined. Studies with strong design scores showed the greatest effect in structural outcomes between intervention and control groups (3% to 4% difference). None of the studies showed negative associations between physical activity and bone structure. Weaver et al[66] examined 18 reports and noted that 8 showed positive, significant effects of exercise on bone structure outcomes. However, of the 10 reports that indicated no significant differences between exercise and control groups, 6 reports were from the same study, which did not intervene with high-impact, dynamic, short duration exercise. Weaver et al[66] also identified eight prospective observational studies; all eight studies found significant differences in bone structure favoring the most active cohort members when compared to the least active.

Dose-response: Almost exclusively, intervention studies that reported positive outcomes used targeted, high-impact exercise with ground reaction forces at least three times body weight for approximately 6 months. Examples of physical activities that typically include this magnitude of ground reaction forces include volleyball, basketball, martial arts, and gymnastics. The duration and frequency of the interventions varied greatly, ranging from 2 to 12 sessions per week and 1 to 60 minutes per session.[65, 66] However, the reviewed trials were not designed to examine dose-response and no trial included multiple arms of exercise using different loading conditions. Therefore, dose-response is not conclusively known. Limited evidence supports the osteogenic effect of resistance training and other muscle-strengthening physical activity.[66] However, dose-response information is not available.

Demographic factors and weight status: The effect of physical activity on bone strength appears greatest around puberty, indicating that maturity is an effect modifier. However, very few studies focused on post-pubertal youth or pre-school children. Males and females benefit similarly from physical activity (though bone structural changes may be different between males and females). Recent reports suggest that when compared to peers of the same body weight and sex, youth with obesity have weaker bones, indicating that weight status may be an effect modifier.[66] Few studies have included children from diverse racial/ethnic groups or addressed socioeconomic status, so their effect on modifying the relationship between physical activity and bone strength is not known.

For additional details on this body of evidence, visit: https://health.gov/paguidelines/second-edition/report/supplementary-material.aspx for the Evidence Portfolio.

Comparing 2018 Findings with the 2008 Scientific Report

The findings and conclusions of this report regarding the associations between physical activity and health in youth are consistent with the findings reported in the 2008 Scientific Report.[2] However, the scientific evidence supporting the conclusions in this report is substantially more robust than was the case in 2008. The evidence has been strengthened by marked increases in the quantity and quality of research on physical activity and two key health indicators, weight status and/or adiposity and bone health. Further, the evidence has been strengthened by the publication of numerous systematic reviews and meta-analyses on topics related to the impact of physical activity on health outcomes in children and adolescents.

The 2008 Scientific Report[2] informed a recommendation that was included in the 2008 Physical Activity Guidelines for Americans. That recommendation called for children and adolescents ages 6 to 17 to do 60 minutes or more of moderate-to-vigorous physical activity per day. It was further recommended that, within the 60 minutes of daily physical activity, children and adolescents should engage in muscle-strengthening, bone-strengthening, and vigorous intensity physical activities at least three days per week.[1] As noted above, the Subcommittee's conclusions are consistent with the conclusions of the 2008 Scientific Report. Accordingly, these conclusions and the evidence summaries supporting the conclusions are consistent with the physical activity recommendation for children and adolescents as included in 2008 Physical Activity Guidelines for Americans.

Public Health Impact

A substantial percentage of U.S. children and youth do not meet the current federal physical activity guideline.[67] That guideline calls for daily participation in 60 or more minutes of moderate-to-vigorous physical activity as well as regular engagement in vigorous physical activity, muscle-strengthening exercise, and bone-strengthening activities. The conclusion that strong evidence demonstrates that higher amounts of physical activity are associated with better status on multiple health indicators during childhood and adolescence points to the important public health benefits that would be associated with increasing the percentage of young persons in the United States who meet physical activity guidelines. The evidence is strong that these health benefits would accrue to children and adolescents during their developmental years. Further, current evidence suggests that it is likely that many of those health benefits would carry forward into adulthood.

Question 3: In children and adolescents, is sedentary behavior related to health outcomes?

a) What is the relationship between sedentary behavior and cardiometabolic health?
b) What is the relationship between sedentary behavior and adiposity or weight status?
c) What is the relationship between sedentary behavior and bone health?
d) Are there dose-response relationships? If so, what are the shapes of those relationships?
e) Do the relationships vary by age, sex, race/ethnicity, weight status, or socioeconomic status?

Sources of evidence: Systematic reviews, meta-analyses, original research articles

Conclusion Statements

Limited evidence suggests that greater time spent in sedentary behavior is related to poorer health outcomes in children and adolescents. **PAGAC Grade: Limited.**

Subquestions

Limited evidence suggests that greater time spent in sedentary behavior is related to poorer cardiometabolic health; the evidence is somewhat stronger for television viewing or screen time than for total sedentary time. **PAGAC Grade: Limited.**

Limited evidence suggests that greater time spent in sedentary behavior is related to higher weight status or adiposity in children and adolescents; the evidence is somewhat stronger for television viewing or screen time than for total sedentary time. **PAGAC Grade: Limited.**

Limited evidence suggests that sedentary behavior is not related to bone health in children and adolescents. **PAGAC Grade: Limited.**

Insufficient evidence is available to determine whether a dose-response relationship exists between greater time spent in sedentary behavior and poorer health outcomes in children and adolescents. **PAGAC Grade: Not assignable.**

Insufficient evidence is available to determine whether the relationship between sedentary behavior and health outcomes in youth is moderated by age, sex, race/ethnicity, or socioeconomic status. **PAGAC Grade: Not assignable.**

Review of the Evidence

Evidence Related to the Overall Question

The conclusion that there is limited evidence that greater time spent in sedentary behavior is related to poorer health outcomes in children and adolescents was based on the conclusions for three subquestions. Specifically, it was concluded that limited evidence demonstrated that greater time spent in sedentary behavior is associated with lower cardiometabolic health and less favorable weight status or adiposity, and limited evidence of no relationship between sedentary behavior and bone health. The evidence supporting these conclusions is summarized below. For Question 3, the Subcommittee relied on systematic reviews and meta-analyses, while a search was conducted for original research articles to address bone health.

Evidence Related to Specific Factors

Cardiometabolic risk factors: The Subcommittee obtained evidence on the relationship between sedentary time and cardiometabolic risk factors from systematic reviews and meta-analyses. The literature search identified 12 systematic reviews and meta-analyses that potentially addressed this question. After review of these articles, it was determined that four articles[68-71] were best suited to answer the question. The systematic review by Chinapaw et al[68] found insufficient evidence for a longitudinal association between sedentary behavior and blood pressure or blood lipids in children and adolescents. Tremblay et al[69] reported that increased screen time was related to increased risk factors in children and adolescents. However, this conclusion was based on nine cross-sectional studies and only two longitudinal studies. Likewise, in an update of the evidence from Tremblay et al,[69] Carson et al[70] reported that results varied across different risk factors, but TV or screen time was more closely related to risk factors than accelerometer-derived estimates of sedentary behavior. This conclusion was based on 25 cross-sectional studies and 6 longitudinal studies. Finally, Cliff et al[71] reported that 8 out of 28 studies found a significant association between sedentary behavior and cardiometabolic outcomes in children and adolescents. In general, the limited evidence from longitudinal studies suggests a positive association between sedentary time and cardiometabolic risk factors in children and adolescents, with somewhat stronger results for TV viewing or screen time as the exposure.

Weight Status or adiposity: Evidence on the relationship between sedentary time and weight status or adiposity was obtained from systematic reviews and meta-analyses. The literature search identified 12 systematic reviews and meta-analyses that potentially addressed this question. After review of these articles by two members of the Subcommittee, it was determined that eight articles[53, 68-74] were best suited to answer the question.

In the most comprehensive review of sedentary behavior and adiposity published to date,[70] which included 162 studies (125 cross-sectional, 32 longitudinal, 5 case-control) the authors reported that there was a positive longitudinal association between TV or screen time and adiposity, but device-based measurements of sedentary time were not associated with adiposity. These results are supported by other systematic reviews that generally reported low levels of evidence for longitudinal associations between sedentary behavior and adiposity in children and adolescents.[53, 68, 69, 71, 73] In a systematic review that focused exclusively on the early years (ages 0 to 4 years),[72] three of four studies in toddlers reported a dose-response association between TV viewing and adiposity and two of five studies in preschoolers demonstrated a significant association. Wu et al[74] conducted a systematic review of interventions to reduce screen time, and reported no significant effect of screen time reduction on body mass index in children, based on evidence from seven studies.

Bone Health: The Subcommittee obtained evidence on the relationship between sedentary time and bone health from primary research. The literature search identified four prospective observational studies,[75-78] with sample sizes varying from 169 to 602 and age ranges from 8 to 20 years. All studies used a device-based measure of sedentary time (i.e., accelerometer). Vaitkeviciute et al[78] and Ivuškāns et al[75] used the same cohort of peri-pubescent boys and showed sedentary time was negatively associated with bone outcomes. However, the method used to construct sedentary time from accelerometry data likely attributed an unknown proportion of sedentary time as non-wear time. One study[77] used a temporal substitution statistical model and, surprisingly, reported that bone outcomes improved when levels of high physical activity intensity were held fixed and sedentary time was statistically exchanged for light-intensity physical activity time. Whereas, Gabel et al[76] reported some negative associations and some positive associations between sedentary time and bone outcomes. Variability in bone outcomes, accelerometry-processing, and statistical approaches may have all contributed to the lack of consensus in results. The literature at this time suggests limited evidence that there is no relationship between sedentary behavior and bone health.

Dose-Response: Few studies of sedentary behavior and health outcomes in children and adolescents have been designed in a manner that allows examination of dose-response relationships. Accordingly, this subquestion was graded as Not Assignable.

Demographic Effect Modifiers: The studies on sedentary behavior and health outcomes in children and adolescents have not been designed in a manner that allowed examination of the potential modifying effects of demographic characteristics such as sex, age, race/ethnicity, weight status, and socioeconomic status. Accordingly, this subquestion was graded as Not Assignable.

For additional details on this body of evidence, visit: https://health.gov/paguidelines/second-edition/report/supplementary-material.aspx for the Evidence Portfolio.

Public Health Impact

Compelling evidence demonstrates that children and adolescents in the United States spend substantial amounts of time engaged in sedentary behaviors. This evidence comes from surveillance systems using device-based assessment of time spent in sedentary behavior and from surveys documenting time spent in specific behaviors that typically involve little or no physical activity. These behaviors include television viewing and other forms of "screen time," such as use of cell phones, tablets, and other devices for text messaging, playing video games, and other recreational pursuits. These discretionary sedentary behaviors are in addition to time spent reading and studying in school and after school. Analyses of data from NHANES have shown that U.S. children and adolescents spend 6 to 8 hours per day in sedentary behavior and that the majority spend more than 2 hours per day watching television and/or engaged with other types of screens.[79-81]

This information plus evidence that sedentary behavior causes adverse health outcomes in adults (see *Part F. Chapter 2. Sedentary Behaviors* for details) raises the concern that this behavior pattern may exert a negative effect on health among youth. Such an outcome could be the result of either direct effects of the sedentary behaviors, displacement of time spent in more physically active behaviors, or both.[69, 82, 83]

As noted above, currently available scientific evidence linking sedentary behavior to health outcomes in young persons is limited. Likewise, the interactive effects of sedentary behavior and physical activity on health in children and adolescents are not well understood. However, as is also noted above, the evidence linking moderate-to-vigorous physical activity to positive health outcomes is strong, and a substantial portion of children and adolescents is insufficiently physically active.[67] Accordingly, replacing some sedentary behavior with moderate-to-vigorous physical activity would improve the health of American youth.

NEEDS FOR FUTURE RESEARCH

1. Conduct randomized controlled trials and prospective observational studies to elucidate the dose-response relationships for physical activity and health outcomes, including adiposity, cardiometabolic health, and bone health in children and adolescents at each developmental stage.

   Rationale: Few studies have been designed to directly examine dose-response relationships between physical activity and health outcomes in young persons. This gap constitutes a major limitation in the process of identifying the types and amounts of physical activity needed to produce health benefits at each developmental stage.

2. Undertake randomized controlled trials and prospective observational studies to determine whether the health effects of physical activity during childhood and adolescence differ across groups based on sex, age, maturational status, race/ethnicity, and socioeconomic status.

   Rationale: Few studies have been designed to directly examine the extent to which the health effects of physical activity may differ across demographic subgroups. This gap substantially limits the ability to determine whether the dose of physical activity needed to produce health benefits varies across population sub-groups. Studies aimed at elucidating the extent to which race/ethnicity modifies the effects of physical activity on health outcomes should consider social, cultural, and biological factors that may influence an effect modifying role of race/ethnicity.

3. Conduct experimental and prospective observational studies to examine the health effects of physical activity in children and adolescents with elevated risk status based on adiposity, cardiometabolic health, and bone health.

Rationale: Most children and adolescents fall within the normal, healthy range on key health indicators, and consequently increased physical activity is unlikely to enhance their already normal status. However, children at elevated risk may manifest improved status with increased physical activity. A considerable volume of research has been conducted in children and adolescents with overweight and obesity, but more research is needed with young persons who have elevated cardiometabolic and bone health risk.

4. Examine the effects of novel forms of physical activity, including high intensity interval training and exergaming, on health outcomes in youth. Both experimental and prospective observational studies should be conducted.

   Rationale: Certain forms of physical activity are particularly prevalent among children and adolescents, and more research is needed to determine the extent to which these forms of physical activity affect key health outcomes.

5. Develop valid instruments for measuring physical activity and examine the health effects of physical activity in very young children between birth and 2 years.

   Rationale: In part because of a lack of validated measures of physical activity in very young children, knowledge of the relationship between physical activity and health outcomes in children between birth and age 2 years is very limited.

6. Undertake studies, using longitudinal research designs, to examine the relationship between specific forms of sedentary behavior (e.g., sitting time, screen time) and health outcomes in children and adolescents using both self-report and device-based assessment of sedentary behavior.

   Rationale: Current research on the relationship between sedentary behavior and health is limited by a dearth of studies using device-based measures of time spent in sedentary behavior. Many studies have focused on television viewing as an indicator of sedentary behavior, but television viewing is confounded by exposures other than sedentary time. Research is needed to differentiate between the health effects of time spent sedentary and time spent in specific behaviors that typically include sedentary time.

7. Conduct intervention studies to test the effects of reducing sedentary behavior on health outcomes in children and adolescents.

Rationale: Very few studies have examined the health effects associated with reduction of time spent in sedentary behavior among children and adolescents. The findings of such studies would inform the process of identifying the levels of time spent in sedentary behavior that may be associated with negative health outcomes. Further, these studies would determine the extent to which reduction of time spent in sedentary behavior influences time spent in moderate-to-vigorous and light-intensity physical activity.

8. Examine the interactive effects of sedentary behavior and physical activity of varying intensities on health outcomes in children and youth.

   Rationale: The relationship between physical activity and health outcomes in children and adolescents may be modified by amount of time spent in sedentary behavior. That is, youth who spend large amounts of time in sedentary behavior may require higher levels of physical activity to produce a particular health outcome. Studies should be undertaken to directly examine this issue.

9. Undertake prospective observational studies to examine the effects of physical activity during childhood and adolescence on health outcomes later in life.

   Rationale: Large-scale cohort studies that have followed children into adulthood and have used state-of-the-art measures of physical activity are rare, particularly in the United States. Accordingly, knowledge of the long-term impact of physical activity status early in life on health outcomes later in life is very limited. Further, the findings of such studies could inform development of physical activity guidelines for individuals in transitional periods, such as early adulthood.

10. Determine in children and adolescents the impact of genetic profiles on behavioral and physiological responses to physical activity and on the health effects of physical activity.

    Rationale: Studies in adults have shown that the health effects of physical activity are moderated by genetic profile such that a given dose of physical activity produces widely varying effects on indicators of health. Our knowledge of the relationship between physical activity and health in children and adolescents would be enriched by undertaking similar studies in young persons. Such studies could expand knowledge of how genes and the environment may interact in influencing indicators of health in young persons.

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PART F. CHAPTER 8. WOMEN WHO ARE PREGNANT OR POSTPARTUM

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INTRODUCTION

Pregnancy is a normal but unique period of life for most women. The multiple hormonal, physiologic, and biomechanical changes that occur, such as increased blood volume and heart rate, weight gain, and shift in center of gravity almost always proceed properly. All women who are pregnant should be under medical care to monitor the progress of pregnancy and assure the continued health of mother and fetus.

This chapter is about the large majority of women whose pregnancy is proceeding normally. For them, regular engagement in physical activity of moderate intensity for 20 to 30 minutes per day on most or all days of the week has been recommended during pregnancy and the postpartum period by the American College of Obstetricians and Gynecologists (ACOG) in 2015 and reaffirmed in 2017.[1]

Similarly, the 2008 *Physical Activity Guidelines for Americans* recommended 150 to 300 minutes per week of moderate intensity aerobic physical activity during pregnancy and postpartum to be spread throughout the week.[2] However, from 2007 to 2014 only 29 percent (95% confidence interval (95% CI): 24%-34%) of pregnant women at any gestation in the United States met the minimum guideline of at least 100 minutes per week of physical activity.[3] However, when increasing the minimum guideline to exercise at least 150 minutes per week, only 23% (95% CI: 15%-35%) met the guideline.

Current recommendations differ markedly from 30 years ago. In 1985, an ACOG Technical Bulletin warned pregnant women to keep their heart rate below 140 beats per minute and not to exercise strenuously for more than 15 minutes.[4] Since then, scientific research has established not only the safety of moderate-intensity physical activity for women with a normal pregnancy but its benefits as well. The restrictions on heart rate and duration of physical activity have been lifted, and recommendations encouraging women with a normal pregnancy and postpartum period to participate in non-contact physical activities of moderate-intensity are common both in the United States[1, 5] and around the world.[6, 7] The normal physiologic changes occurring throughout pregnancy may make perceived exertion a better indicator of moderate intensity than heart rate parameters or estimated absolute energy requirements of specific activities.[1] On a personalized rating of perceived exertion scale of 0 to 10, where 0 is sitting and 10 is the greatest effort possible, moderate-intensity activity would be a middle effort of 5 to 6.[2] Another way to gauge moderate intensity is with a talk test, where carrying on a conversation (but not singing) is still possible while doing moderate-intensity physical activity.[8]

This chapter provides some information about physical activity during the postpartum period, and considers such issues as the return toward pre-pregnancy weight and postpartum depression. The postpartum is a period during which resumption of previous lifestyle practices can be challenging. For this chapter, the postpartum period is defined as the year following delivery.

The benefits and risks of muscle-strengthening physical activity and vigorous-intensity aerobic activity are two issues out of reach of the available searches performed for this Work Group. They are lightly covered by the literature pertaining to physical activity by pregnant women, yet are important to any discussion about health benefits and risks of physical activity. Muscle strengthening activity for pregnant women was not addressed in the *Physical Activity Guidelines Advisory Committee Report, 2008* but is recommended in the 2015 ACOG Committee Opinion as well as in guidelines from other countries.[1, 5, 6] For vigorous-intensity physical activity, the 2008 Guidelines suggested that "women who habitually engage in vigorous-intensity aerobic activity or who are highly active can continue physical activity during pregnancy and the postpartum period, provided they remain healthy and discuss with their health-care provider how and when activity should be adjusted over time."[2] Whether vigorous-intensity physical activity provides unique benefits or risks beyond its contribution to total volume of physical activity has not been well researched, although some physicians still advise against physical activity at greater than 90 percent of maximum heart rate.[9]

REVIEW OF THE SCIENCE

Overview of Questions Addressed

This chapter addresses four major questions:

1. What is the relationship between physical activity and weight gain during pregnancy and weight loss during postpartum?
2. What is the relationship between physical activity and the incidence of gestational diabetes mellitus?
3. What is the relationship between physical activity and the incidence of (1) preeclampsia and (2) hypertensive disorders during pregnancy?
4. What is the relationship between physical activity and (1) affect, (2) anxiety, and (3) depression during pregnancy and postpartum (up to one year)?

Questions 1 through 4 each have the following subquestions:

a) What dose of physical activity is associated with the reported quantitative benefit or risk?
b) Is there a dose-response relationship? If yes, what is the shape of the relationship?
c) Does the relationship vary by age, race/ethnicity, socioeconomic status, or weight status?

Data Sources and Process Used to Answer Questions

The Work Group identified two high-quality existing reports, the Physical Activity Guidelines Advisory Committee Report, 2008[5] and 2015 ACOG Committee Opinion on Physical Activity and Exercise During Pregnancy and the Postpartum Period,[1] that provided summaries of the science about the relationship between physical activity and health outcomes in women who are pregnant and postpartum. After reviewing these high-quality reports and consulting with three outside experts, the Work Group decided that these two documents could serve as a foundation for summarizing the benefits and risks of light- to moderate-intensity physical activity during pregnancy and the postpartum. The Work Group also reviewed its other research questions to identify searches from other Subcommittees that could provide evidence to answer questions related to this issue. Research questions unlikely to provide information pertaining to pregnancy or postpartum were not considered. For example, the Committee decided that all-cause mortality or coronary artery disease would not be suitable outcomes for this age group. Seven searches conducted by the Committee were considered to provide potentially pertinent information.

1. **Cardiometabolic Health and Weight Management Q1:** What is the relationship between physical activity and prevention of weight gain?

2. **Cardiometabolic Health and Weight Management Q2:** In people with normal blood pressure or pre-hypertension, what is the relationship between physical activity and blood pressure?

3. **Cardiometabolic Health and Weight Management Q3***:* In adults without diabetes, what is the relationship between physical activity and type 2 diabetes?

4. **Brain Health Q2:** What is the relationship between physical activity and quality of life?

5. **Brain Health Q3:** What is the relationship between physical activity and: (1) affect, (2) anxiety, and (3) depressed mood and depression?

6. **Brain Health Q4***:* What is the relationship between physical activity and sleep?

7. **Aging Q2:** What is the relationship between physical activity and physical function? (The search for this question was not restricted to older age groups).

For each of these seven questions, the results from the searches for systematic reviews, meta-analyses, pooled analyses, and existing summary reports were reviewed. All search results that included “gestation,” “postp,” “pregn,” “natal,” or “maternal” in the title or abstract were pulled and gathered for the Pregnancy topic. The title, abstract, and full-text triage review process was the same as that used for other 2018 Advisory Committee topics. The Work Group relied on these publications as the sources of potential evidence regarding quantifiable benefits or risks and the associated dose of physical activity. The Committee also completed one supplementary search activity by adding “eclampsia” and “preeclampsia” to the Cardiometabolic Health and Weight Management Question 2 search on hypertension.

After duplicates were removed, a total of 254 articles were identified through this process. The titles were reviewed by two of the three members of the work group. A total of 122 articles were deemed potentially relevant based on the title search, and the abstracts of these papers were reviewed by two members of the Committee. Through expert consultation, two original research articles were added to the group of articles being reviewed at full text. A total of 73 articles were deemed to be potentially relevant and the full papers were retrieved and reviewed.

During the full-text triage process, the Work Group originally recorded all health outcomes addressed in the articles for pregnant and postpartum women, as well as infants at birth. After reviewing the literature, the Committee decided that the available articles adequately addressed: 1) gestational weight gain (GWG) and postpartum weight loss; 2) gestational diabetes mellitus (GDM); 3) eclampsia and preeclampsia; and 4) affect, anxiety, depression. Too few reviews of quality of life, sleep, and physical function were available to provide an adequate assessment of the relationship.

A wide range of potential health-related outcomes during pregnancy, delivery, and the postpartum period exist for both mother and child. Researchers commonly report not only on the outcome of their primary interest, such as gestational diabetes, but on other sometimes related outcomes, such occurrence of Cesarean section or birth weight of the infant. As a result, the review articles captured in our searches provided information on the search topic and, quite often, information on other events related to the pregnancy, delivery, or the postpartum period. The Work Group saw the opportunity to compare these ancillary findings with information in the 2008 Scientific Report[5] to determine whether the ancillary findings were consistent. The ancillary findings are summarized and discussed after presentation of the evidence pertaining to the specific questions addressed by the Work Group (see Table F8-3).

During the Work Group's review of the meta-analyses and systematic reviews, the Work Group sometimes found it necessary to examine the original research papers included in a review to determine which studies met the Committee's requirements for inclusion. The Work Group alludes to a few of the original research articles in the text; however, these original research articles are not included in the evidence portfolio, as they were not part of the original search.

Question 1. What is the relationship between physical activity and: 1) weight gain during pregnancy; and 2) weight loss during postpartum?

a) What dose of physical activity is associated with the reported quantitative benefit or risk?

b) Is there a dose-response relationship? If yes, what is the shape of the relationship?
c) Does the relationship vary by age, race/ethnicity, socioeconomic status, or weight status?

Sources of evidence: Systematic reviews, meta-analyses, and two existing reports

Conclusion Statements

Weight Gain During Pregnancy

Strong evidence demonstrates a significant inverse relationship between physical activity and weight gain during pregnancy. **PAGAC Grade: Strong.**

Limited evidence suggests that a dose of physical activity similar to the 2015 American College of Obstetricians and Gynecologists Guidelines and the 2008 *Physical Activity Guidelines for Americans* is associated with minimized weight gain and a lower risk of excess gestational weight gain. **PAGAC Grade: Limited.**

Limited evidence suggests a dose-response relationship between physical activity and gestational weight gain. **PAGAC Grade: Limited**.

Insufficient evidence is available to determine whether the relationship between physical activity and gestational weight gain varies by age, race/ethnicity, socioeconomic status, or weight status. **PAGAC Grade: Not assignable**.

Weight Loss During the Postpartum Period

Insufficient evidence is available to determine whether physical activity is associated with weight loss during the postpartum period. **PAGAC Grade: Not assignable.**

Insufficient evidence is available to determine what dose of physical activity is effective for weight loss during postpartum. **PAGAC Grade: Not assignable.**

Insufficient evidence is available to determine whether a dose-response relationship exists between physical activity and weight loss during postpartum. **PAGAC Grade: Not assignable.**

Insufficient evidence is available to determine whether any relationship between physical activity and weight loss during postpartum varies by age, race/ethnicity, socioeconomic status, or weight status. **PAGAC Grade: Grade not assignable**.

Review of the Evidence

Weight Gain During Pregnancy

Sources of evidence included systematic reviews, meta-analyses, and two existing reports published between 2006 and 2017. Nine meta-analyses,[10-18] and two systematic reviews[19, 20] were ultimately included in the Work Group's evidence review. Nine of the reviews included only studies with experimental designs,[10, 11, 13-18, 20] one included only cohort studies,[19] and one included both experimental designs and cohort studies.[10] The number of studies included in each of the reviews ranged from 3[12] to 44.[17] The specifics of the exercise interventions varied but most were similar to the volume recommended by 2008 Physical Activity Guidelines and the 2015 ACOG Committee Opinion.[1, 2]

Evidence on the Overall Relationship

The 11 reviews provided strong evidence that women assigned to the physical activity interventions gain about 1 kilogram (kg) less weight during pregnancy than women in the control groups. Of the eight meta-analyses,[10, 11, 13-18] seven reported significantly less weight gained for the experimental group.[10, 11, 13-15, 17, 18] The other meta-analysis included only women with overweight or obesity and reported significantly lower weight gain in pregnant women with obesity, but not in those with overweight, compared with women in the control groups.[16]

The meta-analysis by da Silva et al[10] reviewed 30 randomized controlled trials (RCTs). Based on a meta-analysis of 18 of those RCTs, which included 1,598 women performing a structured exercise program and 1,605 receiving standard care, the standardized mean difference (SMD) in gestational weight gain was -1.11 kg (95% confidence interval (CI): -1.59 to -0.69), with women in the exercise group gaining less weight than women receiving standard care. Seven other meta-analyses of RCTs[11, 13-1617, 18] reported similar standardized mean differences in gestational weight gain between exercising and control women, ranging from -0.36 kg (95% CI: -0.64 to -0.09)[16] to -2.22 kg (95% CI: -3.14 to -1.30).[11]

A systematic review by McDonald et al[20] considered 21 RCTs (18 exercise only and 3 exercise and diet combined). Of the 18 exercise-only interventions in the review, only 6 were deemed "successful" based on statistically significant (P<0.05) differences in weight gain between the exercise and control groups. However, these differences were modest in size. The meta-analysis by Han et al[12] reported findings from each of 3 RCTs because they differed sufficiently to preclude combining them for a meta-analysis. With sample sizes of 12, 83, and 84, each study reported that women in the more active group gained less weight. The differences were not statistically significant for any of the three.

One systematic review paper by Fazzi et al[19] considered the role of sedentary behavior on gestational weight gain. Of the three cohort studies considered, only one observed a significant relation between sedentary behavior and amount of gestational weight gain,[21] in which the "Active" group (labeled according to author´s categorization) gained significantly less weight during the second and third trimesters than the "Sedentary" group (named according to author´s categorization).

Several systematic reviews and meta-analyses[10, 13, 20] examined the relationship between physical activity and "excess" weight gain (defined by the Institute of Medicine (IOM) Guidelines).[22] In general, women who reported physical activity during pregnancy experienced a significantly lower risk of excess weight gain compared with women who did not, with pooled effect sizes ranging from an 18 percent lower risk (odds ratio [OR]=0.82; 95% CI: 0.68-0.99)[10] to 23% (OR=0.77; 95% CI: 0.66-0.88).[13]

Dose-response: The dose of physical activity prescribed in the RCTs varied among the studies. Similarly, the assessment and categorization of reported leisure-time physical activity was not consistent. It appears, however, that most RCT interventions used an exercise regimen involving primarily aerobic activity of moderate-intensity (walking, swimming, aerobic exercise), occurring at least three times per week for a duration of 30 to 60 minutes per bout. This dose of physical activity appears similar to both ACOG Guidelines and the 2008 Physical Activity Guidelines recommendations.[1, 2]

Most of the reviews did not assess whether maternal physical activity and gestational weight gain had a dose-response relationship. The one review that attempted to answer this question[20] reported that prescribed doses of exercise in the RCTs did not differ between those interventions observing significant (P<0.05) differences in weight gain between the exercise and control groups and those that did not. However, indirect evidence of a dose-response is suggested by the observation that adherence to the prescribed exercise program was significantly higher in the "successful" interventions,[20] and the observation in a meta-analysis of 28 RCTs in which the mean difference in gestational weight gain between the exercise and control groups was inversely correlated with both the duration (in weeks) of the intervention (r=-0.51; P=0.023) and the volume (hours per week) of exercise prescribed (r=-0.45; P=0.05).[18]

Evidence on Specific Factors

Demographic factors and weight status: Virtually none of the systematic reviews or meta-analyses assessed whether the purported relationship between physical activity and gestational weight gain varied by age, race/ethnicity, or socioeconomic status. With regard to weight status, the Work Group observed that most of the findings were reported among women of normal weight. However, several systematic reviews[13, 16, 18, 20] stratified their data by weight status (i.e., normal weight, overweight, or obese). These studies tended to observe larger effect sizes among women of normal weight, compared with those with overweight or obesity.[13, 18, 20] In contrast, one review of women, all of whom had overweight or obesity[16] reported a greater standardized mean difference in gestational weight gain between the exercise and control groups among women with obesity (SMD=-0.91 kg; 95% CI: -1.66 to -0.16) compared with women with overweight (SMD=-0.12; 95% CI: -0.52 to 0.26).

Weight Loss during the Postpartum Period

A total of five systematic reviews and/or meta-analyses[11, 23-26] that included only six original research articles and a total of 287 participants addressed the relationship between physical activity and weight loss during the postpartum period. Most of these reviews report no significant difference in weight loss between women who performed physical activity (alone without dietary restriction) up to 1 year during the postpartum period and the control group.

Evidence on the Overall Relationship

In a meta-analysis of 2 studies that included 53 breastfeeding women, Amorim Adegboye and Linne[23] report no significant difference in postpartum weight loss between women who did and did not exercise (SMD=-0.10 kg; 95% CI: -1.90 to 1.71). Nascimento et al[25] reported that the postpartum weight loss observed in three studies between women who exercised (with no dietary intervention) and those who did not was not statistically significant (SMD= -0.79 kg; 95% CI: -2.54 to 0.97). A more recent meta-analysis[11] in 128 women also reported that exercise did not result in significant weight loss during postpartum compared with usual care (SMD= -1.74 kg; 95% CI: -3.59 to 0.10). Similarly, exercise did not cause a significant reduction in body mass index during the postpartum period compared to usual care (SMD= -0.54 kg/m^2; 95% CI: -1.17 to 0.08).

For additional details on this body of evidence, visit: https://health.gov/paguidelines/second-edition/report/supplementary-material.aspx for the Evidence Portfolio.

Question 2. What is the relationship between physical activity and incidence of gestational diabetes mellitus?

a) What dose of physical activity is associated with the reported quantitative benefit or risk?
b) Is there a dose-response relationship? If yes, what is the shape of the relationship?
c) Does the relationship vary by age, race/ethnicity, socioeconomic status, or weight status?

Sources of evidence: Systematic reviews, meta-analyses, existing reports

Conclusion Statements

Strong evidence demonstrates a significant inverse relationship between physical activity and risk of gestational diabetes mellitus. **PAGAC Grade: Strong**

Limited evidence suggests that a dose of physical activity similar to the 2015 ACOG Guidelines and the 2008 Physical Activity Guidelines is associated with a lower risk of gestational diabetes mellitus. **PAGAC Grade: Limited.**

Limited evidence suggests that a dose-response relationship exists between physical activity and gestational diabetes mellitus. **PAGAC Grade: Limited**.

Insufficient evidence is available to determine whether the relationship between physical activity and gestational diabetes mellitus varies by age, race/ethnicity, socioeconomic status, or weight status. **PAGAC Grade: Not assignable**.

Review of the Evidence

Sources of evidence included systematic reviews, meta-analyses, and two existing reports published between 2006 and 2017. Thirteen meta-analyses [10, 12, 14, 27-36] and 2 systematic reviews[37, 38] addressed physical activity and gestational diabetes mellitus (GDM). The number of studies included in each of the reviews ranged from 3[12] to 41[37] and comprised a mixture of RCTs and observational cohort studies. In general, the physical activity exposure in RCTs was an aerobic exercise program, whereas in the observational cohort studies the exposure was self-reported leisure-time physical activity.

Evidence on the Overall Relationship

Eight of 13 meta-analyses reported higher levels of physical activity to be associated with statistically significant reductions in the risk of GDM (Table F8-1),[10, 14, 27, 28, 31, 33, 35, 36] 4 of 13 meta-analyses reported non-significant reductions,[29, 30, 32, 34] and 1 reported a non-significant increase.[12] The reduced risk of GDM, including all estimates regardless of statistical significance (Table F8-1), ranged from 0.45 to 1.01 with a median value of 0.73. This risk reduction in the incidence of GDM is essentially the same as the 25 percent to 30 percent reduction in the risk of incident type 2 diabetes in the general population associated with physical activity in the current target range. (See *Part F. Chapter 5. Cardiometabolic Health and Prevention of Weight Gain* for more details.) The preponderance of articles included in the systematic reviews reported statistically significant reductions in risk.[37, 38]

Table F8-1. Summary of Findings from 13 Meta-Analyses of the Relationship Between Pre-Pregnancy and Early Pregnancy Physical Activity and Risk of Gestational Diabetes Mellitus

Author, year*	Study Design	Effect (95% CI)
PRE-PREGNANCY PHYSICAL ACTIVITY		
Aune et al., 2016[27]	**Cohort (N=8)**	**sRR=0.78 (0.61-1.00)**
Tobias et al., 2011[33]	**RCT (N=7)**	**pOR=0.45 (0.28-0.75)**
EARLY PREGNANCY PHYSICAL ACTIVITY		
Aune et al., 2016[27]	Cohort (N=5) **RCT (N=12)** **Combined (N=17)**	sRR=0.97 (0.73-1.28) **sRR=0.69 (0.50-0.96)** **sRR=0.80 (0.64-1.00)**
da Silva et al., 2017[10]	Cohort (N=6) **RCT (N=10)**	sOR=0.75 (0.55-1.01) **sOR=0.67 (0.49-0.92)**
Di Mascio et al., 2016[28]	**RCT (N=4)**	**sRR=0.51 (0.31-0.82)**
Han et al., 2011[12]	RCT (N=3)	sRR=1.10 (0.66-1.84)
Madhuvrata et al., 2015[29]	RCT (N=3)	pOR=0.77 (0.33-1.79)
Oostdam et al., 2011[30]	RCT (N=3)	risk difference= -0.05 (-0.20-0.10)
Russo et al., 2015[31]	**RCT (N=10)**	**sRR=0.72 (0.58-0.91)**
Sanabria-M et al., 2015[14]	**RCT (N=8)**	**sRR=0.69 (0.52-0.91)**
Song et al., 2016[32]	RCT (N=10)	sRR=0.77 (0.54-1.09)
Tobias et al., 2011[33]	**RCT (N=5)**	**pOR=0.76 (0.70-0.83)**
Yin et al., 2014[34]	RCT (N=6)	sRR=0.91 (0.57-1.44)
Yu et al., 2017[35]	**RCT (N=5)**	**SMD=0.59 (0.39-0.88)**
Zheng et al., 2017[36]	**RCT (N=4)**	**SMD=0.62 (0.43-0.89)**

Legend: sRR=standardized relative risk, sOR=standardized odds ratio, pOR=pooled odds ratio, and SMD= standardized mean difference.
Note: Studies with statistically significant findings are in bold type.

Aune et al[27] reviewed 23 studies of *total* physical activity (leisure-time, occupational, and household activity combined) and of leisure-time activity performed before or during early pregnancy and the incidence of GDM. Those women who reported performing high levels of total physical activity before pregnancy experienced a significantly lower risk of GDM compared with women reporting low levels of total activity (relative risk (RR)=0.62; 95% CI: 0.41-0.94; 4 studies), whereas high versus low levels of total activity performed during early pregnancy did not significantly lower the risk of GDM (RR=0.66; 95% CI: 0.36-1.21; 3 studies).

On the other hand, women performing higher levels of moderate-intensity leisure-time physical activity either before (RR=0.78; 95% CI: 0.61–1.00; 8 studies) or during pregnancy (RR=0.80; 95% CI: 0.64, 1.00; 12 studies) significantly lowered their risk of GDM by about 20 percent.[27] Women who performed such physical activity both before **and** during pregnancy lowered their risk by 59 percent (RR=0.41; 95% CI: 0.23–0.73; 2 studies) compared with those reporting no physical activity during both time-periods. High versus low levels of vigorous activity performed before pregnancy significantly lowered the risk of GDM by nearly 25 percent (summary RR=0.76; 95% CI: 0.66-0.88; 3 studies), but this was not the case for vigorous activity performed during pregnancy (RR=0.95; 95% CI: 0.55-1.63; 2 studies).

Findings from the other meta-analyses for the overall relationship were similar, with the statistically significant findings ranging from an odds ratio of 0.45; 95% CI: 0.28-0.75 (7 studies),[33] to a relative risk of 0.72; 95% CI 0.58-0.91 (10 studies).[31] The three nonsignificant reductions and the nonsignificant increase ranged from a relative risk of 0.77 (0.54-1.09) (10 studies),[32] to a relative risk of 1.10 (0.66-1.84) (3 studies)[12] (Table F8-1).

The meta-analysis by Aune et al[27] also evaluated the independent role of walking, household, or occupational activity on GDM before and during early pregnancy. Women reporting high versus low levels of walking before (RR=0.66; 95% CI: 0.48-0.91; 2 studies) and during (RR=0.80; 95% CI: 0.66-0.97; 2 studies) pregnancy significantly lowered their risk of GDM. The relationship between high versus low levels of household activity and GDM risk was not statistically significant (RR=0.36; 95% CI: 0.12-1.08; 2 studies). Women who reported performing high versus low levels of occupational physical activity were found to have an increase in risk of GDM for occupational activity performed both before pregnancy (RR=1.90; 95% CI: 0.97-3.74; 2 studies) and during pregnancy (RR=0.78; 95% CI: 0.21-2.93; 2 studies), though this increase did not achieve statistical significance.

Dose-response: The dose of physical activity of physical activity prescribed in the RCTs varied among the studies. Similarly, the assessment and categorization of reported leisure time physical activity from observational studies was not detailed nor consistent. It appears, however, that most RCT interventions used a physical activity regimen involving primarily aerobic activity of at least moderate-intensity (walking, cycling, swimming, aerobic dance), occurring at least three times per week for a duration of 30 to 60 minutes per bout. This dose of activity appears similar to both ACOG Guidelines and the 2008 Physical Activity Guidelines[1, 2]

Aune et al[27] performed a dose-response analysis and reported that each 5 hours per week increment in pre-pregnancy physical activity lowered the risk of GDM by about 30 percent (RR=0.70; 95 % CI: 0.49-1.01; 3 studies), with significant evidence of non-linearity (P<0.005). A similar relationship was not observed for physical activity performed during early pregnancy (RR=0.98; 95% CI: 0.87-1.09; 3 studies). Evidence from two observational studies in the meta-analysis by Tobias et al[33] suggests that women who walked at a brisk pace before pregnancy and for a longer duration significantly lowered their risk of GDM compared with women who walked at a casual pace for shorter durations (pooled OR=0.59; 95% CI: 0.30-0.87).

Evidence on Specific Factors

Demographic factors and weight status: Almost none of the systematic reviews or meta-analyses assessed whether the purported relationship between physical activity and GDM varied by age, race/ethnicity, or socioeconomic status. The review by Song et al[32] reported that physical activity during pregnancy had a significant impact on GDM risk in women ages 30 years and older, but not in women younger than age 30 years.

For additional details on this body of evidence, visit: https://health.gov/paguidelines/second-edition/report/supplementary-material.aspx for the Evidence Portfolio.

Question 3. What is the relationship between physical activity and the incidence of (1) preeclampsia and (2) hypertensive disorders during pregnancy?

a) What dose of physical activity is associated with the reported quantitative benefit or risk?
b) Is there a dose-response relationship? If yes, what is the shape of the relationship?
c) Does the relationship vary by age, race/ethnicity, socioeconomic status, or weight status?

Sources of evidence: Systematic reviews and meta-analyses, existing reports

Conclusion Statements

Limited evidence suggests that leisure-time physical activity or exercise training lowers the risk of preeclampsia. **PAGAC Grade: Limited**

Limited evidence suggests that a dose of physical activity similar to the 2015 American College of Obstetricians and Gynecologists Guidelines and the 2008 Physical Activity Guidelines is associated with a lower risk of preeclampsia. **PAGAC Grade: Limited.** Limited evidence suggests that a dose-response relationship exists between physical activity and the incidence of preeclampsia. **PAGAC Grade: Limited**.

Insufficient evidence is available to determine whether the relationship between physical activity and preeclampsia varies by age, race/ethnicity, socioeconomic status, or weight status. **PAGAC Grade: Not assignable**.

Review of the Evidence

Sources of evidence included systematic reviews, meta-analyses, and two existing reports published between 2006 and 2017. Six meta-analyses[10, 13, 28, 36, 39, 40] and three systematic reviews[19, 41, 42] addressed physical activity and blood pressure during pregnancy. Five meta-analyses[10, 13, 36, 39, 40] and two systematic reviews[41, 42] focused on preeclampsia; one meta-analysis[28] and one systematic review[19] focused on incident hypertension. The nine reviews included a mixture of study designs. Three reviews included only experimental designs,[13, 28, 36] one review included experimental designs and cohort studies,[10] one included experimental, cohort, and case-control studies,[40] two included cohort and case-control studies,[39, 42] and two included cohort and cross-sectional studies.[19, 41] The physical activity exposures were primarily aerobic and mostly leisure-time physical activity. One review[41] focused entirely on occupational physical activity, and two others[19, 40] included information about leisure-time physical activity and occupational exposures. Fazzi et al[19] examined sedentary behavior. The experimental studies within the reviews included a mixture of supervised physical activity or prescribed and structured aerobic physical activity programs.[10, 13, 28, 36]

Evidence on the Overall Relationship

The nine reviews provided limited evidence of an inverse relationship between volume of physical activity and risk of preeclampsia or incident hypertension. (Table F8-2) summarizes the findings from the five meta-analyses about preeclampsia. One meta-analysis that included cohort and case-control studies reported a beneficial association between higher levels of physical activity and reduced risk of preeclampsia from both pre-pregnancy (RR=0.65; 95% CI: 0.47-0.89; 5 studies) and early pregnancy physical activity (RR=0.79; 95% CI: 0.70-0.91; 11 studies).[39] Another meta-analysis reported a beneficial association between pre-pregnancy and early pregnancy physical activity and reduced risk of preeclampsia for case-control studies, but not for cohort studies.[40] Three meta-analyses using RCTs and cohort studies found no association; one of them examined pre-pregnancy physical activity,[10] the other two, early pregnancy physical activity.[13, 36]

The meta-analysis of 10 cohort studies by Kasawara et al[40] also reported no association between leisure time physical activity and preeclampsia (OR=0.99; 95% CI: 0.93-1.05). In contrast, their meta-analysis of 6 case-control studies reported a significantly lower odds of preeclampsia (OR=0.77; 95% CI: 0.64-0.91) with physical activity performed in pre-pregnancy (summarized from two studies) being even more effective (OR=0.56; 95% CI: 0.41-0.76).

Muktabhant et al[13] also observed no difference in incident preeclampsia between women who exercised during pregnancy and those who did not (average RR=0.99; 95% CI: 0.58-1.66), based on data from four RCTs (N=1,253). The authors further analyzed data according to weight status: normal weight; overweight or obese; and combined normal and overweight or obese. Even among women with overweight or obesity, there was no difference in risk of preeclampsia in two studies between those in the exercise groups and those in the control groups (RR=1.60; 95% CI: 0.38-6.73). Concurrent evidence from another recent meta-analysis of two RCTs[36] provides additional support of a null association (pooled OR=1.05; 95% CI: 0.53-2.07; *P*=0.88).

da Silva et al[10] reviewed 30 RCTs that examined the relationship between structured exercise programs and the incidence of preeclampsia and provided a meta-analysis of data from three of them. Their findings indicated that exercise training had no effect on lowering this risk (pooled RR=0.93; 95% CI: 0.55 to -1.57), with no evidence of heterogeneity. Their meta-analysis of eight cohort studies (involving 155,414 women) also found that moderate to vigorous leisure-time physical activity did not significantly lower the risk of preeclampsia compared with low or no leisure-time activity (pooled OR=0.88; 95% CI: 0.73-1.06), with low evidence for heterogeneity.

One systematic review examined four case-control studies and seven cohort studies, and reported no observed relationship between physical activity and preeclampsia.[42]

One systematic review[19] and one meta-analysis[28] examined the relationship between physical activity and "hypertensive disorders" during pregnancy. Hypertensive disorders during pregnancy include preeclampsia and gestational hypertension. Gestational hypertension is elevated blood pressure without concomitant signs of preeclampsia such as proteinuria, and its relationship, if any, with preeclampsia is unknown. Of the three pertinent original studies in Fazzi et al,[19] two (Loprinzi et al[43] N=206 and Chasan-Taber et al[44] N=1,240) reported no association between sedentary behavior and gestational hypertension, whereas one study (Li and Zhao[45] N=405) observed that women with persistent sedentary work developed more gestational hypertension than did women in the referent group.[19] Di Mascio et al[28] reported a risk ratio of 0.21 (95% CI: 0.09-0.45; 3 studies) for hypertensive disorders for more active women compared with less active women.[28]

Table F8-2. Summary of Findings from Five Meta-Analyses of the Relationship Between Physical Activity and Risk of Preeclampsia

Author, year	Study Design	Effect (95% CI)
PRE-PREGNANCY PHYSICAL ACTIVITY		
Aune et al., 2014[39]	**Cohort (n=4) + Case-control (n=1)**	**sRR=0.65 (0.47-0.89)**
da Silva et al., 2017[10]	Cohort (n=8) RCT (n=3)	sOR=0.88 (0.73-1.06) sOR=0.93 (0.55-1.57)
Kasawara et al., 2012[40]	Cohort (n=3) **Case-control (n=2)**	sOR=0.85 (0.67-1.09) **sOR=0.56 (0.41-0.76)**
EARLY PREGNANCY PHYSICAL ACTIVITY		
Aune et al., 2014[39]	**Cohort (n=7) + Case-control (n=4)**	**sRR=0.79 (0.70-0.91)**
Kasawara et al., 2012[40]	Cohort (n=10) **Case-control (n=6)**	OR=0.99 (0.93-1.05) **OR=0.77 (0.64-0.91)**
Muktabhant et al., 2015[13]	RCTs (n=4)	avgRR: 0.99 (0.58-1.66)
Zheng et al., 2017[36]	RCTs (n=2)	pOR=1.05 (0.53-2.07)

Legend: sRR=standardized relative risk, sOR=standardized odds ratio, avgRR= average relative risk, and pOR=pooled odds ratio.
Note: Studies with statistically significant findings are in bold type.

In contrast to studies of leisure-time physical activity, the reviews examining occupational activity reported an increased risk of preeclampsia. When occupational physical activity was explored separately from leisure-time activity and in relation to the development of preeclampsia, in two of the case-control studies in the Kasawara et al[40] meta-analysis, the risk of preeclampsia was significantly elevated. Similarly, Bonzini et al[41] observed a higher risk of preeclampsia for lifting heavy loads (1 study) and higher amounts of physical activity (2 studies). The authors note, however, that all these studies were rated as having higher potential for inflationary bias due to the retrospective data collection. It is important to consider that the relationship between occupational activity and preeclampsia may be confounded by factors such as low socioeconomic status, low educational attainment, and obesity.

Dose-response: The systematic review by Aune et al[39] was the only paper to report on the dose-response relation between physical activity and risk of pre-eclampsia. In their analysis of **pre-pregnancy** physical activity, the summary relative risk was 0.72 (95% CI: 0.53–0.99; n=3 studies) per 1 hour per day and 0.78 (95% CI: 0.63–0.96; n=2 studies) per 20 MET-hours per week, indicating a 22 to 28 percent lower risk of pre-eclampsia per unit increase in physical activity. This relationship appeared non-linear with a flattening of the curve at higher levels of activity, with a 40% reduction in risk up to 5–6 hours per week but no further reductions at higher activity levels. With regard to physical activity performed during **early pregnancy**, the summary relative risk per 1 hour per day was 0.83 (95% CI: 0.72–0.95; n=7 studies) and 0.85 (95% CI: 0.68–1.07; n=3 studies) per 20 Met-hours per week. This dose-response relationship appeared to be linear.

Evidence on Specific Factors

Demographic factors and weight status: There was no available evidence that tested whether the relationship between physical activity and preeclampsia varies by age, race/ethnicity, socioeconomic status, or weight status.

For additional details on this body of evidence, visit: https://health.gov/paguidelines/second-edition/report/supplementary-material.aspx for the Evidence Portfolio.

Question 4. What is the relationship between physical activity and (1) affect, (2) anxiety, and (3) depression during pregnancy and postpartum (up to one year)?

a) What dose of physical activity is associated with the reported quantitative benefit or risk?
b) Is there a dose-response relationship? If yes, what is the shape of the relationship?
c) Does the relationship vary by age, race/ethnicity, socioeconomic status, or weight status?

Sources of evidence: Systematic reviews, meta-analyses, existing reports

Conclusion Statements

Affect During Pregnancy or the Postpartum Period

Insufficient evidence is available to determine whether a relationship exists between physical activity and affect during pregnancy and the postpartum period. **PAGAC Grade: Not assignable.**

Insufficient evidence is available to determine whether a specific dose of physical activity is associated with affect during pregnancy and the postpartum period. **PAGAC Grade: Not assignable.**

Insufficient evidence is available to determine whether a dose-response relationship exists between physical activity and affect during pregnancy and the postpartum period. **PAGAC Grade: Not assignable.**

Insufficient evidence is available to determine whether the relationship between physical activity and affect varies by age, race/ethnicity, socioeconomic status, or weight status. **PAGAC Grade: Not assignable.**

Anxiety During Pregnancy

Limited evidence suggests that higher levels of physical activity are associated with reduced symptoms of anxiety during pregnancy. **PAGAC Grade: Limited.**

Insufficient evidence is available to determine the dose of physical activity that is associated with reduced symptoms of anxiety during pregnancy. **PAGAC Grade: Not assignable.**

Insufficient evidence is available to determine whether a dose-response relationship exists between physical activity and reduced symptoms of anxiety during pregnancy. **PAGAC Grade: Not assignable.**

Insufficient evidence is available to determine whether the relationship between physical activity and symptoms of anxiety during pregnancy varies by age, race/ethnicity, socioeconomic status, or weight status. **PAGAC Grade: Not assignable.**

Anxiety During the Postpartum Period

Insufficient evidence is available to determine whether a relationship exists between physical activity and symptoms of anxiety during the postpartum period. **PAGAC Grade: Not assignable.**

Insufficient evidence is available to determine whether a specific dose of physical activity is associated with symptoms of anxiety during postpartum. **PAGAC Grade: Not assignable.**

Insufficient evidence is available to determine whether a dose-response relationship exists between physical activity and symptoms of anxiety during postpartum. **PAGAC Grade: Not assignable.**

Insufficient evidence is available to determine whether the relationship between physical activity and symptoms of anxiety during postpartum varies by age, race/ethnicity, socioeconomic status, or weight status. **PAGAC Not assignable.**

Depression During Pregnancy

Limited evidence suggests that higher levels of physical activity are associated with reduced symptoms of depression during pregnancy. **PAGAC Grade: Limited.**

Insufficient evidence is available to determine whether a specific dose of physical activity is associated with reduced symptoms of depression during pregnancy. **PAGAC Grade: Not assignable.**

Insufficient evidence is available to determine whether a dose-response relationship exists between physical activity and reduced symptoms of depression during pregnancy. **PAGAC Grade: Not assignable.**

Insufficient evidence is available to determine whether the relationship between physical activity and symptoms of depression during pregnancy varies by age, race/ethnicity, socioeconomic status, or weight status. **PAGAC Grade: Not assignable.**

Depression During the Postpartum Period

Strong evidence demonstrates an inverse relationship between physical activity and reduced symptoms of depression during postpartum. **PAGAC Grade: Strong.**

Insufficient evidence is available to determine whether a specific dose of physical activity is associated with reduced symptoms of depression during the postpartum period. **PAGAC Grade: Not assignable.**

Insufficient evidence is available to determine whether there is a dose-response relationship between physical activity and reduced symptoms of depression during postpartum. **PAGAC Grade: Not assignable.**

Insufficient evidence is available to determine whether the relationship between physical activity and symptoms of depression during postpartum varies by age, race/ethnicity, socioeconomic status, or weight status. **PAGAC Not assignable.**

Review of the Evidence

Sources of evidence included 1) systematic reviews, meta-analyses, and two existing reports published between 2006 and 2017; and 2) the relevant original research articles cited by the systematic reviews and meta-analyses. Three systematic reviews[46-48] and two meta-analyses[49, 50] addressed affect, anxiety, and depression during pregnancy and the postpartum period. Three of the reviews included only experimental trials,[46, 49, 50] and two of the reviews included experimental trials, longitudinal studies, and cross-sectional studies.[47, 48] The physical activity exposure in four of the reviews was aerobic activity usually commensurate with current recommendations[47-50] and in one it was yoga.[46]

Evidence on the Overall Relationship

Affect During Pregnancy and the Postpartum Period

No systematic reviews or meta-analyses were found that examined the relationship between physical activity and affect during pregnancy or the postpartum period.

Anxiety During Pregnancy

Two systematic reviews were found examining the relationship between symptoms of anxiety during pregnancy.[46, 47] Sheffield and Woods-Giscombe[46] provided a systematic review of 13 studies (7 of which were RCTs) that examined the effects of yoga on symptoms of anxiety and depression during pregnancy. Of the five studies that evaluated anxiety symptomology, all of them reported statistically significant improvements in the State/Trait Anxiety Inventory (STAI) scores following a yoga intervention. Of note is that three of five studies reported between-group differences, whereas two of five studies reported within-group changes only. Shivakumar et al[47] reported that more physically active women reported reduced symptoms of anxiety in one of three studies that examined symptoms of anxiety.

Anxiety During the Postpartum Period

No systematic reviews or meta-analyses were found that examined the relationship between physical activity and anxiety during the postpartum period.

Symptoms of Depression During Pregnancy

Two systematic reviews were found examining the relationship between symptoms of depression during pregnancy.[46, 47] In the same study described above about symptoms of anxiety, Sheffield and Woods-Giscombe[46] reported that six of seven studies all using the Center for Epidemiologic Studies of Depression (CES-D) scale, reported a statistically significant improvement in depression score. Four of the seven studies reported between-group differences in depressive symptoms score and two of six reported within-group changes only. In another systematic review, two of two studies reported reduced symptoms of depression in the higher physical activity group.[47] These findings should be interpreted cautiously, however, as all of these studies had some methodological limitations, such as small samples sizes, inappropriate or no control group, or lack of control for confounding variables, thereby underscoring the need for more research in this area.

Symptoms of Depression During the Postpartum Period

Two meta-analyses[49, 50] and one systematic review[48] examined the relationship between physical activity and symptoms of depression during the postpartum period. Teychenne and York[48] provided a systematic review of 17 studies, 10 of which were observational studies and 7 of which were intervention trials. Five of the studies examined physical activity performed during pregnancy and 12 examined postpartum activity. Only 2 of 5 studies of physical activity during pregnancy reported a significant inverse relation with postpartum depression, whereas 4 of 10 observational studies and 5 of 7 intervention trials of postpartum physical activity reported beneficial effects, suggesting that physical activity during the postpartum period may be more likely to prevent postpartum depression than physical activity before postpartum.

McCurdy et al[49] examined 16 RCTs comparing exercise to standard care in postpartum women (N=1,327) with (10 trials) and without (6 trials) depression. In general, depressive symptoms scores (based on the Edinburgh Postnatal Depression Scale (EPDS)) were lower among those in exercise intervention groups compared with those in control groups (pooled SMD= -0.34; 95% CI: -0.50 to -0.19). Among the 10 treatment trials in woman with postpartum depression, a moderate beneficial effect of exercise on depressive symptoms was observed (SMD= -0.48; 95% CI: -0.73 to -0.22) relative to the control group. Moreover, in women with depression pre-intervention (defined as an EPDS score greater than12), exercise increased the odds of resolving depression post-intervention by 54 percent (OR=0.46; 95% CI: 0.25–0.84) compared with the control group. In the six prevention trials (i.e., women without depression) a beneficial effect of exercise was observed in the EPDS score (SMD= -0.22; 95% CI: -0.36 to -0.08) compared with standard care. These findings are consistent with a smaller review and meta-analysis by Poyatos-León et al.[50] Indeed, among women performing physical activity during pregnancy and the postpartum period, there was a decrease in postpartum depressive symptom scores (measured by EPDS or by the Beck Depression Inventory) in favor of the physical activity compared with the control group (effect size (ES)=0.41; 95% CI: 0.28-0.54). In the subgroup analysis, the effect size was smaller for women who did not meet criteria for postpartum depression (ES=0.29; 95% CI: 0.14-0.45), but was more pronounced in women who did (ES=0.67; 95% CI: 0.44-0.90). Most (10 of 12) of the interventions were begun during the postpartum period and involved a variety of activities, such as walking, aerobics, Pilates, yoga, and stretching.

In sum, consistent with findings for the general population (see *Part F. Chapter 3. Brain Health*, Question 3), the evidence demonstrates that physical activity has a beneficial effect on postpartum depressive symptoms. The benefits appear to be more pronounced in women who have greater depressive symptomology and when activity is performed during the postpartum period rather than during pregnancy or before.

For additional details on this body of evidence, visit: https://health.gov/paguidelines/second-edition/report/supplementary-material.aspx for the Evidence Portfolio.

Summary of Main and Auxillary Findings Pertaining to Pregnancy-Related Health Outcomes

The above paragraphs summarize information about the relationship between primarily moderate-intensity physical activity during pregnancy and the postpartum period and: 1) gestational weight gain, 2) return to normal weight after delivery, 3) risk of gestational diabetes, 4) risk of preeclampsia and eclampsia, and 5) symptoms of depression. These are questions that could be directly addressed by the systematic reviews and meta-analyses brought in by searches conducted by the Pregnancy Work Group. Several of these studies also provided information about other pregnancy-related outcomes. For example, because women who develop gestational diabetes are more likely than other mothers to have larger-than-normal babies, several reviews focusing on gestational diabetes also provided information about the proportion of newborns who were larger than expected. In this section, we summarize this auxiliary information: for 1) ease of delivery, 2) preterm birth and gestational age at delivery, 3) birth weight, 4) small for gestational age and low birth weight, and 5) large for gestational age and high birth weight. It is important to note that we did not conduct searches to address these specific questions. Our findings cannot be considered conclusive and we have not “graded” the evidence as we have done for questions for which a specific literature search was conducted. We have noted in Table F8-3, however, how the auxiliary information compares with information in the 2008 Advisory Committee Report and the ACOG Committee Opinion of 2015.[1, 5] Significance was interpreted at $P<0.05$.

Ease of Delivery

The auxiliary information suggests that generally, women who are more physically active during pregnancy are less likely than women who are less active to have a Cesarean section at the time of delivery. Five meta-analyses[12, 13, 17, 18, 28] provided information about physical activity level and risk of Cesarean section. Two meta-analyses reported statistically significant reductions in the risk of Cesarean section among women assigned to intervention arms that included aerobic activity and/or resistance training during pregnancy.[18, 28] Two meta-analyses reported statistically non-significant reductions.[13, 17] One meta-analysis reported a statistically non-significant increase in risk of Cesarean section,[12] but it included only 2 studies whereas the other four meta analyses included 5 to 20 studies.

Preterm Birth and Gestational Age at Delivery

The auxiliary information suggests no difference between more active and less active pregnant women in the risk of preterm delivery or gestational age of infant at delivery. One meta-analysis reported a decreased risk of preterm delivery among more physically active women[10]; five meta-analyses reported no difference.[13, 17, 28, 35, 36] Similarly, five meta-analyses reported no difference in gestational age at delivery between women who were more physically active during pregnancy than women who were less physically active.[10, 12, 17, 28, 36] The search also captured one meta-analysis of occupational physical activity and pregnancy outcomes.[41] The exposures of interest were long periods of standing (greater than3 hours) and heavy lifting. The analysis found a significant association between standing for at least 3 hours and an elevated risk of preterm birth.

Birth Weight

The auxiliary information suggests minimal to no difference in the birth weight of babies born to more physically active women than less physically active women. Three meta-analyses reported that babies of more active women weighed fewer grams than babies of less active women; -1.05 grams (95% CI: -1.49 to -0.62),[10] cohort studies only, -60 grams (95% CI: -120 to -10)[17] and -30.60 gm (95% CI: -56.83 to -4.37).[18] Five meta-analyses reported a non-significantly reduced birth weight for babies born to more active women,[10] for RCT only.[12, 28, 35, 36] One systematic review of sedentary behavior and birth weight reported two studies finding no association and one study reporting that more sedentary women were more likely to have low birth weight babies.[19]

Small for Gestational Age and Low Birth Weight

Three meta-analyses reported no difference between more and less active women and the risk of the newborn to be small for gestational age.[10, 17, 18] One reported no difference in the risk for low birth weight between intervention participants engaging in aerobic exercise compared to control participants.[28]

Large for Gestational Age and High Birth Weight

The auxiliary information suggests that babies of more physically active women are less likely to be large for gestational age at birth than babies of less physically active women.[10, 18] However, three meta-analyses reported no statistical differences between babies born to more or less active women,[12, 13, 17] although one reported that the reduction in large for gestational age risk for babies born to more active women became significant if three studies at high risk of bias were removed from the analysis.[13] One meta-analysis reported a statistically significant lower relative risk of macrosomia (newborn weighing greater than 4000 grams) for babies born to more physically active women, but this was based on only two studies.[30]

Apgar Score

Four meta-analyses reported no significant difference in mean Apgar score or risk of Apgar score less than 7 at 5 minutes for babies born to women who were physically more active during pregnancy than women who were less active.[12, 35, 36, 51]

Table F8-3. Effects of Physical Activity on Pregnancy- and Postpartum-Related Events

Events	2008 PAGAC Report	2015 ACOG Committee Opinion	2018 PAGAC Report
Topic-specific searches for PAGAC Report 2018			
Gestational weight gain		Modest decrease in weight gain (page e138)	Strong evidence of reduced risk of excess weight gain
Return to normal weight	Appears not to help (page G11-38)		Insufficient evidence
Gestational diabetes	Probable reduced risk of gestational diabetes (page G11-37)	Reduced risk (page e137)	Strong evidence of reduced risk of gestational diabetes
Preeclampsia	Possible reduced risk of preeclampsia (page G11-37)	Possible reduced risk of preeclampsia (page e138)	Moderate evidence of no association with preeclampsia

Events	**2008 PAGAC Report**	**2015 ACOG Committee Opinion**	**2018 PAGAC Report**
Affect, anxiety, and depression during pregnancy	Appears to improve mood and increase self-esteem (page G11-37-8)	Enhances psychological well-being (page e135)	Limited evidence of reduced anxiety and depression
Affect, anxiety, and depression during postpartum	Enhanced mood (page G11-38)		Strong evidence of reduced symptoms of depression; limited evidence for anxiety; insufficient evidence for affect
Quality of life during pregnancy or postpartum			Insufficient evidence, grade not assignable
Quality of sleep during pregnancy or postpartum			Insufficient evidence, grade not assignable

Events	2008 PAGAC Report	2015 ACOG Committee Opinion	2018 PAGAC Report
Incidental outcomes from searches (partial searches)			
Labor & delivery	Uncertain impact (page G11-38)	Reduced risk of operative delivery (Cesarean or vaginal) (page e137)	Partial search: evidence suggests reduced risk of Cesarean section
Postpartum recovery		Decreased postpartum recovery time (page e138)	Partial search: no auxiliary evidence on this topic; decreased recovery time still applies.
Lactation	No impact (page G11-38)	No impact (page e139)	Partial search: no auxiliary evidence on this topic; no effect on lactation.
Physical fitness during pregnancy	Maintains (page G11-37)	Improves or maintains (page e137)	Partial search: no auxiliary evidence on this topic; maintains or improves fitness.
Physical fitness during postpartum	Improved (page G11-38)	Improves cardiovascular fitness (page e139)	Partial search: no auxiliary evidence on this topic; improves fitness.
Preterm delivery, difference in gestational age	No risk from moderate intensity physical activity (page G11-37)		Partial search: evidence suggests no risk of preterm delivery or difference in gestational age
Low birth weight, small for gestational age	No risk from moderate intensity physical activity (page G11-37)[1]	Minimal to no difference in birth weight (page e137)	Partial search: evidence suggests minimal to no difference in birth weight
High birth weight, Large for gestational age			Partial search: evidence suggests a reduction in risk of high birth weight or large for gestational age
Apgar			Partial search: evidence suggests no difference in Apgar scores

Source: 2008 Scientific Report,[5] 2015 ACOG Committee Opinion.[1]

Comparing 2018 Findings with the 2008 Physical Activity Guidelines Advisory Committee Report

The 2008 Advisory Committee Report concluded that for women with a normal pregnancy, regular physical activity probably reduces the risk of gestational diabetes, possibly reduces the risk of preeclampsia, and appears to improve mood both during and after pregnancy (Table F8-3).[5] The Committee's findings in 2018 support the findings of 2008 and extend them in several ways. Strong evidence now shows that physical activity commensurate with the current target range reduces the risk of excessive weight gain, gestational diabetes, and symptoms of depression postpartum. Physically active pregnant women gain about 1 kg less than their less active peers, reduce their risk of gestational diabetes by 25 percent to 30 percent, and have significantly fewer depressive symptoms. The Committee's findings in 2018 also provide support for the observations in 2008 that moderate-intensity physical activity provides no risk of preterm birth or low birth weight.

The 2008 Physical Activity Guideline reported that "habitual exercisers undergoing a healthy pregnancy need not drastically reduce their physical activity, provided that they remain asymptomatic and maintain open communication with their health care providers so that adjustments can be made if necessary."[5] However, certain activities should be avoided including contact sports, activities with a high risk of falls, hot yoga/pilates, scuba diving, and sky diving. [1] This same communication should be continued into the postpartum period, where the time needed before a woman returns to performing regular physical activity should be governed by medical safety concerns, rather than a set time period.

Public Health Impact

Only about 23-29 percent of women are sufficiently physically active during pregnancy to be in the recommended target range for substantial health benefits.[3] Of course, some of the other women engage in at least some activities of moderate relative intensity and, thereby, accrue some benefits. Nevertheless, around one-half of women who are pregnant receive few or none of the physical and emotional health benefits of habitual physical activity.

Quantifying the benefits not accrued is difficult, but it is clear that a substantial number of current and future health problems and costs could be avoided with regular physical activity during pregnancy. Strong evidence in this Report demonstrates that physically active pregnant women are less likely to exceed the Institute of Medicine recommendations for healthy weight gain during pregnancy than their less active peers.[22] Because they gain less weight, they are at less risk of excessive postpartum weight retention, future obesity, and birth of an infant with macrosomia.[52] They also appear to be at lower risk of Cesarean section, and at no greater risk of preterm delivery.

Strong evidence in this Report demonstrates that physically activity women are about 25 percent to 30 percent less likely to develop gestational diabetes than their inactive peers. Gestational diabetes occurs in around 5 percent to 9 percent of women who are pregnant. Women with gestational diabetes have a seven-fold increased risk of developing type 2 diabetes after pregnancy; they also are at increased risk of delivery by Cesarean section and having an infant with macrosomia and/or neonatal hypoglycemia.[53]

Strong evidence in this Report demonstrates that physically active women experience fewer symptoms of depression during the postpartum. About 10 percent of women experience postpartum depression, with nearly 25 percent of them still in treatment after 1 year.[54] The data in the Report do not enable a quantitative estimate of the reduction in incidence of postpartum depression, but habitual physical activity will help.

Thus, the benefits documented in this Scientific Report—reduced gestational weight gain, reduced risk of gestational diabetes, and a reduction in postpartum depression—confirm the public health importance of physical activity before, during, and after pregnancy.

NEEDS FOR FUTURE RESEARCH

1. Conduct observational and experimental studies of the effects of vigorous-intensity physical activity before and during pregnancy on maternal and fetal outcomes.

   Rationale: The safety and benefits of moderate-intensity physical activity during pregnancy and the postpartum period are now generally accepted. The safety and benefits of vigorous-intensity (absolute and perceived) physical activity are less well-documented and this type of activity may be discouraged by some health care providers. For women who have not been physically active, a program of moderate-intensity physical activity would be recommended. On the other hand, substantial numbers of women participate regularly in vigorous physical activity (e.g., running, stationary cycling, rowing) before pregnancy and may want to continue such activity for as long as possible throughout pregnancy. Information from such studies would provide valuable information on minimal effective levels of vigorous activity and maximal threshold levels for safety.

2. Continue to conduct large-scale observational studies to investigate longitudinally the relationship between various types and volumes of physical activity before and during pregnancy and during the postpartum period on short- and long-term weight status.

   Rationale: Although it is established that habitual moderate-intensity physical activity of a volume in the recommended target zone is associated with reduced weight gain during pregnancy, information about the relationship between various types and volumes of physical activity and weight change during pregnancy and the postpartum period would help guide the development of clinical and public health recommendations.

3. Conduct experimental and observational studies to investigate the effects of various types, intensities, and volumes of regular physical activity on quality of life and symptoms of anxiety and depression and during pregnancy, and quality of life and symptoms of anxiety during the postpartum period.

   Rationale: Although strong evidence demonstrates that regular moderate-intensity physical activity reduces depressive symptoms during the postpartum period, little information exists about the role of physical activity on perceived quality of life and symptoms of anxiety and depression symptoms during pregnancy and quality of life and symptoms of anxiety during the postpartum period. Emerging evidence suggests that maternal mental health affects the health of the developing fetus. Knowledge about the benefits of even low doses of physical activity, as well as about the benefits of various modes of physical activity for women with anxiety or depression can help to promote a healthy pregnancy for both mother and fetus.

4. Conduct experimental and observational studies to determine the influence of regular physical activity on quality of sleep during pregnancy and the postpartum period.

   Rationale: Although regular physical activity is known to improve sleep and feelings of quality of life in the general population, little is known about the effect of regular physical activity on quality of sleep during pregnancy and the postpartum period. Getting enough sleep, especially during the postpartum period, is a common problem for new mothers. If women during pregnancy and postpartum benefit from acute episodes and regular participation in physical activity as do those in the general population, it could improve overall level of energy and quality of life.

5. Conduct large observational studies to determine whether specific types, intensities, and doses of physical activity affect maternal and fetal outcomes, such as preterm birth, low birth weight, and preeclampsia differentially.

   Rationale: Most of the experimental research on physical activity during pregnancy relies on the 2008 Physical Activity Guidelines[5] or the 2015 American College of Obstetricians and Gynecologists[1] recommendations of 150 minutes per week of moderate-intensity activity. Limited evidence suggests that certain types of physical activity, such as prolonged standing or lifting heavy loads performed in an occupational setting, may have different health effects for pregnant women than when performed during leisure time. The veracity of the observation needs to be determined, and, if confirmed, it will be important to determine whether the results are caused by the nature of the activities or the setting or perhaps other confounding factors (socioeconomic status, education level, age). Observing the impact of varying types, intensities, and doses of physical activity in varying domains (leisure-time, occupational, household, transportation) on a range of maternal and fetal outcomes would significantly advance current knowledge and inform both clinical and public health practice.

6. Conduct observational and/or experimental research that has adequate statistical power to determine whether the associations between physical activity and maternal or fetal outcomes vary by age, race/ethnicity, socioeconomic status, or weight status.

   Rationale: Most of the studies reviewed in this report were not designed or powered to test for effect modification by various sociodemographic factors or by body weight. Such information is important for making more specific physical activity recommendations for various population sub-groups in efforts to reduce health disparities among pregnant women.

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PART F. CHAPTER 9. OLDER ADULTS

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INTRODUCTION

Advances in public health and in health care are keeping people alive longer, and consequently, the proportion of older people in the global population is increasing rapidly. As of 2016, individuals ages 65 years and older comprise about 13 percent of the United States population, and their numbers are projected to reach 72.1 million (19% of the total population) by the year 2030. This represents a two-fold increase compared with the older adult population in 2000. Moreover, the number of people 85 years and older is projected to rise to 14.6 million by 2040.[1] Due to these growing demographic trends, the prevention of chronic disease, the maintenance of functional status, and the preservation of physical independence in aging present major challenges that have substantial personal and public health implications.

Ample evidence now exists that regular physical activity is key to preventing and managing major chronic diseases common to older people. Physical activity is also important for preserving physical function and mobility, which can then delay the onset of major disability.[2] Despite the known benefits of physical activity to health and physical function in aging, the proportion of older adults meeting recommended physical activity guidelines remains low (27%), based on data from the 2011-2012 National Health and Nutrition Examination Survey (NHANES) data.[3]

The *Physical Activity Guidelines Advisory Committee Report, 2008*[4] addressed the importance and impact of physical activity in preventing or delaying the onset of substantial functional and/or role limitations in middle-aged and older adults without such limitations. The report further addressed the relationship between physical activity and improvements in functional ability in older adults with mild, moderate, or severe functional or role limitations, as well as the role of physical activity in reducing the incidence of falls and fall-related injuries. Since the 2008 Scientific Report,[4] considerable evidence has emerged regarding the relative benefits of various modes or combinations of physical activity (e.g., progressive resistance training, multicomponent exercise, dual-task training, tai chi, yoga, dance) for specific physical function outcomes (e.g., strength, gait speed, balance, activities of daily living (ADL) function). The term “multicomponent” refers to physical activity interventions that include more than one type (or mode) of physical activity, with common types being aerobic, muscle-strengthening, and balance training. Dual-task interventions combine a physical activity intervention with a cognitive intervention (such as counting backward). Also, there is now convincing evidence of the magnitude of risk reduction in fall-related injuries due to various physical activity interventions. In addition, the current research has begun to address the issues of the dose-response relationship between physical activity and physical function in aging, as well as of the minimal effective dose and the maximal threshold for safety.

The *2018 Physical Activity Guidelines Advisory Committee Report* expands upon the 2008 Scientific Report by examining the relationship between physical activity and the risk of fall-related injuries, as well as the relationship between physical activity and physical function, in both the general aging population and in people living with specific chronic diseases. The 2018 Scientific Report further leverages current research in examining: 1) the dose-response relationship between exposure and outcome; 2) the mode of activity most beneficial to a specific functional outcome; and 3) whether the relationship between physical activity and physical function varies by age, race, sex, socioeconomic characteristics, or by body weight.

REVIEW OF THE SCIENCE

Overview of Questions Addressed

This chapter addresses three major questions and related subquestions:

1. What is the relationship between physical activity and risk of injury due to a fall?
   a) Is there a dose-response relationship? If yes, what is the shape of the relationship?
   b) Does the relationship vary by age, sex, race/ethnicity, socioeconomic status, or weight status?
   c) What type(s) of physical activity are effective for preventing injuries due to a fall?
   d) What factors (e.g., level of physical function, existing gait disability) modify the relationship between physical activity and risk of injury due to a fall?

2. What is the relationship between physical activity and physical function among the general aging population?
   a) Is there a dose-response relationship? If yes, what is the shape of the relationship?
   b) Does the relationship vary by age, sex, race/ethnicity, socioeconomic status, or weight status?
   c) What type(s) of physical activity (single component, dual task, multicomponent) are effective for improving or maintaining physical function among the general aging population?
   d) What impairment(s) (e.g., visual impairment, cognitive impairment, physical impairment) modify the relationship between physical activity and physical function among the general aging population?

3. What is the relationship between physical activity and physical function in older adults with selected chronic conditions?

Data Sources and Process Used to Answer Questions

The Aging Subcommittee determined that systematic reviews, meta-analyses, pooled analyses, and reports provided sufficient literature to answer two of its three research questions. For Question 1 (*What is the relationship between physical activity and risk of injury due to a fall?)* the Subcommittee identified that existing reviews (systematic reviews, meta-analyses, pooled analyses, and reports) covered only a portion of the science. Specifically, the existing reviews provided evidence from randomized controlled trials (RCTs), but not evidence from cohort or case-control studies. A supplementary search for cohort and case-control studies was conducted to capture the most complete literature.

Question 1: What is the relationship between physical activity and risk of injury due to a fall?

a) Is there a dose-response relationship? If yes, what is the shape of the relationship?
b) Does the relationship vary by age, sex, race/ethnicity, socioeconomic status, or weight status?
c) What type(s) of physical activity are effective for preventing injuries due to a fall?
d) What factors (e.g., level of physical function, existing gait disability) modify the relationship between physical activity and risk of injury due to a fall?

Sources of evidence: Systematic reviews and/or meta-analyses, a high-quality existing report, prospective cohort studies, a case-control study.

Conclusion Statements

Strong evidence demonstrates that participation by community-dwelling older adults in multicomponent group or home-based fall prevention physical activity and exercise programs can significantly reduce the risk of injury from falls, including severe falls that result in bone fracture, head trauma, open wound soft tissue injury, or any other injury requiring medical care or admission to hospital. **PAGAC Grade: Strong.**

Limited evidence suggests that a dose-response relationship exists between the amount of moderate-to-vigorous physical activity or home and group exercise and risk of fall-related injury and bone fracture. However, the small number of studies available and the diverse array of physical activities studied make it difficult to describe the shape of the relationship. **PAGAC Grade: Limited.**

Insufficient evidence is available to determine whether the relationship between physical activity and risk of injury and bone fracture due to a fall varies by age, sex, race/ethnicity, socioeconomic status, or weight status. **PAGAC Grade: Not assignable.**

Moderate evidence indicates that the risk of fall-related injury and bone fracture may be reduced using a variety of community-based group and home physical activities. Effective multicomponent physical activity regimens generally include combinations of balance, strength, endurance, gait, and physical function training, along with recreational activities. **PAGAC Grade: Moderate.**

Insufficient evidence is available to determine whether other factors (e.g., level of physical function ability and pre-existing gait disability) modify the relationship between physical activity and risk of injury due to a fall. **PAGAC Grade: Not assignable.**

Review of the Evidence

The 2008 Scientific Report stated that, "clear evidence demonstrates that participation in physical activity programs is safe and can effectively reduce falls in older adults at elevated risk of falls."[4] The 2008 Scientific Report also noted, however, that insufficient information was available from RCTs to assess the effects of regular physical activity on injuries resulting from falls. Since 2008, a number of RCTs have examined this question, and the evidence from these trials is summarized below.

The Subcommittee based its conclusions on evidence published between January 2006 and December 2016. This evidence came from three existing systematic reviews and meta-analyses of RCTs,[5-7] one high-quality report on RCT research in this area,[8] three prospective cohort studies,[9-11] and one case-control study.[12] Participants included in these studies were non-hospitalized, ambulatory adults, ages 50 years and older. The exposure of interest was all types and intensities of physical activity, and the outcomes of interest were all or any injuries from falls; fractures from falls; head injuries from falls; intra-abdominal injury from falls; medically attended injury from falls; neck, back, and spine injuries from falls; "pooled" injuries from falls; and sprains from falls.

Evidence on the Overall Relationship

Results from these systematic reviews and/or meta-analyses of RCTs consistently support that fall prevention physical activity programs effectively reduce the risk of fall-related injuries by 32 to 40 percent and bone fractures by 40 to 66 percent among older adults in community and home settings.[5-8] These RCT findings are supported by data from three prospective cohort studies[9-11] and one case-control study.[12]

El-Khoury et al[5] reviewed 17 individual RCTs and performed a meta-analysis on 10 of them (N=4,305 participants ages 60 years and older). Although the definitions and classifications of injurious falls varied widely among the RCTs, their findings strongly suggest that structured physical activity interventions reduced the risk of all fall-related injuries by approximately 37 percent (pooled relative risk (RR)=0.63; 95% confidence interval (CI): 0.51-0.77). The risk of fall-related injuries requiring medical care was reduced by 30 percent (pooled RR=0.70; 95% CI: 0.54-0.92, based on 8 trials) and the risk of a severe fall-related injury (such as a fracture, head trauma, soft tissue injury requiring suturing, or any other injury requiring admission to hospital) was reduced by 43 percent (pooled RR=0.57; 95% CI: 0.36-0.90, based on 7 trials). Finally, the risk of a fall resulting in a fracture was reduced by 61 percent (pooled RR=0.39; 95% CI: 0.22-0.66, based on 6 trials). Moreover, the benefits of physical activity programs to reduce the risk of these four categories of fall-related injuries were similar between older adults identified as being at high risk of falling versus those who were at an unspecified risk.

More recently, Zhao et al[7] reported that among 15 RCTs including 3,136 participants ages 53 to 83 years, physical activity reduced the risk of fall-related fractures by 40 percent (pooled RR=0.60; 95% CI: 0.45-0.84). A comparable finding of 43 percent reduced risk of fall-related fractures was reported when a sensitivity analysis was performed to retain only the 11 studies deemed "low" overall risk of bias (RR=0.57; 95% CI: 0.41-0.81). Gillespie et al[6] reported that among 6 RCTs including 810 participants, structured physical activity interventions reduced the risk of a fall-related fracture by 66 percent (pooled RR=0.34; 95% CI: 0.18 to 0.63).

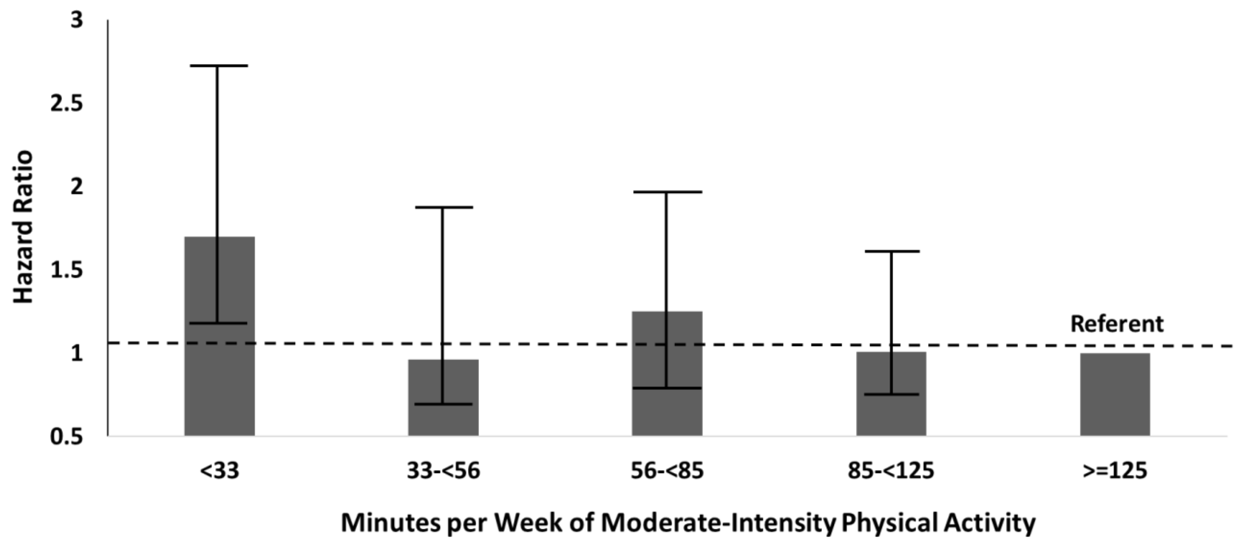
Results from a meta-analysis of studies involving community-dwelling adults ages 65 years and older[8] suggest that participation in physical activity programs tailored to the risk factors and needs of each participant (i.e., "targeted" exercise) reduced the risk of fall-related injury by 33 percent (pooled RR=0.67; 95% CI: 0.51–0.89, based on 3 studies and 546 participants). Those programs designed to be the same for all participants ("untargeted" exercise) reduced the risk of fall-related injury by 56 percent (RR=0.44; 95% CI: 0.27–0.72, based on 2 studies and 426 participants). Long-term (6 months or longer) targeted and untargeted physical activity programs reduced the risk of fall-related injury by 32 percent (RR=0.68; 95% CI: 0.51-0.90, based on 2 studies and 453 participants) and by 39 percent (RR=0.61; 95% CI: 0.33-1.12, based on 2 studies and 358 participants), respectively.

Dose-response: Results of the meta-analyses of RCTs suggest an inverse dose-response relationship between the amount of moderate-to-vigorous physical activity performed and the magnitude of the reduction in risk of fall-related injuries and bone fractures, regardless of whether the intervention is home- or group-based. Multicomponent physical activity regimens that combine aerobic, strength, and balance training appear to be especially effective. The small number of studies and the diverse ways in which the amount of physical activity was operationalized limit confidence in making a strong statement about the shape of the dose-response of physical activity on risk of injuries from falls, however.

Consistent results from four high-quality epidemiologic studies (three cohort and one case-control) suggest that adults ages 65 years and older who participate in physical activity of at least moderate-intensity for 30 or more minutes per day[9] or for 25 or more metabolic equivalents per week,[10] reduce the risk of fall-related injury and bone fracture. Evidence also exists that even adults ages 85 years and older obtain similar benefits from 60 minutes or more per week of home- or group-based physical activity.[11] However, it is important to note that lower amounts of moderate-intensity physical activity[9, 10] and walking[11] may not be sufficient to reduce the risk of fall-related injury and bone fracture in older age.

For example, Heesch et al[10] reported that among 8,188 healthy, Australian community-dwelling women (ages 70 to 75 years), self-reported high or very high levels of physical activity were associated with a 47 percent lower 6-year risk of self-reported bone fracture, compared with women who reported none or very low levels (referent group) (OR=0.53; 95% CI: 0.34-0.83). Those women reporting low (OR=0.84; 95% CI: 0.62-1.13) or moderate (OR=0.88; 95% CI: 0.66-1.19) levels of activity, however, did not significantly lower their risk of fracture. Iinattiniemi et al[11] reported findings from 512 community-dwelling Finnish adults ages 85 years and older (the majority of whom were female). Respondents who reported participating in physical activities such as home exercise, gardening, cross-country skiing, dancing, swimming, bicycling, or group exercise for more than 60 minutes per week reduced their risk of sustaining a fall-related injury by 63 percent, compared with not performing any of these activities (OR=0.37; 95% CI: 0.19-0.72). Among this same sample, however, walking did not appear to affect the risk of injury from a fall. Indeed, those who reported walking fewer than 60 minutes per week (OR=0.87; 95% CI: 0.50-1.50), 60 to 140 minutes per week (OR=0.94; 95% CI: 0.56-1.58), and more than 140 minutes per week (OR=0.83; 0.46-1.48) experienced no significant reduction in risk of fall-related injury. In a case-control study of hip fracture among 387 Australian adults ages 65 years and older (126 cases: 261 controls), Peel et al[12] reported that playing sport in older age independently reduced the risk of hip fracture by 51 percent (adjusted OR=0.49; 95% CI: 0.29-0.83). Simply achieving “sufficient” versus “insufficient” levels of physical activity (based on minutes per week of walking and moderate and/or vigorous activity) did not reduce risk. Finally, Cauley et al[9] studied a cohort of men (N=2,731; mean age 79 years) over an average follow-up period of 3.5±0.9 years. They reported that men in the lowest quintile of daily active energy expenditure (less than190 kilocalories per day) had a significantly higher risk of non-spine fracture compared with men in the highest quintile (greater than or equal to 775 kilocalories per day; referent group) (hazard ratio (HR)=1.82; 95% CI: 1.10-3.00). Those men in the lowest quintile of daily moderate-intensity activity (less than 33 minutes per day) experienced a 70 percent higher risk of fracture compared with those in the highest quintile (greater than or equal to 125 minutes per day; referent group) (HR=1.70; 95% CI: 1.03-2.80). Of note, is that quintiles 2 (33 to less than 56 minutes per day), 3 (56 to less than 85 minutes per day), and 4 (85 to less than 125 minutes per day) of moderate-intensity activity were not associated with an increased rate of fracture, compared with quintile 5. A similar finding was observed for energy expenditure from moderate-intensity activity, suggesting that a minimal threshold of 33 minutes per day of moderate-intensity activity (or of 190 calories per day of active energy expenditure) was sufficient to negate the excess risk of fall-related fractures in these men (Figure F9-1).

Figure F9-1. 3.5 Year Risk of Fracture in Older Men by Quintile of Moderate-Intensity Physical Activity: The Osteoporotic Fractures in Men Study (N=2,731)



Source: Adapted from data found in Cauley et al., 2013.[9]

Evidence on Specific Factors

Demographic factors and weight status: Cauley et al[9] reported that age (younger than 80 years versus 80 years and older) did not influence the relationship between higher levels of active energy expenditure or moderate-intensity physical activity and lower risk of fracture in a cohort of men ages 65 years and older. Consistent with this observation, the benefit of physical activity to reduce the risk of fall-related injury was similar among women ages 70 to 75 years[10] and adults ages 85 years and older.[11]

Although the majority of participants in the reviewed studies were female, the benefit of physical activity to reduce the risk of fall-related injuries appears consistent in cohorts of men[9] as well as women.[10] Of note, is the fact that none of the studies reviewed deliberately tested effect modification by sex. Moreover, among 512 Finnish home-dwelling adults, ages 85 years and older, female sex was one predictor of injurious falls, but its impact on the relationship between physical activity and fall-related injuries was not specifically assessed.[11]

Information on the race/ethnicity and socioeconomic status of participants was limited, inconsistently presented, and not statistically assessed. As a result, no conclusions about these relationships were possible.

Weight status did not significantly influence the relationship between physical activity and bone fracture risk among cohorts of women ages 70 to 75 years[10] or among men ages 65 years and older.[9]

Type of physical activity: The physical activity programs that effectively reduced the risk of fall-related injuries and bone fractures contained a variety of group- and home-based activities.[5, 7, 8, 11, 12] Most programs were multicomponent and included various combinations of moderate-intensity balance, strength, endurance, gait, and physical function training, as well as recreational activities (e.g., dancing, cycling, gardening, sports). Although the research is limited, it does not support the use of low-intensity walking as a primary mode of physical activity to reduce the risk of fall-related injuries and fractures among older adults,[11, 12] although walking may be included in multicomponent physical activity regimens. Unfortunately, insufficient information was available from the systematic reviews to determine the effects of individual elements (e.g., strength training, balance training) of the multicomponent training programs on the risk of fall-related injuries.

Factors modifying the relationship: The impact of physical activity on risk of fall-related injury in older age may be influenced by factors such as level of physical function or pre-existing gait disability. Unfortunately, the eight articles used as sources of evidence do not contain sufficient information to address this subquestion.

For additional details on this body of evidence, visit: https://health.gov/paguidelines/second-edition/report/supplementary-material.aspx for the Evidence Portfolio.

Comparing 2018 Findings with the 2008 Scientific Report

The 2008 Scientific Report[4] presented compelling evidence that older adults may safely participate in physical activity programs to reduce their risk of falling. The evidence evaluated by the Subcommittee further emphasizes that multicomponent physical activity programs can reduce the risk of injuries and fractures due to a fall among older people. These 2018 findings expand upon those from 2008 in providing strong evidence of the magnitude of risk reduction in fall-related injuries (30 to 40 percent) and fractures (40 to 66 percent) resulting from these highly-feasible multicomponent programs.

Public Health Impact

One in four individuals ages 65 years and older falls in the United States every year. Moreover, falls are the leading cause of fatal injury and the most common cause of nonfatal trauma-related hospital admissions among older adults. Physical activity programs that emphasize combinations of moderate-intensity balance, strength, endurance, gait, and physical function training appear most effective in reducing the risk of fall-related injuries and fractures in older adults. Thus, the effectiveness of these programs (performed in community settings or at home) for risk reduction has significant public health relevance in older age, due to the high prevalence of falls and fall-related injuries and fractures among older adults, as well as the consequent morbidity, disability and reduced quality of life.

Question 2: What is the relationship between physical activity and physical function among the general (i.e., non-institutionalized) aging population?

a) Is there a dose-response relationship? If yes, what is the shape of the relationship?
b) Does the relationship vary by age, sex, race/ethnicity, socioeconomic status, or weight status?
c) What type(s) of physical activity are effective for improving or maintaining physical function?
d) What impairment(s) modify the relationship between physical activity and physical function among the general aging population?

Sources of evidence: Systematic reviews, meta-analyses, pooled analyses

Conclusion Statements

Strong evidence demonstrates that physical activity improves physical function and reduces risk of age-related loss of physical function in the general aging population. **PAGAC Grade: Strong.**

Strong evidence demonstrates an inverse dose-response relationship between volume of aerobic physical activity and risk of physical functional limitations in the general aging population. **PAGAC Grade: Strong.**

Limited evidence suggests an inverse dose-response relationship of volume of muscle-strengthening and frequency of balance training with risk of physical functional limitations in the general aging population. **PAGAC Grade: Limited.**

Limited evidence suggests that the relationship between physical activity and physical function does not vary by age, sex, or weight status in the general population of older adults. **PAGAC Grade: Limited.**

Insufficient evidence is available to determine whether the relationship between physical activity and physical function varies by race/ethnicity and socioeconomic status in the general population of older adults. **PAGAC Grade: Not assignable.**

Strong evidence demonstrates that aerobic, muscle-strengthening, and multicomponent physical activity improves physical function in the general aging population. **PAGAC Grade: Strong**.

Moderate evidence indicates that balance training improves physical function in the general aging population. **PAGAC Grade: Moderate**.

Limited evidence suggests that tai chi exercise, dance training, active video gaming, and dual-task training improve physical function in the general aging population. **PAGAC Grade: Limited**.

Insufficient evidence is available to determine the effects of flexibility activity, yoga, and qigong exercise on physical function in the general aging population. **PAGAC Grade: Not assignable**.

Limited evidence suggests that the effect of physical activity on physical function is relatively stronger in older adults with limitations in physical function compared to relatively healthy older adults. **PAGAC Grade: Limited.**

Insufficient evidence is available to determine whether visual impairments or cognitive impairments modify the relationship between physical activity and physical function among the general aging population. **PAGAC Grade: Not assignable**.

Review of the Evidence

Introduction

Age-related limitations in physical function are prevalent in older adults. The National Health Interview Survey ascertained the prevalence of physical limitations in 2001-2007, with limitations defined as great difficulty doing (or inability to do) basic tasks of life (e.g., walk a quarter of a mile, lift a 10-pound bag of groceries).[13] At that time, 22.9 percent of older adults ages 60 to 69 years reported limitations and 42.9 percent of adults ages 80 years and older reported limitations. The 2008 Scientific Report[4] addressed the extent that physical activity reduces risk of limitations in physical function, reasoning that “If physical activity prevents or delays disability, the majority of older Americans stand to benefit.” However, the 2008 strength of evidence rating of “moderate to strong” reflected the fact that evidence was incomplete in some respects, such as a lack of well-designed intervention trials and insufficient evidence for quantifying effects of physical activity.[4] Also, the conclusion did not explicitly address the effect of physical activity on physical function, but rather stated physical activity reduced risk of “function and/or role limitations.”[4] Thus, the Subcommittee deemed this report should determine the extent that additional research is now available on physical activity and physical function in older adults.

Literature Reviewed

To address the relationship between physical activity and physical function among the general aging population, the Aging Subcommittee reviewed 17 systematic reviews,[14-30] 20 meta-analyses,[31-50] and 1 pooled analysis.[51] As described below, the reviews were sorted by the types of physical activity reviewed, and by whether they included or excluded studies of the effects of physical activity on physical function in study samples with a single, diagnosed chronic condition.

Reviews of RCTs of Aerobic, Muscle-Strengthening, Balance, and/or Multicomponent Physical Activity Programs, **Excluding** Studies Limited to Specific Chronic Conditions.

Three meta-analyses and one systematic review focused on healthy or community-dwelling older adults. Of the three meta-analyses, one included 23 RCTs,[39] one included 37 randomized and 5 non-randomized trials,[36] and one included 24 studies of which 13 were RCTs.[43] Total participants in these reviews ranged from 1,220 to 2,495. One systematic review included eight relevant trials.[22]

Three meta-analyses and two systematic reviews included studies in all older adults. Three meta-analyses included between 19 and 94 RCTs, though numbers of comparisons in individual analyses were commonly in the range of 5 to 15.[33, 37, 49] In the Cochrane meta-analyses of 133 separate analyses—many with a very small number of studies—the relevant analyses were deemed to be those reported in the abstract by the authors.[37] Some studies in two systematic reviews address effects of exercise on physical function.[14, 15]

Reviews of RCTs of Aerobic, Muscle-Strengthening, Balance, and/or Multicomponent Physical Activity Programs, **Including** Studies Limited to Specific Chronic Conditions

Three meta-analyses focused on community-dwelling older adults.[31, 35, 38] The total number of included studies ranged from 11 to 28, and total participants ranged from 617 to more than 2,500.

Three meta-analyses and four systematic reviews included studies in all older adults. Two meta-analyses reported the findings of the same review involving 33 RCTs in 2,172 older adults.[41, 42] One meta-analysis included studies in both older and younger adults, so it was regarded as a systematic review of 15 studies in older adults.[34] Some studies in four systematic reviews addressed effects of exercise on physical function.[16, 17, 23, 28]

Other Reviews of Aerobic, Muscle-Strengthening, Balance, and/or Multicomponent Physical Activity Programs

One meta-analysis compared effects of progressive resistance training to power training.[48] Power training involves exercising against moderate resistance at maximum speed ("as fast as possible"), in the range of 33 to 60 percent of the maximum speed without resistance.[48] In contrast, conventional resistance training typically involves exercising against high resistance at relatively slow speeds. This meta-analysis included 11 trials involving 377 participants. Four reviews of cohort studies addressed the effect of physical activity on physical function: one meta-analysis of 9 studies involving 17,000 participants,[46] two broad systematic reviews that included some relevant studies,[24, 29] and one pooled analysis involving 357 participants.[51]

Reviews of Controlled Trials of Tai Chi, Yoga, Qigong, and Flexibility Training

The Subcommittee identified three reviews of RCTs of tai chi, yoga, and/or qigong—one meta-analysis of tai chi,[40] one systematic review of tai chi or qigong,[26] and one meta-analysis of yoga.[50] The total number of included studies ranged from 13 to 36 RCTs. One systematic review of flexibility training included 22 studies in 1,127 participants.[27]

Reviews of Dance, Video Games, and Dual-task Physical Activity Programs

The Subcommittee identified one systematic review of seven RCTs of dance interventions,[18] and one systematic review of 15 training studies and 3 cross-sectional studies of dancing.[21] Three meta-analyses of active video gaming[32, 45, 47] included between 16 and 18 studies.

Five reviews examined effects of dual-task training on physical function. One meta-analysis included 14 RCTs,[44] and four systematic reviews included some relevant studies.[19, 20, 25, 30]

Lifestyle Interventions and Independence for Elders (LIFE) Study

The Aging Subcommittee was aware of a trial called "LIFE", a large RCT of multicomponent exercise on a primary outcome of mobility disability.[2] The trial enrolled older adults with limitations in physical function, had a sample size of 1,635, with an exercise intervention lasting an average of 2.6 years. The trial found exercise significantly reduced risk of mobility disability, defined as inability to walk 400 meters (HR=0.82; 95% CI: 0.69-0.98). The Subcommittee was unable to locate this particular study in the above-cited reviews, so it was not included in the sources of evidence. However, the Subcommittee notes that, had this study been included as source of evidence, it would not change the conclusions of the chapter. In particular, the LIFE results were consistent with the Subcommittee's rating of strong evidence that physical activity has beneficial effects on physical function in older adults. LIFE reported a non-significant trend for stronger effects of exercise in adults with more limited function (HR=0.75; 95% CI: 0.60-0.94) compared to less limited (HR=0.95; 95% CI: 0.73-1.23), which does not contradict (and is consistent with) the Subcommittee's conclusion of limited evidence that effects are stronger in older adults with limitations in physical function than in healthy older adults. LIFE reported that effects of exercise did not differ by sex or age, which is consistent with the Subcommittee's finding of limited evidence that effects of physical activity do not differ by sex or age.

Evidence on the Overall Relationship

The reviews of RCTs and cohort studies of aerobic, muscle-strengthening, balance, and/or multicomponent physical activity programs provided strong evidence that physical activity improves physical function and reduces risk of age-related loss of physical function in the general aging population. Significant effects of physical activity on physical function were reported by all meta-analyses whose results are summarized in Table F9-1, whether or not the meta-analyses (1) excluded studies limited to a specific chronic condition, (2) limited analyses to community dwelling or healthy adults, and (3) included only RCTs. The conclusions of systematic reviews also generally supported this conclusion.[14-17, 22, 28] In most cases, the measure of physical function was an "objective" or performance-based measure. Performance tests are classified by the task involved. For example, a common "gait" measure is speed of walking in meters per second measured over a short 3- or 4-meter course. A common "balance" measure is the ability to stand on one leg, with stance time measured in seconds. In the evidence description below, terminology is simplified. A statement that "physical activity improved balance" means "physical activity improved performance measures of physical function using balance tasks." However, some reviews included self-report measures of physical function, such as the 36-item Short Form Survey (SF-36) physical functioning scale, and ADL scales.

The Subcommittee regarded one meta-analysis[31] as a particularly relevant source of evidence. This review was recent (2017) and included only RCTs that reported objective, composite outcome measures of physical function, such as the Short Physical Performance Battery (SPPB). The review had a good quality score and included a large number (N=28) of RCTs focused on community-dwelling older adults. This meta-analysis reported an effect size (ES) of 0.45 (95% CI: 0.27-0.64).

The findings of the more relevant meta-analyses (which excluded studies limited to a specific chronic condition) supported the conclusion of strong evidence.[33, 36, 37, 39, 43, 49] These six meta-analyses analyzed effects of physical activity according to type (muscle-strengthening, balance, multicomponent, any) and outcome measure (any objective measure, measures of gait speed, measures of balance, chair rise, Timed Up and Go, and ADL). Effect sizes (see Table F9-1) ranged from small (improvement of 1.6 seconds in eyes-closed one-leg stand time[37]) to large (ES=0.84 for resistance training on usual gait speed[36]).

Almost all analyses demonstrated a significant effect of a mode of physical activity on the above measures of physical function, though two analyses found a borderline significant effect and one analysis of ADL measures found a non-significant effect. A meta-analysis of balance training classified measures of balance into five categories (static and dynamic steady state; proactive and reactive balance; and performance on standard test batteries [e.g., Berg Balance Scale]), with significant effects of balance training found for all five categories.[39] However, the most public health relevant balance measure reported was the effect of balance training on composite performance measure of balance—the Berg Balance scale—and only the effect of training on the Berg Balance Scale are included in the table. Other categories of measures of balance generally included some physiologic measures of balance, such as force plate measures of postural sway.

Table F9-1. Effects of Physical Activity from Meta-Analyses of RCTs of Aerobic, Muscle-Strengthening, Balance, and/or Multicomponent Physical Activity Programs

Measure of Physical Function	Muscle-strengthening	Balance
	Effect; (confidence interval), test	**Effect; (confidence interval), test**
Combined Analyses		
Gait speed	ES=0.84; (95% CI: 0.52-1.16)[36] R=0.15; (95% CI: 0.03-0.26)[43] MD=0.13 m/s; (95% CI: 0.09–0.16)[49] SMD=0.25 m/s; (95% CI: 0.05-0.46)[37]	MD=0.07 m/s; (95% CI: 0.03-0.10)[49] #
Balance	MD=1.64 s; (95% CI: 0.97-2.13) OLSC[37]	SMD=1.52; (95% CI: 0.65-2.39), BBS[39]
Chair rise		
Timed Up and Go	MD=-4.30 s; (95% CI: -7.60 to -1.00)[37]	
Activities of Daily Living Scale		

Measure of Physical Function	Multicomponent	Any
	Effect; (confidence interval), test	**Effect; (confidence interval), test**
Combined Analyses		ES=0.37; (95% CI: 0.22- 0.52)[33]
Gait speed	ES=0.86; (95% CI: 0.50-1.23)[36] R=0.18; (95% CI: 0.12-0.24)[43] MD=0.05 m/s; (95% CI: 0.00-0.09)[49] *	ES=0.84; (95% CI: 0.61-1.06)[36] R=0.17; (95% CI: 0.11-0.22)[43] ES=0.26; (95% CI: 0.11-0.41)[33]
Balance	MD=5.03 s; (95% CI: 1.19-8.87), OLSO[37] MD=1.60 s; (95% CI: -0.01-3.20), OLSC[37] * MD=1.84; (95% CI: 0.71-2.97), BBS[37]	ES=0.27; (95% CI: 0.11-0.42)[33]
Chair rise		ES=0.30; (95% CI: 0.04-0.57)[33]
Timed Up and Go	MD=-1.63 s; (95% CI: 95% CI: -2.28 to -0.98)[37]	
Activities of Daily Living Scale		ES=0.05; (95% CI: -1.25-0.22)[33] ns

Legend: CI=confidence interval, ES=effect size, MD=mean difference, m/s=meters per second, s=seconds, SMD=standardized mean difference, R=Pearson correlation coefficient, BBS=Berg Balance Scale, OLSO=one leg stand eyes open, and OLSC=one leg stand eyes closed.
Note: Meta-analyses in this table excluded studies limited to specific chronic conditions. Reported measures of effect and confidence intervals may be rounded to two significant digits. Four meta-analyses included only RCTs.[33, 37, 39, 49] One meta-analysis included both randomized and non-randomized controlled trials[36] and one meta-analysis included randomized trials, non-randomized trials, and single arm trials.[43] Positive effects indicate improvement due to physical activity, except for the Timed Up and Go (where lower scores indicate better function). *=borderline significant effect, where one side of the 95% CI was either 0[43] or -0.01.[37] All other effects are statistically significant unless marked "ns"=non-significant. #=an analysis of dance-like movements was classified as balance training. Muscle strengthening was generally resistance training, but could include studies of power training (e.g., in Howe et al[37]). No meta-analysis analyzed effects of aerobic training only. Combined analyses included resistance, balance, and endurance training[49]; "multiple exercise types"[37]; and "multi-modal training."[36] Analyses of "Any" training generally included trials of single activity types and multicomponent training.

The Subcommittee also reviewed findings of the other meta-analyses (which included studies limited to a specific chronic condition) to assess whether their findings were similar. The findings in these reviews also supported the conclusion of strong evidence and included the review by Chase et al[31] discussed above.[31, 35, 38, 41, 42] The reported effects of physical activity on performance measures were comparable to those in Table F9-1 in analyses including more than two or three comparisons. For example, an analysis of four trials of home-based fall prevention programs reported a significant effect of multicomponent physical activity on the balance measure of functional reach (MD=1.6 cm; 95% CI: 0.37-

2.76).[35] A meta-analysis of 33 RCTs of progressive resistance training reported significant effects on: (1) self-reported physical function or disability measured by a variety of instruments (standardized mean difference (SMD)=0.14; 95% CI: 0.05-0.22), (2) walking ability as measured by gait speed (SMD=0.08 meters per second; 95% CI: 0.04-0.12) (though not when measured by timed walks), (3) Timed Up and Go (SMD= -0.69 seconds; 95% CI: -1.11 to -0.27), and (4) timed chair rise (SMD=0.94; 95% CI: -1.49 to -0.38).[41, 42] Although one meta-analysis of any physical intervention reported a significant effect of physical activity on the SF-36 physical functioning scale (Hedges's g=0.41; 95% CI: 0.19-0.64),[38] a meta-analysis of only muscle-strengthening training found no effect.[42]

The Subcommittee noted that no meta-analysis provided an estimate of the effect of aerobic activity on physical function. However, in one systematic review of 53 RCTs of aerobic training,[16] 7 trials assessed effects of training on physical function. Of these, six reported at least one significant effect. Notably, all 53 studies prescribed aerobic training using relative intensity.

The Subcommittee also noted that one meta-analysis reported a non-significant effect of any activity on ADL score.[33] However, a systematic review prepared for Canada's physical activity guidelines reviewed cohort studies of aerobic activity in older adults.[24] This review concluded that aerobic activity can reduce risk of functional limitations, including ADL dependency, by as much as 50 percent. This finding was supported by a meta-analysis of cohort studies with physical activity measures that focused on aerobic activity.[46] This review reported low versus moderate-to-high amounts of physical activity have a large and significant reduction in risk of ADL dependency (odds ratio (OR)=0.51; 95% CI: 0.38-0.68).

Dose-response: A review of 24 comparisons from prospective cohort studies with covariate adjustment provided strong evidence of an inverse dose-response relationship between aerobic activity and risk of functional limitations.[24] This review classified dose of aerobic activity reported in cohort studies into four ordinal categories, ranging from 1=low level of activity to 4=vigorous activities and/or high activity volume. With this analysis framework, virtually every study showed an inverse dose-response relationship of aerobic activity with risk of limitations in physical function.

A meta-analysis of 23 studies of balance training provided limited evidence of a dose-response relationship between dose of balance training and physical function.[39] This review classified measures of balance into five categories (static and dynamic steady state; proactive and reactive balance; and performance on standard test batteries [e.g., Berg Balance Scale]), but dose-response data were provided for only one category (static steady state balance). When the dose of balance training was measured as number of sessions per week (1 versus 2 versus 3), the number of sessions was associated with amount of improvement in balance in a dose-response manner.

Limited evidence also suggested a dose-response relationship with muscle-strengthening training. One meta-analysis reported the number of repetitions of resistance training was significantly (P<0.01) and positively related to the effect of the training on composite objective measures of physical function, with a trend of more improvement in function with more sets of resistance training (P=0.09).[31] However, the review did not further describe or quantify the dose-response relationship.

Evidence on Specific Factors

Age, sex, weight status: Limited evidence suggests that the relationship between physical activity and physical function does not vary by age, sex, or weight status in the general population of older adults. One meta-analysis reported sex and body mass index (BMI) were not significant effect modifiers of the relationship of physical activity on composite physical function scores.[31] A meta-analysis of cohort studies reported the relationship between aerobic activity and ADL dependency did not differ significantly by age (75 years and younger versus older than 75 years).[46]

Race/ethnicity, socioeconomic status: The available evidence was insufficient to determine whether the relationship between physical activity and physical function varies by race/ethnicity and socioeconomic status in the general population of older adults. No relevant analyses were located in the sources of evidence.

Types of Activity

Aerobic, muscle-strengthening, and multicomponent physical activity: Strong evidence demonstrates that aerobic, muscle-strengthening, and multicomponent physical activity improves physical function in the general aging population. The evidence for this finding was discussed above. In addition, the Subcommittee reviewed one meta-analysis of seven RCTs comparing two types of muscle-strengthening physical activity—power training and resistance training.[48] The meta-analysis reported a small advantage of power training over resistance training in improving physical function in older adults. These results illustrate that conventional resistance training is not the only type of muscle-strengthening activity that improves physical function in older adults.

Tai chi: Limited evidence suggests that tai chi improves physical function. A systematic review reported that 11 of 12 relevant RCTs found tai chi improved at least one measure of physical function (relevant trials included a general sample of older adults and a no-exercise control group).[26] However, this review did not report quality scores. One meta-analysis assessed the effects of tai chi on a single physical function outcome—one leg stand time—and reported a non-significant effect.[40] No analyses were located that addressed how types, forms, and dose of tai chi influence its effects on physical function.

Yoga: Insufficient evidence was available to determine the effects of yoga on physical function. The one review of yoga included only three relevant studies (general sample of older adults and a no-exercise control group).[50] Data in the review showed that only 1 of the 3 studies reported a significant effect on balance-related physical function, and one of two studies reported a significant effect on mobility.

Qigong: Insufficient evidence was available to determine the effects of qigong on physical function. In the review that included studies of qigong, only one of the qigong studies was relevant (general sample of older adults, no-exercise control group, and physical function outcome).[26]

Flexibility: Insufficient evidence was available to determine the effect of flexibility training on physical function. A systematic review of 22 studies concluded the information regarding the relationship between functional outcomes with flexibility interventions was conflicting.[27] A meta-analysis of three studies of flexibility training found a non-significant effect of flexibility training on gait speed.[49]

Dancing: Limited evidence suggests dance interventions improve physical function. One review reported that dancing had positive effects on gait in five of five trials and positive effects on balance in six of six trials.[18] Another reviewed reported that dancing improved either balance and/or gait in 8 of 13 trials.[21] However, both reviews expressed concerns about how to interpret the evidence, given the diversity of dance forms studied, the diversity of outcome measures, and the small sample size of many studies. No analyses were located that addressed how the types of dance and dose influence the effects of dancing on physical function.

Active Video Gaming: Limited evidence suggests active video gaming interventions improve physical function. The meta-analysis with the largest number of trials reported significant effects of active video gaming on balance (SMD=0.77; 95% CI: 0.45-1.09; 16 comparisons) and functional mobility (SMD=0.56; 95% CI: 0.25-0.78; 17 comparisons).[32] However, the sample sizes of the trials were small, with only one trial enrolling more than 20 older adults in the intervention group. These findings were not consistently confirmed by two smaller meta-analyses: one reported a small significant effect on Berg Balance scores (MD=0.73; 95% CI: 01.7-1.29; three comparisons) and no significant effect on Timed Up and Go (six comparisons).[47] The other reported a non-significant effect on Timed Up and Go (three comparisons).[45] One review reported that video game activity was supervised in 17 of 18 trials,[47] indicating the evidence is incomplete that older adults can improve physical function by self-supervised active video gaming.

Dual-task Training: Limited evidence suggests dual-task training improves physical function. As mentioned previously, dual-task interventions combine a physical activity intervention with a cognitive intervention. For example, a dual-task verbal fluency intervention could involve naming words beginning with a particular letter during a walking activity. One meta-analysis of 14 RCTs reported a significant improvement in gait speed under dual-task conditions, with overall mean difference (MD)=0.11 meters per second (95% CI: 0.07-0.15).[44] Significant effects were reported for the subgroup of trials with verbal fluency dual-task condition (MD=0.09 meters per second; 95% CI: 0.05-0.14) and arithmetic dual-task condition (MD=0.11 meters per second; 95% CI: 0.06-0.16). However, most trials were small and trials varied in definition and types of dual-task training, types of physical activity, and quality. Information provided by systematic reviews was consistent with the finding of limited evidence.[19, 20, 25, 30]

Modification of Effects by Impairments

Physical impairments: Limited evidence suggests that physical activity has a stronger effect on physical function in older adults with limitations in physical function, compared with relatively healthy older adults. One meta-analysis compared the effect size in non-frail adults (ES=0.35; 95% CI: 0.17-0.54) to that in frail adults (ES=1.09; 95% CI: 0.55-1.64) and found the effect size was significantly larger in frail adults ($P<0.05$).[31] The strong effects of physical activity on physical function in frail adults (Question 3 below) are consistent with this finding.

Visual or cognitive impairments: The available evidence was insufficient to determine whether visual impairments or cognitive impairments modify the relationship between physical activity and physical function among the general aging population. No relevant analyses were located in the sources of evidence.

For additional details on this body of evidence, visit: https://health.gov/paguidelines/second-edition/report/supplementary-material.aspx for the Evidence Portfolio.

Comparing 2018 Findings with the 2008 Scientific Report

As noted above, the 2008 Scientific Report[4] found consistent observational evidence that physical activity reduces risk of limitations in physical function, but only limited evidence from RCTs and meta-analyses. The evidence grade was “moderate to strong.” The 2008 Committee found “moderate” evidence that aerobic and muscle-strengthening activities were effective, particularly walking.[4] They also found "moderate" evidence of an inverse dose-response relationship between physical activity and risk of physical functional limitations, and limited evidence on the optimal pattern of tai chi that reduces risk of falls but no evidence rating for effects of tai chi on physical function.[4]

The 2018 Scientific Report provides more complete information about the relationship of physical activity and physical function. Evidence from RCTs now provides strong evidence that muscle-strengthening activities and multicomponent physical activity programs improve physical function, and provides moderate evidence that balance activities improve physical function. Hence, even though evidence is limited regarding the minimal dose of balance training (by itself) required to improve physical function, the findings indicate it is appropriate for *all* older adults to engage in multicomponent activity programs that include aerobic activity, muscle-strengthening activity, and activities that improve or maintain balance. In the 2008 Scientific Report,[4] this finding applied only to older adults at increased risk of falls.

Cohort studies provide strong evidence that regular aerobic activity reduces risk of functional limitations, with high levels of aerobic activity associated with approximately a 50 percent reduction in risk of major limitations. In addition, limited information now suggests a dose-response relationship for balance activities and muscle-strengthening activities, with improvement in physical function. Limited evidence now suggests as well that tai chi, dual-task training, active video gaming, and dancing have beneficial effects on physical function. Consistent with the findings of the 2008 Scientific Report,[4] the 2018 evidence review found insufficient evidence that flexibility activity by itself provides beneficial effects on physical function.

The 2008 Scientific Report stated, "Relative intensity is important to consider, as fitness levels are very low in many older adults."[4] A finding in this evidence review is consistent with this statement, as a review of 53 clinical trials of aerobic training reported that all trials used relative intensity to prescribe aerobic training.

Public Health Impact

The finding that physical activity improves physical function and reduces risk of age-related loss of physical function in the general aging population is of major public health importance. It is well known that the percent of older adults in the U.S. population is growing steadily, and by 2050 more than 20 percent of the population will be age 65 years or older. Older adults with lower levels of physical function generally have higher health care expenditures. Older adults strongly prefer to have levels of physical function sufficient to live in community settings, rather than reside in long-term care facilities.

In particular, the finding of moderate evidence that balance activities improve physical function has public health importance. As noted above, this finding indicates it is appropriate for all older adults to engage in multicomponent training that includes balance training as a component.

The absolute size of effects may belie their public health importance. For example, it may appear that a 0.12 meters per second improvement in gait speed with muscle-strengthening training is a small effect,[49] but in older adults, gait speed is strongly related to mortality risk. Predicted 10-year survival at age 75 years varies across the observed range of gait speeds, from 19 percent to 87 percent in men and from 35 percent to 91 percent in women, with significant increments per 0.1 meters per second.[52]

Notably, several findings with "limited" evidence also have high public health importance. It would be concerning if physical activity had smaller beneficial effects in those older adults who have the most need of improvements in physical function. Adults age 75 years and older have more age-related loss of physical function, are more likely to be women, and the majority have a BMI in the range of overweight-to-obese. Limited evidence suggests that these characteristics do not influence the effect of physical activity on function. Further, the effect of physical activity on physical function is of high importance to frail adults. It is reassuring that existing evidence suggests effects of physical activity are *greater* in frail older adults compared to non-frail adults.

Question 3: What is the relationship between physical activity and physical function in older adults with selected chronic conditions?

Question 3 builds upon the previous question by addressing the relationship between physical activity and physical function in discreet populations of older people having selected chronic conditions. The chronic conditions were selected based on their prevalence in older age, as well as on the availability of published research linking physical activity to physical function within each condition. The selected chronic conditions are: 1) cardiovascular disease; 2) chronic obstructive pulmonary disease (COPD); 3) cognitive impairment (e.g., Alzheimer's disease); 4) frailty; 5) hip fracture; 6) osteoporosis and osteopenia; 7) Parkinson's disease; 8) stroke; and 9) visual impairment.

Conclusion Statements

Limited evidence suggests that physical activities such as muscle-strengthening, tai chi, and qigong improve physical function among older people with **cardiovascular disease**. **PAGAC Grade: Limited.**

Limited evidence suggests that tai chi and qigong exercise improves one aspect of physical function (walking ability) in individuals with **chronic obstructive pulmonary disease**. **PAGAC Grade: Limited.**

Limited evidence suggests that for individuals with **cognitive impairment**, physical activity programs improve physical function, including measures of activities of daily living. **PAGAC Grade: Limited.**

Strong evidence demonstrates that physical activity improves measures of physical function in older people with **frailty**. **PAGAC Grade: Strong.**

Moderate evidence indicates that for community-dwelling older adults who sustain a **hip fracture**, extended exercise programs (which begin after formal hip fracture rehabilitation ends) are effective for improving physical function. **PAGAC Grade: Moderate.**

Limited evidence suggests that muscle-strengthening and agility (balance) activities performed on two or more days per week improves physical function in older people who are at risk of fragility fractures due to **osteoporosis or osteopenia**. **PAGAC Grade: Limited.**

Strong evidence demonstrates that physical activity improves a number of physical function outcomes, including walking, balance, strength, and disease-specific motor scores in individuals with **Parkinson's disease**. **PAGAC Grade: Strong.**

Moderate evidence indicates that that mobility-oriented physical activity improves walking function for individuals after a **stroke**. **PAGAC Grade: Moderate.**

Insufficient evidence is available to determine the effects of physical activity on older adults with **visual impairments**. **PAGAC Grade: Not assignable**.

Review of the Evidence

Cardiovascular Disease

Sources of evidence: Systematic review, meta-analyses

The Subcommittee based its conclusion on evidence published in 2016. This evidence came from one existing systematic review[53] and three existing meta-analyses.[54-56] Participants included men and women ages 65 years and older with existing cardiovascular disease (CVD) (ischemic heart disease, coronary artery disease, cerebrovascular disease, or heart failure) from both community and hospital settings. The exposure of interest was all types and intensities of physical activity and the outcomes of interest were performance-based indices of physical function (e.g., 6-minute walk test), Timed Up and Go, and household and physical activity mobility).

Evidence on the Overall Relationship

Based on a meta-analysis of 6 RCTs involving 374 CVD patients, Wang et al[55] reported improvements in the 6-minute walk test among those patients performing alternative and complementary exercises compared with those performing aerobic activity or no activity over 12 weeks (SMD=59.6 meters; 95% CI: 5.0-114.2 meters). Results from a meta-analysis of 3 RCTs among 106 heart failure patients indicated that those performing one hour of tai chi 2 to 3 times per week over 12 weeks also increased their 6-minute walking distance compared with those in usual care or performing aerobic or endurance activity (SMD=1.58; 95% CI: 0.70-2.45).[54] Yamamoto et al[56] performed a meta-analysis of 7 RCTs comparing the effects of muscle-strengthening to usual care or combined muscle-strengthening or aerobic training to aerobic training alone on mobility score in 118 people with CVD who were ages 65 years and older. Those people performing muscle-strengthening activities improved their mobility score compared with those in usual care (SMD=0.61; 95% CI: 0.21-1.01). Because of the small number of systematic reviews and meta-analyses for tai chi or qigong activities, aerobic activities, and muscle-strengthening activities, as well as the limited number of physical function outcomes addressed in these reviews, the Subcommittee rated the evidence as limited.

Chronic Obstructive Pulmonary Disease

Sources of evidence: Meta-analyses

The 2018 systematic search process located five potentially eligible reviews of the effects of physical activity on physical function in older adults with COPD.[57-61] Only 3 of these reviews,[58, 59, 61] however, met the eligibility criteria of: 1) enrolling older adults ages 50 years or older, 2) having intervention studies with a no-exercise control group, and 3) using physical activity interventions that were not part of a formal COPD medical rehabilitation program. The search located two meta-analyses of the effects of tai chi in people with COPD. Upon reviewing the studies in both of these reviews, it was determined that the more recent review[59] was a well-done review in the Cochrane Library and also contained all the tai chi studies in the less recent review by Wu et al,[61] as well as four additional studies. Therefore, the review by Wu et al[61] was not used as source of evidence, leaving only the systematic reviews and meta-analyses by Ding et al[58] and by Ngai et al.[59] One review[59] included 12 RCTs of tai chi and the other[58] included 7 RCTs of qigong (which were not included in Ngai et al[59]) and 3 RCTs of tai chi or of tai chi or qigong (which were included in the Ngai et al[59] review). Thus, there was little overlap in these reviews. The search found no studies of the effects of aerobic, resistance, or a combination of aerobic and resistance activity on physical function in older adults with COPD.

To answer this question, the Subcommittee examined the relationship between physical activity and physical function in older people with COPD.[58, 59] Samples sizes of individual studies ranged from 10 to 206 participants and total participants ranged from 718 to 811 (N=811 overall), and the mean age in studies ranged from 54 to 74 years. The included studies enrolled both men and women living in the community and the duration of the physical activity programs was between 6 weeks and 1 year. The exposure of interest was either tai chi (with a diversity in the tai chi styles and forms included in the interventions), qigong, or a combination of tai chi and qigong. Outcomes of interest were measures of physical performance, but the meta-analyses report findings only for the 6-minute walk test.

Evidence on the Overall Relationship

One meta-analysis involving 6 RCTs (N=318 participants) that compared tai chi to usual care reported improvements in the 6-minute walk test (MD=29.64 meters; 95% CI: 10.5-48.77) in favor of the tai chi group.[59] The other meta-analysis[58] involved 5 RCTs (N=349 participants) and also reported improvements in 6-minute walk test (MD=41.77 meters; 95% CI: 10.2-73.4) in the qigong and tai chi groups compared with the controls. Importantly, heterogeneity was high in both of the meta-analyses (I^2=59%[59] and 85%[58]), and the quality of the studies included were of low or very low methodologic quality.

In sum, consistent, but limited, evidence from two meta-analyses of a modest number of generally low-quality RCTs suggests tai chi and qigong may improve walking ability (as measured by the 6-minute walk test) in older adults with COPD.

Cognitive Impairment

Sources of evidence: Systematic reviews, meta-analyses

The Subcommittee based its conclusions on evidence published between 2010 and 2017, which included seven systematic reviews[19, 62-68] and seven meta-analyses.[69-74] The number of RCTs included in these reviews were as few as 5[69] and were as many as 18.[70] Most reviews included approximately 10 RCTs.[62, 67, 73] Those reviews assessing changes in ADL function tended to have fewer studies (approximately 6 RCTs) with poorer methodological quality. The studies reviewed included adults that were institutionalized or community dwelling[68, 74] and most included all forms of diagnosed dementia, such as Alzheimer's disease, fronto-temporal dementia, or Lewy Body dementia. The exposure of interest was all types and intensities of physical activity, and the outcomes of interest were measures of physical function, such as performance-based measures (6-minute walk test, Timed Up and Go, balance) or measures of ADL.

Evidence on the Overall Relationship

Approximately 20 to 30 percent of adults older than age 65 years suffer from either mild cognitive impairment or dementia. Changes in physical function often co-occur with cognitive losses, which can then accelerate the risk of disability and need for caregiving. The scientific literature indicates that physical activity training is capable of improving some measures of physical function in individuals with cognitive impairment. (For more details, see *Part F. Chapter 3. Brain Health.*) The physical function measures that showed the most consistent improvements with physical activity training include Timed Up and Go, walking speed, and Berg balance measures.[73] Improvements in ADL scales are also reported across several reviews.[66, 70-72] In fact, a meta-analysis of six high-quality RCTs,[74] indicates that physical activity training improves ADL function (effect size [ES]=0.80), as well as measures of physical function (ES=0.53). More recent analyses by Forbes and Blake[70] and Lewis et al[72] also report moderate to strong improvements in ADL function (ES=0.68 and 0.77, respectively). Moreover, one high-quality study reported that physical activity training can delay the deterioration of ADL performance.[69]

The reviews uniformly included interventions that were multicomponent and incorporated aerobic and muscle-strengthening training as well as balance, stretching, and endurance training.[62, 63, 66, 68, 70, 71, 74] The physical activity interventions generally ranged from 3 weeks to 12 months in duration with frequencies of 2 to 7 times per week,[62, 67, 74] with the length of sessions ranging from 20 minutes to 75 minutes. The intensity levels were reported as light-to-moderate but were generally not quantified or measured in many studies. Most interventions were conducted either as "community-based" or took place in senior home or nursing home facilities.

Importantly, attrition was higher in studies that included individuals with more severe cognitive impairment, thereby limiting confidence in the effects of physical activity on measures of physical function in this more severely impaired population.[69, 71] Few studies performed intent-to-treat analyses, and most had inadequate blinding procedures, and a poor description of the physical activity training procedures. Given the small number of well-conducted studies and the low level of precision within them, the Subcommittee graded the evidence as limited.

Frailty

Sources of evidence: Systematic reviews, meta-analyses

The Subcommittee based its conclusions on evidence published between 2008 and 2016. This evidence came from 15 existing systematic reviews of RCTs.[75-89] Only 3 of the 15 papers also included meta-analyses.[78, 83, 84] Most participants included in these studies were individuals ages 65 years and older and all met at least one established criterion for frailty. The majority of the participants were community-dwelling. The exposure of interest was all types and intensities of physical activity, and the outcomes of interest were measures of physical function, such as performance-based measures (6-minute walk test, Timed Up and Go, 30-second chair stands, gait, balance, strength) or self-reported measures of ADL or quality of life (QoL).

Evidence on the Overall Relationship

All of the 15 systematic reviews or meta-analyses reported that physical activity improved some or all measures of physical function in older people with frailty.[75-89]

A recent meta-analysis[84] of 19 RCTs among community-dwelling older adults with frailty reported improvements in normal gait speed (MD=0.07 meters per second; 95% CI: 0.04-0.09) and in fast gait speed (MD=0.08 meters per second; 95% CI: 0.02-0.14) among physical activity groups, compared with control groups. Overall, physical activity decreased the time needed to walk 10 meters by 1.73 seconds, which has important clinical relevance for older people with frailty. In addition, scores on the Short Physical Performance Battery also improved with physical activity (MD=2.18; 95% CI: 1.56-2.80).

A meta-analysis of 8 RCTs involving 1,068 frail older people between the ages of 75 and 87 years (mostly women) reported that compared with a non-physical activity control group, the physical activity groups increased their gait speed by 0.07 meters per second (95% CI: 0.02-0.11).[78] The groups also differed in their Borg Balance Scale score (weighted mean difference (WMD)=1.69; 95% CI: 0.56-2.82)) and in the ADL performance score (WMD=5.33; 95% CI: 1.01-9.64) in favor of the physical activity groups. The physical activity programs associated with these improvements generally were between 60 and 90 min per session and repeated daily for about 3 to 12 months.

Seven of 10 studies in a systematic review by Cadore et al[76] reported a lower incidence of falls among frail older people (ages 70 to 90 years) in physical activity (multicomponent, muscle-strengthening training, combined endurance and yoga, or tai chi) groups, compared with those in control groups, with a reduction ranging from 22 percent to 58 percent. Moreover, 6 of 11 studies in this review reported improvements in gait speed (4 percent to 50 percent); 8 of 10 studies reported improvements in balance (5 percent to 80 percent); and 9 of 13 studies reported improvements in strength (6 percent to 60 percent).

Multicomponent physical activity training comprising aerobic, progressive muscle-strengthening, balance, and functional training appears more effective than single-component training to improve physical function among older people with frailty.[76, 81, 85, 86, 89] After reviewing 47 RCTs, Theou et al[86] concluded that multicomponent training of at least moderate intensity that is performed 3 or more times per week for a duration of 30 to 45 min per session, over at least 3 to 5 months appeared most effective to increase functional ability in older people with frailty. In general, greater improvements were observed with greater intensity of activity (particularly with progressive muscle-strengthening training),[83, 87] greater frequency per week, longer training durations, and greater adherence. Insufficient evidence is available to determine whether a dose-response relationship exists between physical activity and physical function in people with frailty, as only one of the systematic reviews assessed dose-response. It is important to note that only 2 of the 18 systematic reviews or meta-analyses considered adverse events from the exercise training protocols,[84, 87] and neither of these reviews reported any.

Given the robust and consistent literature linking physical activity to improvements in physical function in older people with frailty, the Subcommittee graded the evidence as strong. The majority of subjects in the reviewed studies were women, however, and no information was provided on race, socioeconomic status, or weight status. One observational study in the review by Vermeulen et al[88] reported a 2-fold higher risk of ADL disability in women (OR=8.5; 95% CI: 2.0-36.2), compared with men (OR=4.3; 95% CI: 1.1-17.1) due to low physical activity. Therefore, insufficient evidence is available to determine whether the relationship between physical activity and physical function among people with frailty varies by age, sex, race/ethnicity, socioeconomic status, or weight status.

After Hip Fracture

Sources of evidence: Meta-analyses

The Subcommittee identified two meta-analyses of RCTs. Studies were eligible if the exposure or intervention in the study was physical activity or exercise. Studies of formal rehabilitation programs were not eligible to be included. One of the meta-analyses[90] included only “extended exercise programs,” defined as programs that are “offered after or extended for more than a regular rehabilitation period.” This meta-analysis included 11 RCTs (N=1,012 people) of physical activity judged to be of “good” or “excellent” quality and excluded RCTs of formal rehabilitation programs and with Physiotherapy Evidence Database (PEDro) quality scores of 4 or less. The other meta-analysis[91, 92] included a total of 13 RCTS regarded by the authors as “structured exercise programs” whose purpose was to improve mobility. To be conservative, only 8 of 13 RCTs in this Diong et al[91, 92] paper (N=232 people) were eligible for the meta-analysis. The majority of hip fracture patients in these studies lived in the community at the time of fracture as well as after discharge from usual care rehabilitation programs. The main types of physical activity in the trials were aerobic activity (only) typically involving weight-bearing activities such as walking, muscle-strengthening activity (only), and multicomponent programs involving some combination of aerobic activity, muscle-strengthening activity, balance training, functional training, and gait training. The outcomes of interest were measures of physical function, such as performance-based measures of gait, balance, strength, and ADL function or self-reported mobility.

Evidence on the Overall Relationship

The analyses contributing to this evidence summary are listed in Table F9-2 below. For the 13 analyses in the table, significant effects of physical activity on physical function were reported for 9 analyses (in bold). Effect sizes (ES) ranged considerably, with one ES (for Timed Up and Go) typically regarded as “large” as it exceeded 0.8. The other four analyses showed non-significant trends, but nonetheless favored the physical activity group over the control group.

Table F9-2. Effect Sizes for the Relationship Between Physical Activity and Physical Function in Older Adults After Hip Fracture

	Auais et al., 2012[90]		Diong et al., 2016[91, 92]	
Physical Function Measure	**Test & N of comparisons in MA**	**MA results**	**Test & N of comparisons in MA**	**MA results**
Balance	4 different tests N=7	ES=0.32 (0.15, 0.49)	Berg Balance Scale N=4	+3.09 scale points (1.97, 4.21)
Physical Performance	4 different tests N=4	ES=0.53 (0.27, 0.78)		
	Timed Up and Go N=3	ES=0.83 (.28, 0.14)	Timed Up and Go N=3	-7.14 seconds (3.9, 10.36)
Walking	6-minute walk test N=4	ES=0.22 (-0.12, 0.57)	Gait speed N=9	+ 0.07 m/s (.01, 0.14)
	Usual gait speed N=4	ES=0.16 (-0.17, 0.48)		
	Fast gait speed N=4	ES=0.42 (0.11, 0.73)		
ADL	4 different measures N=4	ES=0.16, (-0.07, 0.35)	An ADL measure N=6	ES=0.24 (0.07, 0.41)
Self-report of physical function	SF-36 PF scale N=4	ES=0.20 (-0.30, 0.44)	Report of mobility as "good" N=2	ES=0.31 (0.10, 0.52)

Legend: MA=meta-analysis, ES=effect size, and ADL=activities of daily living.

Two additional analyses in the Diong et al[91, 92] supported the finding that community physical activity programs after a hip fracture have beneficial effects in older adults. First, in a meta-analysis of all 13 studies, exercise in "other settings" has a stronger effect size (ES=0.55; 95% CI: 0.24-0.85) on mobility measures than does hospital only exercise (ES=0.07; 95% CI: -0.12-0.27). The authors noted the interventions in hospital-based programs usually had fewer exercise sessions than programs in other settings, implying community-based programs are capable of providing an overall "dose" of physical activity sufficient to achieve an effect on physical function. An additional analysis of six RCTs demonstrated that exercise increases leg strength on the side of the body affected by the hip fracture (Hedge's g=0.47, P<0.001).

In most RCTs, the physical activity intervention began a few weeks to a few months after discharge from formal rehabilitation. The intervention duration varied from 1 month to 1 year, with most studies lasting about 3 to 6 months. As stated previously, the most common physical activity component was muscle-strengthening exercise, sometimes in combination with other modes of activity and sometimes as the only mode.

Neither of the meta-analyses conducted subgroup analyses to determine whether the relationship between physical activity and physical function in older adults after hip fracture varied by age, sex, race, socioeconomic status, BMI, baseline physical function or baseline disease status. Also, no evidence was identified with respect to adverse events or injury during exercise.

Osteoporosis or Osteopenia

Sources of evidence: Systematic reviews, meta-analyses

The Subcommittee based its most recent conclusions on evidence published between 2009 and 2016. This evidence came from four existing systematic reviews of RCTs,[30, 93-95] two of which included a meta-analysis.[93, 94] Participants included in these studies were all community-dwelling individuals ages 55 years and older with osteoporosis (with or without fractures). These studies involved only RCTs and the exposure of interest was all types and intensities of exercise, and the outcomes of interest were measures of physical function, such as performance-based measures (gait, balance, strength) or self-reported measures of ADL or QOL.

Evidence on the Overall Relationship

Li et al[94] provided a systematic review and meta-analysis of 4 exercise RCTs among 256 post-menopausal women with a clinical diagnosis of osteoporosis or osteopenia (with and without fractures) and measurements of health-related quality of life (measured by SF-36 and the Quality of Life Questionnaire of the European Foundation for Osteoporosis (QUALEFFO)). The authors reported that in every RCT, the physical activity groups (who participated in programs of strengthening, stretching, agility, and/or balance training) showed significant improvements in self-reported physical function (SMD=2.77; 95% CI: 2.17-3.37), compared with the control groups (no activity or stretching). Group-based programs typically produced better results, compared with the one study of a home-based program. Short-duration physical activity programs (fewer than or equal to 12 weeks) resulted in significant improvements in physical function score (SMD=6.54; 95% CI: 0.15-12.94), as did programs that were more than 12 weeks (SMD=2.74; 95% CI: 2.13-3.34). Importantly, physical activity programs that combine strengthening with agility and balance training resulted in significant ($P<0.05$) improvements in physical function score, whereas programs involving only strengthening did not. In general, the physical activity programs were performed twice per week for approximately 40 to 60 minutes per session. Compliance with the prescribed physical activities in the included studies was high (more than 80 percent) and none of the trials reported any adverse events.

Findings from another systematic review of five RCTs[95] support the benefits of strength training to improved physical function in older people with osteoporosis. Indeed, four of the five trials included in this review demonstrated statistically significant improvements in physical function and ADL (self-reported from the SF-36), with effect sizes ranging from trivial (ES=0.08) to large (ES=1.74). Those studies reporting greater compliance with the physical activity program also reported more positive outcomes. Three of the trials were supervised and involved resistance training that focused on the back, core, and upper and lower extremities 2 to 3 times per week for about 50 to 60 minutes per bout. The two trials of home-based resistance training focused on the abdomen, lower back, and hips and the activity was performed with greater frequency than the supervised programs: 3 times per day on 7 days per week in one study and 10 times per day on 5 days per week in the other.

A more recent review,[93] reports inconsistent findings from 7 trials comparing physical activity or active physical therapy interventions with placebo or non-exercise or non-active physical therapy interventions among 488 people (ages 40 years or older with a history of osteoporotic vertebral fractures). Due to substantial variability among the seven trials, a pooled analysis was performed using data from only two studies, which nonetheless showed significant between-group differences in favor of the physical activity group for the Timed Up and Go performance test (MD -1.13 sec, 95% CI: -1.85 to -0.42). The authors concluded that although individual trials reported benefits for pain, physical function, and quality-of-life outcomes for those people performing physical activity, the findings should be interpreted cautiously. Due to the limited number of studies and outcome measures of physical function, the Subcommittee graded the evidence as limited.

Parkinson's Disease

Sources of evidence: Systematic reviews, meta-analyses

The Subcommittee based its conclusions on evidence published between 2004 and 2016. This evidence came from 20 systematic reviews.[19, 96-115] Only three of the reviews did not include a meta-analysis.[19, 97, 99] Participants included in these studies were community-dwelling older people between the ages of 57 and 88 years diagnosed with mild to moderate Parkinson's disease (based on Hoehn and Yahr scores of 1 to 3). The physical activity training modalities were varied, ranging from conventional forms of training (aerobic or resistance training) to activities such as tango dancing, virtual reality training, yoga, and tai chi (Table F9-3). Outcomes of physical function were performance-based measures, such as Timed Up and Go, 6-minute walk test, gait velocity, balance, strength, and motor skills. As indicated in the table below, the evidence base includes a large number of studies, with large numbers of participants.

Table F9-3. Number of Studies and Sample Sizes According to Training Mode in Individuals with Parkinson's Disease

Training Mode	Number of Studies	Sample Sizes
Mixed mode aerobic	35 total studies (20 RCTs) 18 RCTs 14 RCTs	N=1,210 N=901 N=495
Resistance training	12 RCTs	N=approximately 1000
Treadmill walking	18 RCTs	N=633
Tango/dance	13 total studies (9 RCTs)	N=357
Virtual reality training	8 trials	N=263
Yoga, tai chi	29 studies of various designs	N= approximately 910

Legend: RCT=randomized controlled trial.
Source: Alves Da Rocha et al., 2015,[96] Chung et al., 2016,[98] Cruickshank et al., 2015,[100] de Dreu et al., 2012,[101] Dockx et al., 2016,[102] Goodwin et al., 2008,[103] Kwok et al., 2016,[104] Lamotte et al., 2015,[105, 106] Lima et al., 2013,[107] Lotzke et al., 2015,[108] Mehrholz et al., 2015,[109] Ni et al., 2014,[110] Saltychev et al., 2016,[111] Sharp and Hewitt, 2014,[112] Shu et al., 2014,[113] Tillman et al., 2015,[114] and Yang et al., 2014.[115]

Evidence on the Overall Relationship

Effect sizes for the relationship between any of the physical activity training modes and the physical function outcomes ranged from small to moderate. Table F9-4 shows representative pooled effect sizes across the 6 physical function measures.

Table F9-4. Representative (Pooled) Effect Sizes for Physical Activity and Physical Function for Individuals with Parkinson's Disease

Physical Function Measure	Standardized Mean Differences (SMD) and 95% Confidence Intervals
Gait velocity (meters per second)	SMD=0.33; (95% CI: 0.17-0.49)
6 min walk (meters)	SMD=0.72; (95% CI: 0.08-1.36)
Timed Up and Go (seconds)	SMD=0.46; (95% CI: 0.08-0.76)
Balance score	SMD=0.36; (95% CI: 0.08-0.64)
UPDRS motor score	SMD=0.48; (95% CI: 0.21-0.75)
Strength	SMD=0.61; (95% CI: 0.35-0.87)

Legend: UPDRS=Unified Parkinson's Disease Rating Scale.
Note: Positive values signify improvement versus control conditions.
Source: Shu et al., 2014[113] and Chung et al., 2016.[98]

One recent meta-analyses[98] involving seven RCTs of resistance training (N=401 participants) reported significant improvements in muscle strength (SMD=0.61; 95% CI: 0.35-0.87), balance score (SMD=0.36; 95% CI: 0.08-0.64) and Parkinsonian motor symptoms (SMD=0.48; 95% CI: 0.21-0.75) in the physical activity, compared with control groups. Cruickshank et al[100] also reported significant improvements in strength (SMD=0.88; 95% CI: 0.66-1.09), as well as an 11.4 percent improvement in the Unified Parkinson's Disease Rating Scale (UPDRS) motor score. Another meta-analysis[107] of progressive muscle-strengthening training (four RCTs or quasi-RCTs; N=92 participants) also reported increased muscle strength (SMD=0.50; 95% CI: 0.05-0.95), as well as clinically relevant improvements in walking capacity (SMD=96 meters; 95% CI: 40-152) among people with mild to moderate Parkinson's disease. In contrast, Saltychev et al[111] found no evidence to support the superiority of progressive muscle-strengthening training over other types of physical training for improving physical function in people with Parkinson's disease. This conclusion presumably is due to the fact that 5 of the 12 studies in the review used some other active exercise or balance training comparison group, thereby diminishing the magnitude of effect for progressive muscle-strengthening training.

Kwok et al[104] performed a meta-analysis of nine RCTs involving yoga and tai chi. Beneficial effects in UPDRS III score were reported overall (SMD=-0.91; 95% CI: -1.37 to -0.45). In the subgroup analysis, yoga demonstrated the largest effect in improving UPDRS III score (SMD= -2.35; 95% CI: -3.21 -1.50), balance score (SMD=1.48; 95% CI: 0.91-2.06) and the Timed Up and Go test (SMD= -0.97; 95% CI: -1.46 to -0.47) and 6-Minute Walk Test (SMD=0.78; 95% CI: 0.35-1.21). Interventions with tai chi alone appear more effective than combined therapies for only a few balance and mobility outcomes, however.[110, 115]

Programs involving Argentine tango (N=7 studies) have demonstrated improvements in UPDRS motor severity score (ES= -0.62; 95 % CI:-1.04 to -0.21), balance score on the Mini-BESTest (ES=0.96; 95% CI: 0.60-1.31) and Berg Balance Scale (ES=0.45; 95% CI: 0.01-0.90), and gait with the Timed Up and Go test (ES= -0.46; 95% CI: -0.72 to -0.20).[108] Other forms of dance, such as the foxtrot or Irish dancing, have also demonstrated benefits to UPDRS motor scores (ES= -10.73; 95% CI: -15.05 to -6.16), balance score (ES=0.72; 95% CI: 0.31-1.44) and gait speed (ES=0.14 meters per second; 95% CI: 0.02-0.26) when compared with no intervention.[112] Physical activity programs involving a variety of activities, such as dance, hydrotherapy, aerobic exercise, boxing, Nordic walking, and tai chi[96] also appear effective in improving walking ability on the 6-Minute Walk Test (SMD=35 meters; 95% CI: 21-45), balance score (SMD=3.67; 95% CI: 3.05-4.30), UPDRS score (SMD= -4.22; 95% CI: -4.8 to -3.6), Timed Up and Go score (SMD=2.2 seconds; 95% CI: 1.2-4.1), and stride length (SMD= 0.112 meters; 95% CI: 0.034-2.8) in people living with Parkinson's disease. Due to the robust and consistent literature linking physical activity to improvements in physical function in older people living with Parkinson's disease, the Subcommittee graded the evidence as strong.

Stroke

Sources of evidence: Systematic reviews and meta-analyses

The Subcommittee based its conclusions on evidence published between 2007 and 2015. This evidence came from two systematic review and meta-analyses.[116, 117] Participants included in these studies were individuals who had survived a stroke and were still able to walk, who had a walking speed of at least 0.2 meters per second.[117] The physical activity modalities were primarily strength or mobility training, and outcomes of physical function were performance-based measures of walking (walking velocity and endurance).

Evidence on the Overall Relationship

A pooled analysis of five RCTs of strength training (N=240 participants) reported that strength training did not improve walking velocity following a stroke (Cohen's d (d)= -0.11; 95% CI: -0.46 to 0.24).[116] On the other hand, a pooled analysis of 10 studies of intensive mobility training (N=436 participants) by these same authors indicated a moderate beneficial effect on walking velocity (d=0.45; 95% CI: 0.14-0.77), which translated into an increase in walking speed of 0.23 meters per second (95% CI: 0.18-0.27) in the intervention group.[116] A third and larger pooled analysis of 17 controlled studies also performed by Eng and Tang[116] (N=752 participants) reported that treadmill training improved walking velocity in people following sub-acute and chronic stroke (d=0.23; 95% CI: 0.14-0.59) and following chronic stroke alone (d=0.31 95% CI: 0.06-0.69). Walking endurance also improved (d=0.70; 95% CI: 0.29-1.10). Of note, however, is that the effect sizes for treadmill walking were not different from those involving other over-ground physical therapy mobility training modes. Finally, a meta-analysis of 6 trials (N=171 participants) involving walking with "cuing of cadence" versus walking training alone indicated an increase in walking speed of 0.23 meters per second favoring the cuing with cadence group.[117] The Subcommittee felt that the body of evidence linking mobility-oriented physical activity to improvements in walking function in older people following a stroke (although not large) was adequate and consistent and thus the evidence was graded as moderate.

Visual Impairments

Sources of evidence: Meta-analysis

Older adults with visual impairment may have greater age-related problems with balance and may be in greater need of fall prevention programs compared older adults without this impairment. The only systematic review and meta-analysis by Gleeson et al[118] contained no relevant findings to address the outcomes specified.

For additional details on this body of evidence for all these chronic conditions, visit: https://health.gov/paguidelines/second-edition/report/supplementary-material.aspx for the Evidence Portfolio.

Comparing 2018 Findings with the 2008 Scientific Report

The 2008 Scientific Report did not address the role of physical activity for maintaining or improving physical function in older people with specific chronic conditions. Thus, these current 2018 findings extend the previous report in stressing that it is never too late in life to achieve benefits from regular physical activity. This report further expands on the previous report by identifying specific modes of activity (e.g., progressive muscle-strengthening training, tai chi, tango dancing, multicomponent training) that can best benefit specific chronic conditions.

Public Health Impact

About 80 percent of older adults have at least one chronic condition, and 77 percent have at least two.[119] Chronic diseases account for 75 percent of health care spending in the United States.[119] Low levels of daily physical activity often co-exist with chronic disease, thereby accelerating the risk of functional decline, disability, and mortality. In fact, ample evidence now indicates that physical inactivity is among the strongest predictors of physical disability in older people.[2] Given the rapidly increasing trends in aging demographics in the United States, preventing or delaying loss of physical function and mobility is an important public health concern, and this may be especially so for older people with already established chronic conditions.

OVERALL SUMMARY AND CONCLUSIONS

Strong evidence demonstrates that participation in multicomponent group or home-based fall prevention physical activity and exercise programs can reduce the risk of injury from falls, including severe falls that result in bone fracture, head trauma, open wound soft tissue injury, or any other injury requiring medical care or admission to hospital among community dwelling older adults. The evidence reviewed by the Subcommittee consistently indicated a 30 percent to 40 percent reduction in risk across studies. Limited evidence from RCTs suggest an inverse dose-response relationship between the amount of moderate-to-vigorous physical activity and the magnitude of risk reduction in fall-related injuries and bone fractures. Multicomponent physical activity regimens that combine aerobic, strength, and balance training appear to be especially effective in lowering risk of fall-related injuries, regardless of whether the exercise is home- or group-based.

Among the general aging population, strong evidence demonstrates that physical activity improves physical function and reduces the risk of age-related loss of physical function in an inverse graded manner. Moreover, evidence (albeit limited) now suggest that the benefits of physical activity to physical function may be greater in older adults with limitations in physical function compared with their healthier counterparts. Aerobic, muscle-strengthening, and multicomponent physical activity appear to have the strongest relationship to improvements in physical function in the general aging population, although balance training is also effective. Physical activities such as tai chi, dance training, active video gaming, and dual-task training also improve physical function in the general aging population, although the data are limited at this time.

Strong evidence also demonstrates that physical activity improves physical function in frail older adults. Multicomponent exercise training of at least moderate intensity that is performed 3 or more times per week for a duration of 30 to 45 min per session, over at least 3 to 5 months appears most effective to increase functional ability in frail older people. Strong evidence also demonstrates that physical activity improves a number of physical function outcomes, including walking, balance, strength, and disease-specific motor scores in individuals with Parkinson's disease. The physical activity training modalities associated with these improvements ranged from conventional forms of training (aerobic or resistance training) to activities such as tango dancing, virtual reality training, yoga and tai chi. Moderate evidence suggests that extended exercise programs can improve physical function even following a hip fracture or a stroke. Muscle-strengthening exercise (alone or in combination with other modes) appears effective in individuals following hip fracture, while mobility-oriented physical activity improves walking function for individuals after a stroke. For the other chronic diseases (CVD, cognitive impairment, COPD, osteoporosis, and visual impairment), the evidence is too limited to make conclusions about the relationship between physical activity and physical function. Nonetheless, evidence suggests that it is never too late in life to benefit from physical activity.

NEEDS FOR FUTURE RESEARCH

1. Conduct large-scale randomized controlled trials of older adults at high risk of falls designed with fall-related injuries and bone fractures as the primary outcomes of interest.

   Rationale: The incidence of fall-related injury or bone fracture is typically a secondary outcome of interest for randomized controlled trials designed to assess the effect of physical activity on the rate of falling. This issue results in insufficient sample sizes across studies to assess injurious falls and fractures, increases the potential for selection or information bias, and results in inadequate collection of pertinent injury-related data.

2. Conduct large observational and experimental studies to investigate further the dose-response relationships between physical activity (aerobic, muscle-strengthening, balance, and multicomponent) and fall-related injuries and bone fractures.

   Rationale: Currently, little information is available regarding the dose-response relationship between physical activity and fall-related injuries in older adults. Such information in necessary for setting minimum activity thresholds for effectiveness and maximum thresholds for safety.

3. Conduct large-scale randomized controlled trials comparing various doses of balance training and muscle-strengthening training on physical function in the general population of older people.

   Rationale: Little information is currently available on the amount of balance and muscle-strengthening training necessary to maintain or to improve physical function among generally healthy older people. Such information is important for attenuating the aging-related decline in physical function, thereby delaying the onset of frailty and maintaining physical independence in aging.

4. Conduct large-scale randomized controlled trials to determine the effects of tai chi, qigong, dance, active video gaming, and yoga on physical function in healthy older adults, as well as those with different chronic conditions.

   Rationale: These activities have only recently been considered as effective strategies for maintaining and improving physical function in older people. These forms of physical activity may be especially beneficial for those with already-existing chronic disease and/or limitations to mobility. Such research should address: 1) the types or modes of such activity that are most effective for specific chronic conditions; and 2) the minimal effective doses of these activities for improving physical function.

5. Conduct prospective cohort studies of physical activity and physical function in older adults that include objective measures (e.g., heart rate monitors) of relative intensity of activity.

   Rationale: The relationship of relative versus absolute intensity to the health benefits of regular physical activity remains unclear. Epidemiologic (i.e., observational) studies using objective monitoring would: 1) allow for more robust analyses of how intensity affects health benefits, and 2) facilitate integration of findings from observational studies (which typically measure intensity of activity using absolute intensity) with those from randomized controlled trials (which typically measure intensity of activity using relative intensity).

6. Conduct more meta-analyses with meta-regressions to determine the extent to which the heterogeneity of results often observed among different studies of physical activity and physical function can be explained by variation in the tests used to measure physical function.

Rationale: Composite measures of physical function (such as the combination of measures resulting in a single score used in Diong et al[91, 92] tend to result in stronger effect sizes with physical activity, compared with single measures. This may be due to the fact that physical function comprises a constellation of attributes that may not be adequately captured by a single measure. Moreover, comparisons among studies is difficult due to differences in how physical function is characterized and assessed (performance measures versus self-reported activities of daily living function or quality of life). Such meta-analyses would allow investigators to derive a single best composite measure to be used consistently in future studies of physical function.

7. Conduct more experimental research on dual-task training that clearly describe the dual-task training procedures and the parameters of the secondary task. In addition, these studies should provide evidence of whether dual-task costs were reduced by training and whether dual-task training transfers to untrained tasks.

   Rationale: Dual-task training is a relatively new area of research in aging, and the methodologic quality of the studies reviewed for this report ranged from poor to moderate. To ensure internal validity and reproducibility, future research in this area should provide as much detail as possible in describing the methods and should consider multiple outcome tasks (trained and untrained) in the analysis.

8. Conduct large-scale randomized controlled trials and/or meta-regression analyses to establish dose-response effects of aerobic and resistance training on physical function for people with chronic obstructive pulmonary disease, frailty, osteoporosis, cognitive impairment, Parkinson's disease, visual impairments, and following hip fracture or stroke.

   Rationale: Currently, little information is available regarding the dose-response relationship between aerobic and strengthening activities and physical function in specific vulnerable subgroups of older adults. These modes of activity are proven effective in minimizing the age-related decline in physiological reserve and function among the general aging population, and thus may be especially important for older people with chronic conditions that limited their mobility. Such information in necessary for setting minimum activity thresholds for effectiveness and maximum thresholds for safety.

9. Conduct large-scale randomized controlled trials to investigate the optimal dose and mode of physical activity necessary to improve and maintain balance function and reduce injury-related falls and fractures in persons with frailty, hip fracture, osteoporosis, Parkinson's disease, visual impairments, and stroke.

   Rationale: Balance is essential for maintaining physical function and mobility, particularly among people with existing functional and mobility limitations due to frailty, osteoporosis, Parkinson's disease, visual impairments, or following hip fracture or a stroke. Currently, little information is available regarding the types or optimal dose of exercise for improving balance function. Such information in necessary for setting minimum activity thresholds for effectiveness and maximum thresholds for safety.

10. Conduct large-scale randomized controlled trials with 6- and 12-month post-intervention follow-up assessments to determine the effects of physical activity on activities of daily living mobility, instrumental activities of daily living, free-living physical or ambulatory activity and social participation for older individuals with chronic disease. These individuals are at accelerated risk of functional decline, disability, and social isolation.

    Rationale: Little evidence currently exists on how improvements in strength, balance, and endurance following a physical activity intervention to improve physical function translate into everyday improvements in activities of daily living function and social participation, especially after the formal intervention period is over. Such knowledge would provide important information on how improvements in physiologic function can contribute to and sustain certain behavioral aspects of healthy aging (such as self-care, independence, social engagement) and quality of life.

11. Conduct large cohort and experimental studies to determine the dose-intensity and timing of physical activity necessary to prevent functional decline or to improve physical function across the spectrum of cognitive dysfunction and dementia.

    Rationale: Limited evidence currently exists about the impact of physical activity training on physical function limitations that often co-occur with cognitive dysfunction and dementia. Cognition and mobility are intimately linked, and improving physical function through physical activity in a cognitively impaired population might have broad effects for independence and activities of daily living.

12. Conduct large-scale observational or experimental studies with adequate statistical power to determine whether the relationship between physical activity and risk of fall-related injuries or loss of physical function in older people varies by race/ethnicity, sex, socioeconomic status, or level of existing impairments across the aging spectrum.

    Rationale: The vast majority of available research has been conducted on older white women, thereby limiting the generalizability of the findings to this demographic subgroup alone. Moreover, the potential impact of these influential factors often is not considered in statistical analyses, thus limiting the ability to determine whether effect modification exists at all. Results from this type of research would provide stronger scientific foundations for local, state, and national government, medical, and community wellness entities committed to reducing possible health disparities among various demographic sectors. This research would also support public and private partners in developing effective physical activity programs and policies to help individuals maintain their health and function through older age.

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PART F. CHAPTER 10. INDIVIDUALS WITH CHRONIC CONDITIONS

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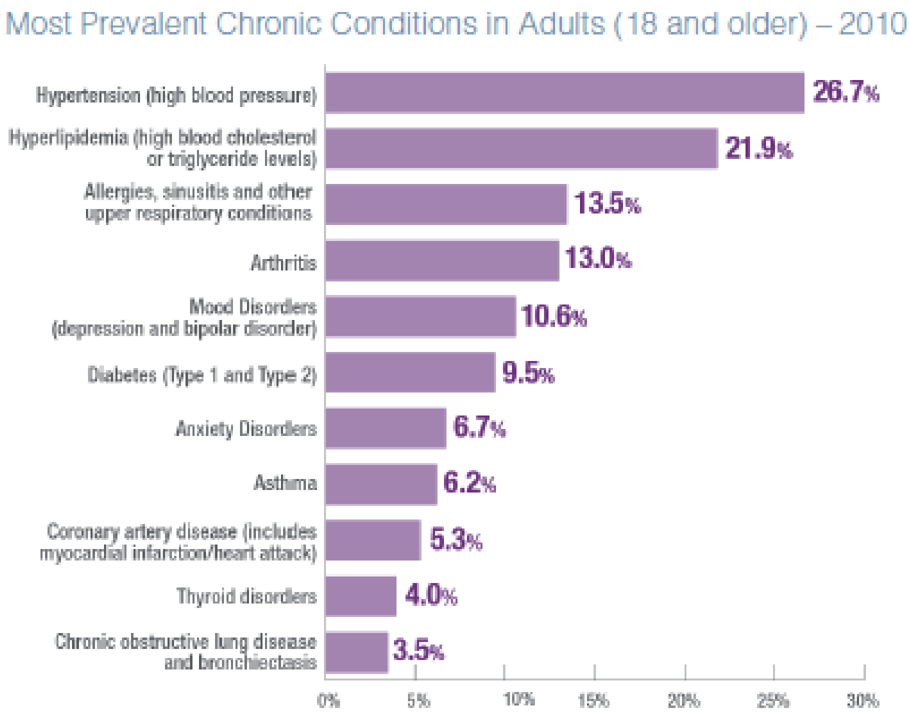
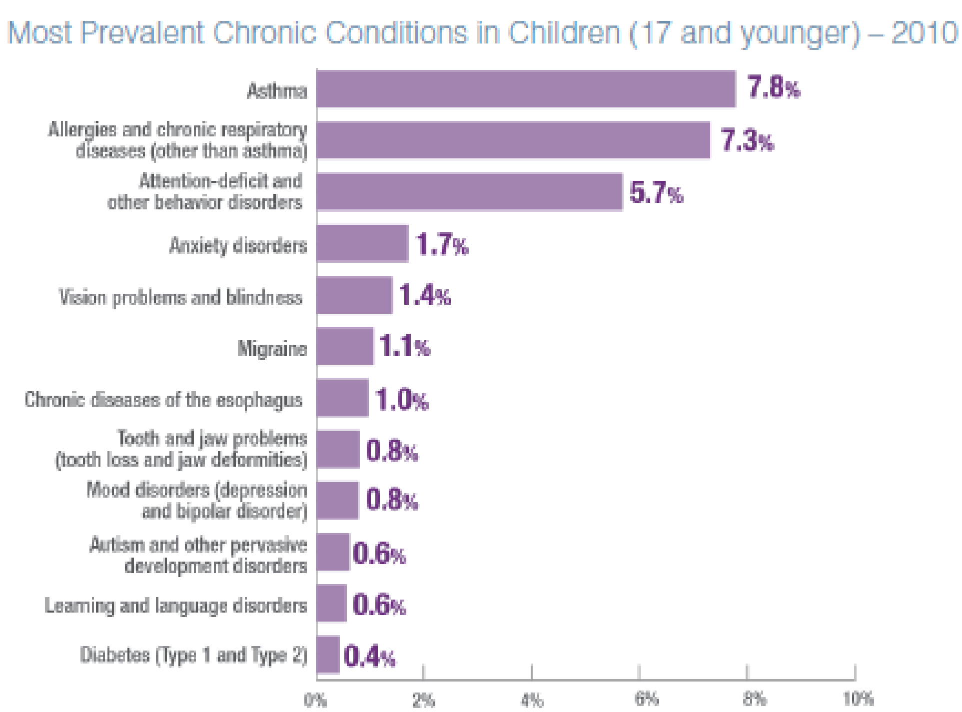
INTRODUCTION

This chapter reviews evidence related to the preventive effects of physical activity in people with chronic conditions. Chronic conditions can be defined as conditions with duration of at least 1 year, which either require medical care and/or limit activities of daily life.[1] A person has multiple chronic conditions if they have two or more chronic conditions at the same time.

Chronic conditions occur in both children and adults. The prevalence of some common chronic conditions (e.g., hypertension) and groups of chronic conditions (e.g., anxiety disorders) are shown in Figure F10-1.[2] In 2010, about half (51.7%) of all Americans had at least one chronic condition, and about one-third (31.5%) had multiple chronic conditions. The prevalence of most common chronic conditions increases with age, and about 80 percent of adults ages 65 years and older have multiple chronic conditions.[2] Given the aging of the U.S. population, the percent of adults with chronic conditions will thus increase over the next few decades. Chronic conditions that are prevalent in older adults have public health importance, even if they are not included in the figure. For example, in adults ages 50 years and older, the prevalence of osteoporosis is estimated at about 10 percent.[3] Osteoporosis increases risk of hip fracture—an important cause of morbidity and mortality in older adults.

Figure F10-1. Most Prevalent Chronic Conditions in Adults and Children, 2010





Source: Gerteis et al., 2014.[2]

Broadly speaking, physical activity has two types of effects in people with chronic conditions: therapeutic and preventive. Therapeutic physical activity is used to treat a disease in the same sense that medication is treatment. An example of therapeutic physical activity is physical activity that is part of formal rehabilitation programs, such as cardiac, stroke, and pulmonary rehabilitation. Generally, therapeutic physical activity is tailored to the medical needs of an individual patient and supervised and/or prescribed by health professionals. The reviews in this chapter do not address therapeutic physical activity per se.

The evidence reviews in this chapter focus on the role of physical activity in prevention in people with an existing chronic condition. Some reviews address primary prevention—not primary prevention of the existing chronic condition, but rather primary prevention of an *additional* chronic condition. For example, evidence reviews in this chapter address whether physical activity reduces risk of cardiovascular mortality in adults with the chronic conditions of type 2 diabetes and hypertension. Questions in this chapter that include the outcome of risk of co-morbid conditions and risk of second primary cancer address primary prevention of additional chronic conditions. Although this chapter does not address primary prevention of type 2 diabetes and hypertension, *Part F. Chapter 5. Cardiometabolic Health and Prevention of Weight Gain* does review the effect of physical activity in reducing risk of incident type 2 diabetes and hypertension.

Other evidence reviews address secondary prevention. Herein, secondary prevention refers to preventing a chronic condition from getting worse over time (i.e., increasing in severity). Worsening of a disease over time is assessed by indicators of disease progression. For example, in the osteoarthritis evidence review of this chapter, indicators of progression are increasing amounts of damaged knee cartilage over time and the need for knee replacement surgery. When a chronic condition progresses, it commonly impairs physical function and lowers health-related quality of life (HRQoL), and may eventually cause mortality. Questions in this chapter that include the outcomes of progression, health-related quality of life, physical function, risk of cancer recurrence, and cancer-specific mortality address secondary prevention.

Admittedly, a clear distinction between therapeutic and preventive effects of physical activity is often not possible. For example, in the evidence review for type 2 diabetes (Question 4 of this chapter), the effects of physical activity on glycated hemoglobin (HbA1C) are regarded as preventive effects, as high levels of HbA1C increase risk of disease progression. Of course, the effects of physical activity on HbA1C can also be regarded as therapeutic, as a goal medical treatment of type 2 diabetes is to lower HbA1C below an individualized target level.

The evidence reviews of this chapter update information and evidence findings of the *Physical Activity Guidelines Advisory Committee Report, 2008* report.[4] The 2008 Scientific Report[4] addressed, to at least some extent, the effects of physical activity in all the chronic conditions of interest in this chapter: cancer survivors, osteoarthritis, hypertension, type 2 diabetes, multiple sclerosis, spinal cord injury, and intellectual disabilities. However, many fewer scientific studies were available at the time the 2008 Scientific Report[4] was written. The evidence reviews of this chapter located substantially more information, and with one exception (progression outcome of osteoarthritis), the evidence reviews of this chapter relied on existing systematic reviews, meta-analyses, and published analyses of pooled data. Comparisons of the findings of this report with the findings of the 2008 Scientific Report[4] are provided for each question.

The evidence reviews of this chapter have substantial public health importance. As the number of chronic conditions increases in an individual and as existing conditions worsen, the risk of functional limitations increases, quality of life decreases, and costs of medical care increase. In 2010, 65 percent of healthcare spending was for individuals with a chronic condition, and notably, most of this spending (71%) was for people with multiple chronic conditions.[2] Thus, in individuals with a chronic condition, it is of large public health importance to prevent another chronic condition from developing and to prevent the existing condition from getting worse.

Other aspects of the importance of prevention in individuals with chronic conditions are: (1) Individuals with chronic conditions generally engage in less physical activity. To the extent physical activity provides benefits, it emphasizes the importance of promoting physical activity in individuals with chronic conditions. (2) Documenting preventive benefits in individuals with chronic conditions increases the confidence that when a research study reports a preventive effect of physical activity in the general population, it is not because of preventive effects that occur only in relatively healthy people. (3) Documenting preventive benefits increases the confidence that effects of physical activity are not blocked by disease effects. (4) Documenting preventive benefits emphasizes that the same physical activity commonly provides both preventive and therapeutic benefits in individuals with chronic conditions.

Prioritization of Chronic Conditions

Early in its work, the 2018 Physical Activity Guidelines Advisory Committee agreed that Question 1 of this chapter would address effects of physical activity in cancer survivors. To identify the chronic conditions for other questions in this chapter, the Individuals with Chronic Conditions Subcommittee identified four criteria for prioritizing conditions: (1) public health importance as indicated by prevalence of the condition; (2) amount of evidence available as indicated by preliminary literature searches for systematic reviews and meta-analyses; (3) diversity (by organ system) in conditions chosen for review; and (4) no review of effects of physical activity in the condition by another Subcommittee.

A list of chronic conditions for possible review was presented at the Committee's second public meeting and discussed by the Committee publicly and in small group break-out sessions. Information on prevalence of chronic conditions was ascertained from a report by the Agency for Healthcare Research and Quality (Figure F10-1[2]) or from published articles. Preliminary searches were done to estimate the size of the literature of the effects of physical activity for conditions on the list. The search used a standard set of physical activity terms, sought only articles designated as systematic reviews or meta-analyses, and used a list of search terms developed separately for each chronic condition. It was originally thought that, for some conditions, available evidence on the health effects of physical activity in people with that condition would be insufficient. However, the preliminary literature searches located tens, if not hundreds, of possible systematic reviews of effects of physical activity for each condition (Table F10-1). That is, the search did not rule out the possibility that, for any chronic condition, at least a few good quality reviews of effects of physical activity would be available.

A table was created that ranked chronic conditions based upon prevalence and size of published literature (Table F10-1). The purpose of this table was to provide background information for discussions by the Subcommittee; it was not intended to provide a decision rule for selecting chronic conditions. The prevalence of each condition was ranked, as was the number of "hits" in the preliminary search. The sum of the two ranks was calculated, and then the sum was ranked. (This table was revised several times; only one version is shown). As an example of the content of deliberations, consider low back pain. There was concern that low back pain is technically a symptom due to a variety of conditions, rather than a single chronic condition comparable to, for example, hypertension. Because effects of physical activity could vary by the etiology of the back pain, a review would require identifying effects of physical activity for each common condition causing back pain. The preliminary search results might overestimate the relevant evidence, as trials of therapeutic activity for acute low back pain might be commonly included in reviews. When it was decided to include a review of physical activity and osteoarthritis, part of the rationale was that osteoarthritis is a common cause of back pain, and thus this review might end up addressing effects of physical activity in back pain due to osteoarthritis.

Several conditions were not selected because of evidence reviews by other Subcommittees. The Aging Subcommittee reviewed effects of physical activity on physical function in older adults with cardiovascular disease (CVD), chronic obstructive pulmonary disease, conditions causing cognitive impairment (including Alzheimer's disease), hip fracture, osteoporosis, Parkinson's disease, and stroke. The Brain Health Subcommittee reviewed the effects of physical activity in several additional chronic conditions, including dementia, schizophrenia, attention deficit hyperactivity disorder, major depression, bipolar disorder, anxiety disorders, and obstructive sleep apnea.

The Subcommittee carefully considered an evidence review addressing a chronic condition in children. As of the fourth (next to last) Committee meeting, a review of a chronic condition prevalent in children was still under consideration. With the Brain Health Subcommittee taking the lead on reviews of physical activity in people with mental health conditions, the leading option was a review of asthma in both adults and children. However, children are at low risk of chronic conditions so it was likely that no information on prevention of co-morbidities in children with asthma would be available. The waxing and waning of asthma symptoms and the effects of treatment on disease severity also could make it challenging to tease out effects of physical activity on progression, physical function, and HRQoL.

Thus, it was decided to do a review of the effect of physical activity on intellectual and physical disabilities, in part because intellectual disabilities, such as Down syndrome, are highly relevant to children. Another set of preliminary searches was done and an outside expert consulted. The preliminary search showed insufficient evidence was available for muscular dystrophy, but sufficient evidence would be available for the final three conditions reviewed in this chapter: multiple sclerosis, spinal cord injury, and intellectual disability.

Table F10-1. Ranking of Chronic Conditions Based on Prevalence and Size of Published Literature

Chronic Condition	Prevalence Children	Prevalence Adults	Sum of Prevalences	# Search Results	Prevalence rank	Search rank	Sum	Overall Rank
Hypertension	2-3%	26.7%	29.0%	436	1	5	6	1
Mood Disorders	0.80%	10.6%	11.4%	490	6	2	8	2
Cancer Survivors		6.3%	6.3%	785	10	1	11	3 T
Type 2 Diabetes	<.4%	9.5%	9.8%	483	8	3	11	3 T
Low Back Pain		18.1%	18.1%	241	3	9	12	5
Osteoarthritis		13.0%	13.0%	294	5	8	13	6
Lipid Disorder		21.9%	21.9%	84	2	14	16	7
Asthma	7.80%	6.2%	14.0%	83 (125 with Exercise-Induced)	4	13	17	8
Coronary Heart Disease		5.3%	5.3%	294	12	7	19	9
Neuromotor Disease			Low	449 (513 including stroke & AD)	18	4	22	10 T
Congestive Heart Failure		2.3%	2.3%	317	16	6	22	10 T
Chronic Renal Disease		10.0%	10.0%	53	7	16	23	12
COPD		3.5%	3.5%	142 (284 with Rehabilitation)	13	11	24	13
Stroke		3.0%	3.0%	185 (356 with Rehabilitation)	15	10	25	14
Peripheral Artery Disease		3.4%	3.4%	91	14	12	26	15
Anxiety Disorders	1.70%	6.7%	8.4%	27	9	18	27	16

Chronic Condition	Prevalence Children	Prevalence Adults	Sum of Prevalences	# Search Results	Prevalence rank	Search rank	Sum	Overall Rank
ADHD	5.70%		5.7%	11	11	19	30	17
Alzheimer's Disease		2.0%	2.0%	73	17	15	32	18
Cystic Fibrosis	<1%		Low	43	19	17	36	19

Legend: ADHD=attention deficit hyperactivity disorder, COPD=chronic obstructive pulmonary disease, AD=anxiety disorders.

In summary, prioritization was a sequential process based upon discussions at public meetings and various Subcommittee meetings. This sequential process ensured adequate time and resources were available to address the final list of questions. Three prevalent conditions were chosen for Questions 2, 3, and 4: osteoarthritis (musculoskeletal), hypertension (cardiovascular), and type 2 diabetes (metabolic). The resources and time available allowed only a more limited review for the last three conditions, selected in part because of the public health importance of physical activity in people with disabilities: multiple sclerosis, spinal cord injury, and intellectual disability. The selection of cancer types for review in Question 1 is discussed below under Question 1.

Principles Guiding the Evidence Review and Terminology

In selecting relevant evidence, the Subcommittee was guided by several principles and definitions. (1) The evidence review would rely on existing systematic reviews, rather than de novo reviews of original research articles. This principle was followed for all reviews with one exception—the review of progression in osteoarthritis. (2) Given the focus on prevention, the review would exclude studies of therapeutic exercise, such as the effects of formal rehabilitation programs. (3) The most relevant experimental evidence would come from controlled trials, preferably randomized trials, comparing physical activity (only) to a no-activity control group. (4) In a person with one condition, the term co-morbid condition would refer to any other chronic condition that could be measured by a medical diagnosis (e.g., coronary heart disease) or by events (e.g., cardiovascular mortality). (5) The term physical function would have the same definition as that developed by the Aging Subcommittee, namely "the ability of a person to move around and to perform types of activity." (6) Given that HRQoL is a multi-dimensional concept that includes physical function, the most relevant HRQoL measures would not be subscale scores, but summary scores aggregating information on quality of life across several subscales (or domains). (7) The term progression would refer to worsening of an existing disease or chronic condition over time, and be assessed by one or more disease-specific indicators.

REVIEW OF THE SCIENCE

Overview of Questions Addressed

This chapter addresses seven major questions and related subquestions:

1. Question 1. Among cancer survivors, what is the relationship between physical activity and (1) all-cause mortality, (2) cancer-specific mortality, or (3) risk of cancer recurrence or second primary cancer?
   a) Is there a dose-response relationship? If yes, what is the shape of the relationship?
   b) Does the relationship vary by age, sex, race/ethnicity, socioeconomic status, or weight status?
   c) Does the relationship vary based on: frequency, duration, intensity, type (mode), and how physical activity is measured?

2. Question 2. In individuals with osteoarthritis, what is the relationship between physical activity and (1) risk of co-morbid conditions, (2) physical function, (3) health-related quality of life, (4) pain, and (5) disease progression?
   a) Is there a dose-response relationship? If yes, what is the shape of the relationship?
   b) Does the relationship vary by age, sex, race/ethnicity, socioeconomic status, or weight status?
   c) Does the relationship vary based on frequency, duration, intensity, type (mode), or how physical activity is measured?

3. Question 3: In people with the cardiovascular condition of hypertension, what is the relationship between physical activity and (1) risk of co-morbid conditions, (2) physical function, (3) health-related quality of life, and (4) cardiovascular disease progression and mortality?
   a) Is there a dose-response relationship? If yes, what is the shape of the relationship?
   b) Does the relationship vary by age, sex, race/ethnicity, socioeconomic status, weight status, or resting blood pressure level?
   c) Does the relationship vary based on frequency, intensity, time, duration, type (mode), or how physical activity is measured?

4. Question 4. In people with type 2 diabetes, what is the relationship between physical activity and (1) risk of co-morbid conditions, (2) physical function, (3) health-related quality of life, and (4) disease progression?
   a) Is there a dose-response relationship? If yes, what is the shape of the relationship?
   b) Does the relationship vary by age, sex, race/ethnicity, socioeconomic status, or weight status?
   c) Does the relationship vary based on: frequency, duration, intensity, type (mode), or how physical activity is measured?

5. Question 5. In people with multiple sclerosis, what is the relationship between physical activity and: 1) risk of co-morbid conditions, 2) physical function, and 3) health-related quality of life?

6. Question 6. In people with spinal cord injury, what is the relationship between physical activity and (1) risk of co-morbid conditions, (2) physical function, and (3) health-related quality of life?

7. Question 7. In people with intellectual disabilities, what is the relationship between physical activity and: (1) risk of co-morbid conditions, (2) physical function, and (3) health-related quality of life?

Data Sources and Process Used to Answer Questions

To allow for coverage of the largest number of chronic conditions, the Subcommittee chose to rely exclusively on existing reviews including systematic reviews, meta-analyses, pooled analyses, and reports for its questions, only answering the questions and sub-questions that could be answered with the information from the existing reviews. For all but one question, additional searches for original research were not needed. For Question 2 (individuals with osteoarthritis) the existing reviews did not identify sufficient evidence to answer the question about disease progression. The Subcommittee and expert consultant regarded progression of osteoarthritis as a question that needed to be answered due to the existing relationship between physical activity and osteoarthritis. A supplementary de novo search for original research was conducted on progression in individuals with osteoarthritis.

In an effort to reduce duplication of efforts, the searches for existing reviews and title triage for Question 3 (individuals with hypertension) and Question 4 (individuals with type 2 diabetes) were done concurrently with the Cardiometabolic Health and Weight Management Subcommittee's Question 2 (blood pressure) and Question 3 (incidence of type 2 diabetes). The search strategies for each of these questions were developed to address the needs of both Subcommittees. Title triage addressed the inclusion criteria of both Subcommittees. Abstract and full-text triage were done separately for both Subcommittees.

Across its questions, the Chronic Conditions Subcommittee reviewed original research articles contained in the included systematic reviews, meta-analyses, pooled analyses, and reports to allow for additional specificity in the understanding of the literature. These original research articles are not included as evidence in the evidence portfolio. For complete details on the systematic literature review process, see *Part E. Systematic Literature Search Methodology.*

Question 1. Among cancer survivors, what is the relationship between physical activity and (1) all-cause mortality, (2) cancer-specific mortality, or (3) risk of cancer recurrence or second primary cancer?

a) Is there a dose-response relationship? If yes, what is the shape of the relationship?
b) Does the relationship vary by age, sex, race/ethnicity, socioeconomic status, or weight status?
c) Does the relationship vary based on: frequency, duration, intensity, type (mode), and how physical activity is measured?

Sources of evidence: Systematic reviews, meta-analyses, pooled analyses

Conclusion Statements

Breast Cancer in Women

Moderate evidence indicates that greater amounts of physical activity after diagnosis are associated with lower risks of breast cancer-specific mortality and all-cause mortality in female breast cancer survivors. **PAGAC Grade: Moderate.**

Insufficient evidence is available to determine whether physical activity after diagnosis is associated with risk of breast cancer recurrence or second primary breast cancer. **PAGAC Grade: Not assignable.**

Moderate evidence indicates that a dose-response relationship exists; as levels of physical activity increase, risks of breast cancer-specific mortality and all-cause mortality decrease in female breast cancer survivors. **PAGAC Grade: Moderate.**

Moderate evidence indicates that greater amounts of physical activity after diagnosis are associated with lower risks of breast-cancer-specific mortality in both pre- and postmenopausal breast cancer survivors, with menopause as a proxy for age, while greater amounts of physical activity are associated with lower risks for all-cause mortality in only postmenopausal breast cancer survivors. **PAGAC Grade: Moderate.**

Moderate evidence indicates that greater amounts of physical activity after diagnosis are associated with lower risks of all-cause mortality in breast cancer survivors with both normal weight and overweight or obesity, while greater amounts of physical activity after diagnosis are associated with lower risks of breast cancer-specific mortality only in breast cancer survivors with overweight or obesity. **PAGAC Grade: Moderate.**

Insufficient evidence is available to determine whether the relationship between physical activity and all-cause mortality or breast cancer-specific mortality differs by sex, race/ethnicity or socioeconomic status in breast cancer survivors. **PAGAC Grade: Not assignable.**

Insufficient evidence is available to determine whether the frequency, duration, intensity, or type (mode) of physical activity is related to all-cause mortality or breast cancer-specific mortality in breast cancer survivors. **PAGAC Grade: Not assignable.**

Colorectal Cancer

Moderate evidence indicates that greater amounts of physical activity after diagnosis are associated with lower risks of colorectal cancer-specific mortality and all-cause mortality in colorectal cancer survivors. **PAGAC Grade: Moderate.**

Insufficient evidence is available to determine whether physical activity after diagnosis is associated with risk of colorectal cancer recurrence or second primary colorectal cancer. **PAGAC Grade: Not assignable.**

Moderate evidence indicates that a dose-response relationship exists; as levels of physical activity increase, risks of colorectal cancer-specific mortality and all-cause mortality decrease in colorectal cancer survivors. **PAGAC Grade: Moderate.**

Moderate evidence indicates that the association between physical activity and both colorectal cancer-specific mortality and all-cause mortality does not vary across age groups from middle to older ages. **PAGAC Grade: Moderate**.

Moderate evidence indicates that the association between physical activity and both colorectal cancer-specific mortality and all-cause mortality does not vary between men and women. **PAGAC Grade**: **Moderate.**

Insufficient evidence is available to determine whether the relationship between physical activity and all-cause mortality or colorectal cancer-specific mortality differs by race/ethnicity, socioeconomic status, or weight status in colorectal cancer survivors. **PAGAC Grade: Not assignable.**

Insufficient evidence is available to determine whether the frequency, duration, intensity, or type (mode) of physical activity is related to all-cause mortality or colorectal cancer-specific mortality in colorectal cancer survivors. **PAGAC Grade: Not assignable.**

Prostate Cancer

Limited evidence suggests an inverse association between highest versus lowest levels of physical activity after diagnosis and all-cause mortality in prostate cancer survivors. **PAGAC Grade: Limited.**

Moderate evidence indicates an inverse association between highest versus lowest levels of physical activity after diagnosis and prostate cancer-specific mortality in prostate cancer survivors. **PAGAC Grade: Moderate.**

Insufficient evidence is available on the association between physical activity level and prostate cancer recurrence or progression. **PAGAC Grade: Not assignable.**

Limited evidence suggests that a dose-response relationship exists; as levels of physical activity increase, risks of prostate cancer-specific mortality and all-cause mortality decrease in prostate cancer survivors. **PAGAC Grade: Limited.**

Insufficient evidence is available on the association between physical activity and prostate cancer survival or recurrence by age, race/ethnicity, socioeconomic status, or weight status. **PAGAC Grade: Not assignable.**

Limited evidence suggests that increased frequency, duration, and intensity of physical activity may be associated with decreased risks for all-cause mortality and prostate cancer-specific mortality in prostate cancer survivors. **PAGAC Grade: Limited.**

Review of the Evidence

According to the U.S. National Cancer Institute, a person is considered to be a cancer survivor from the time of diagnosis until the end of life. Currently, almost 15 million people in the United States are cancer survivors.[5] Trends toward earlier detection of cancer and improved treatments have contributed to increased survival; two-thirds of individuals with cancer survive for at least 5 years.[5] This improved survival has shifted focus in survivorship research toward new outcomes, such as studying long-term survival (i.e., over decades). Increasingly, recognition of the role of host factors in cancer survival, such as obesity, metabolic health, inflammation, immune function, and the endocrine system, has supported the increased focus on lifestyle changes to improve these factors.

Systematic literature searches were conducted to answer Question 1, with conclusions possible for breast cancer in women, colorectal cancer, and prostate cancer. The databases searched included

PubMed, Cochrane, and CINAHL. The literature search to address Question 1 was limited to systematic reviews, meta-analyses and pooled analyses. For prostate cancer, the results of the literature search did not provide information on the physical activity association with all-cause mortality. The Subcommittee therefore also reviewed original research articles contained within the one meta-analysis of physical activity and prostate cancer prognosis in order to examine the association between physical activity and all-cause mortality.

In the studies included in the meta-analyses, systematic reviews, and pooled analyses, physical activity was measured through self-report, with different types of validated physical activity questionnaires. In many studies, participants were presented with a list of typical activities (e.g., walking, running, biking), and asked to indicate the frequency and duration of each activity. Other studies used more general questions about time spent in vigorous- or moderate-intensity activities. Most collected information on recreational activities, several also included occupational activities, and only a few included household activities. Some calculated total physical activity, adding up all of these activities; most limited calculation of amount of activity to leisure-time activity. Some of the meta-analyses calculated MET-hours per week of moderate and vigorous physical activities where data were available, but the cut-points for highest versus lowest activity levels varied across studies. Although most studies that calculated MET-hours assigned a MET value of 6 for vigorous activities, some assigned a value of 8.

Although information was available in some meta-analyses and systematic reviews on pre-diagnosis physical activity levels, the Subcommittee examined only post-diagnosis activity levels in relation to prognosis, because the focus of this chapter is on individuals with chronic disease.

Most of the studies included in the meta-analyses and systematic reviews adjusted for possible confounding factors, although few had data on types of treatments and whether full courses of treatment were received. Therefore, none of the meta-analyses was able to examine the confounding or effect modifying effects of treatment. Because receipt of optimal treatment is a key predictor of survival from cancer, the Subcommittee could not rule out a major confounding or modifying effect of this factor.

The remainder of the discussion of the evidence and findings is organized by the three types of cancer addressed by the review: breast cancer in women, colorectal cancer, and prostate cancer. In addition, a section on other cancers comments on results of searches for evidence for other cancer types.

Breast Cancer in Women

More than three million U.S. women are living with a diagnosis of invasive breast cancer.[6] Breast cancer prognosis is strongly influenced by stage at diagnosis, tumor subtype, and availability and access to appropriate therapies.[7] However, growing evidence suggests that host effects, including weight status, metabolic health, and nutrition influence prognosis.[8-11]

The Subcommittee used information from eight systematic reviews,[12-19] of which six included meta-analyses.[14-19] These reviews included physical activity data collected after diagnosis and between 4 and 14 studies. Sample sizes ranged from several hundred to (in the most recent review) 17,666 breast cancer survivors (1,239 deaths).[14] Median length of follow-up ranged from 3 to 12 years. For recurrence, data were available from four cohort studies and one small randomized controlled trial (RCT). Also reviewed were three reports from a pooling project of four studies with a total of 13,000 breast cancer survivors.[20-22] Where several meta-analyses presented similar risk estimates, the Subcommittee chose to report estimates from the most recent or most comprehensive review. In some cases, subgroup analyses were reported in older reviews, and are therefore presented here.

For this analysis, breast cancer survivors are defined as women who have been diagnosed with invasive breast cancer. All of the systematic reviews and meta-analyses included studies with breast cancer survivors diagnosed at stages I to III, excluding those initially diagnosed with metastatic (stage IV) cancer.

Evidence on the Overall Relationship

Data from this body of evidence show a consistent inverse association between amounts of physical activity after diagnosis and cancer-specific and all-cause mortality in breast cancer survivors. Estimates from a 2015 meta-analysis of eight cohorts found that highest versus lowest levels of physical activity were associated with a 48 percent reduction in risk for all-cause mortality (relative risk (RR)=0.52; 95% confidence interval (CI): 0.43-0.64).[16] A 2016 meta-analysis of ten cohorts found that highest versus lowest levels of post-diagnosis physical activity were associated with a 38 percent reduction in risk of breast cancer-specific mortality (RR=0.62; 95% CI: 0.48-0.80).[14] This latter study found that risk of recurrence was significantly reduced in four cohorts and one trial that collected recurrence data (RR=0.68; 95% CI: 0.58-0.80).[14] It should be noted that the various studies used quite different definitions of recurrence, so it is difficult to interpret the combined effect of these results. The pooling project addressed the association between meeting the 2008 Physical Activity Guidelines[23] recommended activity levels and breast cancer survival. The project found that engaging in 10 or more MET-hours per week was associated with a 27 percent reduction in all-cause mortality (hazard ratio (HR)=0.73; 95% CI: 0.66-0.82) and a 25 percent reduction in breast cancer-specific mortality (HR=0.75; 95% CI: 0.65-0.85).[20]

Dose-response: A meta-analysis of four cohort studies found that, in comparisons of less active to more active individuals, each 5, 10, or 15 MET-hours per week increase in amounts of post-diagnosis physical activity was associated with a 6 percent (95% CI: 3%–8%), 11 percent (95% CI: 6%–15%), and 16 percent (95% CI: 9%–22%) reduction in risk of breast-cancer mortality, respectively.[17] Furthermore, each 5, 10, or 15 MET-hours per week increase in amounts of post-diagnosis physical activity was associated with a 13 percent (95% CI: 6–20%), 24 percent (95% CI: 11%–36%), and 34% (95% CI: 16%–38%) decreased risk of all-cause mortality, respectively.[17]

Evidence on Specific Factors

Age: Although no meta-analyses assessed relationships by age, menopausal status was investigated as an effect modifier in two meta-analyses.[16, 19] In women who were premenopausal at diagnosis, highest versus lowest physical activity was associated with reduced breast cancer death (HR=0.55; 95% CI: 0.37-0.82).[16] In postmenopausal women, highest versus lowest level of physical activity was associated with reduced risk of both breast cancer-specific and all-cause mortality (HR=0.75; 95% CI: 0.58-0.98 and HR=0.44; 95% CI: 0.24-0.80, respectively).[16]

Cancer subtype: Two meta-analyses assessed effects by tumor estrogen receptor status.[15, 16] Women with estrogen receptor positive tumors who were in the highest level of physical activity had reduced risk of all-cause mortality compared with women in the lowest level (HR=0.34; 95% CI: 0.14-0.83), but physical activity did not have a similar effect on all-cause mortality in women with estrogen receptor negative tumors. This meta-analysis further found that the subset of survivors at the highest level of physical activity with both estrogen receptor negative and progesterone receptor negative tumors had reduced risk of all-cause mortality (HR=0.56; 95% CI: 0.41-0.77), while those with estrogen and progesterone receptor positive tumors had reduced risk for breast cancer-specific mortality (RR=0.32; 95% CI: 0.12-0.86).[16] Women with stage I and stage II-III disease at diagnosis had reduced risk of all-cause mortality (HR=0.31; 95% CI: 0.10-0.95 and HR=0.57; 95% CI: 0.41-0.79, respectively).[16] These analyses by cancer subtypes were limited to two to three cohort studies, and therefore should be interpreted with caution. The pooling project found that women with estrogen receptor positive tumors who were in the top two tertiles of post-diagnosis physical activity had significantly reduced mortality (20-30%, P_{trend}<0.0001) after 5-year follow-up, compared with those with lower activity levels.[21]

Sex: Although breast cancer occurs in men, it is 100 times less common than in women. No studies investigated the association between physical activity and survival, recurrence, or second primary in men with breast cancer.

Race/ethnicity and socioeconomic status: No conclusions can be made regarding whether the inverse relationship between physical activity and all-cause mortality, as well as cancer-specific mortality, varies by race/ethnicity, or socioeconomic status. The studies lacked sufficient representation of ethnic and minority populations, as well as outcomes based on socioeconomic status, preventing any systematic conclusions related to these factors.

Weight status: Three meta-analyses estimated effects of physical activity by body mass index (BMI) level, with similar results.[15, 16, 19] In the latest review, for those with BMI <25 kg/m^2, risk of all-cause mortality in those with highest versus lowest physical activity level was reduced (HR=0.44; 95% CI: 0.30-0.64), while risk for breast cancer-specific mortality was not reduced.[16] Among those with BMI ≥25 kg/m^2, risks for both breast cancer-specific and all-cause mortality were reduced in those with highest versus lowest physical activity level (HR=0.51; 95% CI: 0.35-0.74 and HR=0.50; 95% CI: 0.32-0.78, respectively).[16]

Physical activity frequency, duration, intensity, type (mode): Physical activity in the meta-analyses was measured as either hours per week, or more generally expressed as MET-hours per week of moderate and vigorous physical activities. Beyond the total MET-hours per week of moderate-to-vigorous physical activity, presumed primarily aerobic based on surveys and questionnaires, no specific conclusions can be made regarding the nature of the exercise exposure.

Colorectal Cancer

Review of the Evidence

More than 1,317,000 individuals in the United States are colorectal cancer survivors, and about 135,000 new cases occur per year, of which approximately 72 percent are colon and 28 percent are rectal.[24, 25] Colorectal cancer causes approximately 50,260 deaths per year in the United States, accounting for 8.4 percent of cancer deaths as the second leading cause for cancer mortality.

The Subcommittee used information from eight systematic reviews,[12, 14, 17, 26-30] of which six included meta-analyses.[14, 17, 27-30] These reviews included between three and seven studies that assessed post-diagnosis physical activity in relation to survival. Sample sizes in included cohorts ranged from several hundred to (in the most recent review) a total of 9,698 colorectal cancer survivors (1,071 deaths).[14] Median length of follow-up ranged from 4 to 12 years. For recurrence, data were available from only one small cohort study. Where several meta-analyses presented similar risk estimates, the Subcommittee chose to report estimates from the most recent or most comprehensive review. In some cases, subgroup analyses were reported in older reviews, and are therefore presented here.

The studies on physical activity pooled all outcomes for colon and rectal cancer, which are reported at a ratio of approximately two cases of colon cancer for each case of rectal cancer, and adjusted for tumor location, including proximal colon (ascending and transverse), distal colon (descending and sigmoid), and rectal cancer, and for cancer grade. Thus, the conclusions of this report are considered to apply to cancer survivors with a diagnosis of both proximal and distal colon and rectal cancer. Most of the cohort studies included colorectal cancer stages I to III, excluding metastatic stage IV cancer, and the meta-analyses of the cohort studies further excluded stage IV to minimize the bias that could be introduced with its higher mortality. Therefore, this question's conclusions do not apply to stage IV colorectal cancer.

Evidence on the Overall Relationship

Data from this body of evidence show a consistent inverse association between amounts of physical activity after diagnosis and all-cause mortality and colorectal cancer-specific mortality in colorectal cancer survivors. A 2016 meta-analysis including seven cohort studies showed a 42 percent reduced risk of all-cause mortality in survivors with highest versus lowest levels of physical activity (RR=0.58; 95% CI: 0.49-0.68).[30] A different 2016 meta-analysis of six cohorts found that highest versus lowest levels of post-diagnosis physical activity were associated with a 38 percent reduction in risk of colorectal cancer-specific mortality (relative risk (RR)=0.62; 95% CI: 0.45-0.86).[14] This latter study found that risk of recurrence was not statistically significantly related to physical activity, but the data were from only one cohort with 832 survivors (159 deaths).[14]

One meta-analysis assessed dose-response using five cohort studies. In comparisons of less active to more active individuals, each 5, 10, or 15 MET-hours per week increase in post-diagnosis physical activity was associated with a 15 percent (95% CI: 10%-19%), 28 percent (95% CI: 20%-35%), and 35 percent (95% CI: 28%-47%) lower risk for all-cause mortality.[17] Results for colorectal cancer-specific mortality were virtually identical.

Evidence on Specific Factors

Age: Most of the prospective cohort studies included in the meta-analyses consisted of individuals with a median age ranging from 60 to 69 years. Although age was included as an adjustment factor in most studies, no meta-analyses conducted analyses by age group. However, the cohorts that enrolled only older individuals[31, 32] found similar effects of physical activity on mortality compared with younger survivor populations.

Sex: The recent meta-analyses included two prospective cohort studies with women only[32, 33] that showed statistically significant inverse associations between physical activity and both all-cause mortality and cancer-specific mortality. One study with only men showed a non-statistically significant negative association between highest versus lowest physical activity level and risk for either all-cause mortality or colorectal cancer-specific mortality.[34] Results for remaining cohorts lay between the results for women only and men only. Therefore, it appears likely that physical activity reduces all-cause and colorectal cancer-specific mortality in both men and women.

Race/ethnicity and socioeconomic status: No conclusions may be made regarding whether the inverse relationship between physical activity and all-cause mortality or colorectal cancer-specific mortality varies by race/ethnicity, or socioeconomic status. The studies lacked sufficient representation of ethnic and minority populations, as well as outcomes based on socioeconomic status, preventing any systematic conclusions related to these factors.

Weight status: Although most of the source cohorts in the meta-analyses adjusted for BMI, the meta-analyses did not provide estimates of effects of physical activity on mortality by categories of BMI. Therefore, the effect of weight status on the role of physical activity in colorectal cancer survivors is unknown.

Physical activity frequency, duration, intensity, type (mode): Physical activity in the meta-analyses was measured as either hours per week, or more generally expressed as MET-hours per week of moderate and vigorous physical activities. Sedentary to low activity was defined as less than 3 MET-hours per week, while higher physical activity levels were classified at a range from more than 17 to more than 27 MET-hours per week. Beyond the total MET-hours per week of moderate-to-vigorous physical activity (which was presumed as primarily aerobic based on surveys and questionnaires), no specific conclusions can be made regarding the nature of the exercise exposure.

Prostate Cancer

Review of the Evidence

More than three million U.S. men are living with a diagnosis of invasive prostate cancer.[35] Most men diagnosed in older ages (older than age 65 years) do not die of their prostate cancer; rather, the primary cause of death in this survivor population is CVD. Prognosis is influenced by stage at diagnosis and availability and access to appropriate therapies.[36]

The Subcommittee used information from two systematic reviews,[12, 14] of which one included a meta-analysis.[14] The Ballard-Barbash et al[12] review included only one cohort study of prostate cancer survivors, while the Friedenreich et al[14] review included four studies. Therefore, estimates for this report are from the latter review. Available information on the association between physical activity and survival in men with prostate cancer is from prospective cohort studies of prostate cancer survivors for whom data were obtained on physical activity levels after diagnosis. Sample sizes in the four cohorts ranged from 830 to 4,600 prostate cancer survivors. Median length of follow-up ranged from 2 to 15 years. For recurrence, data were available from two cohort studies.

Evidence on the Overall Relationship

Data from this body of evidence show an inverse association between amounts of physical activity after diagnosis and cancer-specific mortality in prostate cancer survivors. Estimates from a 2016 meta-analysis of three cohorts found that highest versus lowest levels of physical activity were associated with a 38 percent reduction in risk for prostate cancer-specific mortality (RR=0.62; 95% CI: 0.47-0.82).[14] Overall mortality was not addressed in the Friedenreich et al[14] meta-analysis. A review of the papers included in the systematic reviews indicates that highest versus lowest levels of total, recreational, non-sedentary occupational, and vigorous physical activity were statistically significantly related to reduced risk for all-cause mortality.[37-39]

Risk of recurrence or progression was not associated with physical activity in a meta-analysis of two cohorts that collected recurrence or progression data (RR=0.77; 95% CI: 0.55-1.08).[14] It should be noted that the various studies used quite different definitions of recurrence, so it is difficult to interpret the combined effect of these results.

A review of the individual papers included in the meta-analysis[14] showed significant dose-response effects, such that men who exercised for greater MET-hours per week or greater numbers of hours per week, or who engaged in vigorous activity, had lower risk for both all-cause mortality and prostate cancer-specific mortality.[37-39] One study found an association between increased walking speed and duration with lower risk of prostate cancer progression,[40] and one study found a statistically significant association between increased walking or biking and both overall and prostate cancer-specific mortality.[38] However, the studies used different categories for gradient of amount of activity, and therefore it is difficult to determine an overall relationship between these components of physical activity and prostate cancer outcomes.

Evidence on Specific Factors

Age: Neither the meta-analysis nor the cohort studies assessed relationships by age groups.

Cancer subtype: The association between physical activity and prostate cancer progression by Gleason score (cancer aggressiveness) was estimated in one study in a recent meta-analysis.[14] For men with Gleason score less than7, the hazard ratio for reduced survival for those walking 7 or more hours per week versus less than 0.5 hours per week was 0.39 (95% CI: 0.11-1.41). For those with Gleason score greater than or equal to 7, the hazard ratio for reduced survival for those walking 7 or more hours per week versus less than 0.5 hours per week was 1.33 (95% CI: 0.54-3.29) ($P_{interaction}$ 0.006). Because neither hazard ratio was statistically significant, it is not clear that the prognosis differs by baseline indicator of disease aggressiveness.

Race/ethnicity and socioeconomic status: None of the studies provided information on effects of physical activity on survival or progression by race/ethnicity, or socioeconomic status.

Weight status: None of the studies provided information on effects of physical activity on survival or progression by weight status.

Physical activity frequency, duration, intensity, type (mode): The individual cohort studies assessed relationships between several domains of physical activity and both all-cause mortality and prostate cancer-specific mortality, including vigorous activity, MET-hours per week, walking speed, and mean time walking or biking. Most physical activity domains were associated with improved survival. However, given the variable ways of measuring and presenting data in the source cohort studies, it is not possible to firmly determine whether the magnitude of effects on prognosis in prostate cancer survivors is similar across these physical activity domains.

Other Cancers

Although the Subcommittee searched for systematic reviews, meta-analyses, and pooled analyses related to post-diagnosis physical activity and prognosis in any cancer, most of the published studies have focused on breast, colorectal, and prostate cancers. The Subcommittee decided that evidence was too limited for other cancers to draw conclusions or assign an evidence grade.

One 2016 systematic review/meta-analysis identified two cohort studies that included any cancer type.[14] One of these studies showed a statistically significant 38 percent reduction in cancer-specific mortality in men with highest versus lowest levels of physical activity,[41] while the other found no significant association of physical activity with cancer-specific mortality in women.[42] The Ballard-Barbash et al[12] systematic review included one study of glioma, which showed a statistically significant 36 percent reduction in all-cause mortality in individuals engaging in 9 or more versus less than 9 MET-hours per week of physical activity (HR=0.64; 95% CI: 0.46-0.91; P_{trend}< .001).[43] The Subcommittee recognizes that additional single studies of physical activity in relation to cancer survival have been published, but all were published after our systematic search was applied.

For additional details on this body of evidence, visit: https://health.gov/paguidelines/second-edition/report/supplementary-material.aspx for the Evidence Portfolio.

Comparing 2018 Findings with the 2008 Scientific Report

The 2008 Scientific Report[4] reviewed the literature on the association between physical activity and cancer prognosis through 2008. From the limited amount of research available at that time, the 2008 Scientific Report[4] tentatively concluded that increased physical activity is associated with reduced mortality for women with breast cancer and for men and women with colorectal cancer. Since that time, the literature on physical activity and cancer survival has grown enough to warrant meta-analyses of survival cohort data, which can provide more precise estimates of these associations, as well as dose-response estimates and information about effects within subgroups of cancer survivors.

The 2008 Scientific Report[4] also considered evidence of associations between physical activity and late and long-term consequences of cancer treatment and quality of life. The 2018 Committee did not review these issues, but rather focused on the considerable new literature available on physical activity and survival.

Public Health Impact

In the United States, an estimated 42 percent of men and 38 percent of women will develop cancer in their lifetimes.[44] For several cancers, the projected number of years that affected individuals will live is increasing, such that many cancer survivors can expect to live for decades after their diagnosis.[45] More than 15.5 million children and adults with a history of cancer were alive on January 1, 2016, in the United States, and of these, 8,319,370 had a history of breast, colorectal, or prostate cancer.[46] By January 1, 2026, it is estimated that the population of cancer survivors will increase to 20.3 million: almost 10 million males and 10.3 million females.[46] Of these, an estimated 10,889,250 will be survivors of breast, colorectal, or prostate cancer.

A growing body of literature supports an inverse association between greater amounts of physical activity and decreased all-cause and cancer-specific mortality in individuals with a diagnosis of breast, colorectal, or prostate cancer, with risk reductions ranging from 38 to 48 percent. The lack of information about confounding or effect modification by type and completion of treatment reduced the strength of the findings. However, given the statistical significance and effect sizes of the observed associations, the Subcommittee supports recommendations to breast, colorectal, and prostate cancer survivors to increase physical activity. Given the lack of information on physical activity in relation to survival in individuals with cancers other than breast, colorectal, or prostate cancer, no conclusions or recommendations can be made for these cancer survivors. Physical activity should be encouraged to improve survival in individuals diagnosed with breast, prostate, or colorectal cancer.

Question 2. In individuals with osteoarthritis, what is the relationship between physical activity and (1) risk of co-morbid conditions, (2) physical function, (3) health-related quality of life, (4) pain, and (5) disease progression?

a) Is there a dose-response relationship? If yes, what is the shape of the relationship?
b) Does the relationship vary by age, sex, race/ethnicity, socioeconomic status, or weight status?
c) Does the relationship vary based on frequency, duration, intensity, type (mode), or how physical activity is measured?

Sources of evidence: Systematic reviews, meta-analyses, existing report, original articles

Conclusion Statements

Risk of Co-morbid Conditions

Insufficient evidence is available to determine whether a relationship exists between greater amounts of physical activity and comorbidities in individuals with osteoarthritis. **PAGAC Grade: Not assignable.**

Physical Function or Pain

Strong evidence demonstrates a relationship between greater amounts of physical activity with decreased pain and improved physical function in adults with osteoarthritis of the knee and hip. **PAGAC Grade: Strong**.

Insufficient evidence is available to determine whether a dose-response relationship exists between physical activity with pain or physical function in individuals with osteoarthritis. **PAGAC Grade: Not assignable.**

Insufficient evidence is available to determine whether the relationship between physical activity with pain or physical function varies by age, sex, race/ethnicity, socioeconomic status, or body weight status in individuals with osteoarthritis. **PAGAC Grade: Not assignable**.

Limited evidence suggests that greater intensity or duration of aerobic and muscle-strengthening physical activity is related to improvement in pain and physical function in individuals with osteoarthritis of the knee and hip. **PAGAC Grade: Limited.**

Health-related Quality of Life

Moderate evidence indicates a relationship between greater amounts of physical activity and improved health-related quality of life in individuals with osteoarthritis of the knee and hip. **PAGAC Grade: Moderate.**

Insufficient evidence is available to determine whether a dose-response relationship exists between physical activity and health-related quality of life in individuals with osteoarthritis. **PAGAC Grade: Not assignable.**

Insufficient evidence is available to determine whether the relationship between physical activity and health-related quality of life varies by age, sex, race/ethnicity, socioeconomic status, or body weight status in individuals with osteoarthritis. **PAGAC Grade: Not assignable**.

Insufficient evidence is available to determine whether the frequency, duration, intensity, or type (mode) of physical activity is related to health-related quality of life in individuals with osteoarthritis. **PAGAC Grade: Not assignable.**

Disease Progression

Moderate evidence indicates a relationship between physical activity and disease progression in individuals with osteoarthritis. Moderate evidence indicates that up to the range of 10,000 steps per day, ambulatory physical activity does not accelerate osteoarthritis of the knee. **PAGAC Grade: Moderate.**

Moderate evidence indicates a dose-response relationship between physical activity and disease progression in individuals with osteoarthritis. The relationship appears to be U-shaped. **PAGAC Grade: Moderate.**

Insufficient evidence is available to determine whether the relationship between physical activity and progression varies by age, sex, race/ethnicity, socioeconomic status, or body weight status in individuals with osteoarthritis. **PAGAC Grade: Not assignable**.

Insufficient evidence is available to determine whether the frequency, duration, intensity, or type (mode) of physical activity is related to progression in individuals with osteoarthritis. **PAGAC Grade: Not assignable.**

Review of the Evidence

Evidence on the Overall Relationship

Risk of Co-morbid Conditions

Available evidence was insufficient to determine whether a relationship exists between greater amounts of physical activity and comorbidities in individuals with osteoarthritis (OA). A search for systematic reviews, meta-analyses, pooled analyses, and reports failed to locate any reviews of the effects of physical activity on risk of co-morbid conditions. Thus, no additional discussion is provided for the outcome of risk of co-morbid conditions.

Osteoarthritis and Pain, Physical Function, and Health-related Quality of Life

The original literature search revealed 18 meta-analyses and systematic reviews meeting the criteria for inclusion in the analysis of OA and pain, physical function, and health-related quality of life (HRQoL).[47-64] However, these meta-analyses included significant overlap in the studies included. In an attempt to minimize redundancy, the Subcommittee reviewed the overlap of studies within all the meta-analyses. Meta-analyses with considerable overlap, with fewer than five unique additional studies, and that did not add additional information to the larger studies were not retained for purposes of the final analyses. This resulted in retention of six meta-analyses.[47-50, 52, 53]

Of these six studies, five covered physical function as an outcome,[47, 49, 50, 52, 53] five covered pain as an outcome,[47-49, 52, 53] and two dealt with HRQoL as an outcome.[47, 52]

Pain: The meta-analyses examined a variety of physical activity interventions, including land-based therapeutic strength and aerobic exercises,[48, 52] aquatic activities,[47, 48] and tai chi.[49, 52] Juhl et al[53] examined single or combination exercises, including aerobic, resistance, and performance training. The included reviews[47-49, 52, 53] addressed pain as outcomes using a variety of scales (Western Ontario and McMaster's Osteoarthritis Index, Lequesne Osteoarthritis Index).

Physical Function: The meta-analyses examined a variety of physical activity interventions, including land-based strength and aerobic exercises,[50, 52] aquatic activities,[47, 50] and tai chi.[49, 50, 52] Juhl et al[53] examined single or combination exercises, including aerobic, resistance, and performance training. The included reviews addressed physical function and outcomes related to physical function in a variety of ways, including perceived self-efficacy, and cognitive and emotional impairment,[49] functional aerobic capacity,[49, 50] and disability and physical function measured using the Activities of Daily Living Scale, Western Ontario and McMaster's Osteoarthritis Index, and Global Disability Scores.[47, 52, 53]

Health-related Quality of Life (HRQoL): Fransen et al[52] examined the effects of a variety of types of land-based exercise, including muscle strengthening, balance training, aerobic walking, cycling, and tai chi. Bartels et al[47] assessed various types of exercises (range of motion, strength, aerobics) with HRQoL as an outcome using a variety of scales.[47, 52]

In sum, these six reviews included:

- 131 individual studies and meta-analyses dealing with knee OA alone, covering 9,798 individuals with physical function as an outcome, 10,948 with pain as an outcome, and 2,771 with HRQoL as an outcome;
- 13 individual studies dealing with hip OA alone, covering 3,021 individuals with physical function as an outcome, 1,320 with pain as an outcome, and 1,190 with HRQoL as an outcome; and

- 13 individual studies dealing with aquatic exercise on knee and hip OA together, covering 1,076 participants with pain as an outcome, 1,059 participants with function as an outcome, and 971 participants with HRQoL as an outcome.

The effect sizes on pain, physical function and quality of life for those with hip OA did not seem to vary from those considering knee OA alone.

Most of the studies in these meta-analyses consisted of RCTs of the effects of one or more modalities of exercise (land-based and aquatic; aerobic, muscle-strengthening, and tai chi) on knee and hip OA. Most used the Western Ontario and McMaster Arthritis Index (WOMAC) scale—common in the OA research arena—to assess pain, physical function, and quality of life. Some studies examined land-based exercise exclusively.[52] Others examined pool-based exercise effects only.[47] The effect sizes on pain, physical function, and quality of life did not seem to vary whether the exercise was land-based or aquatic exercise.

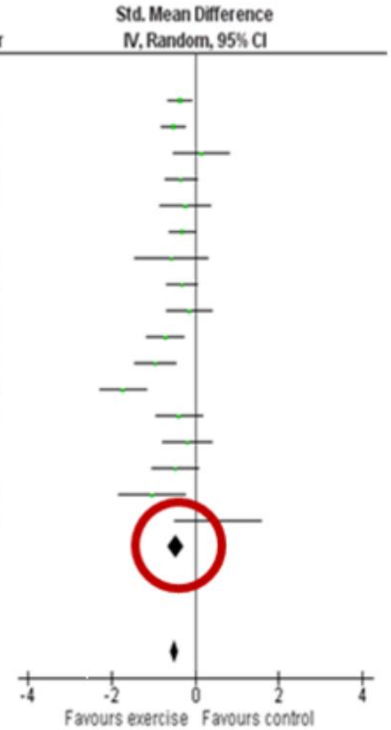
The findings on pain, physical function, and HRQoL are illustrated in Figures F10-2 and F10-3, which present results from one review dealing with land-based exercise effects on the knee (adapted from Fransen et al[52]) and one review dealing with aquatic exercise effects on the knee (adapted from Bartels et al[47]), respectively. In Figure F10-2, the direction to the left favors exercise (decreased pain and improved physical function), whereas, improved HRQoL is to the right. In Figure F10-3, the direction to the left favors exercise (decreased pain, and improved physical function and HRQoL).

The results of these two reviews reported effect sizes that are roughly equivalent for land-based and aquatic exercise. That is, for the outcomes of pain, physical function, and HRQoL, land-based exercise appears to be as efficacious as water-based exercise. Also, the evidence in these reviews suggests that physical activity effects on pain and physical function persist for up to 6 months following cessation of the intervention.[52]

Figure F10-2. Effects of Land-based Exercise on Pain, Physical Function, and Quality of Life in Knee Osteoarthritis

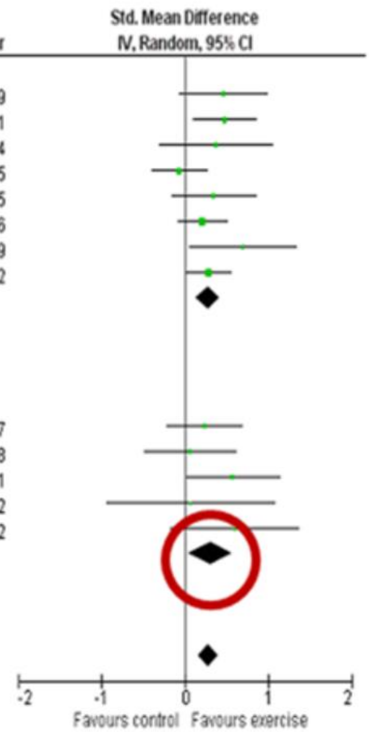
Pain

	Exercise			Control				Std. Mean Difference	
Study or Subgroup	**Mean**	**SD**	**Total**	**Mean**	**SD**	**Total**	**Weight**	**IV, Random, 95% CI**	**Year**
1.1.2 End of treatment scores									
Ettinger 1997a/b	2.21	0.72	146	2.46	0.61	75	3.6%	-0.36 [-0.64, -0.08]	1997
Ettinger 1997a/b	2.14	0.6	144	2.46	0.61	75	3.6%	-0.53 [-0.81, -0.24]	1997
Talbot 2003	1.35	0.93	17	1.2	0.95	17	1.5%	0.16 [-0.52, 0.83]	2003
Hughes 2004	4.9	3.4	68	6.2	4.3	43	2.9%	-0.34 [-0.73, 0.04]	2004
Brismée 2007	15.39	5.7	22	16.64	4.7	19	1.7%	-0.23 [-0.85, 0.38]	2007
Yip 2007	37.33	21.1	79	44.41	23.2	74	3.3%	-0.32 [-0.64, 0.00]	2007
An 2008	71.1	110.1	11	138.2	112.6	10	1.0%	-0.58 [-1.46, 0.30]	2008
Doi 2008	22.55	20.68	61	29.59	23.44	56	3.0%	-0.32 [-0.68, 0.05]	2008
Lund 2008	38	12.5	25	39.7	12	27	2.0%	-0.14 [-0.68, 0.41]	2008
Jan 2008	4.8	3.1	68	7.1	3.4	30	2.5%	-0.71 [-1.16, -0.27]	2008
Lin 2009	4.2	3	36	7.3	3.4	36	2.3%	-0.96 [-1.45, -0.47]	2009
Salli 2010	3.35	1.8	47	6.5	1.8	24	1.9%	-1.73 [-2.30, -1.16]	2010
Bezalel 2010	7	7.5	25	10	7.5	25	2.0%	-0.39 [-0.95, 0.17]	2010
Foroughi 2011	3.8	2.7	20	4.4	3.7	25	1.8%	-0.18 [-0.77, 0.41]	2011
Wang 2011	24	15	26	32	18	26	2.0%	-0.48 [-1.03, 0.08]	2011
Salacinski 2012	18.6	13.4	13	34.3	15.9	15	1.2%	-1.03 [-1.83, -0.23]	2012
Bruce-Brand 2012	10.78	4.31	10	8.33	4.36	6	0.8%	0.54 [-0.50, 1.57]	2012
Subtotal (95% CI)			**818**			**583**	**37.3%**	**-0.47 [-0.65, -0.29]**	
Heterogeneity: $Tau^2 = 0.08$; $Chi^2 = 38.16$, df = 16 (P = 0.001); $I^2 = 58\%$									
Test for overall effect: Z = 5.03 (P < 0.00001)									
Total (95% CI)			**1992**			**1545**	**100.0%**	**-0.49 [-0.59, -0.39]**	
Heterogeneity: $Tau^2 = 0.05$; $Chi^2 = 84.97$, df = 45 (P = 0.0003); $I^2 = 47\%$									
Test for overall effect: Z = 9.64 (P < 0.00001)									
Test for subgroup differences: $Chi^2 = 0.08$, df = 1 (P = 0.77), $I^2 = 0\%$									



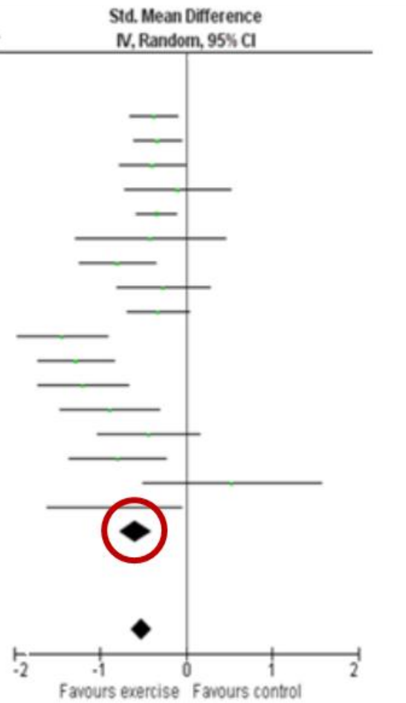
Quality of Life

Study or Subgroup	Exercise Mean	Exercise SD	Exercise Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Year
1.3.1 Change scores									
Minor 1989	-1.7	1.3	28	-2.4	1.7	28	5.3%	0.46 [-0.07, 0.99]	1989
Fransen 2001	2	6.4	83	-0.7	3.7	43	10.7%	0.48 [0.10, 0.85]	2001
Keefe 2004	0.38	1.22	16	0.05	0.33	18	3.2%	0.37 [-0.31, 1.05]	2004
Bennell 2005	0.5	0.13	73	0.51	0.17	67	13.5%	-0.07 [-0.40, 0.27]	2005
Thorstensson 2005	4	13	30	-0.7	14	31	5.8%	0.34 [-0.16, 0.85]	2005
Hay 2006	0.14	2	93	-0.28	2	89	17.5%	0.21 [-0.08, 0.50]	2006
Lee 2009	19.2	15.9	29	9.1	10.3	15	3.6%	0.69 [0.05, 1.34]	2009
Kao 2012	2.1	9.3	114	-0.33	7.9	91	19.4%	0.28 [0.00, 0.55]	2012
Subtotal (95% CI)			**466**			**382**	**78.8%**	**0.27 [0.13, 0.42]**	
Heterogeneity: Tau² = 0.00; Chi² = 7.61, df = 7 (P = 0.37); I² = 8%									
Test for overall effect: Z = 3.70 (P = 0.0002)									
1.3.2 End of treatment scores									
Fransen 2007	49.61	8.83	41	47.6	8.2	36	7.4%	0.23 [-0.22, 0.68]	2007
Lund 2008	43.8	12.5	25	43.1	11.5	27	5.0%	0.06 [-0.49, 0.60]	2008
Wang 2011	74	11	26	67	13	26	4.8%	0.57 [0.02, 1.13]	2011
Bruce-Brand 2012	66.64	20.36	10	65	27.77	6	1.4%	0.07 [-0.95, 1.08]	2012
Salacinski 2012	59.2	17.5	13	46.7	22.6	15	2.6%	0.59 [-0.17, 1.36]	2012
Subtotal (95% CI)			**115**			**110**	**21.2%**	**0.30 [0.04, 0.57]**	
Heterogeneity: Tau² = 0.00; Chi² = 2.55, df = 4 (P = 0.64); I² = 0%									
Test for overall effect: Z = 2.23 (P = 0.03)									
Total (95% CI)			**581**			**492**	**100.0%**	**0.28 [0.15, 0.40]**	
Heterogeneity: Tau² = 0.00; Chi² = 10.20, df = 12 (P = 0.60); I² = 0%									
Test for overall effect: Z = 4.45 (P < 0.00001)									
Test for subgroup differences: Chi² = 0.03, df = 1 (P = 0.86), I² = 0%									



Physical Function

Study or Subgroup	Exercise Mean	Exercise SD	Exercise Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Year
1.2.2 End of treatment scores									
Ettinger 1997a/b	1.72	0.48	144	1.9	0.48	75	3.1%	-0.37 [-0.66, -0.09]	1997
Ettinger 1997a/b	1.74	0.48	144	1.9	0.48	75	3.1%	-0.33 [-0.61, -0.05]	1997
Hughes 2004	17.3	12.6	68	22.3	12.8	43	2.7%	-0.39 [-0.78, -0.01]	2004
Brismée 2007	39.5	12.96	22	40.69	11.89	19	1.9%	-0.09 [-0.71, 0.52]	2007
Hurley 2007	20	18.5	229	25.9	13.6	113	3.3%	-0.35 [-0.57, -0.12]	2007
An 2008	347.5	383.8	11	511.8	381.6	10	1.3%	-0.41 [-1.28, 0.46]	2008
Jan 2008	14.8	8.9	68	22.5	10.9	30	2.5%	-0.80 [-1.24, -0.36]	2008
Lund 2008	35.9	11.5	25	38.9	11	27	2.1%	-0.26 [-0.81, 0.28]	2008
Doi 2008	13.69	13.47	61	18.59	16.38	56	2.8%	-0.33 [-0.69, 0.04]	2008
Lin 2009	10.1	8.3	36	24.9	11.8	36	2.2%	-1.44 [-1.96, -0.91]	2009
Jan 2009	11.2	10.1	71	25	11.8	35	2.5%	-1.28 [-1.72, -0.84]	2009
Salli 2010	20.65	8.9	47	32.6	11.6	24	2.2%	-1.20 [-1.73, -0.66]	2010
Bezalel 2010	25	10	25	34	10	25	2.0%	-0.89 [-1.47, -0.30]	2010
Foroughi 2011	13.3	9.4	20	18.1	12	25	2.0%	-0.43 [-1.03, 0.16]	2011
Wang 2011	18	14	26	31	18	26	2.1%	-0.79 [-1.36, -0.23]	2011
Bruce-Brand 2012	33.91	12.91	10	26.11	15.33	6	1.0%	0.53 [-0.50, 1.57]	2012
Salacinski 2012	15.8	13.9	13	28.9	16.2	15	1.5%	-0.84 [-1.62, -0.06]	2012
Subtotal (95% CI)			**1020**			**640**	**38.0%**	**-0.59 [-0.78, -0.40]**	
Heterogeneity: Tau² = 0.10; Chi² = 47.46, df = 16 (P < 0.0001); I² = 66%									
Test for overall effect: Z = 6.00 (P < 0.00001)									
Total (95% CI)			**2260**			**1653**	**100.0%**	**-0.52 [-0.64, -0.39]**	
Heterogeneity: Tau² = 0.11; Chi² = 135.50, df = 44 (P < 0.00001); I² = 68%									
Test for overall effect: Z = 8.23 (P < 0.00001)									
Test for subgroup differences: Chi² = 0.83, df = 1 (P = 0.36), I² = 0%									



Reproduced from [Exercise for osteoarthritis of the knee: A Cochrane systematic review. Marlene Fransen et al.,[52] 49, 2015] with permission from BMJ Publishing Group Ltd.

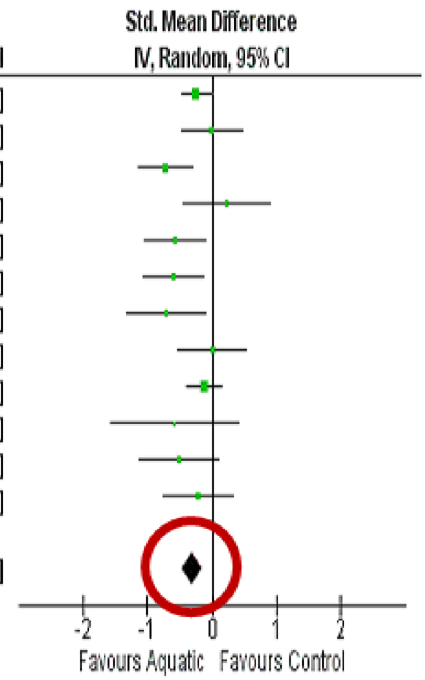
Figure F10-3. Effects of Aquatic Exercise on Pain, Physical Function, and Quality of Life in Knee Osteoarthritis

Pain

Study or Subgroup	Aquatic Mean	Aquatic SD	Aquatic Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI
Cochrane 2005	8.46	3.74	152	9.35	3.54	158	18.3%	-0.24 [-0.47, -0.02]
Foley 2003	10	2.96	35	10	2.96	35	8.3%	0.00 [-0.47, 0.47]
Fransen 2007	27.3	18.7	55	40	16.2	41	9.7%	-0.71 [-1.13, -0.30]
Hale 2012	7.8	3.66	20	7.1	1.67	15	4.8%	0.23 [-0.44, 0.90]
Hinman 2007	143	79	36	198	108	35	8.1%	-0.58 [-1.05, -0.10]
Kim 2012	6.14	1.8	35	7.26	1.92	35	8.0%	-0.60 [-1.07, -0.12]
Lim 2010	3.27	1.67	24	4.55	1.88	20	5.5%	-0.71 [-1.32, -0.10]
Lund 2008	-60.2	12.47	27	-60.3	12.47	27	6.9%	0.01 [-0.53, 0.54]
Patrick 2001	1.38	0.74	98	1.46	0.62	117	15.8%	-0.12 [-0.39, 0.15]
Stener-Victorin 2004	30	30.37	10	48.5	29.63	7	2.4%	-0.58 [-1.58, 0.41]
Wang 2006	43.5	18.6	21	54.9	25.2	21	5.5%	-0.51 [-1.12, 0.11]
Wang 2011	-72	18	26	-68	18	26	6.6%	-0.22 [-0.76, 0.33]
Total (95% CI)			**539**			**537**	**100.0%**	**-0.31 [-0.47, -0.15]**

Heterogeneity: $Tau^2 = 0.02$; $Chi^2 = 16.28$, df = 11 (P = 0.13); $I^2 = 32\%$

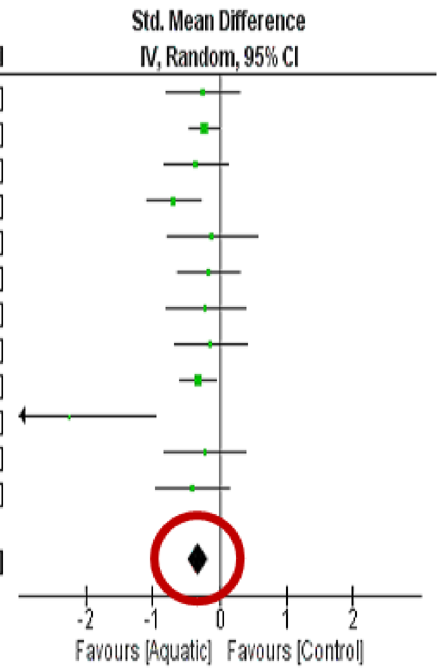
Test for overall effect: Z = 3.80 (P = 0.0001)



Physical Function

Study or Subgroup	Aquatic Mean	Aquatic SD	Aquatic Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI
Arnold 2008	9.94	4.3	25	10.91	3.04	26	6.1%	-0.26 [-0.81, 0.29]
Cochrane 2005	29.26	14.48	149	32.42	13.25	156	21.6%	-0.23 [-0.45, -0.00]
Foley 2003	33	12.59	35	37	9.63	35	7.9%	-0.35 [-0.83, 0.12]
Fransen 2007	34.8	23.7	55	49.9	19	41	9.7%	-0.69 [-1.10, -0.27]
Hale 2012	24	8.33	20	24.9	6.48	15	4.3%	-0.12 [-0.79, 0.55]
Hinman 2007	598	316	36	656	373	35	8.1%	-0.17 [-0.63, 0.30]
Lim 2010	-38.8	7.7	24	-36.9	9.6	20	5.3%	-0.22 [-0.81, 0.38]
Lund 2008	-62.7	11.95	27	-61.1	11.43	27	6.4%	-0.13 [-0.67, 0.40]
Patrick 2001	0.93	0.55	101	1.13	0.67	121	18.0%	-0.32 [-0.59, -0.06]
Stener-Victorin 2004	23.5	7.03	10	45	11.48	7	1.2%	-2.25 [-3.54, -0.95]
Wang 2006	0.9	0.4	21	1	0.5	21	5.2%	-0.22 [-0.82, 0.39]
Wang 2011	-76	16	26	-69	18	26	6.1%	-0.40 [-0.95, 0.14]
Total (95% CI)			**529**			**530**	**100.0%**	**-0.32 [-0.47, -0.17]**

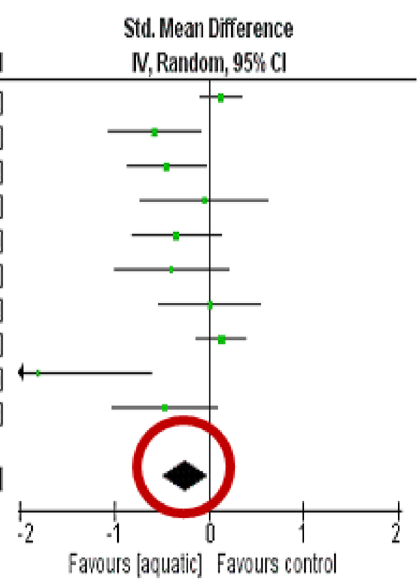
Heterogeneity: Tau² = 0.01; Chi² = 13.74, df = 11 (P = 0.25); I² = 20%
Test for overall effect: Z = 4.28 (P < 0.0001)



Quality of Life

Study or Subgroup	Aquatic Mean	Aquatic SD	Aquatic Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI
Cochrane 2005	-48.02	24.78	159	-51.32	27.17	151	15.3%	0.13 [-0.10, 0.35]
Foley 2003	-49.4	20.04	35	-38.3	17.8	35	10.4%	-0.58 [-1.06, -0.10]
Fransen 2007	-45.15	9.36	55	-40.55	11.01	41	11.6%	-0.45 [-0.86, -0.04]
Hale 2012	24.81	10.04	20	25.36	9.23	15	7.4%	-0.06 [-0.72, 0.61]
Hinman 2007	0.43	0.2	36	0.5	0.2	35	10.5%	-0.35 [-0.82, 0.12]
Lim 2010	-46.8	8.27	24	-42.65	12.18	20	8.4%	-0.40 [-1.00, 0.20]
Lund 2008	-43	12.47	27	-43.1	11.95	27	9.4%	0.01 [-0.53, 0.54]
Patrick 2001	0.61	0.07	101	0.6	0.08	121	14.5%	0.13 [-0.13, 0.40]
Stener-Victorin 2004	0.37	0.83	10	3	1.93	7	3.3%	-1.81 [-3.00, -0.62]
Wang 2011	-73	12	26	-67	13	26	9.1%	-0.47 [-1.02, 0.08]
Total (95% CI)			**493**			**478**	**100.0%**	**-0.25 [-0.49, -0.01]**

Heterogeneity: Tau² = 0.09; Chi² = 25.48, df = 9 (P = 0.002); I² = 65%
Test for overall effect: Z = 2.04 (P = 0.04)



Source: Bartels et al.,[47] Aquatic exercise for the treatment of knee and hip osteoarthritis, Cochrane Database of Systematic Reviews, John Wiley and Sons. Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Dose-response: Most studies of the effects of physical activity on pain, physical function and quality of life are RCTs of one mode, intensity, or duration. Further there is significant heterogeneity for these factors in the studies included within each meta-analysis. Therefore, very limited information on dose-response is available and the minimum dose associated with significant response could not be estimated.

Evidence on Specific Factors

The findings of these six reviews were consistent in that physical activity is associated with reductions in pain and improvements in physical function and quality of life for both knee and hip OA, irrespective of the mode (aquatic versus land-based). The relationships with pain relief, physical function, and quality of life appear to be applicable for aerobic physical activity, for muscle-strengthening activity, and for tai chi. However, some modest difference in effect sizes was seen across these exposures. The evidence reviewed did not contain sufficient information to determine if intensity or duration was related to changes in HRQoL. Evidence was also insufficient to determine if the relationship between physical activity and pain, physical function and quality of life varied by age, sex, race/ethnicity, socioeconomic status or body weight.

Osteoarthritis Disease Progression

Concern that high-intensity physical activity and large amounts of weight-bearing activity may have harmful effects on OA progression prompted the Subcommittee to conduct a targeted review for this outcome. This review required a separate search for evidence from searches related to pain, physical function, and HRQoL. The Subcommittee reviewed the literature addressing the association of physical activity with progression of OA in those with pre-existing disease. For the purposes of this review, progression of OA was defined as worsening of OA as assessed by structural OA imaging (radiograph or magnetic resonance imaging, MRI), or as clinical progression to total knee replacement (TKR). The Subcommittee did not identify any studies examining the effects of physical activity on circulating biomarkers associated with a worsening disease state.

Existing Systematic Review and Meta-Analyses

The Subcommittee identified one systematic review including 49 studies[65] and one meta-analysis[62] including three studies. The systematic review[65] included exposures of low-impact therapeutic physical activity combining muscle-strengthening, stretching, and aerobic elements. All of the primary literature studies in this systematic review dealt with knee OA (no included studies dealt with progression of hip

OA) and used structural OA imaging progression or progression to TKR as outcomes. This systematic review examined 48 longitudinal cohort studies composed of 8,614 total participants.

The systematic review[65] provided no evidence of harmful effects of activity on progression in its comparisons of individuals with greater amounts of low-impact physical activity to individuals with the least amounts of physical activity, when progression was assessed by adverse events of increased pain, decreased physical function, progression of structural OA on imaging or increased TKR at a group level. Of the studies in this review, only six (five of which were RCTs) included objective imaging outcomes or TKR as measures of osteoarthritis progression. Objective measures and need for joint replacement were considered the standards for assessing effects on OA progression. Although the number of joint replacements was small across the five RCTs, these trials found no evidence of more TKRs within physical activity groups (N=8 TKR) compared to groups that did not engage in physical activity (N=10 TKR). Based upon this review, the Subcommittee was not able to comment on the impact of greater intensity physical activity on OA progression.

The meta-analysis[62] assessed self-reported running or jogging (including running-related sports such as triathlon and orienteering). Timmins et al[62] used radiography, other imaging, and questionnaires to examine diagnosis of knee OA, radiographic markers of knee OA, knee joint surgery for OA, knee pain, and knee-associated disability as markers of OA progression. This review, containing 10 individual studies with a total of 6,962 individuals, examined running and development of knee OA, including joint surgery, as outcomes considered indicative of progression from subclinical to clinical disease.[62] Although this meta-analysis included prevention of primary OA, the data are instructive for understanding the role of running in the development of OA. In this meta-analysis, three studies examined TKR as an outcome. The meta-analysis revealed runners had significantly less risk of having TKR than did non-runners (odds ratio (OR)=0.46; 95% CI: 0.30-0.71; P=0.0004).

Original Research

Although providing highly relevant evidence, the Subcommittee did not believe that one systematic review dealing with knee OA alone was adequate to assess the entire range of the literature. Therefore, for the question of the effects of physical activity on OA disease progression, the Subcommittee elected to perform a primary literature review. Five original research studies examining the relationship between physical activity and disease progression were identified.[66-70] All studies were prospective cohort studies, published from 2013 to 2016. The analytical sample size ranged from 100[68] to 2,073[67];

three were U.S. studies,[67, 69, 70] one Tasmanian,[66] and one did not report. Three studies used self-reported physical activity on the Physical Activity Scale for the Elderly (PASE)[67-69]; two had device-measured physical activity from accelerometer or pedometer.[66, 70] All included studies examined OA progression (knee structural change, cartilage loss) as the outcome.

These five longitudinal cohort studies with imaging or TKR as outcomes were deemed of adequate quality to address the question.[66-70] Two of these studies had device-based measures of physical activity and all used MRI to assess OA progression. Outcome measures included radiographic progression with the Kellgren Lawrence (KL) grading system, MRI with a measure of cartilage damage (T2 relaxation) and, in one study, subchondral bone marrow lesions. Collectively, these five studies focused on one of three longitudinal cohort studies: the Osteoarthritis Initiative,[67-69] the Multicenter Osteoarthritis Study[67, 70] and a longitudinal cohort study of 405 community dwelling adults from Australia.[66] The Osteoarthritis Initiative assessed physical activity with the Physical Activity Scale for the Elderly survey; the Multicenter Osteoarthritis and the Australian cohort assessed exposure by device-based step count measures.

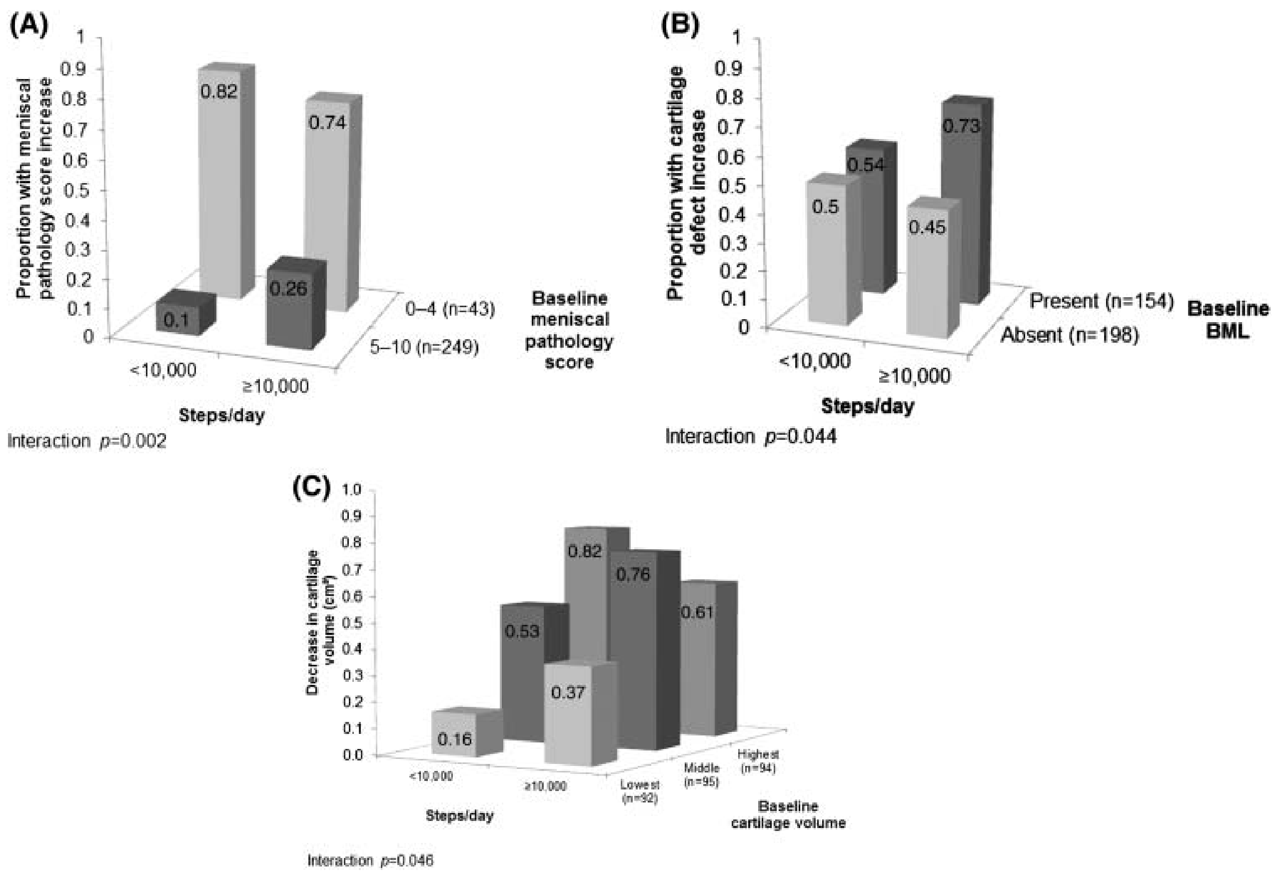
Overall, the findings in these studies were mixed:

- The Osteoarthritis Initiative assessed knee OA in 100 participants using MRI and saw no disease progression with physical activity, as measured by the Physical Activity Scale for the Elderly.[68]
- The Multicenter Osteoarthritis study assessed knee OA in 1,179 participants using radiographic (X-ray) cartilage loss and saw no disease progression with physical activity, as measured by accelerometry (steps).[70]
- The Osteoarthritis Initiative assessed knee OA in 205 individuals with asymptomatic OA using MRI to ascertain cartilage quality. The authors examined large and small amounts of physical activity as measured by high and low Physical Activity Scale for the Elderly scores; they found that 15 percent of the population in each category were associated with OA progression.[69]
- Felson et al[67] assessed OA in 3,542 knees of 2,073 Osteoarthritis Initiative and Multicenter Osteoarthritis participants with asymptomatic OA; they found that those in the greatest physical activity quartile, as measured by the Physical Activity Scale for the Elderly, showed no OA progression.
- Dore et al[66] assessed knee OA in 405 Australian individuals using MRI with four structural measures. Steps per day were measured with pedometer counts. Individuals with fewer than 10,000 steps per day showed no knee OA progression; those with more than 10,000 steps per

day showed some progression. The effect of physical activity appeared to be modified by baseline state (Figure F10-4).

Thus, the Subcommittee's review identified at least two studies demonstrating a U-shaped relationship between aerobic exercise and OA progression in those with pre-existing OA.[66, 69] For land-based exercise, benefit is seen at step counts up to 10,000 steps per day. Greater ambulation (more steps per day) appears to be associated with some OA progression.[66]

Figure F10-4. Interaction of Underlying Joint Pathology by MRI and Ambulatory Physical Activity Amounts (Step Counts) on Osteoarthritis Progression, as Shown on MRI



Note: Greater meniscal pathology scores, presence of bone mineral lesions and less cartilage volume all indicate more severe disease. Bone mineral lesions are areas of increased signal adjacent to the subcortical bone at the medial tibial, medial femoral, lateral tibial, and lateral femoral sites and indicate more severe joint pathology. All figures show an interaction effect, wherein for those individuals with less baseline meniscal pathology, steps are not related to pathology score increases. In contrast, in adults with greater baseline pathology scores, a greater percent of adults with more than 10,000 steps per day show worsening of pathology scores over time (26%) compare to adults with fewer than 10,000 steps day (10%).
Source: Reproduced from [The association between objectively measured physical activity and knee structural change using MRI, Dawn A Dore et al.,[66] 72, 2013] with permission from BMJ Publishing Group Ltd.

Evidence on Specific Factors

Demographic factors and weight status: The issue of effect modification by sex, age, race/ethnicity, and socioeconomic status was not examined in the meta-analyses used as sources of evidence. Although a relationship between BMI and osteoarthritis is generally recognized, no one has investigated through meta-analyses whether these translate to effect modifications of these factors in the physical activity-OA relationship.

Due to exposure heterogeneity, it is not possible estimate an energy expenditure exposure of aerobic exercise associated with effects. Moderate-level evidence indicates that physical activity up to about 10,000 steps per day does not accelerate knee OA. One study indicated that lifetime running was not associated with increased risk of primary OA; in fact, a significant reduction in risk occurred in these cohorts.

Type of physical activity: The relationships with pain relief, physical function, and quality of life appear to be applicable for aerobic exercise, muscle-strengthening exercise, and tai chi.[52] In its review, the Subcommittee did not discover any studies investigating the relationships among greater amounts of aquatic exercise and OA progression. It was not possible to determine if effects of physical activity on progression varied by frequency, duration, intensity, or type of physical activity.

For additional details on this body of evidence, visit: https://health.gov/paguidelines/second-edition/report/supplementary-material.aspx for the Evidence Portfolio.

Comparing 2018 Findings with the 2008 Scientific Report

The 2008 Scientific Report[4] included a broad review of physical activity and osteoarthritis, including review of effects of activity on risk of incident OA as well as effects of physical activity in people with OA. That report found clear evidence of benefits of physical activity on pain, HRQoL, and physical function in people with OA.

The findings of this report are generally consistent with those of the 2008 Scientific Report,[4] but expand the information related to these findings. For example, this report comments more extensively on the types of physical activity that provide benefits, e.g., that aquatic exercise can provide benefits similar in magnitude to those of land-based exercise, that tai chi provides benefits in people with OA, and that benefits can persist after cessation of physical activity. This report adds considerably to information on the effects of physical activity on progression of OA. There appears to be U-shaped relationship between amount of ambulatory physical activity and progression in OA, with moderate evidence that step counts up to the range of 10,000 steps per day do not accelerate progression of OA. However, the Subcommittee located some evidence suggesting that step counts above the range of 10,000 steps per day may have adverse effects on progression.[66, 69]

Public Health Impact

There are approximately 100 different arthritic conditions affecting a total of 54.4 million Americans. Among these, OA is the most common joint disorder in the United States, affecting an estimated 30.8 million adults (13.4 percent of the civilian adult U.S. population).[71] Methodological issues make it highly likely that the real burden of OA has been underestimated.[72] Lower extremity OA is the leading cause of mobility impairment in older adults in the United States.[73] OA affects a broad spectrum of age groups in the United States, including 2 million Americans younger than age 45 years with knee OA.[74] By the year 2040, an estimated 78.4 million (25.9% of the projected total adult population) adults ages 18 years and older are expected to have medically diagnosed arthritis,[75] the majority of whom will have OA. As expected, based on these prevalence and disability figures, OA is associated with an extremely high economic burden—by one national estimate equal to $185.5 billion in aggregate annual medical care expenditures.[76]

From this review, it is clear that regular exercise at amounts up to those consistent with the 2008 Physical Activity Guidelines[23]—at least 150 minutes per week of moderate-intensity aerobic exercise and 2 days per week of muscle-strengthening exercise—has substantial beneficial effects on the overall population of those with pre-existing OA, and will have a substantial public health impact. Physical activity should be encouraged in the general population of those individuals with pre-existing OA for pain relief, improved physical function, and improved quality of life without concern of causing worsening of the condition for exposures of less than 10,000 steps per day. Measurable benefits of physical activity seem to persist for periods of up to 6 months following cessation of a defined program.

Question 3: In people with the cardiovascular condition of hypertension, what is the relationship between physical activity and (1) risk of co-morbid conditions, (2) physical function, (3) health-related quality of life, and (4) cardiovascular disease progression and mortality?

a) Is there a dose-response relationship? If yes, what is the shape of the relationship?
b) Does the relationship vary by age, sex, race/ethnicity, socioeconomic status, weight status, or resting blood pressure level?

c) Does the relationship vary based on frequency, intensity, time, duration, type (mode), or how physical activity is measured?

Source of evidence: Systematic reviews, meta-analyses

Conclusion Statements

Co-morbid Conditions

Insufficient evidence is available to determine whether a relationship exists between physical activity and risk of co-morbid conditions among adults with hypertension. **PAGAC Grade: Not assignable.**

Physical Function

Insufficient evidence is available to determine whether a relationship exists between physical activity and physical function among adults with hypertension. **PAGAC Grade: Not assignable.**

Health-related Quality of Life

Insufficient evidence is available to determine whether a relationship exists between physical activity and health-related quality of life among adults with hypertension. **PAGAC Grade: Not assignable.**

Disease Progression

Strong evidence demonstrates that physical activity reduces the risk of progression of cardiovascular disease among adults with hypertension. **PAGAC Grade: Strong.**

Strong evidence demonstrates that, among adults with hypertension, physical activity reduces the disease progression indicator of blood pressure. **PAGAC Grade: Strong.**

Moderate evidence indicates an inverse dose-response relationship between physical activity and the disease progression indicator of cardiovascular disease mortality among adults with hypertension. **PAGAC Grade: Moderate.**

Insufficient evidence is available to determine whether a dose-response relationship exists between physical activity and blood pressure among adults with hypertension. **PAGAC Grade: Not assignable.**

Insufficient evidence is available to determine whether the relationship between physical activity and the disease progression indicators of blood pressure and cardiovascular disease mortality varies by age, sex, race/ethnicity, socioeconomic status, or weight status among adults with hypertension. **PAGAC Grade: Not assignable.**

Limited evidence suggests that, among adults with hypertension, the blood pressure response to physical activity varies by resting blood pressure level, with the greatest blood pressure reductions occurring among those adults who have the highest resting blood pressure levels. **PAGAC Grade: Limited.**

Insufficient evidence is available to determine whether the relationship between physical activity and the disease progression indicators of blood pressure and cardiovascular disease mortality varies by the frequency, intensity, time, and duration of physical activity, or how physical activity is measured among adults with hypertension. **PAGAC Grade: Not assignable.**

Moderate evidence indicates the relationship between physical activity and the disease progression indicator of blood pressure does not vary by type of physical activity, with the evidence more robust for traditional types (modes, i.e., aerobic, dynamic resistance, combined) of physical activity than for other types (tai chi, yoga, and qigong) among adults with hypertension. **PAGAC Grade: Moderate.**

Review of the Evidence

Cardiovascular disease is the leading cause of death in the United States and the world, accounting for approximately 1 in 3 deaths (807,775, or 30.8%) in the United States and 17.3 million (31%) worldwide.[77, 78] Hypertension is the most common, costly, and preventable CVD risk factor. According to the *Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure* (JNC 7)[79] blood pressure classification scheme, hypertension affects 86 million (34%) adults in the United States and 1.4 billion (31%) adults globally.[77, 78] The lifetime risk of acquiring hypertension is 90 percent.[79] Furthermore, hypertension is the most common primary diagnosis in the United States, and the leading cause for medication prescriptions among adults older than age 50 years.[80] By 2030, it is estimated that 41 percent of adults in the United States will have hypertension. From 2010 to 2030, the total direct costs attributed to hypertension are projected to triple ($130.7 to $389.9 billion), while the indirect costs due to lost productivity will double ($25.4 to $42.8 billion).[77] Curbing this growing and expensive public health crisis is a national and global priority.[78, 81]

To answer this question, the Subcommittee reviewed one systematic review,[82] and 14 meta-analyses.[83-96] The coverage dates ranged from inception of the database to 2016, the total number of included studies ranged from 4 to 93, and the total included study sample size consisted of 125,986 adults ranging from 216 to 96,073 participants. The systematic review examined 6 large longitudinal prospective cohort studies, and the 14 meta-analyses included RCTs that examined the blood pressure response to physical activity among adults with hypertension compared to a control condition among similar adults who were sedentary at baseline.

All studies in the meta-analyses included adults with hypertension,[82-96] six included adults with prehypertension,[82-84, 88, 93, 95] and eight included adults with normal blood pressure.[82-85, 93-96] Because the literature reviewed for this question was based upon the JNC 7 blood pressure classification scheme, the Subcommittee used the JNC 7 blood pressure classification scheme[79] for data extraction purposes. The JNC 7 defines these blood pressure classifications as follows: Hypertension is defined as having a resting systolic blood pressure of 140 mmHg or greater and/or a resting diastolic blood pressure 90 mmHg or greater, or taking antihypertensive medication, regardless of the resting blood pressure level. Prehypertension is defined as a systolic blood pressure from 120 to 139 mmHg and/or diastolic blood pressure from 80 to 89 mmHg. Normal blood pressure is defined as having a systolic blood pressure less than 120 mmHg and diastolic blood pressure less than 80 mmHg. However, it should be noted that during the preparation of this report, the American College of Cardiology and American Heart Association Task Force on Clinical Practice Guidelines released the 2017 *Guideline for the Prevention, Detection, Evaluation and Management of High Blood Pressure in Adults*.[97] The new Guidelines define hypertension as a resting systolic blood pressure of 130 mmHg or greater and/or a resting diastolic blood pressure 80 mmHg or greater, or taking antihypertensive medication, regardless of the resting blood pressure level. Furthermore, the term prehypertension was eliminated and elevated blood pressure was added indicating a resting systolic blood pressure between 120 to 129 mmHg and a diastolic blood pressure <80 mmHg. However, the new hypertension guidelines did not alter the conclusion statements made in this report.

Co-morbid Conditions, Physical Function, and Health-related Quality of Life

Evidence on the Overall Relationship

Hypertension co-morbidities include CVD, obesity, diabetes mellitus, chronic kidney disease, congestive heart failure, and the metabolic syndrome, among others. However, because of a lack of evidence, the Subcommittee was unable to draw any conclusions about whether a relationship exists between physical activity and risk of co-morbid conditions among adults with hypertension, or about whether a relationship exists between physical activity and physical function.

The available evidence also was insufficient to determine whether a relationship exists between physical activity and HRQoL among adults with hypertension. Of note, several of the meta-analyses commented on the potential favorable nature of this relationship (Xiong et al[89] relating to a type of qigong—Baduanjin). However, few primary level studies in these meta-analyses addressed this relationship.

Disease Progression

The Subcommittee defined CVD progression in two ways. Because blood pressure is considered a proxy measure of the risk of CVD,[88, 98] the Subcommittee regarded the blood pressure response to physical activity as an indicator of CVD progression, and the outcome of CVD mortality as an indicator of longstanding hypertension. The evidence on the blood pressure response to physical activity is discussed below, and the evidence on CVD mortality outcomes follows in the section on dose-response.

Evidence on the Overall Relationship

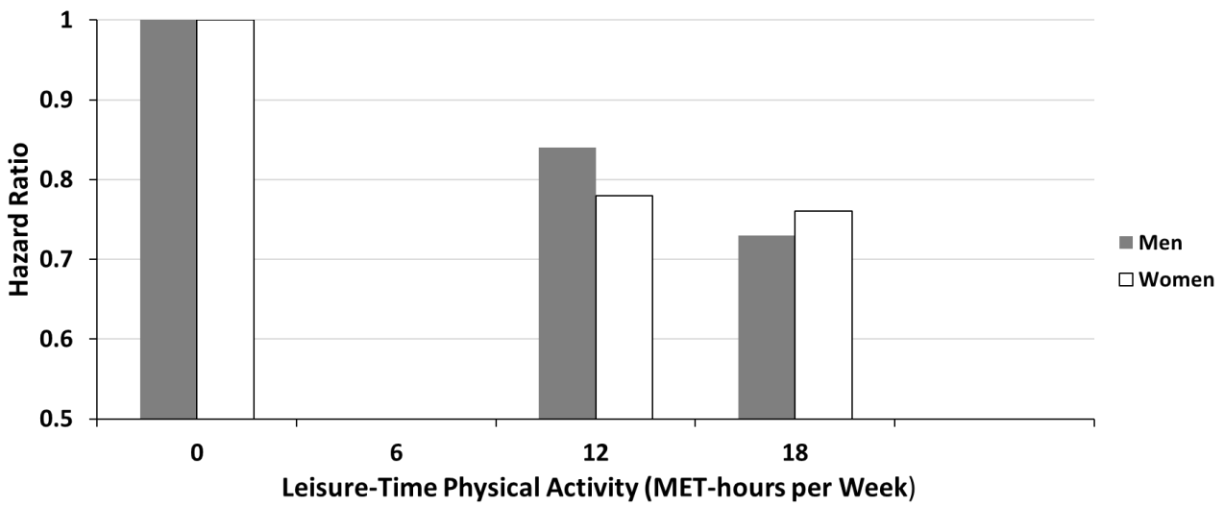
Strong evidence demonstrates that physical activity reduces blood pressure among adults with hypertension. All 14 meta-analyses included RCTs that examined the blood pressure response to physical activity among adults with hypertension compared to a control condition of adults who were inactive.[83-96] Of these, 13 reported a statistically significant reduction in systolic blood pressure and 14 reported a statistically significant reduction in diastolic blood pressure (see Supplementary Table S-F10-1). The magnitude of the reductions ranged from 5 to 17 mmHg for systolic blood pressure and 2 to 10 mmHg for diastolic blood pressure. Blood pressure reductions of this magnitude may be sufficient to reduce risk of coronary heart disease 4 to 22 percent and stroke by 6 to 41 percent among adults with hypertension.[79, 99, 100] Furthermore, the magnitude of these blood pressure reductions to physical activity may be sufficient to reduce the resting blood pressure of some of the samples with hypertension into prehypertensive to normotensive ranges.

When studies disclosed the information, the frequency of physical activity ranged from 1 to 7 days per week, with 3 days per week most common; the intensity ranged from low to vigorous, with low to moderate most common; the time ranged from 12 to 100 minutes per session, with 30 minutes to 45 minutes per session most common; and the study duration ranged from 4 weeks to 24 years, with 4 weeks to 16 weeks most common. Due to the imprecise disclosure of the frequency, intensity, and time of the physical activity interventions, the dose-response of the blood pressure response to physical activity could not be determined.

Dose-Response: Moderate evidence indicates an inverse dose-response relationship between physical activity and CVD mortality among adults with hypertension. One systematic review addressed the impact of self-reported general and leisure-time physical activity on CVD mortality among adults with hypertension who were followed from 5 to 24 years.[82] This systematic review included six large prospective cohort studies[101-106] of approximately equal numbers of mostly white men and women who had hypertension, prehypertension, and normal blood pressure. Only the findings relating to CVD mortality among the samples with hypertension are discussed here.

Hu et al[104] investigated the associations among occupational, daily commuting, and leisure-time physical activity and cardiovascular mortality among 26,643 Finnish men and women with overweight and hypertension, ages 25 to 64 years, who were followed for 20 years. The covariate-adjusted hazard ratios of CVD mortality associated with low (almost completely inactive), moderate (some physical activity more than 4 hours per week, about 12 MET-hours per week or more), and high (vigorous physical activity more than 3 hours per week, about 18 MET-hours per week or more) leisure-time physical activity were 1.00, 0.84 (95% CI: 0.77-0.92), and 0.73 (95% CI: 0.62-0.86) among men, respectively; and 1.00, 0.78 (95% CI: 0.70-0.87), and 0.76 (95% CI: 0.60-0.97) among women, respectively (Figure F10-5). The covariate-adjusted hazard ratios of CVD mortality associated with low (very easy physical activity), moderate (standing and walking at work), and high (walking, lifting, or heavy manual labor at work) occupational physical activity were 1.00, 0.84 (95% CI: 0.85-1.05), and 0.86 (95% CI: 0.78-0.96) among men and 1.00, 0.85 (95% CI: 0.74-0.98), and 0.84 (95% CI: 0.73-0.96) among women (see Supplementary Table S-F10-1). Among women only, the hazard ratios for active daily commuting to and from work associated with reduced CVD mortality were 1.00 for motorized transport or no work, 0.83 (95% CI: 0.72-0.96) for walking or bicycling 1 to 29 minutes per day, and 0.86 (95% CI: 0.74-0.99) for 30 or more minutes per day.

Figure F10-5. The Inverse Relationship Between Cardiovascular Mortality and Leisure-time Physical Activity by MET-hours per Week Among Adults with Hypertension



Source: Adapted from data found in Hu et al., 2007.[104]

In summary, leisure-time moderate physical activity equating to about 12 MET-hours per week or more reduced CVD mortality by 16 percent among men and 22 percent among women, while higher amounts of leisure-time vigorous physical activity equating to about 18 MET-hours per week or more reduced CVD mortality by 27 percent among men and 24 percent among women, indicating an inverse dose-response relationship between physical activity and cardiovascular mortality among adults with hypertension. However, no dose-response relationship was found between occupational and commuting physical activity and cardiovascular mortality.

Collectively, the prospective cohort studies in the systematic review of Rossi et al[82] indicated that greater amounts of physical activity reduced CVD mortality by 16 percent (RR=0.84; 95% CI: 0.73-0.97) to 67 percent (RR=0.33; 95%CI: 0.11-0.94) compared to lower amounts of physical activity or being sedentary. In addition, the greatest amounts of physical activity reduced CVD mortality by 20 percent (HR=0.80; 95% CI: 0.66-0.96) to 67 percent (RR=0.33; 95%CI: 0.11-0.94) compared to lower amounts of physical activity or being sedentary; and low to moderate amounts of physical activity reduced CVD mortality by 16 percent (HR=0.84; 95% CI: 0.73-0.97) to 22 percent (HR=0.78; 95% CI: 0.70-0.87) compared to being physically inactive or sedentary. The protective benefits of physical activity against CVD mortality were similar for men and women. Nonetheless, it was difficult for the Subcommittee to summarize the magnitude and precision of the protective effect based upon the studies of Engstrom et al,[101] Fan et al,[102] and Fossum et al.[103] In these studies there was considerable variation in the definition of hypertension and measurement of blood pressure, and the self-reported measurements of physical activity did not quantify the frequency, duration, and intensity of physical activity.

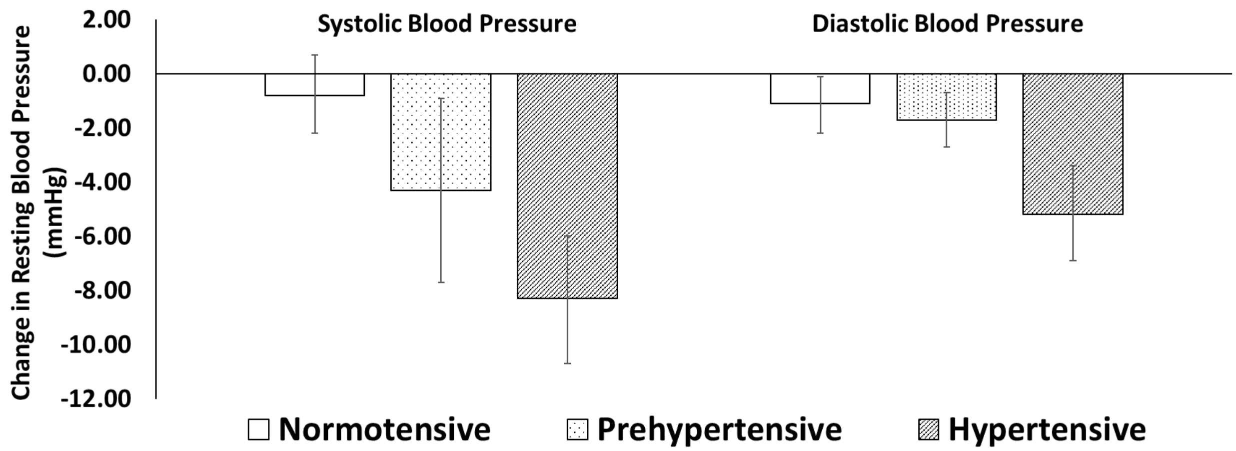
Vatten et al[106] found that among men with a resting systolic blood pressure between 140 to 159 mmHg, those who were highly physically active (RR=1.21; 95% CI: 0.97-1.52) reduced their risk of CVD mortality by 30 percent compared to those who were physically inactive (RR=1.73; 95% CI: 1.37-2.19). Among men with a resting systolic blood pressure >160 mmHg, those who were highly physically active (RR=1.82; 95% CI: 1.46-2.28) reduced their risk of CVD mortality by 19 percent compared to those who were physically inactive (RR=2.24; 95% CI: 1.78-2.83). In addition, among women with a resting systolic blood pressure between 140 to 159 mmHg, those who were highly physically active (RR=1.47; 95% CI: 1.04-2.09) reduced their risk of CVD mortality by 24 percent compared to those who were physically inactive (RR=1.93; 95% CI: 1.39-2.69). Among women with a resting systolic blood pressure >160 mmHg, those who were highly physically active (RR=1.77; 95% CI: 1.26-2.54) reduced their risk of CVD mortality by 27 percent compared to those who were physically inactive (RR=2.41; 95% CI: 1.76-3.30). Therefore, as systolic blood pressure increases within hypertensive ranges, the risk of CVD mortality increases. However, the increased risk is attenuated with higher levels of physical activity.

Evidence on Specific Factors

Demographic characteristics and weight status: The available evidence is insufficient to determine whether the relationship between physical activity and the disease progression indicators of blood pressure and CVD mortality varies by age, sex, race/ethnicity, socioeconomic status, or weight status among adults with hypertension. In the few instances where these factors were examined, the findings were too disparate to synthesize because they were often not reported separately for adults with hypertension but were reported for the overall sample that included adults with hypertension, prehypertension, and normal blood pressure. Two meta-analyses found age not to be a significant moderator of the blood pressure response to physical activity among samples with mixed blood pressure levels.[83, 84] One meta-analysis reported that men exhibited blood pressure reductions twice as large as women following aerobic exercise training among a sample with mixed blood pressure levels.[84] Race/ethnicity was poorly reported, and when reported in seven of the meta-analyses,[87-92, 95] the samples were largely White or Asian. One meta-analysis reported that nonwhite samples with hypertension experienced greater blood pressure reductions than did White samples with hypertension.[95] MacDonald et al[95] found reductions of systolic/diastolic blood pressure of -14.3/-10.3 mmHg after moderate-intensity dynamic resistance training among nonwhite samples with hypertension versus reductions of -9.2/-9.5 mmHg among White samples with hypertension, respectively. No meta-analyses disclosed the socioeconomic status of their samples. Five meta-analyses reported the weight status of their samples, which ranged from normal weight to obese.[83, 87, 88, 93, 95] Cornelissen and Smart[84] found the systolic blood pressure reductions resulting from aerobic training tended to be larger with greater (β1=0.49, *P*=0.08) than less (β1=0.45, *P*=0.06) weight loss among 5,223 adults with mixed blood pressure levels.

Resting blood pressure level: Limited evidence suggests the disease progression indicator of the blood pressure response to physical activity varies by resting blood pressure level among adults with hypertension (Figure F10-6). Of the six meta-analyses examining blood pressure classification as a moderator of the blood pressure response to physical activity,[83-85, 93, 95, 96] four[84, 85, 93, 95] found that the greatest blood pressure reductions occurred among samples with hypertension (5 to 8 mmHg, 4 to 6 percent of resting blood pressure level) followed by samples with prehypertension (2 to 4 mmHg, 2 to 4 percent of resting blood pressure level), and normal blood pressure (1 to 2 mmHg, 1 t to 2 percent of resting blood pressure level) (Supplementary Table S-F10-2). Consistent with the law of initial values,[107, 108] adults with hypertension experience blood pressure reductions from exercise training that are about 2 times greater than the blood pressure reductions among adults with prehypertension and about 4 to 5 times greater than the blood pressure reductions among adults with normal blood pressure (see Supplementary Table S-F10-2). Blood pressure reductions of this magnitude may be sufficient to reduce the resting blood pressure of some of the samples with hypertension into prehypertensive ranges. They may also be sufficient to reduce the risk of coronary heart disease 4 to 22 percent and stroke by 6 to 41 percent among adults with hypertension.[79, 99, 100]

Figure F10-6. Blood Pressure Response to 16 Weeks of Aerobic Physical Activity, by Resting Blood Pressure Level



Source: Adapted from data found in Cornelissen and Smart, 2013.[84]

Frequency: The frequency of the physical activity interventions was reported by 10 meta-analyses,[83-86, 88-90, 92, 93, 95] and ranged from 1 to 7 days per week. However, no conclusions can be made about the influence of frequency on the blood pressure response to physical activity because the findings were too scarce and too disparate to synthesize.

Intensity: The intensity of the physical activity interventions was quantified in nine of the meta-analyses,[83-85, 88, 92-96] and ranged from low to vigorous-intensity. However, no conclusions can be made regarding the influence of intensity on the blood pressure response to physical activity as the magnitude and precision of the effect could not be determined from findings that were too scarce to synthesize.

Time: The time of the exercise session was reported in nine of the meta-analyses,[84-86, 88-90, 92, 93, 96] and ranged from 12 minutes to 100 minutes. However, no conclusions can be made regarding the influence of time on the blood pressure response to physical activity as the magnitude and precision of the effect could not be determined from a lack of findings on the time of the exercise session.

Duration: All chronic (i.e., training) meta-analyses reported the duration of the physical activity intervention, and they ranged from 1 to 60 months.[83-93, 95, 96] However, no conclusions can be made regarding the influence of duration on the blood pressure response to physical activity as the magnitude and precision of the effect could not be determined from findings that were too scarce to synthesize.

Type (Mode): Moderate evidence indicates the relationship between physical activity and the disease progression indicator of blood pressure does not vary by type of physical activity, with the evidence more robust for traditional types (i.e., aerobic, dynamic resistance, combined) of physical activity than for other types (i.e., tai chi, yoga, qigong) among adults with hypertension.

Traditional type (mode): Five meta-analyses examined the blood pressure response to aerobic exercise training,[84-88] three meta-analyses examined the blood pressure response to resistance exercise training (one acute[94] and two chronic[83, 95]), one meta-analysis examined the blood pressure response to combined aerobic and resistance exercise training,[93] and one meta-analysis examined the blood pressure response to isometric resistance training.[96] Cornelissen and Smart[84] examined aerobic exercise training performed, on average, at moderate- to-vigorous intensity for 40 minutes per session 3 days per week for 16 weeks and reported systolic/diastolic blood pressure reductions of: -8.3 (95% CI: -10.7 to -6.0)/-5.2 (95% CI: -6.9 to -3.4), -4.3 (95% CI: -7.7 to -0.9)/-1.7 (95% CI: -2.7 to -0.7), and -0.8 (95% CI: -2.2 to +0.7)/-1.1 (95% CI: -2.2 to -0.1) mmHg among adults with hypertension, prehypertension, and normal blood pressure, respectively (see Supplementary Table S-F10-1). MacDonald et al[95] examined dynamic resistance training performed, on average, at moderate intensity for 32 minutes per session 3 days per week for 14 weeks and reported systolic/diastolic blood pressure changes of -5.7 (95% CI: -9.0 to -2.7)/-5.2 (95% CI: -8.4 to -1.9), -3.0 (95% CI: -5.1 to -1.0)/-3.3 (95% CI: -5.3 to -1.4), and 0.0 (95% CI: -2.5 to 2.5)/-0.9 (95% CI: -2.1 to 2.2) mmHg among adults with hypertension, prehypertension, and normal blood pressure, respectively. Corso et al[93] examined combined aerobic and dynamic resistance exercise training performed, on average, at moderate intensity for 58 minutes per session 3 days per week for 20 weeks and reported systolic/diastolic blood pressure changes of -5.3 (95% CI: -6.4 to -4.2)/-5.6 (95% CI: -6.9 to -3.8), -2.9 (95% CI: -3.9 to -1.9)/-3.6 (95% CI: -5.0 to -0.2), and +0.9 (95% CI: 0.2 to 1.6)/-1.5 (95% CI: -2.5 to -0.4) mmHg among adults with hypertension, prehypertension, and normal blood pressure, respectively.

Carlson et al[96] investigated the blood pressure response among adults with hypertension (N=61) and normal blood pressure (N=162) to 4 or more weeks of isometric resistance training at 30 to 50 percent maximal voluntary contraction, with four contractions held for 2 minutes with 1 to 3 minutes of rest between contractions. Among the adults with hypertension, all of whom were on medication, training resulted in reductions of systolic, diastolic, and mean arterial blood pressure of -4.3 (95% CI: -6.6 to -2.2)/-5.5 (95% CI: -7.9 to -3.3)/-6.1 (95% CI: -8.0 to -4.0) mmHg, respectively. Among adults with normal blood pressure, training resulted in reductions of systolic, diastolic, and mean arterial blood pressure of -7.8 (95% CI: -9.2 to -6.4)/-3.1 (95% CI: -3.9 to -2.3)/-3.6 (95% CI: -4.4 to -2.7) mmHg, respectively. Carlson et al[96] were unable to explain the larger reductions in systolic blood pressure among the adults with normal blood pressure compared to adults with hypertension, and the reverse pattern of blood pressure response for diastolic blood pressure and mean arterial pressure. The sample size of adults with hypertension (N=61), all of whom were on medication, in the meta-analysis by Carlson et al[96] investigating isometric resistance training was much smaller than the sample size of the adults with hypertension in the meta-analyses investigating aerobic,[84] dynamic resistance,[95] and combined aerobic and dynamic resistance[93] exercise training. For these reason, any conclusions made about the antihypertensive benefits of isometric resistance training should be made with caution.

Collectively, these findings indicate the systolic/diastolic blood pressure reductions following physical activity among adults with hypertension are -8.3/-5.2 mmHg for aerobic, -5.7/-5.2 mmHg for dynamic resistance, and -5.3/-5.6 mmHg for combined aerobic and dynamic resistance exercise training. These blood pressure reductions are about 2 times greater among adults with hypertension than among adults with prehypertension and about 4 to 5 times greater among adults with hypertension than among adults with normal blood pressure, independent of type of exercise. These blood pressure benefits occurred at about 6 MET-hours per week or more of moderate-to-vigorous physical activity.

Tai chi, yoga, qigong: Evidence of lower quality suggests that the relationship between physical activity and the disease progression indicator of blood pressure does not vary by for other types of physical activity (i.e., tai chi, yoga, qigong). Four meta-analyses examined these types of physical activity. Xiong et al[89] investigated the blood pressure response to Baduanjin (a type of qigong), an ancient Chinese mind-body exercise characterized by simple, slow, and relaxing movements, among 572 Asian adults with hypertension, and reported systolic/diastolic blood pressure reductions of -13.0 (95% CI: -21.2 to -4.8)/-6.1 (95% CI: -11.2 to -1.1) mmHg following 3 to 12 months of Baduanjin, respectively. These investigators also found in four trials that Baduanjin plus antihypertensive medications was superior to antihypertensive medications alone in lowering systolic/diastolic blood pressure by a magnitude of -7.5 (95% CI: -11.4 to -3.6)/-3.6 (95% CI: -5.2 to -1.8) mmHg, respectively. The authors acknowledged that the primary levels studies in their meta-analyses were of poor quality.

Xiong et al[90] investigated the blood pressure response to qigong, an ancient Chinese healing art that consists of breathing patterns, rhythmic movements, and meditation, among 2,349 Asian adults with hypertension, and reported systolic/diastolic blood pressure reductions of -17.4 (95% CI: -21.1 to -13.7)/-10.6 (95% CI: -14.0 to -6.3) mmHg, respectively, following 8 weeks to 1 year of qigong. These investigators also found in two trials that exercise was superior to qigong in lowering systolic blood pressure by a magnitude of -6.5 (95% CI: -2.8 to -10.2) mmHg, in four trials that qigong was superior to antihypertensive medications in lowering diastolic blood pressure by a magnitude of -6.1 (95% CI: -9.6 to -2.6) mmHg, and in five trials that qigong plus antihypertensive medications was superior to antihypertensive medications alone in lowering systolic/diastolic blood pressure by a magnitude of -12.0 (95% CI: -15.6 to -8.5)/-5.3 (95% CI: -8.1 to -2.4) mmHg, respectively. The authors acknowledged that the primary levels studies in their meta-analyses were of poor quality.

Wang et al[91] investigated the blood pressure response to tai chi, an ancient Chinese exercise that combines deep diaphragmatic breathing with continuous body movements to achieve a harmonious balance between body and mind, among 1,371 mostly Asian adults with hypertension. They reported systolic/diastolic blood pressure reductions of -12.4 (95% CI: -12.6 to -12.2)/-6.0 (95% CI: -6.2 to -5.9) mmHg, respectively, following 2 to 60 months of all forms and types of tai chi. These investigators also found in 14 trials that tai chi was superior to routine care in lowering systolic/diastolic blood pressure by a magnitude of -12.4 (95% CI: -12.6 to -12.2)/-6.0 (95% CI: -6.2 to -5.9) mmHg, respectively, and in 3 trials that tai chi plus antihypertensive medications was superior to antihypertensive medications alone in lowering systolic/diastolic blood pressure by a magnitude of -9.3 (95% CI: -10.9 to -7.8)/-7.2 (95% CI: -7.7 to -6.6) mmHg, respectively. The authors acknowledged that the primary levels studies in their meta-analyses were of poor quality.

Park and Han[92] investigated the blood pressure response to yoga, which incorporates meditation with physical movement, among 394 adults with hypertension. They reported systolic/diastolic blood pressure reductions of -11.4 (95% CI: -14.6 to -8.2)/-2.4 (95% CI: -4.3 to -0.4) mmHg, respectively, among older adults ages 60 years and older following 6 to 12 weeks of yoga. In contrast to the other meta-analyses addressing effects of tai chi, yoga, and/or qigong, the primary level studies in this meta-analysis were described by Park and Han[92] to be of high methodological study quality.

Collectively, the four meta-analyses addressing effects of tai chi, yoga, and/or qigong found blood pressure reductions in systolic blood pressure that ranged from -12 to -17 mmHg and diastolic blood pressure reductions of -2 to -11 mmHg. Except for traditional types of exercise[90] that were superior to qigong in lowering blood pressure, these types of physical activity (tai chi, yoga, and or qigong) proved to be superior to routine care and when combined with antihypertensive medication than compared to antihypertensive medication alone. However, these apparent positive findings of the antihypertensive effects of these types of physical activity types must be interpreted with caution due to the low study methodological quality of this literature, lack of disclosure of important study design considerations, considerable heterogeneity in this literature, inability to generalize findings to other racial/ethnic groups, and lack of long-term follow-up.

How physical activity was measured: All meta-analyses that examined the blood pressure response to physical activity included interventions that were structured by the frequency, intensity, time, duration, and type (mode) of physical activity, but the details of these features of the physical activity interventions were not well disclosed. None of these meta-analyses reported any physical activity measure outside of the structured physical activity intervention. No conclusions can be made regarding how physical activity was measured, as the magnitude and precision of the effect could not be determined from findings that were too scarce to synthesize.

For additional details on this body of evidence, visit: Supplementary Tables S-F10-1, S-F10-2, and https://health.gov/paguidelines/second-edition/report/supplementary-material.aspx for the Evidence Portfolio.

Comparing 2018 Findings with the 2008 Scientific Report

The 2008 Scientific Report[4] concluded that both aerobic and dynamic resistance exercise training of moderate-to-vigorous intensity produced small but clinically important reductions in systolic and diastolic blood pressure in adults, with the evidence more convincing for aerobic than dynamic resistance exercise. The 2018 Scientific Report extends findings from the 2008 Scientific Report[4] among adults with hypertension in four ways. First, the 2018 Scientific Report provides strong evidence that physical activity reduces the risk of progression of cardiovascular disease, as is evident from its moderate to large reductions in blood pressure. Second, the 2018 Scientific Report provides moderate evidence that an inverse, dose-response relationship exists between physical activity and the risk of cardiovascular disease mortality among adults with hypertension. Third, the 2018 Scientific Report suggests that greater blood pressure reductions occur among adults with hypertension who have the highest resting blood pressure levels. Fourth, reflecting on the accumulating evidence over the past decade, the 2018 Scientific Report indicates that, in the range of physical activity volume effective in lowering blood pressure, aerobic and dynamic resistance exercise may be equally effective in reducing blood pressure at volumes in the lower part of this range.

Public Health Impact

Hypertension is the most common, costly, and preventable CVD risk factor. According to the JNC 7 blood definition of hypertension, by 2030 it is estimated that 41 percent of adults in the United States will have hypertension. The lifetime risk of acquiring hypertension is 90 percent. Curbing this growing and expensive public health crisis with the adoption and maintenance of lifestyle interventions, such as habitual physical activity, is a national and global priority.[78, 81] Accordingly, professional organizations throughout the world recommend habitual physical activity for the prevention, treatment, and control of hypertension and the associated reduction in risk of CVD progression (Supplementary Table S-F10-1).[79, 108-116] Due to the clinically important role of physical activity in preventing, treating, and controlling hypertension as well as its CVD protective effects, adults with hypertension are encouraged to engage in 90 minutes per week or more of moderate intensity or 45 minutes per week or more of vigorous intensity aerobic and/or dynamic resistance physical activity, or some combination of these. Greater amounts of physical activity confer greater cardiovascular health benefit so that even greater amounts of physical activity should be encouraged. Adults with hypertension may supplement their physical activity programs with tai chi, yoga, or qigong until sufficient evidence exists to make a more precise conclusion.

Question 4. In people with type 2 diabetes, what is the relationship between physical activity and (1) risk of co-morbid conditions, (2) physical function, (3) health-related quality of life, and (4) disease progression?

a) Is there a dose-response relationship? If yes, what is the shape of the relationship?
b) Does the relationship vary by age, sex, race/ethnicity, socioeconomic status, or weight status?
c) Does the relationship vary based on: frequency, duration, intensity, type (mode), or how physical activity is measured?

Sources of evidence: Systematic reviews, meta-analyses, pooled analyses

Conclusion Statements

Risk of Co-morbid Conditions

Strong evidence demonstrates an inverse association between volume of physical activity and risk of cardiovascular mortality among adults with type 2 diabetes. **PAGAC Grade: Strong.**

Moderate evidence indicates an inverse, curvilinear dose-response relationship between physical activity and cardiovascular mortality among adults with type 2 diabetes. **PAGAC Grade: Moderate.**

Insufficient evidence was available to determine whether the relationship between physical activity and cardiovascular mortality among adults with type 2 diabetes varies with age, sex, race/ethnicity, socioeconomic status, or weight status. **PAGAC Grade: Not assignable.**

Insufficient evidence was available to determine whether the relationship between physical activity and cardiovascular mortality among adults with type 2 diabetes varies with frequency, duration, intensity, or type (mode) of physical activity or how physical activity is measured among people with type 2 diabetes mellitus. **PAGAC Grade: Not assignable.**

Physical Function

Insufficient evidence was available to determine the relationship between physical activity and physical function in adults with type 2 diabetes. **PAGAC Grade: Not assignable.**

Health-related Quality of Life

Insufficient evidence was available to determine the relationship between physical activity and health-related quality of life in adults with type 2 diabetes. **PAGAC Grade: Not assignable.**

Disease Progression: Indicators of Neuropathy, Nephropathy, Retinopathy, and Foot Disorders.

Insufficient evidence was available to determine the relationship between physical activity and indicators of progression of neuropathy, nephropathy, retinopathy, and foot disorders. **PAGAC Grade: Not assignable.**

Disease Progression: Indicators of HbA1C, Blood Pressure, Body Mass Index, and Lipids

Strong evidence demonstrates an inverse association between aerobic activity, muscle-strengthening activity, and aerobic plus muscle-strengthening activity with risk of progression among adults with type 2 diabetes, as assessed by overall effects of physical activity on four indicators of risk of progression: glycated hemoglobin A1C, blood pressure, body mass index, and lipids. **PAGAC Grade: Strong.**

Insufficient evidence was available to determine the relationship between tai chi, qigong, and yoga exercise on four indicators of risk of progression: hemoglobin A1C, blood pressure, body mass index, and lipids. **PAGAC Grade: Not assignable.**

Moderate evidence indicates an inverse dose-response relationship between volume of aerobic activity and two indicators of risk of progression—blood pressure and hemoglobin A1C —among adults with type 2 diabetes. **PAGAC Grade: Moderate.**

Limited evidence indicates an inverse dose-response relationship between volume of resistance training and one indicator of risk of progression— hemoglobin A1C —among adults with type 2 diabetes. **PAGAC Grade: Limited.**

Limited evidence indicates that longer periods of consistent physical activity have a larger effect on three indicators of risk of progression— hemoglobin A1C, body mass index, and lipids—than do shorter periods among adults with type 2 diabetes. **PAGAC Grade: Limited.**

Moderate evidence indicates that the effects of physical activity on the disease progression indicator of blood pressure are larger in hypertensive individuals with type 2 diabetes than in those without hypertension. Similarly, moderate evidence indicates that the effects of physical activity on the disease progression indicator of hemoglobin A1C are larger in individuals with type 2 diabetes who have higher levels of hemoglobin A1C than in those with lower hemoglobin A1C. **PAGAC Grade: Moderate.**

Insufficient evidence was available to determine whether the effects of physical activity on indicators of risk of progression in adults of type 2 diabetes vary by age, sex, race/ethnicity, socioeconomic status, or weight status. **PAGAC Grade: Not assignable.**

Limited evidence suggests, when adults with type 2 diabetes engage in equal amounts of moderate-intensity and vigorous-intensity aerobic activity, vigorous-intensity activity is more efficient than moderate-intensity activity in improving one indicator of risk of progression— hemoglobin A1C. **PAGAC Grade: Limited.**

Insufficient evidence was available to determine the effects of frequency, bout duration, and method of measuring physical activity on indicators of risk of progression in adults with type 2 diabetes. **PAGAC Grade: Not assignable.**

Review of the Evidence

Type 2 diabetes is characterized by relative insulin deficiency, usually combined with an insufficient cellular response to insulin (insulin resistance), resulting in elevated blood glucose. The extent that blood glucose is persistently elevated is commonly assessed by measuring glycated hemoglobin, abbreviated as HbA1C. In 2015, an estimated 30.3 million people of all ages in the U.S. population had diabetes, with type 2 diabetes representing 90 to 95 percent of all cases of diabetes and type 1 diabetes representing the other cases.[117] The number of adults diagnosed with diabetes (either type 1 or type 2) has more than tripled in the past 20 years.[118] The estimated prevalence of diabetes is age-related, with prevalence in 2015 of 17.0 percent and 25.2 percent in adults ages 45 to 64 years and ages 65 years and older, respectively.[117]

Type 2 diabetes is a major cause of morbidity and mortality. For example, it is the leading cause of kidney failure, lower limb amputations, and adult-onset blindness.[118] For purposes of this evidence review, the Subcommittee classified morbidity and mortality into two types: (1) morbidity and mortality due to co-morbid conditions and (2) morbidity and mortality related to the progression (or worsening) of type 2 diabetes.

Co-morbid conditions: People with type 2 diabetes are at higher risk of co-morbid conditions, with CVD (hypertension, stroke, coronary heart disease, heart failure) as the most common cause of death among people with type 2 diabetes. Because people with type 2 diabetes have a higher prevalence of obesity, they are at increased risk of obesity-related conditions, such as osteoarthritis.[119]

Progression: Progression of type 2 diabetes can lead to complications and organ damage, with four well-known conditions regarded as indicators of progression: (1) retinopathy; (2) peripheral neuropathy; (3) nephropathy; and (4) diabetes-related foot infections and foot ulcers. In addition, four conditions were regarded as indicators of risk of progression: HbA1C, blood pressure, BMI, and lipids. For example, hypertension is a strong risk factor for development and progression of diabetic kidney disease.[120] The Subcommittee recognizes that hypertension, lipid disorders such as hypercholesterolemia and obesity can be classified in more than one way, including as co-morbid conditions. However, for the purposes of this evidence review, the Subcommittee focused on these conditions as indicators of risk of progression.

Regular physical activity is recommended for people with type 2 diabetes.[121] Thus, the Subcommittee asked, to what extent does regular physical activity have important preventive effects in people with type 2 diabetes, including reducing risk of co-morbid conditions and reducing risk of disease progression?

To address this question, the Subcommittee considered evidence contained in 40 reviews, which comprised systematic reviews, meta-analyses, and pooled analyses. Individual studies of type 2 diabetes in children were unusual, so evidence was only sufficient for conclusions in adults. The main focus of the evidence review for three outcomes (physical function, quality of life, and progression) was on evidence provided by meta-analyses of RCTs in adults with type 2 diabetes that compared (only) physical activity or exercise interventions to a no-exercise control group. Such meta-analyses could be included as a source of evidence if the percent of studies with a co-intervention (e.g., a diet intervention) was so small it would not affect the conclusions of the meta-analysis, and the authors deemed their results applied to physical activity-only interventions. However, some additional evidence was provided by meta-analyses comparing effects of different types of physical activity, by systematic reviews, and by pooled analyses.

The main focus of the evidence review for the co-morbidity outcome was a review of cohort studies. Large cohort studies in adults with CVD endpoints were included even though adults with type 1 diabetes were included as well as adults with type 2 diabetes. The rationale was: (1) large cohort studies may measure diabetes by self-report where it is likely difficult to reliably ascertain type of diabetes, (2) type 2 diabetes typically represents about 95 percent of cases of diabetes in the population and inclusion of adults with type 1 diabetes in the cohort would not appreciably affect the strength of association between type 2 diabetes with CVD endpoints; and (3) the results of one analysis limited to people with type 2 diabetes could be compared to other results.

Risk of Co-morbid Conditions

Evidence on the Overall Relationship

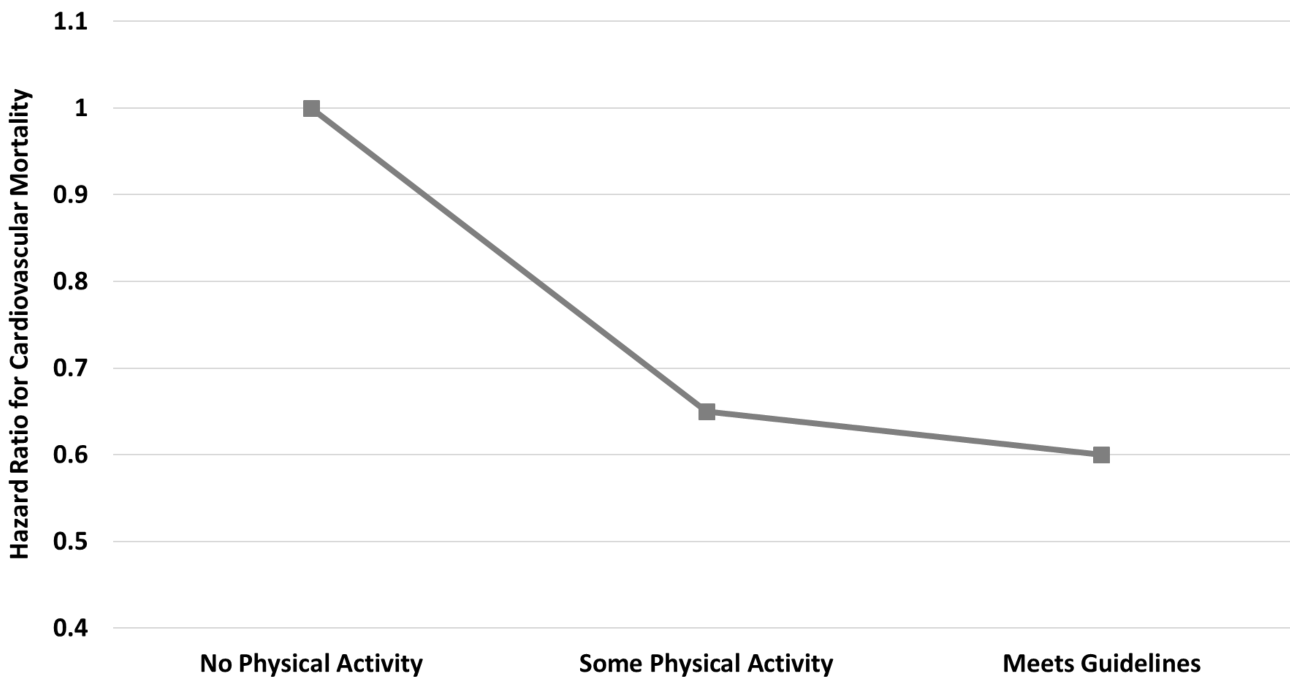
CVD mortality was the only condition for which the Subcommittee located sufficient evidence. The Subcommittee recognized that mortality is not a co-morbidity per se, but included this outcome in its review of co-morbid conditions due to importance and because CVD mortality is related to the prevalence of CVD co-morbidity.

The sources of evidence were two meta-analyses and one pooled analysis. One meta-analysis of CVD mortality included eight cohort studies with a total sample size of nearly 20,000.[122] A second meta-analysis analyzed CVD risk as an outcome, with CVD risk representing a composite outcome of CVD mortality and CVD events (e.g., stroke).[123] This meta-analysis comprised 11 studies, with a total sample size also of about 20,000. Overall, the meta-analyses included 14 individual studies, with five studies included in both meta-analyses. One pooled analyses had a sample size of more than 3,000 adults.[124] The pooled analysis used a single questionnaire assessing leisure-time moderate-to-vigorous physical activity.

These reviews provided strong evidence that regular physical activity reduced risk of CVD mortality in adults with type 2 diabetes. One meta-analysis found a significant and strong inverse relationship between physical activity and CVD mortality, with similar results in comparisons of highest amounts versus lowest amounts of physical activity categories for: total physical activity (HR=0.61; 95% CI: 0.47-0.80); leisure-time physical activity (HR=0.63; 95% CI: 0.48-0.83), and walking (HR=0.58; 95% CI: 0.42-0.79).[122] The other meta-analysis found a significant and strong inverse relationship between high versus low amounts of physical activity with the combined outcome of CVD events or CVD mortality (RR=0.71; 95% CI: 0.60-0.84).[123] When the analysis was limited to six studies known to enroll only adults with type 2 diabetes, the effect was slightly stronger (RR=0.64; 95% CI: 0.56-0.71). The pooled analysis also reported a significant effect of physical activity on CVD mortality in a comparison of highest versus lowest physical activity categories (HR=0.60; 95% CI: 0.44-0.82).[124] In other words, these reviews found that regular physical activity resulted in a 30 to 40 percent reduction in risk of CVD mortality.

Dose-response: The pooled analysis reported a substantially reduced risk of CVD mortality in a dose-response manner (Figure F10-7).[124] Compared to no activity, engaging in some activity was associated with a 32 percent reduction in risk of CVD mortality (adjusted HR=0.68; 95% CI: 0.51-0.92), while engaging in higher amounts of activity (meeting physical activity guidelines) was associated with a larger 40 percent reduction in risk of CVD mortality (adjusted HR=0.60; 95% CI: 0.44-0.82) (P_{trend} <.001).[124] The shape of the dose-response curve was similar to that in adults without type 2 diabetes. The Kodama et al[123] review also reported a significant (*P*<.001) inverse dose-response relationship. The findings of these two reviews were judged to provide moderate evidence of dose-response.

Figure F10-7. Dose-Response Relationship Between Physical Activity and Cardiovascular Disease Mortality in Individuals with Type 2 Diabetes



Source: Adapted from data found in Sadarangani et al., 2014.[124]

Evidence on Specific Factors

These three reviews[122-124] did not address how effects of physical activity may vary based upon individual characteristics (e.g., age, sex) or by characteristics of the physical activity (e.g., intensity, type).

Physical Function

The Subcommittee's search located only one systematic review of the effects of physical activity on physical function in type 2 diabetes.[125] This review included studies of multicomponent fall prevention programs in people with type 2 diabetes and peripheral neuropathy.

Evidence on the Overall Relationship

The review included insufficient evidence to assess the effect of physical activity on physical function. Only 4 of the 10 included studies had a no-exercise control group, and the author's quality rating for two of these four trials was low (3/10 and 4/10).[125] The remaining two RCTs enrolled 182 participants for 10 to 12 weeks of exercise. One RCT reported a significant effect of exercise on four out of four measures of physical function, while the other reported a significant effect of exercise on one out of six measures of physical function. Notably, the authors of the review characterized the evidence as preliminary.

Health-related Quality of Life

The search located six systematic reviews of the effects of physical activity on HRQoL in adults with type 2 diabetes. The sources of evidence were:

- Two large systematic reviews of controlled trials of various exercise types, including walking, muscle-strengthening activities, video games, tai chi, and yoga.[126, 127] One review included 20 RCTs which enrolled a total of 1,719 participants[127] and the other review included 30 clinical trials (not limited to RCTs) that enrolled a total of 2,785 participants.[126] The two reviews included a total of 37 studies, with 13 studies covered in both reviews. HRQoL was most commonly assessed using the 36-item Short Form Health Survey (SF-36).
- Two reviews of tai chi exercise. As one review[128] was an update of a previous review,[129] only the most recent review was used as a source of evidence. The more recent review included three RCTs, which enrolled a total of 157 participants.
- One review of yoga exercise.[130] This review included three RCTs and one non-randomized trial that enrolled a total of 420 participants.
- One systematic review is not discussed below as it included only one study assessing HRQoL.[131]

Evidence on the Overall Relationship

For physical activity generally, the two large systematic reviews provided conflicting evidence.[126, 127] One review[127] summarized the results of the 16 included studies as: "Between group comparisons showed no significant results for aerobic training with the exception of one study, and mixed results for resistance and combined training." The abstract of this review characterized overall results as "conflicting."[127] The other review[126] summarized the results of the 20 included studies quite differently: 15 studies "reported a significant effect of aerobic exercise on quality of life…." The abstract of this review characterized aerobic exercise as "effective," effects of resistance and combined exercise as "mixed," and yoga as needing "more research."[126] The conclusion of conflicting evidence was supported by two additional observations. One of the larger trials reported that HRQoL improved more in the control group than the exercise group.[132] In 13 of 20 studies of aerobic training that assessed HRQoL with the SF-36 in one review, no two studies reported the same pattern of significant changes in SF-36 subscales (except the negative studies).[126] It was not possible to confidently reconcile the different conclusions of these reviews based upon the information presented in the reviews.

The reviews included insufficient evidence on tai chi and yoga to determine the effect of physical activity on HRQoL in people with type 2 diabetes. The systematic review of tai chi included only three RCTs. Although these RCTs reported positive effects of physical activity on HRQoL, the author's quality scores for these RCTs (on a 7-point scale) was only a 2 or a 3. The authors characterized the evidence as "not convincing enough."[128] The systematic review of yoga included four controlled trials of which three were RCTs. Three of the four trials reported positive effects of physical activity on HRQoL. However, the author's quality scores for these trials (on a 10-point scale) ranged from 1 to 4. The authors concluded that, due to the methodological limitations of existing trials, additional high-quality studies are required to establish effects of yoga on HRQoL in individuals with type 2 diabetes.[130]

Disease Progression

The Subcommittee used two sets of indicators to assess the effects of physical activity on progression of type 2 diabetes. The first set included the indicators of retinopathy, nephropathy, neuropathy, and diabetes-related foot conditions. However, no reviews were located on the relationship of physical activity to progression, as assessed by these indicators.

The second set of indicators for progression comprised four indicators of risk of progression: HbA1C, blood pressure, BMI, and lipids. These indicators are also referred to as risk factors for progression. A large number of reviews were located on effects of physical activity on these risk factors. The reviews were sorted by mode of physical activity and by risk factor:

- Primary sources of evidence for effects of *aerobic activity, resistance training, or both* on risk factors for progression were meta-analyses of RCTS.
    - **HbA1C**. Twelve meta-analyses included HbA1C as an outcome.[133-144]
    - **Blood Pressure**. Six meta-analyses included blood pressure as an outcome.[134, 136, 137, 140, 144, 145]
    - **BMI**. Six meta-analyses included BMI as an outcome.[133, 134, 136, 137, 140, 146]
    - **Lipids.** Five meta-analyses included lipids as an outcome.[134, 136, 137, 140, 144]

- Secondary sources of evidence for effects of *aerobic activity, resistance training, or both* on risk factors for progression were other types of reviews.
    - Three meta-analyses compared different types of physical activity.[147-149]
    - Three meta-analyses which included non-randomized trials.[131, 150, 151]
    - Six systematic reviews (or systematic reviews plus meta-analyses where the meta-analysis part was not used as evidence due to inclusion of non-relevant studies in summary statistics).[152-157]

- Primary sources of evidence of the effects of *tai chi, qigong, and yoga* on risk factors for progression were meta-analyses of RCTs.
    - **HbA1C**. Six meta-analyses included HbA1C as an outcome.[128, 139, 158-161]
    - **Blood Pressure**. No meta-analyses included blood pressure as an outcome.
    - **BMI**. No meta-analyses included BMI as an outcome.
    - **Lipids.** One meta-analysis included lipids as an outcome.[161]

- Secondary sources of evidence for effects of *tai chi, qigong, and yoga* on risk factors for progression were other reviews.
    - One meta-analyses included comparisons of different types of physical activity.[128]
    - Three systematic reviews.[129, 130, 162]

Evidence on the Overall Relationship

Effects of Aerobic Activity, Resistance Training, or Both on Risk Factors for Progression

Overall, the reviews provided strong evidence that aerobic activity and muscle-strengthening activity reduced risk of progression of type 2 diabetes, though the strength of evidence varied somewhat by risk factor. This evidence is summarized below for each of the four risk factors. Meta-analyses generally summarized the effects of physical activity using the standard measurement units for each indicator. For example, HbA1C is measured in percent of hemoglobin which is glycated, so an effect size of -0.50 percent indicates a net lowering of HbA1C from, for example, 6.5 percent to 6.0 percent. Blood pressure is measured in mm Hg (millimeters of mercury). BMI units are (body weight in kilograms)/(height in meters)^2. Lipids LDL (low-density lipoprotein), HDL (high-density lipoprotein), total cholesterol, and triglycerides are measured in mg/dL (1 mg/dL=0.01 gram per liter) or in mmol/L. However, some reviews used other measures to quantify exercise effects.

HbA1C. Meta-analyses of RCTs consistently reported aerobic activity reduced HbA1C in adults with type 2 diabetes. The five largest meta-analyses involved 19 to 26 comparisons of aerobic exercise with control groups, and reported similar significant effects of aerobic exercise on HbA1C of -0.50 to -0.73 percent: weighted mean difference (WMD)=-0.73 percent (95% CI: -1.06% to -0.40%)[142]; WMD=-0.70 percent (95% CI: -1.02 to -0.38)[143]; mean difference (MD)=-0.71 percent (95% CI: -1.11 to -0.31)[135]; WMD=-0.50 percent (95% CI: -0.78% to -0.21%)[140]; and WMD=-0.60 percent (95% CI: -0.98% to -0.27%).[134] One of these meta-analyses included only studies of walking interventions.[140] Although one meta-analysis of device-based walking interventions reported no effect of walking on HbA1C, the authors essentially attributed this lack of effect to problems with intervention implementation.[141]

Fewer individual studies have been conducted on the effects of muscle-strengthening on HbA1C. Two overlapping meta-analyses involving four and five comparisons of supervised progressive resistance training reported significant effects of WMD=-0.62 percent (95% CI: -1.14% to -0.11%)[143] and WMD=-0.57 percent (95% CI: -1.14% to -0.01%).[142] Another meta-analysis reported a smaller effect of resistance training on HbA1C of WMD=-0.32 percent (95% CI: -0.60% to -0.04%). However, a meta-analysis of seven studies of resistance band exercise reported a non-significant trend on HbA1C of WMD=-0.18 percent (95% CI: -0.49% to 0.14%)[138] and a meta-analysis in which one of seven studies used resistance bands also reported a non-significant trend.[134]

The results of meta-analyses of combined aerobic and resistance training provided further evidence that combined aerobic and muscle-strengthening activity reduces HbA1C in adults with type 2 diabetes. Four meta-analyses, involving 7 to 14 comparisons, reported similar significant effects of combined exercise on HbA1C of -0.47 to -0.74 percent: WMD=-0.74 percent (95% CI: -1.13% to -0.35%)[137]; WMD=-0.51 percent (95% CI: -0.79% to -0.23%)[142]; WMD=-0.47 percent (95% CI: -0.64% to -0.31%)[143]; and WMD=-0.67 percent (95% CI: -0.93% to -0.40%).[134]

Two overlapping meta-analyses involving 14 and 12 RCTs compared exercise types,[148, 149] and both reported aerobic exercise alone lowered HbA1C more than resistance training alone. However, combined aerobic and resistance training had a larger effect on HbA1C than aerobic exercise alone (difference in exercise effect on HbA1C favoring combined training of MD=-0.17 percent; 95% CI: -0.31% to -0.03%).[148] This finding further supports the conclusion that resistance training alone has an effect on HbA1C, and suggests combined training is most effective in lowering HbA1C in adults with type 2 diabetes.

The other meta-analyses not discussed above generally supported the conclusion that aerobic, resistance, or combined activity improves HbA1C. The secondary sources of evidence also generally supported these conclusions. Notably, a systematic review of pedometer-based walking programs found only two of seven programs reported significant improvements in HbA1C,[155] thus supporting the negative findings of the meta-analysis of device-based walking interventions.[141]

BMI*.* Meta-analyses that included at least 10 RCTs reported small but significant effects of physical activity on BMI. The effects were: WMD=-1.05 BMI units (95% CI: -1.31 to -0.80) for free living exercise[133]; effect size (ES)=-0.53 (95% CI: -0.81 to -0.26) for aerobic activity[137]; MD=-1.56 BMI units (95% CI: -2.41 to -0.71) for aerobic activity[135]; WMD=-0.91 BMI units (95% CI: -1.22 to -0.59) for walking[140]; and ES=-0.50 (95% CI: -0.75 to -0.26) for aerobic plus resistance exercise.[137] Meta-analysis including fewer studies generally reported a non-significant trend favoring an effect of activity on BMI.

Systolic blood pressure*.* Meta-analyses of the effects of physical activity on systolic blood pressure in adults with type 2 diabetes consistently reported significant moderate size effects. The summary effects ranged from WMD=-2.42 mmHg (95% CI: -4.39 to -0.45)[137] to WMD=-7.98 mmHg (95% CI: -9.87 to -6.08),[144] with significant effects found for aerobic activity alone (three analyses), resistance exercise alone (two analyses), combined activity (two analyses) and any activity (one analysis)[134, 137, 140, 144, 145] (note the effect on aerobic activity on blood pressure in one study was only significant after an outlier was removed from the analysis[140]).

Diastolic blood pressure*.* Meta-analyses of the effects of physical activity on diastolic blood pressure in adults with type 2 diabetes consistently reported significant small size effects. The summary effects ranged from WMD=-1.97 mmHg (95% CI: -3.94 to -0.00)[140] to WMD=-2.84 mmHg (95% CI:-3.88 to -1.81),[145] with significant effects found for aerobic activity alone (two analyses), resistance exercise alone (one analysis), combined activity (one analysis) and any activity (one analysis).[137, 140, 144, 145]

Lipids. Compared to HbA1C, blood pressure, and BMI, less evidence was available that physical activity improved lipids in adults with type 2 diabetes. One large meta-analysis pooled the effects of aerobic, resistance, and combined exercise.[137] This review reported a significant but small benefit of physical activity on HDL (35 studies with N=2,059 participants; WMD=0.4 mmol/L; 95% CI: 0.02-0.07) and LDL (25 studies with N=1,807 participants; WMD=-0.16 mmol/L; 95% CI: -0.30 to -0.01). The effect of exercise on triglycerides (WMD=-0.03 mmol/L; 95% CI: -0.17 to 0.10) was not significant. The review also reported: (1) the effects of physical activity on lipids did not differ by type (aerobic, resistance, combined), and (2) exercise interventions of longer durations produced significantly (P<.03) stronger effects on LDL. Consistent with this latter finding, a meta-analysis found no significant effects of exercise on HDL and triglycerides after 4 months of training, but found significant effects of exercise on HDL and triglycerides in two exercise studies that assessed outcomes at 12 months.[144] Two other meta-analyses with fewer studies generally found non-significant trends,[134, 140] though one reported a significant effect of exercise on triglycerides for both aerobic (WMD=-0.03 mmol/L; 95% CI: -0.48 to -0.11) and combined training (WMD=-0.03 mmol/L; 95% CI: -0.57 to -0.02).[134] It is plausible that smaller meta-analyses will not reliably detect a small effect of physical activity on lipids when the size of the effect depends upon the duration of exercise programs included in the analysis.

Effects of Tai Chi, Qigong, and Yoga on Risk Factors for Progression

Tai Chi. Evidence was insufficient to determine the effect of tai chi exercise on risk factors for progression. Three meta-analyses, including a total of five RCTs[128, 139, 161] were found. One reported a significant effect of tai chi on HbA1C (WMD=-0.75 percent; 95% CI: -1.15% to -0.35%) but the analysis included only two comparisons.[139] The other two reviews reported non-significant effects of MD=-1.58 percent (95% CI: -3.83% to 0.67%)[128] and MD=-0.19 percent (95% CI: -0.41% to 0.03%).[161] The mean differences varied considerably among the reviews (-1.58%, -0.75%, and -0.19%), with one analysis including a study with an exercise control group.[161] The meta-analysis of the effects of tai chi on lipids had only two or three comparisons per lipid outcome, and at least one of the studies in the analysis had an exercise control group.[161] No meta-analyses examined the effects of tai chi on blood pressure or BMI.

Qigong. Evidence was insufficient to determine the effect of qigong exercise on risk factors for progression. One meta-analysis of 3 RCTs[139] reported a non-significant effect of qigong on HbA1C. No meta-analyses examined the effects of qigong on blood pressure, BMI, or lipids.

Yoga. Insufficient evidence was available to determine the types and forms of yoga that may affect risk factors for progression. Three meta-analyses analyzed the effect on yoga exercise on HbA1C, involving a total of 12 RCTs, with each review comprising 5 to 8 studies and 220 to 392 participants.[139, 158, 160] Two reviews reported a significant effect on yoga on HbA1C of WMD=-0.47 percent (95% CI: -0.87% to -0.07%)[158] and WMD=-0.81 percent (95% CI: -1.22 to -0.39).[139] One meta-analysis of five RCTS showed significant effects of yoga on total cholesterol (-8.50 mg/dl; 95% CI: -29.88 to -7.11) and LDL cholesterol (- 12.95 mg/dl; 95% CI: -18.84 to -7.06) but not on triglycerides.[158] A fourth meta-analysis did not contribute any additional evidence, as its analyses included studies that did not compare yoga (only) to a no-exercise control group.[159]

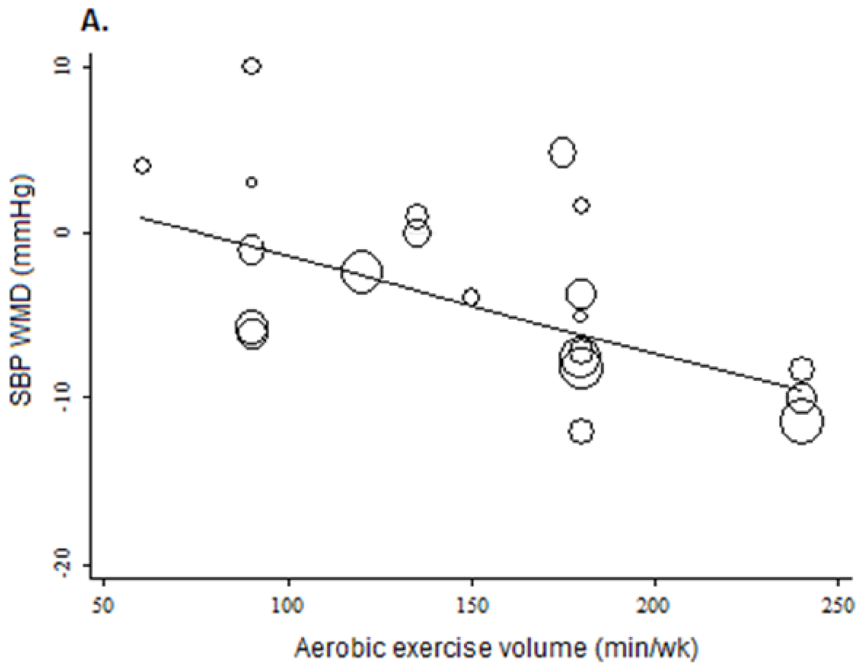
However, the types and forms of yoga studied in the RCTs of yoga varied widely, with substantial heterogeneity in two analyses of the effects of yoga on HbA1C (I^2=82%[158] and 97%[160]). The authors of one review concluded that the appropriate exercise parameters for yoga in adults with type 2 diabetes are unknown.[158] The rating of insufficient evidence reflects that it appears that some forms of yoga are effective while others are not, but current information is insufficient to determine whether this is the case and to identify a subset of effective yoga exercises.

The conclusions of the secondary evidence sources (systematic reviews) were generally consistent with the above conclusions. All three reviews commented that the existing studies of tai chi, qigong, and yoga have methodologic limitations.[129, 130, 162]

Dose-response: The evidence reviewed indicates a dose-response relationship between physical activity and some risk factors for progression of type 2 diabetes.

Aerobic activity and blood pressure. Moderate evidence indicates an inverse dose-response relationship of aerobic activity on blood pressure. A weighted regression found a correlation of r=-0.59 (*P*<.005) between systolic blood pressure and weekly exercise volume, over the range of 50 to 250 minutes per week of activity[145] (Figure F10-8).

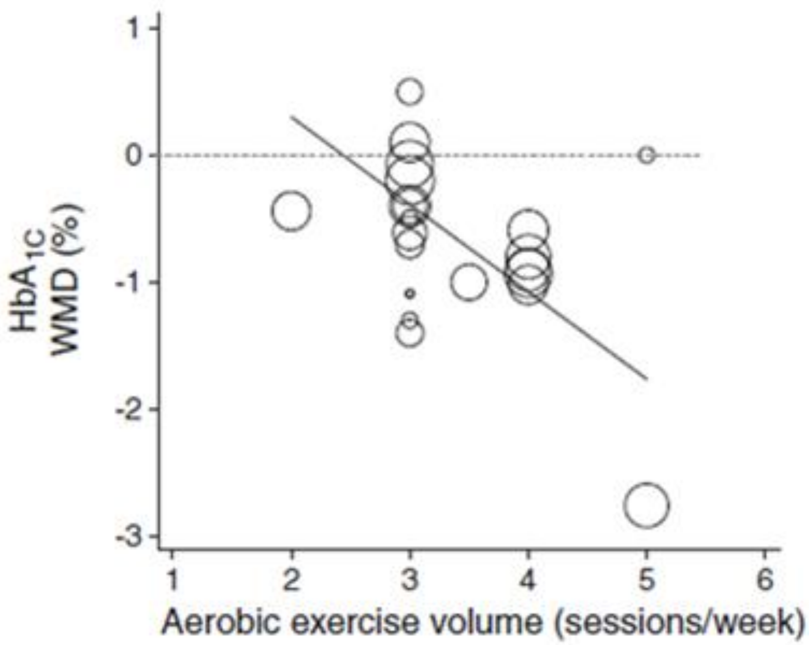
Figure F10-8. Dose-response Relationship between Aerobic Activity and Systolic Blood Pressure in Adults with Type 2 Diabetes



Legend: SBP=systolic blood pressure, WMD=weighted mean difference.
Note: Aerobic exercise volume is measured in minutes per week. The effect on exercise on systolic blood pressure is expressed as the weighted mean difference for each study. The size of the circles is proportional to the inverse variance of each study in the meta-analysis.
Source: Springer Sports Medicine, Association between physical activity advice only or structured exercise training with blood pressure levels in patients with type 2 diabetes: A systematic review and meta-analysis, 44, 2014, 1557-1572, Franciele R. Figueira, Daniel Umpierre, Felipe V. Cureau, Alessandra T. N. Zucatti, Mériane B. Dalzochio, Cristiane B. Leitão, Beatriz D. Schaan,[145] with permission of Springer.

Aerobic activity and HbA1C. Moderate evidence also indicates an inverse dose-response relationship between the dose of aerobic activity and HbA1C. A categorical analysis of aerobic exercise studies reported 150 or more minutes per week had a stronger effect on HbA1C (-0.89 percent; 95% CI: -1.26% to -0.51%) than less than 150 minutes per week (-0.36 percent; 95% CI: -0.50% to -0.23%).[142] A weighted regression showed more sessions per week of aerobic exercise were associated with a greater reduction in HbA1C[143] (Figure F10-9). The weighted correlation between volume and change in HbA1C was r=-0.64 (*P*=.002).

Figure F10-9. Dose-response Relationship between Aerobic Activity and hemoglobin A1c (HbA1C)



Legend: HbA1c=hemoglobin A1c, WMD=weighted mean difference.
Note: Aerobic exercise volume is measured as frequency of sessions per week. The effect on exercise on HbA1C is expressed as the weighted mean difference for each study. The size of the circles is proportional to the inverse variance of each study in the meta-analysis.
Source: Springer Diabetologia, Volume of supervised exercise training impacts glycaemic control in patients with type 2 diabetes: a systematic review with meta-regression analysis, 56, 2012, 242-251, D. Umpierre, P.A.B. Ribeiro, B.D. Schaan, and J.P. Ribeiro,[143] with permission of Springer.

Muscle-strengthening activity and HbA1C. The Subcommittee found only limited information on dose-response effects in muscle-strengthening training. One meta-regression showed 21 or more sets of resistance training per bout of exercise had greater effects on HbA1C (MD=-0.65 percent; 95% CI: -0.97 to -0.32) compared to fewer than 21 sets (MD=-0.16%; 95% CI: -0.38 to -0.05) (*P*=.03).[150]

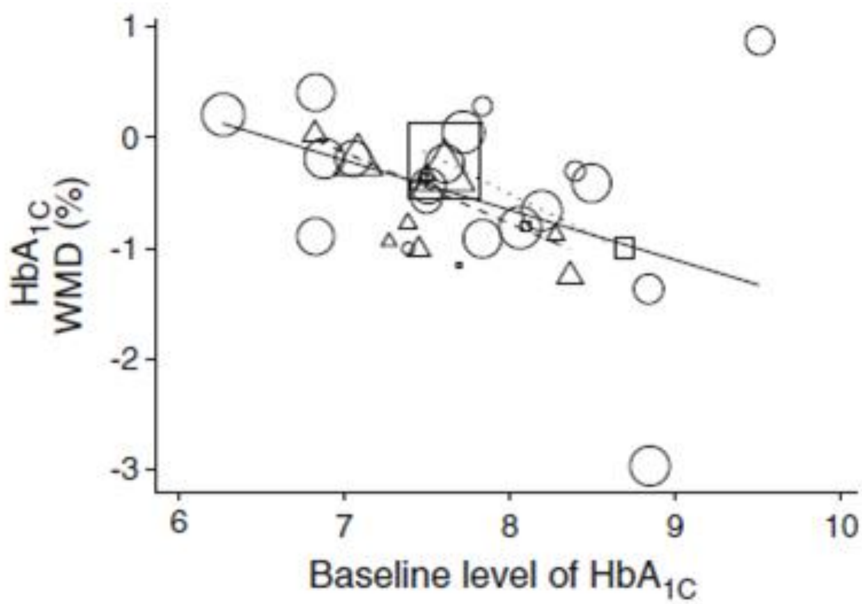
Evidence on Specific Factors

The Subcommittee sought evidence on specific factors related to individual factors (age, sex, race/ethnicity, socioeconomic status, and weight status) and exposure factors (frequency, duration, intensity type, and measurement method). When evidence was located on additional individual factors (blood pressure before physical activity and HbA1C level before physical activity), the Subcommittee deemed this evidence was relevant to the intent of question 4b dealing with variation of effects according to individual characteristics.

Blood pressure before physical activity: In one meta-analysis, the effects of aerobic and resistance training on systolic blood pressure were significantly larger (*P*<.001) in studies in hypertensive patients with type 2 diabetes compared to normotensive patients with type 2 diabetes. Hypertensive studies were defined as those where more than 70 percent of participants with diabetes had blood pressure readings of >140/90.[145]

HbA1C level before physical activity: In one meta-analysis, the effects of physical activity on HbA1C were greater in adults with type 2 diabetes who had higher levels of HbA1C before the exercise intervention began, than in adults with type 2 diabetes who had lower levels of HbA1C before exercise began.[143] The weighted correlation between baseline HbA1C and change in HbA1C was r=-0.52 (*P*=.001) (Figure F10-10).

Figure F10-10. Association between HbA1C Before a Supervised Exercise Intervention, with Change in HbA1C After Different Types of Exercise Interventions



Legend: HbA1c=hemoglobin A1c, WMD=weighted mean difference.
Note: The size of the symbols is proportional to the inverse variance calculated for use in a pooled analysis. The continuous line and circles are for aerobic training studies; the dotted line and squares for resistance training studies; and the dashed line and triangles for combined training.
Source: Springer Diabetologia, Volume of supervised exercise training impacts glycaemic control in patients with type 2 diabetes: a systematic review with meta-regression analysis, 56, 2012, 242-251, D. Umpierre, P.A.B. Ribeiro, B. D. Schaan, and J.P. Ribeiro,[143] with permission of Springer.

Demographic characteristics and weight status: Insufficient evidence was available in the studies reviewed to determine whether the effects of physical activity on risk factors for progression in adults of type 2 diabetes vary by age, sex, race/ethnicity, socioeconomic status, or weight status.

Duration of physical activity programs: Meta-analyses that analyzed the effects of physical activity programs of varying duration generally found stronger effects on HbA1C, BMI, and lipids with programs that last longer. One analysis reported the effects of free-living activity on HbA1C and BMI increased as follow-up intervals increased.[133] With follow-up intervals of less than 6 months, 6 months, 12 months, and 24 months, the effect of activity on HbA1C increased (-0.18%, -0.33%, -0.33%, -0.56%, respectively) and the effect of activity on BMI also increased (-0.75, -0.77, -1.32, -1.52 BMI units, respectively). One review reported that every additional week of aerobic exercise reduced HbA1C an additional 0.009 percent to 0.04 percent,[135] while another reported long-term studies of 6 or more months showed stronger effects of activity on HbA1C than shorter term studies of less than 6 months.[148] As noted above, longer exercise programs had significantly stronger effects on LDL ($p<.03$).[137] However, one review reported the effect of duration of aerobic exercise on BMI was not significant.[135]

Intensity of exercise: Limited evidence suggests that vigorous-intensity aerobic activity is more efficient in reducing HbA1C in individuals with type 2 diabetes compared to moderate-intensity activity. Evidence on effects of intensity on HbA1C was available from a meta-analysis which summarized results of eight RCTs that directly compared effects of moderate-intensity versus high-intensity aerobic activity (either continuous high-intensity or high-intensity interval training).[147] Six of these studies were relevant, as they enrolled adults and matched on volume of aerobic activity. The review reported a stronger effect of vigorous-intensity aerobic activity on HbA1C (WMD=-0.22%; 95% CI: -0.38 to -0.06) across all eight of the trials, which would be similar to the effect in the six relevant trials, as these trials had a total weight of 94.2 percent in the analysis. Although a meta-regression reported no effect of aerobic or resistance training intensity on HbA1C,[143] evidence from RCTs directly comparing effects of different intensities was regarded as preferable and stronger evidence.

Other characteristics: Insufficient evidence was available in the reviews located by the search strategy to determine the effects of frequency, bout duration, and method of measuring physical activity on risk factors for progression in adults with type 2 diabetes.

For additional details on this body of evidence, visit: https://health.gov/paguidelines/second-edition/report/supplementary-material.aspx for the Evidence Portfolio.

Comparing 2018 Findings with the 2008 Scientific Report

The Metabolic Health chapter of the *Physical Activity Guidelines Advisory Committee Report, 2008*, which considered the effects of physical activity on diabetes, had a broader scope than this chapter. For example, the chapter addressed both therapeutic and preventive effects of physical activity in individuals with type 1 and type 2 diabetes.[4] The report regarded the cardiovascular health benefits of physical activity as reducing macrovascular risks and regarded the role of physical activity in preventing neuropathy, nephropathy, and retinopathy as reducing micro-vascular risks.[4]

This chapter adds to the conclusions of the 2008 evidence review in three important ways through its focus on the preventive effects of physical activity in adults with type 2 diabetes. First, the 2008 Scientific Report concluded that strong data supported the benefits of physical activity for CVD protection in type 2 diabetes,[4] but lacked a quantitative summary estimate of the effect of physical activity on CVD mortality. Data now exist to quantify the effect of physical activity (mainly aerobic leisure-time physical activity) on risk of CVD mortality—a 30 to 40 percent reduction in risk. Further, moderate evidence indicates a dose-response effect.

Second, strong evidence now demonstrates that aerobic, muscle-strengthening, and combined activity reduce risk factors for progression of type 2 diabetes: HbA1C, blood pressure, BMI, and lipids. Although the 2008 Scientific Report commented on the effects of physical activity on these risk factors, the only evidence grade stated in that report's Integration chapter was limited evidence for a beneficial effect of physical activity on HbA1C.[4] The evidence available in 2008 on benefits of muscle-strengthening activity was limited, and the report stated resistance training has "shown promise" of beneficial effects in people with type 2 diabetes.[4]

Third, the current findings suggest that for two risk factors for progression—HbA1C and blood pressure—those at greatest risk experience the greatest benefit from physical activity. Further and not surprisingly, evidence is growing that the beneficial effects of physical activity on three risk factors—BMI, HbA1C, and lipids—become larger as adults with type 2 diabetes participate in physical activity over longer periods of time.

Public Health Impact

The public health impact of these findings is large. Type 2 diabetes is prevalent in the population, and the leading cause of death in people with type 2 diabetes is CVD. Physical activity is associated with a 30 to 40 percent reduction in risk of CVD mortality.

Small-to-moderate size beneficial effects of physical activity on HbA1C, blood pressure, BMI, and lipids are consistently reported by randomized trials. Essentially, this finding represents a triple benefit of physical activity in type 2 diabetes: a primary prevention benefit (co-morbidities) as these are risk factors for chronic conditions, a secondary prevention benefit as these are risk factors for progression of type 2 diabetes, and a therapeutic benefit as these are indicators of treatment effectiveness. Importantly, the effects of physical activity on HbA1C and blood pressure appear to be largest in adults with highest levels of risk. Also, the effects of physical activity on some risk factors (BMI, lipids, HbA1C) increase with more months of exercise, and thus may be underestimated by short-term randomized trials.

Overall, the findings emphasize the importance of physical activity in people with type 2 diabetes. There are two main types of physical activity that produced benefit—aerobic and muscle-strengthening—the same two types of activities emphasized in public health guidelines. The volume of activity required to obtain benefits is similar to that in current public health guidelines.

Question 5. In people with multiple sclerosis, what is the relationship between physical activity and: 1) risk of co-morbid conditions, 2) physical function, and 3) health-related quality of life?

Sources of evidence: Systematic reviews, meta-analyses

Conclusion Statements

Risk of Co-morbid Conditions

Insufficient evidence is available to determine the relationship between physical activity and risk of co-morbid conditions in adults with multiple sclerosis. **PAGAC Grade: Not Assignable.**

Physical Function

Strong evidence demonstrates that physical activity—particularly aerobic and muscle-strengthening activities—improves physical function, including walking speed and endurance, in adults with multiple sclerosis. **PAGAC Grade: Strong.**

Health-related Quality of Life

Limited evidence suggests that physical activity improves quality of life, including symptoms of fatigue and depressive symptoms, in adults with multiple sclerosis. **PAGAC grade: Limited.**

Review of the Evidence

Multiple sclerosis (MS) is a neurological disease involving intermittent episodes of focal inflammation that damage the central nervous system. The frequency and neurological location of these immune-mediated, inflammatory episodes vary among affected individuals, resulting in variation in disease progression over time and a heterogeneous mixture of physical and cognitive impairments among people with MS. Multiple sclerosis is the most prevalent chronic disabling neurological disease among U.S. adults,[163] affecting approximately 400,000 individuals.[164]

In considering the importance of preventive effects of physical activity in MS, several issues raised in recent reviews are relevant to this evidence review. First, more than 80 percent of people with the disease live with it for more than 35 years,[165] so physical activity has the potential to provide long-term benefits. Second, in the past, people with MS were advised not to exercise due to concern that exercise would worsen fatigue or symptoms.[165] Because of growing evidence of its benefits, regular physical activity is now generally recommended for people with MS. People with more severe MS may require adapted exercise training, such as body-weight support treadmill training,[166] but people with mild-to-moderate MS can commonly participate in types of physical activity recommended by public health guidelines, such as walking and muscle-strengthening activity.

Third, effects of physical activity on fatigue and depressive symptoms are important to understand, as these are common symptoms in people with MS[165, 167] and they impair HRQoL.[168] About 80 percent of people with multiple sclerosis experience fatigue[169] and about one-fourth have depression.[170]

Finally, the effects of physical activity on physical function are of importance, as impairments in physical function and mobility are also common.[163] Of particular importance are impairments in walking, as impaired walking is common and life-altering and level of impairment in walking can be used to track disease progression over time.[171]

The Subcommittee considered evidence contained in 16 reviews, which comprised both systematic reviews and meta-analyses. All studies included in the reviews were experimental studies (no cohort studies were included). The Subcommittee focused on studies of physical activity interventions with a no-exercise control group. Studies of formal rehabilitation programs, adapted exercise training, and uncontrolled studies were not included as sources of evidence. All reviews were published between 2011 and 2017 inclusive. Some reviews addressed the effects of specific types of physical activity, including aquatic exercise,[172, 173] yoga,[174] tai chi,[175, 176] and muscle strengthening activity.[177] Most reviews summarized effects across a variety of activity types, such as walking, muscle-strengthening activity, video game activity, and balance training.[163, 166, 167, 171, 178-183]

Reviews commonly reported a clinical measure of severity of multiple sclerosis, called the Expanded Disability Status Scale (EDDS).[184] The vast majority of existing trials have enrolled people with mild-to-moderate multiple sclerosis, as indicated by an EDDS score of less than 6.5. Only one review focused on people with severe disability,[166] and this review located only one relevant study (i.e., a physical activity intervention with a no-exercise control group).

In considering the evidence, the Subcommittee noted that trials in individuals with multiple sclerosis often have small sample sizes and/or fewer than 10 weeks of exercise. For example, in one of the earlier meta-analyses published in 2012, five of seven exercise trials had an intervention group of fewer than 20 participants.[182] Such trials potentially have low statistical power. Thus, the Subcommittee regarded larger meta-analyses as the primary source of evidence, as these reviews quantify effects and increase statistical power.

Unlike several other questions in this chapter, the review of multiple sclerosis did not focus on effects of physical activity on the outcome of progression. However, the Subcommittee notes one review concluded that some evidence supports the possibility of a disease-modifying effect of exercise on multiple sclerosis.[165]

Evidence on the Overall Relationship

Risk of Co-morbid Conditions

The Subcommittee was unable to find sufficient evidence to determine the relationship between physical activity and risk of co-morbid conditions in people with MS. The search did not locate any systematic reviews or meta-analyses that addressed risk of co-morbid conditions, including the co-morbidity of major depressive disorder. Although some trials measured depressive symptoms in all participants, no review addressed the effect of physical activity on the percent of participants with diagnosed depressive illness.

Physical Function

Strong evidence demonstrated that physical activity improves physical function in adults with MS. The evidence was strongest for the programs that included moderate-to-vigorous aerobic and/or muscle-strengthening activity, sometimes combined with balance training. A meta-analysis that included 13

RCTs included 5 relevant analyses.[178] First, this review reported that exercise improved walk time in the 10-meter walk test—a measure of gait speed (MD=-1.76 seconds; 95% CI: -2.47 to -1.08).[178] This analysis included 8 comparisons and 234 total participants, and 7 of the 8 interventions tested 4 to 12 weeks of aerobic, resistance, and/or balance training. In the second analysis, the review reported exercise improved walking endurance in the 6-minute walk test (MD=36.46 meters; 95% CI: 15.14-57.79). This analysis included four comparisons and 191 total participants, and all studies tested 12 weeks of aerobic, resistance, and/or balance training. Only one study was included in both of these analyses. In the third analysis, the effect of exercise on 2-minute walk distance involving five comparisons was also significant (MD=12.51 meters; 95% CI: 4.79-20.23).[178] In the fourth analysis, a trend was reported for an exercise effect on the Timed Up and Go test in an analysis including four comparisons (MD=-1.05 seconds; 95% CI: -2.19 to 0.09, *P*=.07). However, the fifth analysis—of the timed 25-foot walk test—found non-significant improvement.

Systematic reviews and another meta-analysis also found some evidence that physical activity improves physical function in people with multiple sclerosis.[163, 171, 177, 183] In some cases, the positive effects were noted for outcomes other than walking, such as balance,[163] and composite measures of physical function.[177] However, these reviews all included fewer RCTs with measures of walking ability than the above meta-analysis (which included 13 trials).[178]

Important supporting evidence that physical activity improves function comes from evidence that physical activity improves measures of physical fitness in adults with MS. Although the Subcommittee did not emphasize reviews of effects of physical activity on fitness, this review of fitness was deemed important in this case because MS has the potential to impair the physiologic effects of exercise. An effect of exercise on physical function is not plausible if exercise has no effect on fitness. It is expected that in individuals with MS, improvements in aerobic capacity and muscular endurance will translate into improvements in walking.[171] For example, one study reported a correlation of r=0.62 between peak aerobic capacity and 6-minute walk distance.[185]

Reviews of the effects of physical activity on fitness consistently reported physical activity improves fitness in people with MS. A meta-analysis that included 20 RCTs reported a small significant effect of exercise on muscular fitness (ES=0.27; 95% CI: 0.17-0.38) and moderate effect on cardiorespiratory fitness (ES=0.47; 95% CI: 0.30-0.65).[179] A meta-analysis of 10 comparisons from 6 studies found strength training increased muscle strength in people with MS (ES=0.31; 95% CI=0.15 to 0.48).[177] A systematic review concluded that strong evidence shows that moderate-intensity exercise increases aerobic capacity and muscular strength in people with MS.[171] Fitness benefits may occur even in severe MS. In a review of effects of exercise training in adults with EDDS score of at least 6.5, a small controlled trial of aerobic exercise reported that exercise improved peak aerobic capacity.[166]

Insufficient evidence was available to determine whether aquatic exercise improves physical function in people with MS. One systematic review of three trials reported significant positive effects of aquatic exercise on physical function.[172] However, these three trials were described as non-randomized trials and a total of only 36 participants were allocated to aquatic exercise in these trials. A more recent systematic review located three RCTs and three non-randomized controlled trials of aquatic exercise.[173] However, this review did not specify how outcomes in these six trials were measured, making it difficult to determine which trial included tests of physical function. It appeared that only one trial found a significant beneficial effect of exercise on a physical function outcome (walking endurance).

Evidence that yoga or tai chi improves physical function in people with multiple sclerosis also was insufficient. A meta-analysis of effects of yoga on mobility located only two trials with a mobility outcome, and the summary effect of yoga was not significant.[174] One systematic review of tai chi located four trials with a no-exercise control group, with significant between group differences in tests of physical function reported for only one non-randomized trial.[176] Another systematic review of tai chi located two RCTs and five non-randomized controlled trials. However, study quality was rated as low in five of the seven trials, and between-group comparisons on effects of exercise on function were not reported for the remaining two higher quality trials.[175]

Health-related Quality of Life

Limited evidence suggests that physical activity improves HRQoL in people with MS. The evidence focused on three measures of quality of life: overall HRQoL, depressive symptoms, and fatigue symptoms.

Overall HRQoL: One meta-analysis of 13 RCTs with 535 total participants reported significant effects of physical activity on quality of life questionnaires, including the SF-36 and the Multiple Sclerosis Quality of Life (MSQOL).[180] The summary effect of physical activity on measures of overall HRQoL was standardized mean difference (SMD)=0.85 (95% CI: 0.51-1.18). However, the analyses combined diverse physical activity interventions (aquatic, yoga, stretching, treadmill, aerobic, resistance, and combined), with the most common intervention being aquatic exercise. The trials' study populations had limited diversity in that 90 percent of participants were women who (apparently) all lived in Iran. One meta-analysis of effects of yoga reported a non-significant effect of yoga on measures of HRQoL (5 comparisons in the analysis).[174] The quantitative results of a meta-analysis were not used as source of evidence because its analysis combined effects of physical activity interventions with effects of rehabilitation interventions.[182] However, results of individual exercise studies were reviewed and, consistent with an effect of physical activity on HRQoL, the five individual studies that reported the largest positive effects on HRQoL were all exercise interventions. Also, one small controlled trial of aerobic exercise in adults with severe disability reported a benefit of exercise on HRQoL.[166]

Depressive symptoms: The strongest evidence that physical activity improves HRQoL was for the effect of physical activity on depressive symptoms, though the size of the effect was small. Two overlapping meta-analyses examined the effects of physical activity on depressive symptoms, one with 15 RCTs and a total of 591 participants,[167] and one with 13 RCTs and a total of 477 participants.[181] Twelve studies were included in both reviews. The interventions in most of the studies were aerobic training, muscle-strengthening activity, or both. Both reviews reported a small, significant effect of physical activity on depressive symptoms of Hedge's g=-0.37 (95% CI: -0.56 to -0.17) and (when improvement was scored as a positive number) Hedge's g=0.36 (95% CI: 0.18-0.54).[181] A meta-analysis of yoga interventions reported a significant effect of yoga on mood (SMD=-0.55; 95% CI: -0.96 to -0.130), but the analysis included only three studies.[174]

Fatigue: One meta-analysis reported a small but significant effect of yoga on measures of fatigue (SMD=-0.52; 95% CI: -1.02 to -0.02; four comparisons).[174] A systematic review located 30 studies of the effects of exercise on fatigue and concluded that the findings from some positive, good quality studies among them suggest that the evidence was promising.[171] A meta-analysis of strength training reported effects on fatigue were assessed by three trials, and all three reported improvements in fatigue.[177] A systematic review noted some high-quality training studies report positive effects on measures of fatigue.[183]

In terms of types of physical activity that improve quality of life in people with MS, the meta-analyses which focused on depressive symptoms indicate that both aerobic and muscle-strengthening activities have benefits.[167, 181] The evidence from a meta-analysis that yoga improved mood and fatigue (summarized above) was based upon only a few studies in each analysis. Evidence for effects of aquatic activity is also limited.

Insufficient evidence was available on the effects of tai chi on measures of HRQoL. One systematic review of tai chi reported a between-group difference in quality of life measures in only one non-randomized controlled trial.[176] As noted in the section on physical function, one systematic review of tai chi included primarily low-quality trials.[175]

For additional details on this body of evidence, visit: https://health.gov/paguidelines/second-edition/report/supplementary-material.aspx for the Evidence Portfolio.

Comparing 2018 Findings with the 2008 Scientific Report

The 2008 Scientific Report reviewed the effects of physical activity in people with MS on the outcomes of cardiorespiratory fitness, muscle strength, mobility (walking speed and distance), and quality of life. For each outcome, only two to four RCTs were located.[4] The evidence was rated as moderate to strong for effects of physical activity on cardiorespiratory fitness, walking speed, and walking distance. The evidence was rated as strong for muscle strength, and very limited for HRQOL. The report did not provide summary measures that quantified the size of the benefits of physical activity on these outcomes.

In comparison, the evidence review and conclusions in this report are based upon a much larger number of RCTs, and meta-analyses are available that quantify effects of physical activity. Strong evidence now exists for a small-to-moderate size effect of physical activity on physical function, as mainly assessed by effects on walking speed and endurance. Systematic reviews provide some evidence that the effects of physical activity are broader than just effects on mobility. For example, it may also improve measures of balance. Although the Subcommittee did not formally rate the evidence of fitness effects, a systematic review done to inform guideline development rated the evidence as strong.[171] A meta-analysis that included 20 RCTs quantified effects of (typically short-term) training studies on fitness as small to moderate. A growing body of evidence is now showing that physical activity improves HRQoL in people with MS, though the evidence for overall quality of life is limited. The Subcommittee did not rate the evidence separately for effects of physical activity on depressive symptoms, and mood is only one component of HRQoL. But clear evidence shows that physical activity has a small beneficial effect on depressive symptoms, as determined by meta-analyses of at least 13 RCTs.

Consistent with the 2008 Scientific Report,[4] evidence is strongest for beneficial effects of conventional aerobic and muscle-strengthening activity. However, data are emerging that other forms of physical activity may have benefits in individuals with MS, particularly on quality of life. This report clarifies that evidence of benefit is limited to people with mild-to-moderate multiple sclerosis. The 2008 Scientific Report noted it did not locate any evidence "to support the notion that exercise imposes a higher risk of exacerbation or harm in people with Multiple Sclerosis."[4] Although the 2018 Scientific Report did not have a question addressing adverse events, the included systematic reviews and meta-analyses provided no findings that were inconsistent with the 2008 conclusion.

Public Health Impact

The review supports the importance of promoting physical activity in people with MS. Indeed, people with MS are less physically active than non-disability age-matched populations.[186] The main finding was that physical activity improves physical function in adults with MS. Although meta-analyses summarize effects of physical activity as small to moderate, the duration of exercise in most trials is 12 weeks or less. Potentially, regular physical activity over long periods of time has moderate-to-large benefits. Indeed, a stronger effect of physical activity on walking speed was reported in a meta-analysis when the analysis was limited to studies of at least 12 weeks duration.[178] Although effects on gait speed are modest, effects that may seem small (e.g., an improvement of 0.1 meters per second) are associated with substantial reductions in risk of all-cause mortality in the general population of older adults.[187] Further, walking speed is a key measure of level of disability in people with MS.

The meta-analyses of effects of activity on depressive symptoms indicate that physical activity is a modestly beneficial non-pharmacologic approach to reducing symptoms of depression generally in people with MS. As noted above, depression is common in adults with MS.

Question 6. In people with spinal cord injury, what is the relationship between physical activity and (1) risk of co-morbid conditions, (2) physical function, and (3) health-related quality of life?

Sources of evidence: Systematic reviews, meta-analyses

Conclusion Statements

Risk of Co-morbid Conditions

Limited evidence suggests that physical activity reduces shoulder pain and improves vascular function in paralyzed limbs in individuals with spinal cord injury. **PAGAC Grade: Limited.**

Physical Function

Moderate evidence indicates that physical activity improves walking function, muscular strength, and upper extremity function for persons with spinal cord injury. **PAGAC Grade: Moderate**.

Health-related Quality of Life

Limited evidence suggests physical activity improves health-related quality of life in individuals with spinal cord injury. **PAGAC Grade: Limited.**

Review of the Evidence

The effects of a traumatic spinal cord injury (SCI) on individuals and their families and friends are immediate and enormous.[188] Upon sustaining a SCI, individuals who were previously healthy and independent must suddenly cope with effects of partial or complete paralysis on body movement, as well as cope with partial or complete loss of control over bowel, bladder, and sexual function. SCIs can lead to negative effects on emotions, relationships with family and friends, and on occupational status. In the United States, about 12,000 new cases of SCI occur each year, and about 260,000 individuals are living with a spinal cord injury.[189]

In individuals affected by SCI, prevention of co-morbidities and mitigating effects of SCI on physical function and HRQoL are of great importance. Addressing the effects of physical activity on risk of co-morbidities, physical function, and HRQoL in individuals with SCI is thus important. A review of the effects of physical activity in individuals affected by SCI necessarily deals with different types of physical activity than are common in the general population. Because SCI restricts physical activity behaviors, the types of activity of interest in SCI include arm ergometry, wheelchair-based exercise, underwater treadmills, and adapted forms of physical activity (e.g., adaptations that partially support body weight).

In terms of preventing co-morbidity, measures of improvement in cardiovascular status and CVD risk due to physical activity assume more than the usual importance. With loss of autonomic control due to SCI, the response to physical activity by blood vessels in the areas affected by the injury may not be normal. An impaired cardiovascular response to activity can limit exercise capacity, accelerating development of CVD.[190] Individuals with SCI are at two to four times higher risk of CVD than those without SCI.[191]

In terms of understanding effects of physical activity on physical function, the effects are obviously influenced by the location and severity of the injury. The severity of the injury is commonly described using the American Spinal Injury Association's Standard Neurological Classification of Spinal Cord Injury (ASIA) (Table F10-2).

Table F10-2. American Spinal Injury Association Impairment and Motor Function Scales

Impairment Scale	
Group A	Complete: No motor or sensory function is preserved in the sacral segments S4-S5.
Group B	Incomplete: Sensory but not motor function is preserved below the neurological level and includes the sacral segment S4-S5.
Group C	Incomplete: Motor function is preserved below the neurologic level and more than half of key muscles below the neurologic level have a muscle grade <3 (less than full range of motion against gravity).
Group D	Incomplete: Motor function is preserved below the neurologic level and at least half of key muscles below the neurologic level have a muscle grade of 3 or more.
Group E	Normal: Motor and sensory function are normal.
Motor Function Scale	
Grade 0	Total paralysis
Grade 1	Palpable or visible contraction
Grade 2	Active movement, gravity eliminated
Grade 3	Active movement against gravity
Grade 4	Active movement against some resistance
Grade 5	Active movement against full resistance
NT	Not testable

Source: Kirshblum et al., 2011.[192]

In reviews of effects of physical activity located by the search strategy, several outcomes were specific to SCI. This led the Subcommittee to consider how such outcomes should be classified for the three outcomes in Question 6.

1. *Shoulder pain* is an important problem for individuals with SCI, affecting 38 to 67 percent of manual wheelchair users.[193] It is usually related to high workloads placed on the shoulders for transfers and wheelchair mobility in individuals with paraplegia[194] and weakness of shoulder muscles in individuals with quadriplegia. Shoulder pain was deemed to be a co-morbid condition—essentially a surrogate outcome for the group of shoulder conditions that occur commonly with SCI (which including overuse injuries like tendinitis).
2. *Measures of vascular function* are important indicators of CVD risk. Lacking reviews on relationships between greater physical activity and CVD events, measures of vascular function were deemed appropriate as surrogate markers of CVD risk.

3. *Wheelchair skills and propulsion*, including ability to start and stop, change directions, and maneuver through doorways, affect an individual's mobility and hence were regarded as measure of physical function.
4. *Physical fitness outcomes* were included in the review of effects on physical function. Physical fitness (aerobic capacity and muscular strength) are clear determinants of physical function in individuals with SCI. Documenting activity-related improvements in fitness outcomes was regarded as important supporting evidence for a finding of effects of physical activity on physical function.

The evidence reviewed comprised nine systematic reviews[195-203] and two meta-analyses.[204, 205] The number of studies included in each review ranged from seven to 82, with a median of 13. About half of all studies were pre-post designs, and about one-third were experimental designs with a comparison group. Other study designs included cohort and cross-sectional studies, case series and case reports, and a chart review.

Evidence Identified on Risk of Co-morbid Conditions

Three systematic reviews[196, 198, 202] provided information about physical activity and the development of co-morbid conditions. One review[196] focused on shoulder pain and included 7 studies (3 RCTs, 4 cohort studies), with a total of 197 adult wheelchair users. Another review[202] assessed changes in vascular function associated with either a single acute episode of physical activity or longer term physical activity. The review included 14 studies (8 with a comparison group and 6 with only pre-post-assessments) of a single episode of activity with a total of 215 adults, and 15 studies (1 RCT, 2 case-control, 11 pre-post, and 1 case report) of habitual physical activity, with a total of 179 adults. Lack of mobility, impaired autonomic regulation of the cardiovascular system, and reduced vascular compliance place individuals with SCI at higher risk of CVD.[202]

Evidence Identified on Physical Function

Six systematic reviews[195, 197, 198, 200, 201, 203] and two meta-analyses[204, 205] provided information about the relationship between physical activity and physical function in individuals with SCI.

Cardiovascular fitness and muscular strength: Three systematic reviews[195, 198, 200] provided information about measures of cardiovascular fitness and muscular strength. The review by Bochkezanian et al[195] included two randomized controlled studies, four pre- post studies, and one case series with a total of

149 adults. The review by Hicks et al[198] included 12 experimental studies with comparison groups and 70 studies with pre-post designs and a total of 1,207 participants. The review by Li et al[200] included four experimental studies with comparison groups, two pre-post designs, one case series, and one case report with 143 adults. The physical activity exposures in one of the reviews[200] was limited to aquatic activities, such as swimming or underwater treadmill walking. The physical activity exposures in the more than 80 studies included in the other two reviews[195, 198] were various combinations of aerobic exercise, mostly arm ergometry or wheelchair use, and muscle strengthening exercises with pulleys, bands, and free weights. Outcome measures in all three reviews included VO_2max, power output, and various task-specific measures of upper body strength.

Walking: Four systematic reviews[197, 198, 200, 203] provided information about walking as an outcome. The review by Gandhi et al[197] included one case series and 11 case reports with a total of 43 children and adolescents of whom 40 were ages 10 to 17 years. The review by Li et al[200] included one pre-post study and one case report with walking outcomes with a total of 12 adults. The review by Hicks et al[198] included 3 studies of individuals with acute (≤12 months) and 11 studies of individuals with chronic (>12 months) SCI. The review by Yang and Musselman[203] included 7 experimental studies with comparison groups, 11 pre-post designs, and 2 case series. The physical activity exposures in one of the reviews[200] was limited to aquatic activities such as swimming or underwater treadmill walking. The exposure in the other three reviews[197, 198, 203] included overground walking, robotic-assisted or body weight supported treadmill training, and muscle-strengthening exercises. Change in walking ability in the four reviews[197, 198, 200, 203] was assessed with measures of walking speed and walking distance.

Upper extremity function: One systematic review[201] focused on upper extremity function among individuals with SCI at the cervical level. Of the 16 studies included in the review, 6 RCTs provided physical activity exposures beyond standard physical therapy. The physical activity exposures included arm ergometry, progressive resistance training, or electrical stimulation. Outcomes included tests of hand function, functional independence, and activities of daily living.

Postural stability: One meta-analysis[205] examined postural control in sitting and standing. The meta-analysis included six experimental studies with comparison groups, 11 pre-post, and 4 cohort studies. The four studies included in the meta-analyses included 153 participants. Exposures included unsupported sitting, rockerboard, tai chi, balance exercises, and task based training; outcomes included sit and reach test and the Berg Balance Scale.

Evidence Identified on Health-related Quality of Life

Two systematic reviews[195, 199] provided information about physical activity and quality of life. One[195] included 7 studies, of which two randomized controlled trials, each with 34 total participants, examined the relationship between physical activity and quality of life. The physical activity exposure in both studies included arm ergometry, free weights, and pulleys. Both studies used the Perceived Quality of Life questionnaire and one also used a body satisfaction questionnaire. The other systematic review[199] included six cross-sectional studies and five experimental trials with a total of 634 adults that examined the relationship between physical activity and quality of life. In the cross-sectional studies, the physical activity practices were obtained from six different self-report instruments; in the experimental trials, the physical activity programs included swimming, treadmill, or combined aerobic and strength training.

Evidence on the Overall Relationship

Risk of Co-morbid Conditions

Shoulder Pain: Evidence that shoulder strengthening and stretching reduces shoulder pain in individuals with SCI comes from a single systematic review that included 3 RCTs and 4 cohort studies with a total of 199 subjects. The exercise exposure included arm ergometry, resistive strengthening with or without electromyelogram biofeedback, and stretching the muscles of the shoulder girdle. Training was three times per week and spanned 2 to 6 months. Shoulder pain was assessed with the Wheelchair Users Shoulder Pain Index (WUSPI).[206] All seven studies reported significantly improved (reduced) scores on the WUSPI.[196] Systematic use of WUSPI as a well-validated outcome measure across studies increases the consistency and strength of this relationship, with benefits consistently exceeding the 5.1 points minimal clinical detectable difference on WUSPI, indicating a significant effect size.

Vascular Function: A single systematic review examined the effect of both acute episodes of physical activity (14 studies, 215 total subjects) and regular episodes of physical activity (15 studies, 179 total subjects) on arterial function among individuals with SCI.[202] The most common exercise exposure was arm cycling for both acute and non-acute studies, but also included passive arm or leg exercise, electrical stimulation, and, for non-acute only body-weight supported treadmill training. Vascular function in paralyzed limbs was significantly improved in both groups.[202]

Physical Function

Walking Function: Four systematic reviews examined the relationship between physical activity and parameters of walking function; all four reviews reported improved walking function associated with either task-oriented exercise[197, 198, 203] or aquatic treadmill or swimming exercise.[200] Yang and Musselman[203] reported increased walking speeds ranging from 0.06 to 0.77 meters per second and increased 6-minute walking distances from 24 to 357 meters. In the review by Hicks et al,[198] 3 of the 13 studies of individuals with acute spinal cord injury reported on walking function as an outcome; 11 of the 69 studies of individuals with chronic spinal cord injuries reported on walking function as an outcome. Quantification was not provided, but all reported general improvements in a variety of assessments of walking. Of the eight studies of aquatic exercise, two examined the effect on walking performance and both reported improvements.[200] Gandhi et al[197] reported uniform improvements in walking across all 13 studies of children and adolescents with spinal cord injury.

Upper Extremity Function: Most studies in the one systematic review that examined upper extremity function reported improvements in muscle strength, arm and hand function, and activities of daily living.[201] However, limited quantitative information was provided, and the outcomes were diverse.

Postural Stability and Balance: The meta-analysis[205] suggests that task-oriented training has negligible effect on postural stability and balance during sitting and standing. Two studies with inactive control groups and two studies with active control groups were included in meta-analyses and both comparisons had nonsignificant differences between groups.

Cardiovascular Fitness and Muscular Strength: The three systematic reviews all provide evidence indicating a positive relationship between greater amounts of aerobic or muscle-strengthening physical activity and higher cardiovascular or muscular fitness.[195, 198, 200] Hicks et al[198] report "clear improvements" among individuals with older (>12 months) and newer (≤12 months) SCI. Summarizing the findings reported from 30 studies of interventions of arm or wheelchair ergometry among individuals with older injuries, Hicks et al[198] report that "it was clear" that the exercise "produced significant improvements in aerobic capacity." Similarly, 16 studies mostly of combined muscular strengthening and arm ergometry reported improved power output; all 11 studies of muscular strengthening and arm ergometry reported improved muscular strength, and all 9 studies of wheelchair skills and propulsion showed significant improvements.[198] Fewer studies of individuals with newer lesions were identified but findings were similar.[198] Bochkezanian et al[195] reported that nine of nine within-group comparisons for aerobic fitness showed improvements associated with the exercise exposure and two of the improvements were statistically significant. Similarly, all 22 within-group comparisons for muscular strength showed improvement and 11 of them were statistically significant. Finally, three of four studies of aquatic exercise (treadmill or swimming) reported improved cardiovascular fitness; the fourth showed no superiority compared with land-based exercise but the review provided no information about whether or how much both aquatic and land-based exercise produced changes in fitness or strength.[200]

Health-related Quality of Life

The two systematic reviews[195, 199] provide limited support for a beneficial relationship between greater participation in physically active endeavors and higher reported perceptions of quality of life. Bochkezanian et al[195] included two RCTs each of which included 32 participants. Of the six comparisons in the two studies, all six showed a beneficial effect of physical activity on quality of life but only one of the six achieved statistical significance. Kawanishi and Greguol[199] included 11 studies, 6 cross-sectional and 5 experimental studies (4 pre-post, 1 RCT that was also one of the two studies in Bochkezanian et al[195]), with a total of 634 individuals.[199] Five of the six cross-sectional studies and four of the five experimental studies reported positive associations, but no quantification was provided. Therefore, although these two systematic reviews describe generally positive associations between greater participation in physically active endeavors and greater perceived quality of life, life-satisfaction, or functional independence irrespective of the SCI level or ASIA classification, the evidence is weak.

For additional details on this body of evidence, visit: https://health.gov/paguidelines/second-edition/report/supplementary-material.aspx for the Evidence Portfolio.

Comparing 2018 Findings with the 2008 Scientific Report

The 2008 Scientific Report summarized the evidence that physical activity improves physical function broadly in individuals with disabilities. The report found evidence across several types of disability that physical activity reduces pain, improves fitness, improves physical function and improves quality of life.[4]

In contrast, Question 6 focused on one type of disability—spinal cord injury. This report located more individual studies in individuals with SCI than were available for the 2008 Scientific Report,[4] allowing conclusions specific for SCI and more precise quantification of effects of physical activity. Moderate evidence now indicates that physical activity improves physical function specifically in individuals with SCI. Also specific for SCI, this report found limited evidence that physical activity opposes the elevated risk of CVD in individuals with SCI, limited evidence that physical activity improves shoulder pain, and limited evidence for benefits of physical activity on HRQoL.

Public Health Impact

This evidence review documents that benefits of physical activity in individuals with chronic conditions extend beyond common age-related chronic conditions such as osteoarthritis and type 2 diabetes. SCI has a different pathogenesis even when compared to other chronic neurological conditions, and yet evidence of limited to moderate strength indicates benefits of physical activity extend to individuals affected by SCI. Notably, these benefits appear to accrue in individuals with both recent (≤12 months) and older (>12 months) injuries, and occur across a range of injury severity. Overall, this review is important to understanding the breadth of beneficial effects of physical activity on health. As about half of individuals with SCI are estimated to have no leisure-time physical activity,[207] the review emphasizes the importance of public health strategies for promoting physical activity in individuals with disabilities.

Question 7. In individuals with intellectual disabilities, what is the relationship between physical activity and: (1) risk of co-morbid conditions, (2) physical function, and (3) health-related quality of life?

Sources of evidence: Systematic reviews, meta-analyses

Conclusion Statements

Risk of Co-morbid Conditions

Insufficient evidence is available to determine the relationship of physical activity with risk of comorbid conditions in individuals with intellectual disabilities. **PAGAC Grade: Not assignable.**

Physical Function

Limited evidence suggests that physical activity improves physical function in children and adults with intellectual disabilities. **PAGAC Grade: Limited.**

Health-related Quality of Life

Insufficient evidence is available to determine the relationship of physical activity with health-related quality of life in individuals with intellectual disabilities. **PAGAC Grade: Not assignable.**

Review of the Evidence

Intellectual disability is historically defined by significant cognitive deficits, most commonly an IQ score of below 70 (two standard deviations below 100, which is the mean IQ of the general population), significant deficits in functional skills, and reduced adaptive skills to carry out age-appropriate activities of daily life. The Diagnostic and Statistical Manual of Mental Disorders defines intellectual disabilities as neurodevelopmental disorders beginning in childhood and characterized by intellectual difficulties, as well as difficulties in adaptive functioning in conceptual, social, and practical areas of living.[208] When the definition of intellectual disability is based only upon IQ, the prevalence of intellectual disability has been historically 2 to 3 percent of the U.S. population. However, a prevalence of 1.37 percent in children and a prevalence of about 1 percent of the total population are more consistent with the contemporary DSM-5 definition.[208-210] Down syndrome, which occurs in 1 of every 700 births, is the most common genetic cause, with more than 250,000 individuals in the United States affected and prevalence rising, in part due to a major increase in lifespan to a mean of 60 years in age.[211] A majority of the systematic reviews and meta-analyses in this report focused either exclusively or primarily on children and/or adults with Down Syndrome.

Risk of Co-morbid Conditions

The one systematic review available examined co-morbid conditions among individuals with intellectual disabilities.[212] The systematic review included 20 studies and covered a timeframe from 1980 to May 2013. The studies examined aerobic exercise and muscle-strengthening activities. Aerobic activities included running, jogging, soccer, basketball, and dancing. Studies assessed a variety of co-morbid conditions, including different types of challenging behaviors and hyperactivity.

Evidence on the Overall Relationship

Only 2 of the 20 studies had a control group; 5 were case reports involving a total of 5 individuals with intellectual disability, and the remaining 13 studies included a total of 53 participants. The review showed a small significant beneficial effect consisting of a mean behavioral improvement of 30.9 percent (95% CI: 25.0-36.8) signifying a decrease in challenging behaviors based on observational ratings or questionnaires scoring aggressive/destructive, self-injurious, hyperactive, and stereotypical behaviors. However, the Subcommittee was unable to grade the relationship between physical activity and co-morbid conditions because of limitations in experimental design, with few controlled studies and small sample sizes.

Physical Function

One meta-analysis[213] and two systematic reviews[214, 215] were available to assess the relationship between physical activity and physical function among individuals with intellectual disabilities.

The Valentín-Gudiol et al[213] meta-analysis of 7 studies included 175 children younger than age 6 years of age with Down syndrome, cerebral palsy, developmental delay, or at moderate risk for developmental delay. The review studied the effects of treadmill locomotor training on walking function and gross motor function, and in a subset of 30 children with Down syndrome, the age of independent walking onset.

The Hardee and Fetters[214] systematic review used 19 studies published up to March 2016 to assess effects in 428 children and adults ages 3 to 66 years with Down syndrome. The review examined traditional exercise programs (e.g., aerobic and/or muscle-strengthening training) and non-traditional exercise programs (e.g., bike riding, dancing, swimming, judo) on a function domain (e.g., strength and endurance) and an activity domain (e.g., gross motor activity tests) using appropriate tests by age group (<18 years and ≥18 years).

The Bartlo and Klein[215] systematic review examined the relationship of physical activity and physical function (walking and balance) using 11 studies over the interval 1990 to 2010 in 310 adults ages 21 to 64 years with intellectual disability.

Evidence on the Overall Relationship

In the systematic reviews,[214, 215] a variety of physical activity modalities were associated with small improvements in walking velocity in adults. These improvements were typically on the order of 10 to 11 percent. Measures of balance scores increased across a range of 10 percent to 25 percent. However, meta-analyses were not available to determine effects sizes due to variability in the outcome measures used and small sample sizes. In children, a variety of physical activities significantly improved some physical function measures, including walking velocity and Timed Up and Go test.[214] However, no meta-analyses were available to examine effect sizes due to the large variability in outcome measures and small sample sizes. Treadmill locomotor training in children resulted in a small positive effect on walking velocity (MD=0.23; 95% CI: 0.08-0.37). A subset analysis in 30 children with Down syndrome showed earlier age of independent walking onset (MD=-4.00; 95% CI: -6.96 to -1.04), improved walking skills in children with developmental delay and gross motor skills in children with cerebral palsy. Thus, limited evidence suggests that, in children and adults with intellectual disability primarily associated with Down syndrome, greater physical activity improves walking, balance, and gross motor skills. The findings and conclusions, though limited by experimental design issues, provide a promising consistency that greater physical activity can produce significant and meaningful improvements in mobility function that are of similar magnitude to those we report for other chronic disability populations in this report.

Health-related Quality of Life

One systematic review of 11 total studies covering a timeframe from 1990 to January 2010 examined relationships between physical activity and health outcomes, including HRQoL in adults with intellectual disabilities, primarily Down syndrome.[215] This study assessed the effects on balance, strength, and cardiovascular fitness of physical activity programs using different modalities, including walking, bicycle ergometer, muscle strengthening, stepping activities, elliptical training, rowing, balance activities, dancing, and plyometric activities. A second systematic review of 11 studies covering a timeframe from 1978 to 2016 examined relationships between greater physical activity and health outcomes, including HRQoL, in children and adults with Down syndrome.[214]

Evidence on the Overall Relationship

The systematic review in adults included one study in which aerobic training was associated with a significant 50 percent improvement in HRQoL scores and one study that resulted in a small but significant positive effect in life satisfaction.[215] In the systematic review including children and adults with Down syndrome, greater physical activity was associated with increased life satisfaction scale in one study, and improved participation in social and environmental activities in five of eight studies examining this outcome. Both outcomes have been related to HRQoL in this population.[214] However, no other significant changes in HRQoL outcomes were reported. Collectively, these findings in a small number of studies are insufficient to establish a grade for the relationship between physical activity and HRQoL for children and adults with intellectual disabilities.

For additional details on this body of evidence, visit: https://health.gov/paguidelines/second-edition/report/supplementary-material.aspx for the Evidence Portfolio.

Comparing 2018 Findings with the 2008 Scientific Report

The 2008 Scientific Report summarized the evidence that physical activity improves physical function broadly in individuals with disabilities.[4] In contrast, this question focused on one type of disability—intellectual disability. The evidence review located many more individual studies in the sources of evidence than were available for the 2008 Scientific Report,[4] allowing a conclusion specific for intellectual disability. Limited evidence now suggests that physical activity improves physical function specifically in individuals with intellectual disabilities. This conclusion applies to both children and adults and generalizes to more types of physical activity than just aerobic activity. Some reviews included studies of individuals with intellectual disabilities other than Down syndrome, and provided quantitative estimates of the effects of physical activity. In particular, the finding applies to children with developmental delay, in which greater physical activity has potential to improve walking velocity and lower the age of walking onset.

Public Health Impact

Individuals with intellectual disabilities represent an important and growing population in the United States. Increased prevalence is due in part to increasing longevity for many intellectual disability populations. For Down syndrome, the mean lifespan has risen from 25 in 1983 to a current mean of 60 years in age.[216] The profiles of disability change with aging, typically with delayed motor development in younger years, followed by increasing disability across adulthood that becomes multi-factorial due to changes resembling accelerated aging in many sensory systems, and early onset Alzheimer's Disease.[217]

The emerging evidence is that greater physical activity has benefits across the lifespan, improving walking function and hastening earliest age of walking onset in children with developmental delay. In adults, a diversity of physical activity modalities is associated with improved walking and gross motor function. Such diversity in physical activity modalities brings choices and many avenues for participation, helping to overcome the many barriers that currently limit the more than 70 percent of adults with disabilities who do not engage in health and wellness programs.[218]

NEEDS FOR FUTURE RESEARCH

This section is organized into two parts. First, five cross-cutting needs for research are discussed that integrate similar research needs relevant to more than one chronic condition (involving conditions reviewed by this chapter or chronic conditions generally). Then, research needs specific to each chronic condition are listed. Research needs within each topic area are listed in order of priority.

Priority Research Needs on Preventive Effects of Physical Activity in Individuals with Chronic Conditions

For the five research priorities in this section, research designs should generally include and compare self-report and device-based measures of physical activity. All the questions in this chapter found insufficient evidence to determine whether method of measurement of physical activity influences reported relationships between physical activity and health outcomes.

1. Conduct research on how characteristics of aerobic activity, muscle-strengthening activity, balance training, and combined activity (e.g., dose, duration, intensity, frequency, and type) influence the relationship between physical activity and health outcomes in individuals with chronic conditions.

   Rationale: A basic element of public health recommendations in physical activity is to specify the frequency, duration, intensity, types, and amounts of physical activity that provide health benefits. Hence, it is remarkable that the reviews of this chapter provided so few data on how these characteristics of physical activity influence health effects. For example, in osteoarthritis, no reviews were located comparing the relative effects of different types of physical activity or of different amounts of physical activity. Yet this chapter has some provocative findings illustrating the importance of research in this area. For example, in type 2 diabetes, research indicated (1) muscle-strengthening activity and aerobic activity have independent effects on hemoglobin A1C (indicating the importance of combined activity), and (2) vigorous-intensity activity is more efficient in lowering hemoglobin A1C (larger effect on hemoglobin A1C for a given volume of aerobic activity) than moderate-intensity activity. The increased interest in health benefits of light-intensity activity makes it an even higher priority to conduct randomized trials comparing different intensities and types of physical activity, and to conduct long-term cohort studies that provide dose-response data. For uncommonly performed types of activity (e.g., balance training), cohort studies are not feasible, so dose-response randomized trials are needed. To some extent, such as in individuals with hypertension, studies are needed to understand how characteristics of physical activity influence acute physiologic and health effects of activity.

2. Conduct research in individuals with chronic conditions on the effects of physical activity in reducing risk of developing additional chronic conditions (co-morbidities).

   Rationale: The introduction of this chapter explains the public health importance of preventing multiple chronic conditions. In essence, as the number of chronic conditions afflicting a person increases, generally physical function worsens, health-related quality of life decreases, and cost of medical care increases. Despite a broad search for preventive effects of physical activity on reduced risk of any co-morbid condition, this chapter could make only a few conclusions related to prevention of co-morbidity. This lack of evidence is despite higher risk of co-morbid conditions in some chronic diseases, as illustrated by the higher risk of cardiovascular disease in individuals with spinal cord injury. Whereas the incidence of a few chronic conditions may be high enough to study in randomized controlled trials, generally prospective cohort studies are needed of long-term effects of physical activity on risk of common co-morbidities.

3. Conduct research on the secondary prevention effects of physical activity in individuals with chronic conditions, that is, research on how physical activity reduces risk of progression of the chronic condition and mitigates the effects of the chronic condition on physical function and health-related quality of life.

   Rationale: The amount of information located on secondary prevention by the evidence reviews varied substantially by chronic condition. Except for osteoarthritis, in individuals affected by the chronic conditions of this chapter, high-quality randomized controlled trials of effects of exercise on physical function and health-related quality of life are needed, including longer term studies (e.g., 4-6 months) that have adequate statistical power. For effects of physical activity on progression, generally prospective cohort studies are needed. For example, cohort studies are needed on effects of physical activity in type 2 diabetes on risk of neuropathy, nephropathy, retinopathy, and foot disorders.

4. Conduct systematic and coordinated randomized controlled trials on the health effects of tai chi, qigong, and yoga in individuals with chronic conditions.

   Rationale: With one exception (osteoarthritis), the evidence for health benefits of tai chi, qigong, and yoga was rated as insufficient by the evidence reviews of this chapter. Although randomized controlled trials of these forms of physical activity were located, often they were few in number, small, and/or of low methodologic quality. Although higher quality randomized controlled trials of these types of physical activity are a priority, it is important that such trials be conducted in a systematic and coordinated fashion. Currently, the types and forms of these physical activity types studied in trials vary substantially, as do reported effects. Public health guidelines need to specify details about physical activity—in this case for each exercise type, to specify the specific movements and minimal dose that are effective in improving health. Such information is not currently available, and systematic and coordinated randomized controlled trials are necessarily to provide this information.

5. Conduct research on whether or not individual characteristics influence the effects of physical activity interventions on health outcomes in individuals with chronic conditions.

   Rationale: The evidence reviews of this chapter found little information on whether or not the effects of physical activity vary by individual characteristics, such as age, sex, race/ethnicity, body weight, socioeconomic status, and severity of the chronic condition. The importance of such information is illustrated by findings in type 2 diabetes. The evidence suggested effects of physical activity on hemoglobin A1C were larger in individuals with the highest levels of hemoglobin A1C, thus emphasizing those at higher risk of progression with more severe disease were not less likely to benefit from physical activity. From the standpoint of evidence needed for public health guidelines, this is a lower priority need for research because beneficial effects of physical activity have been demonstrated across a wide variety of populations. However, it is desirable for prevention guidelines be appropriately tailored to individuals. Thus, this topic remains a research priority.

Priority Research Needs on Preventive Effects of Physical Activity in Individuals with a Specific Chronic Condition

Question 1: Cancer Survivors

6. Continue long-term follow-up of cohorts of cancer survivors, with repeated self-report and device-based measures of physical activity, to determine long-term effects of physical activity on recurrence and survival.

   Rationale: Although survival from breast cancer is improving, the risk of mortality continues for 20 years or more, especially for women with hormone receptor positive tumors. Survival from prostate cancer tends to be long-term for most men, but for some, progression occurs in spite of optimal treatment. Furthermore, many men with prostate cancer have increased risk for cardiovascular disease, and the primary cause of death in these patients is cardiovascular disease. Therefore, the effect of physical activity on long-term all-cause mortality in prostate cancer survivors will need to be assessed. Colorectal cancer survival is increased with lower stage at diagnosis, and many individuals survive long-term. However, little is known about effects of physical activity on long-term colorectal cancer survival. Continued follow-up of large cohorts will allow for identification of individuals with less common cancers, who can then be followed to determine associations between physical activity level and survival from these other cancers.

7. Conduct randomized controlled trials and cohort studies of physical activity and cancer survival, recurrence, and second primary cancer, aimed at eliminating effects of possible confounders.

   Rationale: Treatment type, adherence, and completion are strong predictors of cancer outcomes and can reduce physical activity levels. Fatigue from the cancer and its treatments can reflect adverse clinical processes, and can also reduce physical activity interest and ability. Therefore, randomized controlled trials to test the effect of physical activity on survival, recurrence, and second primary cancer are needed. In addition, cohort studies with appropriate adjustment for clinical sources of confounding can provide additional information, especially if randomized controlled trials are not feasible.

8. Conduct prospective cohort studies and randomized controlled trials to determine effects of physical activity on cancer survival, recurrence, and second primary cancer in understudied groups, such as survivors from diverse races, ethnicities, and socioeconomic groups; individuals with metastatic cancer; men with breast cancer; individuals with cancers other than breast, colorectal, and prostate cancer; and patients treated with cardiotoxic drugs (such as doxorubicin and trastuzumab), radiotherapy, and hormonal treatments.

   Rationale: Few studies have investigated the effects of physical activity on cancer prognosis and survival within specific race, ethnic, or socioeconomic groups. Some of these groups have high risk for poor survival, and are also less likely to meet recommended levels of physical activity. Therefore, determining whether physical activity can improve survival and reduce recurrence and second primary cancers in specific groups is important. Patients treated with cardiotoxic drugs, radiotherapy, or hormonal therapies may have increased risk for cardiac events; it is not known whether physical activity could be cardioprotective in such patients, or whether some forms of physical activity could increase risk of cardiac events.

Question 2: Osteoarthritis

9. Conduct prospective cohort and longer-term randomized controlled trials on osteoarthritis disease progression, with device-based measures used to quantify physical activity exposures and with molecular and imaging disease status biomarkers as outcomes.

   Rationale: There is great confusion in the field on whether physical activity and exercise causes osteoarthritis in the absence of underlying injury and whether specific physical activity and exercise exposure amounts and intensities lead to disease progression. Studies are needed to address these critical issues. Because it takes years for disease activity to result in structural, detectable radiographic changes in the joint, sophisticated imaging modalities, such as magnetic resonance imaging, and biological biomarkers of disease activity (circulating systemic or intra-articular) are required to measure the outcomes.

10. Conduct research to clarify how osteoarthritis progression is modified by baseline demographic and disease characteristics.

    Rationale: For the outcome of disease progression induced by physical activity, some evidence suggests that baseline disease status plays a role in modifying the effect of physical activity, but this role has not yet been fully explained. In addition, although a relationship between body mass index and osteoarthritis is generally recognized, no studies have investigated through meta-analyses whether body mass index modifies the physical activity-osteoarthritis relationship.

11. Conduct direct head-to-head comparisons of the relative effectiveness of physical activity and analgesics for pain control in individuals with osteoarthritis.

    Rationale: The current of the literature revealed that the effect sizes of pain control for exercise therapy is very similar to that of analgesics, including narcotic analgesics.[54] If true, this would be a critical observation with profound implications for patient care, especially as the effects of physical activity on osteoarthritis-related pain seem to be durable for up to six months following cessation of an intervention. Determining the comparative effects of physical activity and analgesics on osteoarthritis pain could contribute greatly to effective clinical management of osteoarthritis.

Question 3: Hypertension

12. Conduct research in people with hypertension on the relationships among physical activity and risk of co-morbid conditions, physical function, health-related quality of life, and cardiovascular disease progression and mortality, which compares effects of physical activity in African Americans to effects in other racial/ethnic groups.

    Rationale: Due to the disproportionate burden of hypertension among African Americans, large trials are needed that are sufficiently powered to perform stratified analyses between African Americans and other racial/ethnic groups. Gaining this information will inform public health recommendations about demographic characteristics that influence the relationship between physical activity and blood pressure, and provide insight into the populations that will experience the greatest cardiovascular health benefits from physical activity.

13. Conduct research that discloses the standard criteria and methods that were used to determine the blood pressure status of the study sample to better isolate samples with hypertension from those with normal blood pressure and prehypertension.

    Rationale: Limited evidence suggests the magnitude of the blood pressure response to physical activity varies by resting blood pressure level, with the greatest blood pressure reductions occurring among adults with hypertension that have the highest resting blood pressure levels. Study sample often include mixed samples of adults with hypertension, prehypertension, and normal blood pressure, and findings are frequently not reported separately by blood pressure classification. Consistent with the law of initial values, this practice underestimates the antihypertensive benefits of physical activity. Reporting findings by blood pressure classification will inform public health recommendations on the magnitude and precision of the blood pressure reductions that result from physical activity among adults with hypertension.

14. Conduct research that discloses and quantifies medication use, particularly antihypertensive medication use among samples with hypertension.

    Rationale: Medication use is poorly reported and is a significant confounder in interpreting the clinical significance of the blood pressure response to physical activity. In addition, evidence is lacking on the interactive effects of physical activity and antihypertensive medication use, another important clinical outcome on that has insufficient evidence. Gaining this information is important to determine whether the influence of physical activity on blood pressure varies by antihypertensive medication use.

Question 4: Type 2 Diabetes

15. Conduct randomized controlled trials comparing the effects of shifting time from sedentary behavior to low-intensity aerobic activity, moderate-intensity aerobic activity, low-intensity muscle-strengthening activity, and moderate-intensity muscle-strengthening activity on indicators of risk of progression of type 2 diabetes.

    Rationale: Evidence is growing of the benefits of reducing sedentary behavior, particularly in individuals with chronic conditions affecting metabolic health. Research is needed on whether shifting sedentary time to light-intensity activities affects progression of type 2 diabetes. If light-intensity activities are beneficial, it is important to compare the efficiency and effectiveness of light-intensity versus moderate-intensity activity. Given the well-documented health benefits of shifting time to moderate-intensity aerobic and muscle-strengthening activities, randomized controlled trials are needed that answer questions such as: Does it require shifting, say, 2 to 3 hours from sedentary to light-intensity activity to obtain the same benefits? Or does it take more like 6 to 8 hours?

16. Conduct randomized controlled trials of fall prevention exercise in adults with type 2 diabetes who are at increased risk of falls and fall injuries.

    Rationale: A major finding in the Older Adults chapter (see *Part F. Chapter 9. Older Adults*) is that fall prevention exercise programs can substantially reduce risk of serious fall injuries in the general aging population. However, the risk factor profile for falls in adults with type 2 diabetes may differ substantially from the profile in the general population, due to effects specific to type 2 diabetes-related on fall risk factors (e.g., neuropathy, myopathy, impaired vision, and foot disorders). The search for evidence located one small review of fall prevention programs in type 2 diabetes. Thus, RCTs are needed on effects of fall prevention exercise in individuals with type 2 diabetes at increased fall risk.

Question 5: Multiple Sclerosis

17. Conduct randomized controlled trials to determine the effects of physical activity on basic and instrumental activities of daily living, participation, and community engagement for individuals with multiple sclerosis.

    Rationale: Strong evidence now exists that greater physical activity can improve walking function, strength, and fitness for individuals with multiple sclerosis. This supports a rationale for further research to determine whether this translates into improved basic and instrumental activities of daily living, increased free-living physical activity, and improved safety in mobility.

18. Conduct longitudinal cohort studies to determine the potential for physical activity to serve as a moderator of disease progression and changes in brain health in individuals with multiple sclerosis.

    Rationale: Systematic reviews of controlled studies find no evidence that physical activity alters disease progression, in contrast to epidemiological studies that indicate possible disease-modifying effects.[165] However, these controlled studies are limited by relatively brief intervention lengths, small sample sizes, and lack of measures of brain disease activity; factors that multi-site studies of disease-modifying medications show are needed to fully explore the natural history of multiple sclerosis. This discrepancy between epidemiological and controlled studies, and bench neuroscience findings that physical activity can provide neuroprotective effects and stimulate neuroplasticity, including for brain white matter, support a rationale for further research into disease modification.

Question 6: Spinal Cord Injury

19. Conduct randomized controlled trials in children and adolescents with spinal cord injury to determine effects of physical activity on psychosocial and social environmental development and participation.

    Rationale: A knowledge gap exists regarding health benefits in this population, which differs from adults in terms of mechanisms for injury and greater potential for neuroplasticity and recovery. Future research in pediatric spinal cord injury is needed to determine age-appropriate modalities and prescriptions for physical activity to facilitate recovery of mobility, optimize functional recovery and independence in daily activities, prevent or reduce comorbid and secondary complications, and optimize psychosocial and psychological development across the formative childhood and adolescent years.

20. Conduct research in individuals with spinal cord injury to determine effects of physical activity on basic and instrumental activities of daily living, free-living physical activity, social participation and engagement, balance and risk for injurious falls and fractures.

    Rationale: The evidence in this report that selected modes of physical activity can produce clinically significant improvements in physical function supports a rationale for randomized studies to determine whether such gains translate into improved daily function, participation, and engagement in activities in the living space and social environment. Systematic analyses of relationships between age, race/ethnicity, socioeconomic status, and weight status need to be built into all such research recommendations. Generally, randomized controlled trials are necessary to address the research need.

Question 7: Intellectual Disabilities

21. Conduct randomized controlled trials to determine the effects of physical activity on cognitive function, neurodevelopmental profiles, instrumental activities of daily living, and adaptive functioning that are related to neuropsychological status in individuals with intellectual disabilities.

    Rationale: Only limited evidence is available on the effects of physical activity on four important outcomes in people with intellectual disabilities: cognitive function, neurodevelopmental profiles, instrumental activities of daily living, and adaptive functioning. Randomized studies are needed to determine whether physical activity can improve cognition for individuals with intellectual disabilities across the age spectrum. Likewise, future research is needed to investigate effects of greater physical activity on neurodevelopment and adaptive functioning. In addition, research should also consider these broader outcomes in an age- and intellectual disability-specific fashion.

22. Conduct randomized controlled trials and cohort studies on effects of physical activity in individuals with a variety of etiologies for intellectual disabilities, and determine whether health effects vary by age, race/ethnicity, socioeconomic status, and weight status.

    Rationale. As the most common genetic cause of intellectual disability in the United States, Down syndrome has received the most research attention. Major gaps exist on the potential health benefits of physical activity in most other conditions, including autism spectrum disorder and autistic traits, Fragile X syndrome, tuberous sclerosis, neurologic sequelae of toxins (e.g., alcohol, lead), maternal and fetal infections, and nutritional deficiencies (e.g., iodine, protein-calorie malnutrition), and neurological sequelae associated with prematurity. Future research is needed to address race/ethnicity, socioeconomic status, and weight status as factors that influence relationships between physical activity and health outcomes for individuals with disabilities.

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Promoting Physical Activity

- Part F. Chapter 11. Promoting Regular Physical Activity

PART F. CHAPTER 11. PROMOTING REGULAR PHYSICAL ACTIVITY

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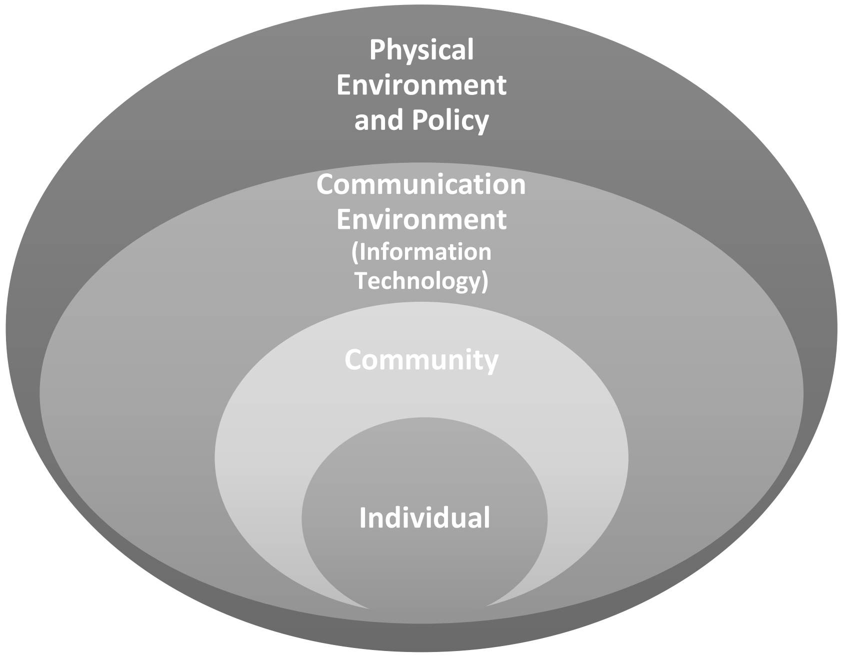
INTRODUCTION

In the preceding chapters of this report, the breadth and depth of the current evidence base on the physical and mental health benefits of regular physical activity have been described. This evidence base and the solid foundation for action that it provides, leads to one of the major challenges facing public health: Given its numerous benefits for individuals across the life course, what strategies and approaches can increase regular physical activity in the U.S. population?

Simply understanding the variety of benefits accompanying an active lifestyle is, for most in the population, insufficient to create a regularly active lifestyle. In fact, research indicates that many Americans understand that regular physical activity is beneficial to their health and well-being, and know that they should include more physical activity in their daily lives.[1] Yet, current national surveillance data continue to show that the physical activity levels of many in the United States remain insufficient to attain the full benefits of an active lifestyle described in the earlier chapters of this report. For instance, in 2015, only 49.8 percent of U.S. adults reported levels of aerobic physical activity consistent with federal guidelines for Americans,[2] while 30 percent of U.S. adults reported being inactive during their leisure time.[3] Similarly, in 2015, only 27.1 percent of U.S. high school students reported levels of physical activity that met the federal guideline of 60 minutes or more of physical activity per day.[4] Interventions designed to supplement knowledge with specific approaches and strategies that effectively promote and sustain physical activity are thus critical. This chapter represents the first evidence review of the physical activity promotion area included in a Physical Activity Guidelines Advisory Committee Report.

Early conceptualizations of physical activity behavior focused largely on individuals' personal motives and behaviors that could influence their physical activity levels. However, over the past several decades, the powerful role that environmental, sociocultural, and community contexts play in shaping and maintaining active lifestyles has been increasingly recognized. The realization that multiple levels of influence affect short- as well as long-term physical activity patterns underlies our use of a social ecological framework (Figure F11-1) to organize the current evidence base in the physical activity promotion field.[5] Applying an adapted version of this framework, the research evaluating physical activity promotion approaches that were available from the completed literature search is divided broadly into four levels of impact or influence—individual, community, the communication environment (which focuses on interventions delivered through information and communication technologies [ICT]), and physical environments and policy. ICT can be employed in interventions emanating from the other levels of impact (individual, community, physical environment, and policy). However, because of its unique potential to influence populations, the accelerating growth of its evidence base, and the distinctive methods and opportunities it presents for physical activity intervention development, implementation, and evaluation, this topic merited a separate description. In addition, in light of the accelerating evidence base pertaining to the health risks accrued by extended periods of sedentary time, even among individuals who achieve recommended amounts of daily physical activity (see *Part F. Chapter 2. Sedentary Behavior*), the Physical Activity Promotion Subcommittee has included in its review the 2011-2016 evidence base of interventions to reduce daily sedentary time among youth and adults, and within worksite settings.

Figure F11-1. Social Ecological Framework



Source: Adapted from data found in Napolitano et al., 2013.[5]

REVIEW OF THE SCIENCE

Overview of Questions Addressed

This chapter addresses 2 major questions, which discuss evidence in the following intervention areas:

1. What interventions are effective for increasing physical activity at different levels of impact?
   a) Individual Level
      - Older Adults
      - Postnatal Women
      - Youth
      - Theory-based Behavioral Interventions and Techniques
         - Rewards and Incentives
         - Behavior Change Theories and Strategies
      - Peer-led Interventions
   b) Community Level
      - Community-Wide Interventions
      - Child Care and Preschool Settings
      - Faith-based Community Interventions
      - Nurse-delivered Interventions in Home or Other Community Settings
      - Interventions in Primary Care Settings
      - School Interventions

- Worksite Interventions

c) Communication Environment Level (Information and Communication Technologies)
- Wearable Activity Monitors
- Telephone-assisted Interventions
- Web-based or Internet-delivered Interventions
- Computer-Tailored Print Interventions
- Mobile Phone Programs
- Social Media
- Interactive Video Games Promoting Active Play or Exercise

d) Physical Environment and Policy Level
- Point-of-Decision Prompts to Promote Stair Use
- Built Environment Characteristics that Support Active Transport
- Community Design and Characteristics that Support Recreational Physical Activity
- Access to Indoor and/or Outdoor Recreation Facilities or Outlets

2. What interventions are effective for reducing sedentary behavior?
   a) Youth Interventions
   b) Adult Interventions
   c) Worksite Interventions

Data Sources and Process Used to Answer Questions

The nature and size of the evidence base in the physical activity promotion field, which dates back more than 50 years, and the fact that this area was not included in the *Physical Activity Guidelines Advisory Committee Report, 2008*,[6] required the Physical Activity Promotion Subcommittee to reduce the scope of the literature reviewed in this area. This was accomplished by using global key word terms targeted to the physical activity promotion and sedentary behavior reduction fields to search the evidence base, and including only systematic reviews, meta-analyses, and government reports that met the Physical Activity Guidelines Advisory Committee's eligibility criteria (for more details on these criteria, see *Part E. Systematic Review Literature Search Methodology*).

To optimize efficiency during the evidence acquisition phase, the global key word terms for both the physical activity promotion and sedentary behavior reduction fields were included in one comprehensive search. Relevant articles for each of these fields were subsequently sorted to specifically address physical activity promotion interventions (Question 1) and sedentary behavior interventions (Question 2). In addition, when an initial search beginning in the year 2000 yielded a vast number of reviews that proved unwieldy in light of the time period under which the Subcommittee was operating, the search was necessarily limited to the years 2011 through the end of 2016.

Global key word terms related to physical activity promotion and sedentary behavior reduction identified relevant literature that was subsequently sorted into categories used to describe the evidence if a category had one or more systematic reviews, meta-analyses, and/or government reports that met the eligibility criteria set by the Committee (see *Part E. Systematic Review Literature Search Methodology*) and these articles contained a sufficient number of studies to determine an evidence grade of Strong, Moderate, or Limited. In some cases, articles contained sufficient information in both areas (physical activity interventions and sedentary behavior interventions) to be used for both questions. The final categories that were used to organize the evidence review were agreed upon by the Subcommittee with approval from the Physical Activity Guidelines Advisory Committee. These categories reflect the enormous heterogeneity of research that is being conducted in the physical activity promotion and sedentary behavior reduction fields.

As reflected in the organizational layout of the chapter, investigators have employed different rubrics or foci in conducting their reviews. They have grouped the evidence by target population (e.g., older adults, youth), intervention location (e.g., schools, worksites), intervention targets (e.g., built environments), intervention delivery channels (e.g., websites, phones), intervention delivery sources (e.g., peer-led interventions), and intervention content (e.g., theory-derived interventions). This diversity made categorization of the literature challenging. Note that the categories that were arrived at by the Subcommittee were not identified a priori and were not specifically included as search terms. Such a condensed approach necessarily limits the size and, potentially, the types of evidence considered in this review (i.e., the chapter review is not exhaustive and does not include a systematic review of the evidence base for the general population).

The major focus of the reviews in this chapter pertains to changes in physical activity levels and sedentary behaviors occurring through different approaches or strategies. The majority of the systematic reviews, meta-analyses, and reports in the physical activity promotion area consist of studies in which physical activity behavior change was measured through a variety of means, including through self-report and/or ambulatory devices (i.e., accelerometers or pedometers), or, in some cases, through behavioral observation. When a physical activity promotion topic area used primarily one of these physical activity outcome measures (e.g., the wearable activity monitors section), it is noted in the methods section describing that topic area.

In contrast to other chapters in this report, the evidence grading for the physical activity promotion field focused on those topic areas that had sufficient evidence-based systematic reviews, meta-analyses, and/or governmental reports to assign an evidence grade of either Strong, Moderate, or Limited. (That is, we did not use a “Not assignable” designation). This decision was due to the fact that the evidence review was necessarily condensed, as described above, with a possible outcome being that a number of topic areas might not have been sufficiently represented in the evidence search to receive any designation, including the “Not assignable” designation.

In grading the available physical activity promotion and sedentary behavior reduction evidence, the Subcommittee often used the evidence grade of “Limited” to refer to a nascent or emerging topic area that has not yet received sufficient rigorous attention from the scientific community to achieve a higher grade. In addition, some topic areas had a larger evidence base but less rigorous designs and methods, small sample sizes, and short intervention periods. Such areas also received a “Limited” evidence grade. “Moderate” or “Strong” evidence grades were assigned when more systematic scientific attention had been given to a topic, and the evidence demonstrated a more consistent effect across more rigorously designed studies. “Strong” evidence grades were distinguished from “Moderate” evidence grades by virtue of the larger pool of more rigorously designed studies available (e.g., randomized controlled trials [RCTs], natural experiments), which generally yielded more consistent positive effects across typically longer time periods.

The following chapter sections on the different levels of impact include comments, when evidence existed from the articles reviewed, on results for specific population subgroups (e.g., by age, sex, chronic disease status, race/ethnicity, socioeconomic status, weight status). They also include, when available from the search, any evidence of dose-response relationships, adverse events, cost-effectiveness, and the specific effects on physical activity levels when the interventions included physical activity combined with other health behaviors, such as dietary change. In general, these factors were rarely reported in the literature that was reviewed, although it is possible that such information was contained within individual articles included in the systematic reviews, meta-analyses, and reports that were evaluated, but simply not discussed at any length in the reviews themselves.

Question 1: What interventions are effective for increasing physical activity at different levels of impact?

INDIVIDUAL LEVEL

Physical activity interventions at the Individual level of impact have been among the earliest types of interventions that have been tested systematically in the physical activity promotion field. This form of intervention generally consists of in-person individual or small group-based physical activity advice and support that can take place in a variety of settings or locales. The articles included in this evidence level did not explicitly target a particular setting as part of their reviews (e.g., schools). Intervention formats typically include one-on-one or group-delivered programs that can involve actual structured exercise and/or educational approaches that teach participants how to employ different types of cognitive and/or behavioral strategies to increase their regular physical activity levels. As such, individual-level interventions can provide a flexible means for providing tailored advice and support to meet individual needs and preferences. However, they also may require a level of staff involvement that can be costly or burdensome over the long run.

The decades of physical activity promotion research at the Individual level have created a rich foundation upon which to build a solid evidence base, particularly in relation to general adult populations.[7] The following systematic review of the evidence in this area, beginning in 2011, highlights areas that extend the evidence base from general adult populations to specific population subgroups, including older adults, postnatal women (i.e., women 0 to 5 years postpartum), and youth. The increasing focus on population subgroups reflects the growing understanding of the importance of developing interventions that are specific to the needs, preferences, and capabilities of different groups. Two other intervention areas containing a sufficient body of systematic reviews and/or meta-analyses since 2011 to support an evidence grade also are described. These two areas—theory-based programs and peer-led programs—reflect specific types of intervention approaches that have received increasing attention in the literature. Peer-led programs are a type of intervention delivery source that has the potential for mitigating the staff burden and costs noted earlier.

As described previously, the categories were not identified a priori and were not specifically included as search terms, but rather emerged during the broad 2011-2016 evidence search that the Subcommittee undertook. Such a condensed approach necessarily limits the size and, potentially, the types of evidence considered at this level.

Older Adult Interventions

Sources of evidence: Systematic reviews, meta-analysis

Conclusion Statement

Strong evidence demonstrates that physical activity interventions that target older adults have a small but positive effect on physical activity when compared with minimal or no-treatment controls, particularly over time periods of 6 to 12 months. **PAGAC Grade: Strong**

Review of the Evidence

Three systematic reviews were included.[8-10] The largest review included 158 studies and covered a timeframe from 1990 to December 2014.[8] A second review covered 24 studies from inception of the database to November 2013,[9] and the third review included 18 studies from 2006 to 2011.[10] The included reviews examined interventions among individuals after retirement,[8] community-dwelling adults ages 60 years and older,[9] and older adults in general, defined as ages 55 years and older.[10] Baxter et al[8] found few studies focused on retirement, but were still interested in the retirement age; thus, that review also focused on older adults in general, defined as ages 50 to 74 years. French et al[9] assessed behavior change techniques that contributed to increases in self-efficacy and physical activity behavior. Nigg and Long[10] reviewed single versus multiple health behavior interventions of physical activity among older adults. However, they identified too few multiple health behavior change studies to allow comparison to single health behavior change interventions.

Evidence on the Overall Relationship

The effectiveness of the interventions was consistently positive when compared to minimal or no-intervention control arms. However, the magnitude of the effect was not easy to determine. Of the reviews included, only French et al[9] provided effect sizes for the effectiveness of the physical activity interventions. Baxter et al[8] stated that the diverse range of physical activity outcomes, as well as the limited number of studies comparing interventions to control groups that did not have an active control group, precluded the use of meta-analysis to provide a statistical summary of intervention effectiveness. Overall, French et al[9] reported that interventions had a small effect on physical activity, with Cohen's d=0.14 (95% confidence interval (CI): 0.09-0.20, P<0.001) and effect sizes ranging from d= −0.02 to d=0.63. They found that three behavior change techniques were significantly associated with higher physical activity behavior effect sizes when present: the use of barrier identification or problem solving, the provision of rewards contingent on successful behavior, and the use of modeling and similar demonstrations of the physical activity behavior being targeted.

Baxter et al[8] commented on the importance of considering the appeal and enjoyment of physical activity, as well as the social aspects of interventions. They reported that advice and counseling, group sessions, and individual sessions were moderately effective at increasing physical activity. Advice and counseling were delivered by various delivery sources, including peer mentors, trained physicians, nurses, and exercise professionals, and at times used combined physician and exercise professional input. For interventions with group sessions, all but one of 15 interventions reviewed resulted in positive physical activity effects.

Nigg and Long[10] reported that, overall, the evaluated interventions were effective. All but one of the physical activity interventions reviewed were conducted in a community setting. Of the 12 single health behavior change studies evaluating physical activity or exercise among older adults, participants were reported to have significantly improved their level of activity at 6- and 12-month follow-ups relative to controls. Only two studies of multiple health behavior change were included in the review, and both were conducted in a community setting. Both included physical activity and diet as the health behaviors studied, but it was not reported whether the behaviors were simultaneously or sequentially targeted. In one study, interventions combining physical activity and fruit and vegetable consumption among older adults improved only the nutrition behavior, and physical activity actually decreased.[11] In the other study, participants improved in both the weight loss behavior and the physical activity behavior compared to the control group.[12]

Overall, studies in this area were of short duration (less than 6 months), with a few that were of medium (between 6 to 11 months), or longer-term (12 months or more) duration.

Evidence on Specific Factors

Evidence in the reviews evaluating different racial/ethnic groups, adverse events, and cost-effectiveness is currently lacking or infrequently reported. Few reviews were found that specifically targeted subgroups of older adults that are increasingly prevalent, including informal family caregivers,[13] and those with chronic conditions.[14-16] As noted above, some studies evaluated interventions that included both physical activity and another health behavior (e.g., dietary change), with mixed results. Nigg and Long[10] found too few multiple health behavior intervention studies in older adult populations to allow confidence when comparing single health behavior interventions with multiple health behavior interventions in this age group.

Features of physical activity intervention targets and measures: Physical activity outcome variables consisted primarily of self-reported minutes per week of moderate-to-vigorous physical activities, as well as the proportion of the sample achieving the physical activity guidelines.[2] Several studies used pedometer-derived step counts and/or accelerometer-derived activity. The review articles did not provide details about prescribed or targeted physical activity types or modes, or duration given to participants.

For additional details on this body of evidence, visit: https://health.gov/paguidelines/second-edition/report/supplementary-material.aspx for the Evidence Portfolio.

Public Health Impact

The number of older adults in the United States is rapidly growing. Given that many older adults have one or more chronic conditions, sometimes co-occurring, which may be ameliorated by participating in regular physical activity, interventions targeted to their needs and preferences are strongly indicated. (For more details on this issue, see *Part F. Chapter 9. Older Adults* and *Part F. Chapter 10. Individuals with Chronic Conditions.*) However, due to a number of barriers, physical activity participation rates often remain low among many older adults. Older adults who are isolated, frail, have mobility limitations or disabilities, and have fewer resources available may be particularly vulnerable to the effects of inactivity. Research also has identified disparities in health conditions, such as chronic pain and arthritis, in low-income and African American adults ages 50 years and older.[17] Chronic pain and arthritis could represent additional barriers to physical activity among populations who are already at high risk of poor health outcomes associated with low levels of physical activity.

Postnatal Women

Postnatal interventions refer to programs that seek to improve physical activity in women with young children, typically 0 to 5 years postpartum, when adequate physical activity is often difficult to increase or maintain.[18]

Sources of evidence: Systematic reviews, meta-analysis

Conclusion Statement

Limited evidence suggests that postnatal interventions are effective for increasing physical activity in postnatal women compared with minimal or no-treatment control conditions. **PAGAC Grade: Limited.**

Review of the Evidence

One meta-analysis[18] and two systematic reviews[19, 20] were included. The meta-analysis[18] included 20 studies overall, of which 14 studies were reviewed meta-analytically. The systematic reviews covered 11[19] and 10 studies.[20] The timeframe reviewed was 1980 to 2015, with the majority of studies reviewed since 2010. Studies targeted postnatal women who were inactive but healthy, postnatal women who experienced gestational diabetes, and postnatal women with other chronic diseases. The defined postnatal period varied across studies from 1 year postpartum[18] to 5 years postpartum[19, 20] and interventions were reviewed that focused either solely on physical activity or were weight and diabetes management studies that targeted diet and physical activity simultaneously.

Evidence on the Overall Relationship

Only limited evidence is available overall that interventions are effective at increasing physical activity in postnatal women. Gilinsky et al[18] reported a moderate and variable effect size for increases in frequency of physical activity (standardized mean difference (SMD)=0.53; 95% CI: 0.05-1.01, *P*=0.03) but small and non-significant effect sizes for increases in overall volume of physical activity (SMD=0.15; 95% CI: -0.6 to 0.35) and for walking (SMD=0.07; 95% CI: -0.21 to 0.36). The most promising effects concerned the six of seven studies targeting postnatal women who were previously inactive but otherwise healthy. These studies reported significant increases in moderate-to-vigorous physical activity and walking after 6 weeks to 6 months of intervention.[18] Intervention approaches that included goal setting, behavioral self-monitoring, setting graded tasks, and reviewing behavioral goals were more commonly delivered in efficacious studies.[18]

The evidence for successfully increasing physical activity or walking within the context of weight management,[18] or among women with gestational diabetes[20] or postnatal depression[18] also was limited. The studies reviewed were generally short (i.e., less than 6 months) to medium (i.e., 6 to 11 months) in length and of poor to moderate quality with respect to nonrandomized designs, high dropout rates, inadequate missing data handling and poor measurement approaches.

Features of physical activity intervention targets and measures: The postnatal interventions ranged in duration from 6 weeks to 6 months and the most prevalent intervention strategies included goal setting, self-monitoring, and instruction. The frequency and duration of contacts was not clear. Studies focused primarily on increasing physical activity generally without a particular focus toward a specific type or intensity of activity. An exception was the three studies that specifically targeted walking.[21-23] However, these interventions were not found to be more effective than other physical activity interventions. Most studies reported outcomes from self-reported measures of physical activity (i.e., minutes per week of moderate-to-vigorous physical activity; MET-minutes per week, and activity kilocalories per week), while four studies also used pedometers and/or accelerometers to assess increases in steps per day. Little information was systematically reported in relation to intervention effects on specific step per day increases.

Evidence on Specific Factors

Evidence in the reviews evaluating different racial/ethnic groups, adverse events, and cost-effectiveness is currently lacking or infrequently reported.

For additional details on this body of evidence, visit: https://health.gov/paguidelines/second-edition/report/supplementary-material.aspx for the Evidence Portfolio.

Public Health Impact

The postnatal period is a critical and challenging period to increase and maintain adequate physical activity levels to promote weight management and reduce disease risk factors. Although the evidence remains limited, interventions that include prominent behavior change strategies (e.g., goal setting, behavioral self-monitoring) as well as those that target generally healthy (albeit inactive) women appear to yield the most promising results.

Youth

Sources of evidence: Systematic reviews, meta-analyses

Conclusion Statement

Strong evidence demonstrates that interventions focused on promoting physical activity in healthy youth have a small but positive effect on physical activity when compared with a variety of control conditions. Interventions directly targeting youth are effective, and effects are further enhanced when interventions also incorporate family or are delivered in school settings during the school day. **PAGAC Grade: Strong**.

Review of the Evidence

The Subcommittee reviewed two meta-analyses[24, 25] designed to explain outcome patterns within the wider systematic review.[24] Included studies were from inception through April 2013[25] and September 2015.[24] Brown et al[24] identified 47 family-based interventions studies focused on children ages 5 to 12 years in the systematic review, 19 of which provided sufficient information to be included in the meta-analysis. Cushing et al[25] identified 89 unique papers, 58 of which focused on physical activity among youth younger than age 18 years. Both reviews focused on generally healthy youth, with Cushing et al[25] specifically excluding studies of youth with chronic illnesses, including obesity, cancer, and asthma. Brown et al[24] focused specifically on interventions that engaged families to increase physical activity in children, while Cushing et al[25] focused on any intervention strategies that included health behavior as a dependent variable. A range of intervention strategies and comparison groups were identified in both reviews. The Subcommittee also reviewed *The Physical Activity Guidelines Midcourse Report: Strategies to Increase Physical Activity Among Youth,*[26] which included a review of reviews of physical activity intervention studies focused on youth ages 3 to 17 years that were published January 2001 through July 2012; a total of 31 reviews containing 910 studies (not mutually exclusive) were included.

Evidence on the Overall Relationship

The effectiveness of the intervention strategies and reported effect sizes were consistent across both reviews. Cushing et al[25] reported an aggregate random-effects effect size for immediate post-intervention effects, expressed as Hedges' *g* (*g*). Assessments of the impact of intervention strategies targeting physical activity showed significant effect sizes for interventions targeting individuals only (g=0.27; 95% CI: 0.12-0.42), which were further enhanced when individual interventions also included families (g=0.44; 95% CI: 0.23-0.66) or school and print or digital media (e.g., newspaper, radio; g=0.30; 95% CI: 0.04-0.57). The interventions included self-report and objective measures of physical activity. When only studies with objective measures of physical activity were considered, effect sizes were smaller but still significant. The Brown et al[24] meta-analysis of family-based physical activity interventions found a small but significant effect size favoring the intervention group (SMD=0.41; 95% CI: 0.15-0.67).

The types of intervention strategies evaluated within the reviews primarily included in-person and web-based education, hands on experiential activities (e.g., supervised exercise sessions, dance classes, sports or recreational activities), physical education classes, and advice to reduce sedentary behaviors (e.g., television turnoff) and replace those sedentary behaviors with increased physical activity. Physical activity interventions were delivered in school settings (in-school and after school), day camps, community-based settings, participant's households, and over the Internet. Family-based interventions included primarily group-based educational activities and interactive physical activity during group sessions, with encouragement (e.g., homework, websites for parents to monitor children's activities, tips for increasing physical activity, home-based exercise programs, step counters) to participate in additional physical activity outside of the sessions.

Features of physical activity intervention targets and measures: Although the reviews included general information about the duration of interventions, they did not provide significant detail about the level of physical activity that was encouraged in interventions or specific physical activity goals within interventions. Physical activity outcomes included objectively and subjectively monitored participation in moderate-to-vigorous physical activity, step counts, and self-reported participation in specific types of physical activity (e.g., outdoor sports, physical education, general physical activity). When interventions were stratified by type of physical activity outcome, Brown et al[24] found that 63 percent of accelerometer-derived moderate-to-vigorous physical activity or counts per minute assessments, 71 percent of pedometer-derived step count assessments, 67 percent of self-reported physical activity frequency assessments, and 67 percent of self-reports of sport, dance, physical education, or outdoor play participation or outdoor observation assessments favored the intervention.

Evidence on Specific Factors

Evidence in the reviews evaluating different racial/ethnic groups, adverse events, and cost-effectiveness is currently lacking or infrequently reported. A large proportion of studies included in the two reviews did not provide race/ethnicity information for participants. Only four studies included in the Cushing et al[25] discussed adverse events, with only one study[27] reporting injuries to two participants that might have been related to study participation; adverse events were not addressed in the meta-analysis by Brown et al.[24] The studies provided some evidence of intervention impact by health status. Although Cushing et al[25] excluded studies of children with chronic disease, Brown et al[24] evaluated studies by weight status of the target child and found that 80 percent of studies including mostly children with normal weight favored the intervention arm while only 59 percent of studies that focused mostly on children with overweight or obesity and 50 percent of studies that did not report weight status favored the intervention arm. Few studies included in the meta-analysis by Brown et al[24] focused on boys; 15 percent of studies focused on girls only, with 86 percent favoring the intervention arm, while 63 percent of mixed sex studies favored the intervention arm.

For additional details on this body of evidence, visit: https://health.gov/paguidelines/second-edition/report/supplementary-material.aspx for the Evidence Portfolio.

Public Health Impact

Among children, individually-focused interventions delivered in a variety of settings can be successful for increasing physical activity levels. Evidence also indicates that their efficacy can be further enhanced when families and schools are incorporated within individual intervention approaches. (See the *Community Level: School Interventions* section of this chapter). Given the potential for family-based interventions to have a positive impact, additional attention should be provided to identify strategies to promote physical activities that appeal to family members of different ages within the same program or setting.

Opportunities to encourage the adoption of lifetime physical activities (e.g., leisure-time pursuits, non-competitive sports) should be encouraged among all youth. This could help youth identify activities during childhood that they could enjoy and participate in across the lifespan, including outside of school. Several evidence-based population approaches to support increases in physical activity that are relevant for youth at the individual level during out-of-school times include improving accessibility of recreation and exercise spaces through creating new spaces, enhancing existing spaces, implementing shared use agreements (e.g., use of school facilities during non-school hours) and improving sidewalk and street design and traffic safety, which could promote active commuting to or from school (see the *Physical Environment and Policy Level* section of this Chapter). High-risk population subgroups, particularly those living in high poverty and congested urban areas, often have limited safe spaces for recreation and physical activity. Children living in suburban areas also may have limited opportunities to engage in active commuting or to easily access recreational or play facilities without having a parent available for transportation.

Theory-Based Behavioral Interventions and Techniques

A range of behavioral theories, along with a number of different strategies and techniques derived from such theories, have been applied in developing physical activity interventions. The evidence review methods employed by the Subcommittee resulted in two distinct areas of evidence that are described below: the use of tangible rewards and incentives contingent upon physical activity behavior change, and the systematic evaluation of behavior change theories and strategies employed in physical activity programs.

Rewards and Incentives

Source of evidence: Systematic reviews

Conclusion Statements

Limited evidence suggests that providing rewards based on achieving physical activity goals is effective for improving device-measured physical activity behavior when goals include opportunities for sedentary adults to earn money, or opportunities for children to earn inexpensive recreational items or television access.[28, 29] **PAGAC Grade: Limited.**

Limited evidence suggests that, for general adult populations, providing guaranteed rewards is effective for increasing exercise session attendance when rewards are contingent upon achieving specific goals; lottery incentives were generally not effective strategies for increasing attendance at supervised exercise sessions.[28, 29] **PAGAC Grade: Limited.**

Limited evidence suggests that, for youth and different populations of adults, providing unconditional incentives contingent upon physical activity behaviors performed is no more effective than providing the same intervention without added incentives for increased physical activity levels, physical activity group session attendance, or fitness levels.[28] **PAGAC Grade: Limited.**

Review of the Evidence

One systematic review[28] and one meta-analysis[29] that included 12 and 11 studies, respectively, provided evidence. The reviews covered a time frame from inception to June 2012[29] and from January 1980 to March 2013.[28] Both reviews examined the effect of incentives on physical activity or exercise outcomes (e.g., exercise session attendance, aerobic fitness, and physical activity participation). Barte and Wendel-Vos[28] considered both unconditional incentives (provided regardless of whether some goal or related condition was met) and rewards (provided only when a specific goal or condition related to physical activity was met), and included studies focused on adults (N=9) and children (N=3). Incentives included financial rewards (adults), television access (youth), inexpensive items (adults and youth), or free access to exercise facilities or activities (adults). Mitchell et al[29] considered financial incentives, including cash and noncash rewards with a monetary value that was contingent on a pre-specified physical activity behavior or outcome, and included studies focused only on adults. Both reviews assessed changes in physical activity-related behaviors. Assessment of physical activity levels and intervention adherence outcomes varied across studies.

Evidence on the Overall Relationship

The effectiveness of rewards and incentives varied depending on the outcome of interest. With regard to exercise session adherence, one meta-analysis[29] reported a positive effect of providing lottery and escalating incentives on exercise session attendance when compared with no incentive for short-duration interventions lasting 4 to 26 weeks; pooled results showed an increase in exercise attendance of 11.55 percent; 95% CI: 5.61%-17.50%. Examples of the types of incentives that were tested included requiring participants to deposit $3 for a 1 in 7 chance to win $21; allowing participants to earn a weekly lotto token for attending 4 of 5 weekly aerobics sessions compared with providing a $5 deposit that could be earned back at a rate of $1 per week for attending 4 of 5 sessions; and allowing participants to earn up to $491, in an escalating fashion, over 18 months by participating in walk/run sessions ($1 for each of the first 25 walks, $1.50 for the next 50 walks, $2 for the next 50 walks, and then $3 per walk until the end of the program) compared with no incentive. Although such incentives improved exercise session attendance, they did not improve overall fitness or physical activity levels.

Both reviews[28, 29] reported that chance- or lottery-based financial incentives did not influence overall physical activity behaviors, including self-reported physical activity, objectively assessed physical activity, or fitness variables. In contrast, the studies in the two reviews[28, 29] generally showed that providing guaranteed direct rewards for reaching physical activity behavior goals was effective for increasing immediate post-intervention physical activity. For example, direct financial incentives and rewards ranging from $2.79 to $46.82 were effective for improving physical activity behaviors in general adult populations, with larger incentives (e.g., $26.75 to $46.82 per week) yielding larger effects.[30, 31] This was also true among sedentary older adults (ages 50 years and older) who were able to earn $10 to $25 per week, with a maximum of $100 in 4 weeks compared to control participants, who received a fixed payment of $75. These participants increased their daily aerobic minutes 16 more minutes than did the control group (P<0.001).[31] Among youth, children ages 7 to 11 years who were able to earn inexpensive recreational items (e.g., balls, Frisbees) for each day they reached pedometer target goals increased their steps per day compared with children who did not earn incentives (2,456 versus 1,033 steps per day, P<0.001).[32] Similarly, children ages 8 to 12 years with overweight or obesity who were able to earn tokens for television access or other inexpensive items, compared to control participants who had free television access, significantly increased their daily step counts (+160.8 versus +33, P=0.019) and daily minutes of moderate-to-vigorous physical activity (+9.4 versus +0.3 minutes, P=0.05).[33, 34]

Guaranteed direct rewards also appear to be effective for increasing attendance at supervised walks, fitness facilities, or group sessions in general adult populations. A study of paying members at a university fitness facility showed an increase in visits to the facility for those who had the opportunity to earn free attendance-based facility memberships compared to control participants who were not provided with an incentive (5.45 versus 3.77 visits, $P=0.003$).[35] An 18-month study of adults ages 25 to 55 years[36] included five conditions: standard behavior therapy (SBT); SBT with supervised walks (SW) 3 times per week; SBT + SW with personal trainers (PT), who walked with participants, made phone reminders, and did make-up SW; SBT + SW with monetary incentives (I) for completing SW; and SBT + SW + PT + I. Participants could earn $1 for their first 25 walks, $1.50 for the next 50 walks, $2 for their next 50 walks, and $3 for the remaining walks. The study found higher attendance at SW sessions among individuals who received behavioral counseling and the opportunity to earn financial rewards compared with individuals who received the same intervention with no opportunity to earn incentives (65.8 versus 35.0 walks in rewards versus non-reward groups without a personal trainer, and 103.4 versus 80.4 walks in reward versus non-reward groups with a personal trainer, $P<0.05$).

The impact of providing rewards or incentives for physical activity behaviors does not appear to extend beyond the immediate post-intervention period. In the aforementioned study that provided incentives to children for reaching activity goals and showed a positive impact on daily steps compared with children who did not receive incentives, effects were reversed in the 14 weeks after the intervention, with controls engaging in significantly higher daily steps compared to intervention participants. This suggests the possibility that rewards for achieving physical activity goals, while useful in inducing short-term increases in physical activity behavior, may undermine longer-term efforts to maintain those physical activity increases. One putative mechanism underlying this type of finding may relate to using extrinsic motivators, such as external rewards, for behavior change, which may serve to undercut the development of intrinsic motivators for such change that can potentially drive behavioral maintenance.[37]

Features of physical activity intervention targets and measures: Physical activity outcome variables consisted of self-report, pedometer-, or accelerometer-assessed step counts and daily moderate-to-vigorous physical activity, and adherence to intervention conditions (e.g., fitness facility attendance, supervised walking sessions, group exercise sessions). Very few details were provided about the intensity, type, and timing of physical activity prescribed in the interventions. Studies in the reviews[28, 29] that provided specific activity goals all showed positive impacts on physical activity attendance and behaviors. Examples of goals included attendance at fitness facilities (range equal to or greater than 11 times per month to 2 to 5 visits per week), increasing daily walking (e.g., to 1,500 steps more than baseline), and minutes of weekly aerobic physical activity (e.g., 15, 25, and 40 minutes daily).

Evidence on Specific Factors

Evidence in the reviews evaluating different racial/ethnic groups, adverse events, and cost-effectiveness is currently lacking or infrequently reported. Interventions focused on previously inactive adults,[30, 31, 38] and incentives provided to lower income adults (with household incomes less than $50,000 in 2008 dollars) compared with higher income adults (with household incomes great than or equal to $50,000 in 2008 dollars),[31] yielded larger effects.

For additional details on this body of evidence, visit: https://health.gov/paguidelines/second-edition/report/supplementary-material.aspx for the Evidence Portfolio.

Public Health Impact

Some population subgroups may be responsive to opportunities to earn rewards for achieving physical activity goals or attending supervised exercise sessions. However, providing unconditional incentives that are not associated with achieving a specific goal does not appear to provide additional benefit above and beyond providing a behavioral intervention alone. The success of small-to-moderate sized behaviorally based tangible incentives (e.g., financial rewards, television access, inexpensive recreational items, gym memberships based on facility use) in increasing physical activity adherence and behavior change in some populations of youth as well as adults suggests that such incentives could be potentially useful strategies for promoting physical activity while addressing some known barriers to physical activity participation (e.g., access to facilities). In addition, escalating or indexed incentives (e.g., reimbursement contingent upon completing a certain number of activities or opportunities to earn higher or more frequent incentives based on greater physical activity participation), cash or reimbursement incentives, and incentives that include a deposit that is held in escrow until a certain physical activity goal or condition is met may enhance the effectiveness of financial incentives in some subgroups.

Behavior Change Theories and Strategies

Sources of evidence: Systematic review, meta-analysis

Conclusion Statement

Strong evidence demonstrates that behavior change theories and techniques are effective for increasing physical activity levels in general adult populations. **PAGAC Grade: Strong**.

Review of the Evidence

One meta-analysis[39] provided evidence on the impact of theory-based interventions to promote physical activity. This meta-analysis contained 82 RCTs that included adults and that were published from inception through May 2013. Of the 61 studies based on a single behavioral theory, 31 were based on the Transtheoretical Model (TTM), 16 were based on Social Cognitive Theory (SCT), 8 were based on the Theory of Planned Behavior (TPB), 5 were based on Self-Determination Theory (SDT) and 1 was based on Protection Motivation Theory (PMT); 14 studies reported combining 2 theories, and 7 studies reported combining 3 to 5 theories. One systematic review[40] that included 41 controlled studies of individual-level walking and cycling interventions among adults provided evidence on behavior change techniques used to promote walking and cycling. The review covered studies published between 1990 and 2011 that compared an intervention strategy with no intervention or standard care; studies with alternate, more active intervention control conditions were not considered in that review. Intervention duration ranged from 1 week to multiple years.

Evidence on the Overall Relationship

The meta-analysis of theory-based interventions[39] (N=82 RCTs) found an overall average effect size of 0.31 (95% CI: 0.24-0.37) for such interventions compared with control groups; single theory intervention effect sizes ranged from 0.26 to 0.61. Analyses did not identify significant differences in physical activity changes between theories. However, interventions based on a single theory had stronger impacts than interventions based on a combination of theories. The effect size for single theory interventions was 0.35 (95% CI: 0.26-0.43) and for combined theories was 0.21 (95% CI: 0.11-0.32).

Of the 41 studies included in the Bird et al[40] review, 21 reported a statistically significant effect on walking and/or cycling outcomes, 12 reported an effect in the positive direction that was not statistically significant, and 13 did not provide information about statistical significance when testing the effect of the intervention on walking and/or cycling behavior. The mean number of behavior change techniques coded in the studies was 6.43 $\pm$ 3.92, 4.42 $\pm$ 3.29, and 1.69 $\pm$ 1.32 for studies reporting statistically significant, non-statistically significant, and no reported statistical significance information, respectively. When effect sizes were presented, studies using combinations of behavior change techniques were successful for increasing walking and cycling behaviors. Although a wide range of behavior change techniques were employed across the 41 studies included in the systematic review, they provided no evidence that a specific combination of techniques was more or less effective for influencing walking and/or cycling behavior. Among interventions that showed a statistically significant effect on walking or cycling, the post-intervention change in physical activity behavior ranged from +0 to +87 minutes per week in walking or cycling, +1.38 to +1.42 days of walking per week, +6,482 to +24,227 steps per week, and +1.1% walking and cycling trips. Effect sizes, where provided, ranged from 0.14 to 0.75. The most commonly reported behavior change technique among studies that reported changes in physical activity behavior (significant and non-significant) was self-monitoring of behavior and intention formation. Providing general encouragement was most commonly cited in interventions that did not provide information about the statistical significance of the effects.

Evidence on Specific Factors

Evidence in the reviews comparing different racial/ethnic groups or specifically reporting adverse events and cost-effectiveness is currently lacking or infrequently reported. Several systematic reviews were found aimed at a specific subgroup which may particularly benefit from more targeted interventions, including low-income adults,[41] adults with obesity,[42] and men.[43]

Features of physical activity intervention targets and measures: Physical activity outcome variables consisted primarily of self-reported or objectively measured minutes of physical activity over a specified time period (i.e., per day or per week), daily step counts, and/or proportion of trips taken using a specific mode of physical activity (e.g., walking, cycling). Few details were provided about the types of physical activities that were prescribed or targeted by the interventions.

For additional details on this body of evidence, visit: https://health.gov/paguidelines/second-edition/report/supplementary-material.aspx for the Evidence Portfolio.

Public Health Impact

The evidence that theory-based interventions are effective suggests that strategically incorporating intervention components that include theoretical constructs is important. Programming that includes key individual, social, and environmental theoretical constructs that relate to diverse age groups and populations could be potentially useful.

Given the broad availability of physical activity self-monitoring tools (e.g., pedometers incorporated into mobile devices, popularity of wearable devices), theoretically derived behavior change strategies such as self-monitoring are a particularly promising technique for increasing awareness of, and adherence to, physical activity goals and guidelines, and enhancing feedback related to self-behavior.

Peer-Led Interventions

Peer-led interventions are defined as interventions that are delivered in part or full by non-professionals who share similar characteristics, health conditions, or situations as the target population of the intervention.[44]

Source of evidence: Meta-analysis

Conclusion Statement

Moderate evidence indicates that peer-led behavioral self-management interventions are effective in older adults and individuals with chronic disease and produce small but meaningful increases in physical activity when compared with minimal or no-treatment control conditions, particularly over short time periods (i.e., 6 to 12 weeks). **PAGAC Grade: Moderate.**

Review of Evidence

The Subcommittee reviewed one meta-analysis that included 21 studies overall, 17 of which were reviewed meta-analytically.[45] The timeframe reviewed was 1989 to 2015. All studies adopted a self-management approach through employing self-regulatory skill building strategies derived from social cognitive theory to promote self-efficacy (i.e., increased confidence in one's ability to engage in regular physical activity), which in turn was presumed to increase physical activity levels. The vast majority of interventions were group-based, ranged from 1 to 13 sessions in length, and targeted inactive but otherwise healthy older adults, or individuals with multiple sclerosis, arthritis, diabetes, physical limitations, or a mix of chronic conditions.

Evidence on the Overall Relationship

The effectiveness of the interventions was small but consistent when compared to minimal intervention or no-treatment control arms. Best et al[45] reported moderate effects for increases in physical activity overall among the 17 studies where effects sizes were available (SMD=0.4; 95% CI: 0.22-0.55, $P<0.001$). A more refined analysis of a small number of studies where active control groups were comparators also appeared promising (four studies; SMD=0.3; 95% CI: 0.08-0.43, $P=0.004$). Fourteen of the 21 studies overall reported significant between-group increases in physical activity relative to control groups. Methodological quality of studies was fair to good overall. The duration of the interventions was typically short (less than 6 months) and variable across studies (range: 1 to 16 weeks). The intensity of the intervention varied from 1 to 3 hours per week of group-based contact. In those studies that included follow-up periods occurring after the intervention was completed, the follow-up duration varied from 2 to 18 months. The maintenance of physical activity improvements was promising in these studies (four studies; SMD=1.5; 95% CI: 0.13-2.83, *P*=0.03).

Features of physical activity intervention targets and measures: Studies focused primarily on increasing physical activity generally without a particular focus on a specific type or intensity of activity. All studies (N=21) described outcomes from self-reported measures of physical activity only (i.e., minutes per week of moderate-to-vigorous physical activity; MET-hours per week and activity kilocalories per week). A sub-analysis among nine studies that all reported minutes of physical activity per week suggested small but consistent effects for physical activity (SMD=0.2; 95% CI: 0.17-0.29, *P*<0.001).

Evidence on Specific Factors

Evidence in the reviews evaluating different racial/ethnic groups, adverse events, and the cost-effectiveness of peer-led interventions is currently lacking or infrequently reported.[46]

For additional details on this body of evidence, visit: https://health.gov/paguidelines/second-edition/report/supplementary-material.aspx for the Evidence Portfolio.

Public Health Impact

Given their potential for lower costs, peer-led interventions may increase the likelihood of broad dissemination of physical activity promotion strategies among populations with chronic diseases, compared with interventions delivered by trained professionals. The actual cost-effectiveness of such approaches, however, awaits further systematic evaluation. The careful fidelity and process measures contained in a number of the reviewed studies suggest that it is feasible for peer volunteers to be trained to deliver theory-driven interventions with adequate fidelity to ensure program success.

COMMUNITY LEVEL

Community level interventions include multi-component interventions aimed at a defined population (i.e., community-wide interventions) as well as interventions targeting a particular setting. Community settings can be defined generally as those locales where people gather for educational, housing, consumer-related, health-related, or social purposes. Community interventions can be initiated through specific settings that reach people in their homes or other locations (e.g., nurse-based outreach programs), or that span multiple settings or locales (i.e., community-wide interventions). A growing number of such settings have served as potentially convenient points of contact in which to deliver physical activity interventions. Some settings serve as important focal points for reaching diverse portions of the population across a wide age range (e.g., primary care settings, faith-based settings), while others can be useful in targeting specific age groups (e.g., schools, child care settings, senior centers, or housing sites).

Attractive elements of community settings include potential population reach, ability to segment audiences, and the potential convenience of intervention delivery. However, such settings can create challenges for intervention delivery in terms of gaining cooperation of setting-specific decision-makers and stakeholders and responding to turnover of personnel in the setting. In addition, while community settings can be useful intervention delivery sites for those groups who regularly use them, it is important to understand which segments of the population do not visit such venues. Intervention fidelity across different settings is another challenge. Meanwhile, community-wide interventions, which typically span multiple community settings and levels of impact (e.g., individuals, institutions, physical environments) produce their own set of challenges. These include issues of cost, true population reach (i.e., the number and types of people actually receiving the interventions), and sustainability.

Although decades of physical activity promotion research have occurred at the community-wide level as well as across a diverse set of community settings, the robustness of the current evidence in this area continues to be curtailed by the use of less rigorous study designs and assessment methods, uneven application of procedures to enhance intervention fidelity, and relatively short intervention durations. Evidence related to different population segments will be discussed to the extent possible when available. As noted previously, the categories were not identified a priori and were not specifically included as search terms, but, rather, emerged during the broad 2011-2016 evidence search that was undertaken. Such a condensed approach necessarily limits the size and, potentially, the types of evidence considered at this level.

Community-Wide Interventions

Sources of evidence: Meta-analysis, systematic reviews

Conclusion Statements

Moderate evidence indicates that community-wide interventions that employ intensive contact with the majority of the target population over time can increase physical activity across the population. **PAGAC Grade: Moderate.**

Limited evidence suggests that community-wide interventions using strategies that reach a smaller proportion of the target population, employ less intensive contact over time, and focus on a relatively narrow set of strategies are effective in promoting community-wide physical activity change. **PAGAC Grade: Limited.**

Review of the Evidence

Three systematic reviews were included[47-49] along with the PAG Midcourse Report.[26] The systematic reviews included a range of 10 to 33 studies. The systematic reviews covered the following timeframes: inception to June 2013,[47] 1980 to 2008,[48] and 1995 to January 2014.[49]

The included reviews examined the effects of community-wide interventions on physical activity participation. Brown et al[48] examined the effectiveness of stand-alone mass media campaigns to increase physical activity at the population level. The included reviews addressed changes in physical activity levels measured largely through a variety of self-report instruments. The PAG Midcourse Report included a review of reviews of physical activity intervention studies focused on youth ages 3 to 17 years that were published January 2001 through July 2012; a total of 31 reviews containing 910 studies (not mutually exclusive) were included.[26]

Evidence on the Overall Relationship

Evidence on intensive multi-component interventions: The small number of community-wide interventions that reported significant increases in physical activity across the entire target population reported intensive contact with the majority of the population over time. Two such studies, conducted in China, reported significant adjusted relative risk (RR) scores of 1.03 to 1.20 (95% CI: 1.05-1.05 and 1.09-1.31, respectively).[50, 51] Among the strategies included in the Chinese interventions were quarterly door-to-door delivery of instructional handouts, health counselor advising, and identification of high-risk community residents.[49] Several other studies have reported significant physical activity increases in one sex but not the other. For example, significant physical activity improvements were reported in men (*P*=0.047) though not women (*P*=0.15) in a Norwegian study,[52] although the adjusted relative risk for the entire population was 1.10 (95% CI: 0.84-1.43) and was not significant. A U.S. study[53] with an independent cross-sectional survey sample, had similar results with *P* values of 0.004 in men versus 0.237 in women, though with no statistically significant differences found in either sex in the cohort sample of this study. In contrast, significant physical activity improvements were found in women though not men in an Australian study.[54] The latter study, however, is complicated by the observation that the baseline physical activity between the intervention and comparison communities was different.

In a regional cardiovascular disease prevention program in the Netherlands,[55] while both the intervention and control arms reported an overall decrease in leisure-time physical activity across a 5-year period in women, those receiving the intervention had significantly less of a decrease over time than did those in the control arm ($P<0.05$). In addition, when comparing reported walking hours per week over the 5-year period for participants overall, this physical activity variable decreased less in the intervention community than in the control community (adjusted percentage change between the two communities=29.41%).

A similar lessening of the decrease over time in physical activity was reported in the intervention relative to control arm in a study conducted in Ghent, Belgium,[56] with the adjusted percentage change between the two arms reported to be 25.6 percent. This community study also reported statistically significant increases in walking, measured by step-counter and self-reported minutes per week of walking, in intervention versus control arms (adjusted changes of 10.8% and 17.34%, respectively).[56] In a multi-community U.S. study that used a dichotomous physical activity outcome,[57] statistically significant intervention effects for the proportion of the population reporting being regularly physically active during leisure time were found for some measurement time points and methods (e.g., at 1 and 3 years using independent cross-sectional surveys; at 7 years post-intervention using cohort surveys), though not for all time points. For this latter study, the overall adjusted relative risk using data extracted from year zero to the final measurement year was reported to be 1.08 (95% CI: 0.97-12.0) and 1.11 (95% CI: 0.94-1.30) for the cohort and independent cross-sectional data, respectively.[49]

Evidence on other community-wide interventions using less-intensive or fewer-component interventions: For less-intensive community-wide intervention efforts, some evidence of positive effects has been reported when the interventions were specifically targeted to specific populations (e.g., primarily school-based settings[58]) or to specific forms of physical activity (e.g., cycling, walking). In the school-based cluster-RCT of adolescents by Simon et al,[58] for example, the authors reported a statistically significant adjusted mean difference of 1.1 hours per week of leisure-time physical activity favoring the intervention arm at 4-year follow-up. Similarly, while some studies reported significant increases in physical activity in response to specific intervention components (e.g., increases in the use of trails and pathways), such increases did not result in a measurable uptake of physical activity across the community as a whole.[49]

A number of investigations in this area, including more recent studies, lack reliable measures of physical activity and report incomplete data collection. Those studies that did not employ randomization methods often reported baseline differences between study arms and other potential threats to internal validity, leading to an assessment of high or unclear risk of bias. Despite study objectives aimed at community-wide interventions, many of the interventions did not reach a sizable portion of the community, interventions varied considerably with respect to intensity (i.e., amount, frequency, and reach of the interventions into the target population over time), and a variety of continuous and dichotomous physical activity outcomes were employed. In addition, a number of studies included a focus on other health behaviors and outcomes of relevance to chronic disease, which potentially could have interfered with or reduced the successful uptake of the physical activity interventions.

The effects of stand-alone mass media campaigns on population-level physical activity are currently unclear, due to a relatively small number of studies that were often accompanied by poor or inadequate measurement of physical activity and weak designs.[48] In contrast, a national 5-year social marketing-based mass media campaign called VERB™ that used multiple social communication channels and targeted a specific population group, i.e., U.S. youth ages 9 to 13 years, showed increased physical activity awareness as well as reported physical activity participation,[59] described in the PAG Midcourse Report.[26] For additional description of this study, see the *Communication Environment Level: Social Media* section of this chapter.

Evidence on Specific Factors

Evidence in the reviews evaluating intervention effects on different racial/ethnic groups and adverse events is currently lacking or infrequently reported. Although some studies did specifically target underserved or lower income communities, only a few studies specifically evaluated intervention differences by socioeconomic strata, with results found to be indeterminate or inconclusive.[49] When the cost-effectiveness of population-level physical activity interventions was compared systematically among the relatively small number of studies for which this information was available,[47] the most efficient interventions for increasing physical activity were community rail trails, step-counters (pedometers), and school health education programs. In general, smaller scale environmental interventions (e.g., trails) produced lower (better) cost-effectiveness ratios than the most expensive large environmental interventions (a light-rail trail system), although the latter was estimated to produce higher physical activity gains. The evidence indicated that monetary incentives and controlled access to local recreational centers free of charge might be less cost-effective than other strategies.[47]

For additional details on this body of evidence, visit: https://health.gov/paguidelines/second-edition/report/supplementary-material.aspx for the Evidence Portfolio.

Public Health Impact

In light of the potential population impact of physical activity interventions aimed across a community as a whole, studies employing various community-level interventions have been conducted across a range of geographic locations and community settings. Several systematic investigations that have employed intensive multicomponent strategies to reach a majority of the target community over an extended period of time have shown success in promoting increases in physical activity. The majority of interventions in this area, however, have been unable to deploy a sufficient number of strategies over time to a large enough proportion of the population to achieve consistent community-wide physical activity increases. Of note, several large-scale interventions were able to achieve smaller decrements in physical activity levels over time relative to control communities—an important finding given prevalent age-related decreases in physical activity levels. In light of the substantial challenges and resources often involved in delivering high-quality community-wide interventions of sufficient intensity, population penetrance, and sustained engagement to produce measurable increases in community physical activity levels over time, more targeted approaches aimed at specific population segments or specific forms of physical activity may be indicated. For example, the national VERB™ multi-component mass marketing campaign was able to report some successes in increasing physical activity among the 9 to 13 year age group for which it was targeted. Alternatively, finding ways to leverage increasingly prevalent information and communication technology platforms as part of community interventions may facilitate higher population penetrance and program sustainability.

Child Care and Preschool Settings

Sources of evidence: Systematic reviews, meta-analysis, published report

Conclusion Statement

Limited evidence suggests that interventions occurring in child care or preschool settings are effective for increasing physical activity in children ages 6 years and younger. **PAGAC Grade: Limited.**

Review of Evidence

One systematic review of 23 studies,[60] one systematic review of 17 studies that included 16 studies in a meta-analysis,[61] and the PAG Midcourse Report[26] were included. Studies included reviews of interventions conducted from inception to September 2014 in center-based and licensed child care settings in children ages 0 to 6 years[61] and inception to May 2013 among children ages 2 to 6 years.[60] The PAG Midcourse Report included a review of reviews of physical activity intervention studies focused on youth ages 3 to 17 years that were published January 2001 through July 2012; a total of 31 reviews containing 910 studies (not mutually exclusive) were included.[26] Intervention strategies included incorporating structured active lessons into classroom activities, play area modifications, scheduling additional play time (indoor and outdoor, structured and unstructured), and parental involvement. Interventions were either led by trained teachers or trained research staff. Several interventions included an additional parent component, primarily consisting of newsletters to parents regarding intervention activities. Several interventions also included physical alterations or redesign of outdoor play space. All of the reviews addressed changes in physical activity. Studies in child care settings primarily used device-based (accelerometer, pedometer, heart rate) measures of physical activity to assess changes in light-, moderate-, and/or vigorous-intensity physical activity. Some studies also assessed sedentary behavior. A few studies used parental assessments to estimate children's physical activity levels or direct observation in classroom or intervention settings.

Evidence on the Overall Relationship

The PAG Midcourse Report concluded that evidence was Suggestive (similar to a grade of "Limited" in the current report) that preschools and child care centers were effective settings for increasing physical activity in children.[26] The PAG Midcourse Report define a grade of "Suggestive" as "reasonably consistent evidence of effect, but cannot make strong definitive conclusions." The conclusion was based primarily on evidence from three reviews focused on childcare settings.[26] Promising strategies deserving of further investigation included: 1) providing portable play equipment on playgroups and other play spaces; 2) providing staff with training in the delivery of structured physical activity sessions and increasing the time allocated for such sessions; 3) integrating physical activity teaching and learning activities into pre-academic instructional routines; and 4) increasing time that children spend outside.

Two additional reviews[60, 61] in preschool and child care settings provided evidence to further support the conclusions from the PAG Midcourse Report.[26] Physical activity outcomes included daily step counts, accelerometer counts, time spent walking, and/or time in sedentary and light-, moderate-, and/or vigorous-intensity physical activity. Although the systematic reviews included a sufficient number of studies from which to draw conclusions, many studies did not provide enough information regarding the magnitude of the effects of the intervention strategies on physical activity behavior change in children. When the magnitude of the effect was presented, effect sizes were reasonably small, with some not reaching statistical significance, and study durations often were relatively brief. One meta-analysis by Finch et al[61] found an overall pooled SMD of 0.44 (95% CI: 0.12-0.76; *P*=0.007), though pooled effect estimates were no longer significant after an outlier was excluded from the meta-analysis (SMD 0.28; 95% CI: -0.01 to -0.56; *P*=0.06). SMD estimates ranged from 0.07 to 1.26 based on an analysis of individual study characteristics. When comparing the eight identified pragmatic trials (delivered under "real world" conditions) and the nine identified non-pragmatic trials (explanatory or efficacy trials), pooled analysis results suggested that the pragmatic interventions were not effective for improving physical activity in children (SMD 0.10; 95% CI: -0.13 to 0.33; *P*=0.40), although the non-pragmatic trials showed a significant effect (SMD 0.80; 95% CI: 0.12-1.48; *P*=0.02). In their review, Mehtala et al[60] provided limited information on the magnitude of effects or effect sizes, although they noted that 14 of 16 studies that focused on increasing physical activity levels reported significant physical activity changes. When available, mean differences across studies ranged from +4.8 percent to +61 percent for percent time in moderate-to-vigorous physical activity, -5 percent to -26.5 percent for sedentary time, and +3 to +58 minutes for minutes of moderate-to-vigorous physical activity.

With respect to the evaluation of different intervention elements, the Finch et al[61] review noted that although both structured and unstructured active lessons produced statistically significant physical activity-related SMDs, the SMD produced by structured active lessons was larger (SMD 0.53 vs. 0.17, respectively, *P*<0.05). Including theory-based interventions also showed promise. Theory-based interventions had a larger and statistically significant SMD (0.76, *P*=0.03) compared with interventions that were not theory-based (0.25, *P*=0.14). Intervention strategies with no parent component had a statistically significant SMD (0.54), while strategies that included a parent component did not (SMD=0.41). Strategies that included changes to the physical environment produced SMDs that were similar to strategies that did not include changes to the physical environment (SMD 0.41 and 0.73, *P*<0.05). Expert-led interventions were more effective than teacher-led interventions (SMD 1.26, *P*=0.02

versus 0.27, *P*=0.19). Interventions lasting 6 or fewer months yielded a statistically significant SMD (0.58, *P*=0.02), while the effect size for interventions lasting more than 6 months was not statistically significant (SMD 0.07, *P*=0.25).

Features of physical activity intervention targets and measures: The most common types of physical activity interventions implemented in child care or preschool settings included group-based interventions lasting 30 or more minutes on 2 to 5 days per week. The types of activities typically included outdoor play activities, activities focused on large muscle or gross motor skills (e.g., jumping, hopping, skipping), dancing, and jogging or running. Physical activity intensity level was typically not defined in intervention descriptions. However, time spent in light-, moderate-, and vigorous-intensity physical activity was listed as common physical activity outcomes of interest.

Evidence on Specific Factors

Populations included in the systematic reviews and meta-analysis included children from low-income communities, children of various races and ethnicities, and males and females. The studies were conducted within and outside the United States. These types of populations may be of interest for subgroup analyses because of reported differences in physical activity levels between groups. Limited evidence was provided to evaluate differences in intervention impact between population groups, with the exception of sex-based differences. Some evidence suggests that intervention strategies focused on increasing playground space were more effective for boys than girls, possibly due to the types of activities (e.g., sports) that occur on playgrounds. Differences between the sexes were not apparent in environments or activities that were not sports-based.[60] Strategies that focused on adding more recess opportunities and reducing playground density appeared to be more effective for girls compared with boys.[60] Evidence in the reviews evaluating intervention effects for children of different races and ethnicities, as well as the reporting of adverse events, are currently lacking or infrequently reported.

For additional details on this body of evidence, visit: https://health.gov/paguidelines/second-edition/report/supplementary-material.aspx for the Evidence Portfolio.

Public Health Impact

Given that 24 percent of young children are cared for in organized care facilities, and children are in these facilities approximately 8 hours per day,[62] the potential impact of increasing physical activity levels in child care and preschool settings could be substantial. Several studies offered information about promising strategies that deserve further evaluation, including physical activity-specific in-service teacher training, structured active lessons, and theory-based interventions.

Faith Based Community Interventions

Faith-based settings are organizations with religious or spiritual components as part of their mission and decision-making.[63] Programs or interventions delivered in concert with these settings can be faith-"based" (i.e., integrated with religious or spiritual aspects) or faith-"placed" (i.e., delivered within or through these settings).[64]

The reach of faith-based organizations into diverse populations, along with the support and community-connectedness they provide, have made them an appealing milieu for designing, implementing, and evaluating physical activity interventions.[65, 66]

Source of evidence: Systematic reviews

Conclusion Statement

Limited evidence suggests that interventions that are either faith-based or faith-placed may be effective for promoting physical activity. **PAGAC Grade: Limited.**

Review of the Evidence

The Subcommittee considered two reviews.[64, 67] Parra et al[64] included studies from inception to January 2016, and Bopp et al[67] included studies from inception to May 2011. Within the Parra et al[64] review, 18 studies used study designs consisting of either RCTs or quasi-experimental studies with a control or comparison group. Of the 18 studies, 3 were faith-placed and the other 15 were faith-based. Additional inclusion criteria in that systematic review were that the interventions had to be delivered in faith-based organizations and have at least one active physical activity component. Fourteen of the studies were conducted in the United States. The remaining studies were conducted in New Zealand (N=2) and Australia (N=2). Nine of the studies were non-RCTs and nine were RCTs with randomization occurring at the cluster level. The majority of participants in the studies were female and African American. A range of ages were represented in the studies and the intervention length ranged from 8 weeks to 3 years. Half of the studies (N=9) included weekly physical activity intervention sessions and some included training of lay health educators, while others were delivered by the research team.

Bopp et al[67] included 27 articles (19=faith based; 8=faith placed). Similar to the Parra et al[64] review the majority of studies (N=21) targeted African American adults, with two studies including Latino adults and one including children. The Bopp et al[67] review described intervention characteristics by type (faith-based or faith-placed). Briefly, for faith-based studies, the intervention length ranged from 4 weeks to 2 years. Most studies (N=10) were theory based, and most (N=15) had weekly class sessions. Common characteristics across studies included education and a guided exercise session. Studies ranged from 13 weeks to 2 years, with faith-placed studies generally reporting longer intervention durations compared with faith-based studies. Details regarding the theoretical foci of the interventions were limited, with only one of the studies explicitly reporting the theoretical basis, while two others cited specific health promotion frameworks. Intervention content and length were heterogeneous, as was the health focus of the intervention (e.g., some focused on diabetes, some specifically on physical activity).

Evidence on the Overall Relationship

Thirteen of the 18 studies included in the Parra et al[64] systematic review reported on change in physical activity behavior or session attendance, with 7 of the 18 studies (3=RCT; 4=non-RCT) finding significant effects for physical activity behavior when comparing the intervention to control. Of the seven, two were faith-placed and five were faith-based. Some common characteristics of those studies with positive effects included interventions with weekly sessions, a basis in theory (e.g., Social Cognitive Theory, Transtheoretical Model), and trained staff or peer educators. The physical activity outcomes reported were heterogeneous (e.g., moderate-to-vigorous physical activity; session attendance, walking behavior, overall time spent in physical activity).

For the faith-based studies reviewed by Bopp et al,[67] 10 of 19 reported positive changes in physical activity behavior. For the faith-placed studies reviewed by Bopp et al,[67] four of eight reported changes in physical activity behavior.

Evidence on Specific Factors

Evidence in the reviews evaluating intervention effects on different racial/ethnic groups, adverse events, or cost-effectiveness is currently lacking or infrequently reported. None of the studies included in the systematic reviews[64, 67] provided evidence of an increased risk of adverse events.

Features of physical activity intervention targets and measures: Outcomes of interest were change in physical activity assessed both by self-report and accelerometry, and included a range of physical activity targets (e.g., moderate-vigorous physical activity, walking, leisure-time physical activity).

Intervention effects were generally small, ranging from a difference between intervention and control in moderate-intensity physical activity of 2.7 minutes (as measured by accelerometry) to 103 minutes (as measured by interview recall). The intervention durations of the included studies in the Parra et al[64] review were variable, with 8 out of 18 being short-term (less than 6 months), 5 out of 18 medium-term (6 to 11 months) and 4 out of 18 long-term (12 months or more). For the faith-based studies in the Bopp et al[67] review, most had intervention durations between 8 to 12 weeks, with two being 6 weeks or less and four with longer durations (one=16 weeks; one=6 months; one=1 year; one=2 years). The faith-placed studies in the Bopp et al[67] review generally had longer intervention durations compared with the faith-based studies; three were 12 to 14 weeks, two were between 6 and 8 months, two were 1 year, and one lasted 2 years. Specific intervention effects related to study duration were not reported consistently in the Bopp et al[67] review.

For additional details on this body of evidence, visit: https://health.gov/paguidelines/second-edition/report/supplementary-material.aspx for the Evidence Portfolio.

Public Health Impact

Faith-based organizations provide many individuals with support, guidance, leadership, and connectedness. Many faith-based organizations are sources of health-related information and delivery of health programming and services. Physical activity adoption and maintenance is a natural intervention target for these faith-based organizations as it is synergistic with the view of health as a multifaceted construct incorporating spiritual, physical, and emotional aspects. Delivering physical activity programming through these community systems offers potential for dissemination and long-term sustainability.

Faith-based organizations may be appropriate health promotion partners for improving physical activity in high-risk populations, particularly as 77 percent of Americans affiliate with a religion and 36 percent attend worship services at least once per week, with affiliation and attendance higher for women and for those from some racial and ethnic populations, including African American and Latino populations.[68, 69] In addition, faith-based organizations often have physical space to hold activities and tend to be a trusted entity in the community with deep social networks.

Nurse-Delivered Interventions in Home or Other Community Settings

Source of evidence: Systematic reviews

Conclusion Statement

Limited evidence suggests that nurse-delivered interventions in community settings are effective for increasing physical activity in adults. **PAGAC Grade: Limited.**

Review of Evidence

Two systematic reviews were included.[70, 71] These reviews included a range of 8 to 13 studies. Both reviews covered the 1990 to 2015 timeframe. Both reviews[70, 71] examined physical activity intervention studies delivered by a registered nurse or nurse practitioner. Richards and Cai[70] specifically examined studies conducted by a nurse at participants' homes. Richards and Cai[71] included interventions delivered in other community settings (i.e., community centers, senior centers, places of worship, outpatient clinics, health or fitness centers). Both reviews addressed changes in physical activity. They examined physical activity through self-report and wearable devices (e.g., daily step counts measured by pedometer). The reviews also addressed other outcomes, including adherence to exercise.

Evidence on the Overall Relationship

A small number of studies have been conducted on the topic. Studies occurred in several different countries. In the review of community-based interventions,[71] only 5 of the 13 studies were RCTs. Of those five RCTs, three reported significant differences between treatment and control arms, although precise, quantified information regarding the magnitude of the effects of the intervention strategies relative to controls on physical activity behavior change was not included.[72-74] In the review of home-based interventions, only four of the eight studies reviewed were RCTs, and two of the four reported significant differences in physical activity between treatment and control arms, although information on the magnitude of intervention effect was not presented.[75, 76] Follow-up data collection (beyond intervention end) was available for 4 out of 21 (19%) of studies, with reported follow-ups often of 6 months or longer. As reported in the experimental trials, some useful intervention components appear to include nurse involvement in establishing physical activity goals, selecting types of physical activity and related lifestyle improvements, and providing direct physical activity advice and counseling.[75-77]

Features of physical activity intervention targets and measures: Physical activity outcomes varied considerably, and included daily step counts,[75, 78-80] accelerometer-based activity counts,[81] aerobic activity,[72] self-reported frequency of exercise,[82] reported walking and/or minutes per week of moderate-to-vigorous physical activity,[77, 83] self-reported walking frequency,[73] walking frequency and intensity,[84] and total physical activity.[74, 85] Most interventions were not reported as prescribing specific physical activity frequency, intensity, time, and/or type.

Evidence on Specific Factors

Evidence in the reviews evaluating different racial/ethnic groups, adverse events, and cost-effectiveness is currently lacking or infrequently reported.

For additional details on this body of evidence, visit: https://health.gov/paguidelines/second-edition/report/supplementary-material.aspx for the Evidence Portfolio.

Public Health Impact

Community-based physical activity interventions delivered through nurse outreach can be particularly useful, given their convenience for populations, such as frail adults and those with chronic conditions, who can benefit from clinical oversight and instruction. Nurses can provide the personal contact and program customization that may be particularly beneficial for behavior change with such populations. Nurses who see patients in their home environments also can involve family members and local support networks as part of the intervention, which can facilitate physical activity participation. Continuity of care also may be a benefit of this type of community outreach intervention.

Interventions in Primary Care Settings

Primary care interventions encompass different delivery types and programs, including counseling sessions with primary care providers that range in duration from short (2 to 10 minutes) to long (e.g., 40 minutes). Counseling can be provided by physician contact only as well as in combination with printed materials. Additionally, some primary care interventions focus solely on prescription schemes in which a general practitioner (e.g., nurse or physician) gives a written prescription to a patient to participate in a physical activity program. Primary care interventions, as reviewed here, do not include intensive lifestyle interventions where primary care serves only as a referral source, or interventions that have not tested the delivery of a behavioral intervention within the clinical setting.

Sources of evidence: Systematic reviews, meta-analysis, review of reviews

Conclusion Statement

Limited evidence exists that primary care-based interventions targeting increases in physical activity among adults are effective when compared with minimal or usual care conditions, particularly over medium (i.e., 6 to 11 months) and longer periods (i.e., 12 months or more). **PAGAC Grade: Limited.**

Review of the Evidence

Two meta-analyses,[86, 87] nine systematic reviews,[88-96] and two systematic reviews of previous systematic reviews[97, 98] were included. The meta-analyses included 14[86] and 17[87] studies. The systematic reviews included a range of 3 to 32 studies. The two systematic reviews of previous systematic reviews included 10[97] and 16[98] reviews. Studies overall covered an extensive timeframe, including a number from inception[86, 91, 98] through 2016.[92, 93] The majority of studies examined interventions among generally healthy adults and older adults[86, 87, 89-92, 94, 95] while one examined African American and Latino groups specifically.[87] The majority of studies focused on the efficacy of a varied range of intervention strategies within primary care settings, while one focused exclusively on motivational interviewing techniques.[90]

Evidence on the Overall Relationship

The effectiveness of the interventions was variable when compared to minimal or usual care control arms. The magnitude of the effect was not easy to determine and many systematic reviews and review of reviews did not report effect sizes. Orrow et al[86] reported small to medium effects for likelihood of achieving 30 minutes of moderate-intensity physical activity on 5 days per week (odds ratio (OR)=1.42; 95% CI: 1.17-1.73) and increases in overall physical activity behavior (SMD=0.25; 95% CI: 0.11-0.38) in previously inactive adults and older adults. The majority of these studies were short in duration (i.e., less than 6 months). Ramoa Castro et al[92] reported increases in physical activity from 5 percent to 26 percent relative to controls in studies of 6 to 12 months in length. However, it should be noted that the magnitude of the effects varied widely, as both of these reviews reported that the majority of studies reviewed had null or non-significant improvements in physical activity. Morton et al[90] reviewed studies implementing motivational interviewing techniques, a common intervention strategy in clinical settings, to increase physical activity. Only 11 of 22 studies reviewed showed significant improvements in physical activity (length of intervention periods was not reported). However, the authors noted that strategies that combined motivational interviewing with other strategies (e.g., vouchers for an exercise facility) tended to be the most effective. For those studies focusing on physical activity prescription schemes in particular, 37 studies were included. Studies were conducted in 11 different countries (United Kingdom=13; Sweden=7; Netherlands=2; Denmark=3; Finland=1; Spain=2; Germany=1; Canada=2; United States=3; New Zealand=1; Australia=1).

Several characteristics were important to the design of prescription-based programs, including the reason for referral, prescriber (e.g., general practitioner or other health professional), location of physical activity implementation (i.e., community facility or home), type of activity, and cost.[96] These characteristics varied by country, particularly in relation to referral reason and cost.[96] Of the studies included from European countries, all except those from the Netherlands had a disease (e.g., cardiovascular disease, diabetes) as the reason for referral, with sedentary lifestyle being a consistent reason for referral across all countries. General practitioner was listed as a prescriber across all countries, although other health professionals were included in the United Kingdom, Sweden, Australia, and New Zealand. All countries included a specific facility in which the recommendation would be implemented, although Sweden, Australia, New Zealand, and the United States included both facilities and home-based locations. In all countries except Spain and Canada, participant payments were required, although a reduced price was noted for the U.K.-based studies. Meta-analyses showed small effects for physical activity adherence (i.e., proportion participating in greater than or equal to 80% of the prescription recommendations: I-squared=98.4%; *P*=0.000; effect sizes ranged from -0.53 to 0.58).[96] One study of more than 6,600 adults found of those referred, 79 percent attended their first appointment.[96] However, such positive effects were not found for self-reported physical activity behavior (I-squared=34.5%; *P*=0.081; effect sizes ranged from -10.34 to 2.12). Many studies in this area were of short duration (less than 6 months), with a few that were of medium (6 to 11 months) or longer-term (12 months or more) duration.[96]

Support for the supplementation of physical activity advice with written prescriptions was mixed, and the amount of contact time spent between the provider and the patient did not appear to have a significant effect on physical activity behavior. More promising effects were observed for those brief interventions with short-term follow-ups (4 to 12 weeks), and those that included motivational interviewing approaches.[98]

Features of physical activity intervention targets and measures: Most of the studies reported that brief advice by the healthcare provider was given, although the nature of the advice was not clearly described. Some studies described brief follow-up with a physical activity specialist,[95] while others clearly described systematic approaches to the delivery of motivational interviewing techniques for increasing physical activity.[90] Briefly, these techniques were specific to motivational interviewing (e.g., empathetic counseling, active or reflective listening, use of “importance” and “confidence” rulers or metrics) as well as other common behavior change techniques (e.g., goal setting, social support, action planning, and feedback). The majority of studies reported outcomes from self-reported measures of physical activity (i.e., minutes per week of moderate-to-vigorous physical activity; MET-hours per week, and activity kilocalories per week) and amounts of walking, with a few studies that reported pedometer-derived step counts and/or accelerometer-derived activity. For prescription schemes specifically, physical activity adherence to recommendations was a prevalent outcome assessed.[87]

Evidence on Specific Factors

Melvin et al[89] reported on a limited number of studies specifically involving African American (N=2) and Latino (N=2) adults and found no significant increases in physical activity.

Orrow et al[86] described one study that reported on adverse events. This study observed small increases in musculoskeletal injury (7%) and falls (11%), relative to usual care, in women ages 40 to 74 years.

One study,[99] reviewed by Gagliardi et al,[95] provided a cost analysis, estimating that an initial monthly cost for adding a physical activity counseling into a primary care practice would be $91.43 (in Canadian dollars) per month. Another study found favorable cost effectiveness for prescription schemes, relative to usual care, in inactive individuals without a medical condition, inactive individuals with obesity, inactive individuals with hypertension, and inactive individuals with depression.[96] Although not analyzed systematically, factors noted to be of potential importance for prescription schemes were the reasons for referral and participant-related payments. Health status was a reason for referral in most of the European studies included, but not for all countries. The fees associated with access to locations and exercise professionals also were found to vary across countries and were not consistently reported or analyzed.[87]

For additional details on this body of evidence, visit: https://health.gov/paguidelines/second-edition/report/supplementary-material.aspx for the Evidence Portfolio.

Public Health Impact

The primary care setting may be an appealing venue for offering physical activity counseling or referral. Despite increasing demands upon clinical providers during primary care visits, the primary care setting represents a scalable opportunity to influence population-level physical activity if effective approaches can be implemented. The current state of the evidence suggests that brief interventions in the context of a clinic visit have limited efficacy for significantly increasing physical activity. Intervention efficacy may be enhanced by providing more standardized interventions (e.g., delivered in a similar manner across providers and health care systems) and more robust strategies (e.g., strategies beyond brief advice that include messaging from one or more members of the provider team using motivational interviewing or other theory-based approaches). Such strategies can be supplemented with written "prescriptions" involving specific physical activity recommendations.

School Interventions

Sources of evidence: Meta-analyses, systematic reviews

Conclusion Statements

Strong evidence demonstrates that interventions that affect multiple components of schools are effective for increasing physical activity during school hours in primary school-aged (typically ages 5 to 12 years) and adolescent youth. **PAGAC Grade: Strong.**

Strong evidence demonstrates that interventions that revise the structure of physical education classes are effective for increasing in-class physical activity in primary school-aged and adolescent youth. **PAGAC Grade: Strong.**

Limited evidence suggests that interventions that modify the designs of school playgrounds or that change recess sessions in other ways are effective for increasing physical activity in youth. **PAGAC Grade: Limited.**

Review of the Evidence

A total of nine documents—five systematic reviews,[100-104] two meta-analyses,[105, 106] one scientific statement (report),[107] and the PAG Midcourse Report[26] —were included. The systematic reviews included a range of 8 to 129 studies. The systematic reviews covered the following timeframes: 1900 to May 2012,[101] 1986 to May 2011,[102] January 2000 to April 2011,[103] 2001 to 2010,[104] and July 2008 to December 2010.[100] The meta-analyses included a range of 13 to 15 studies, and covered an extensive timeframe: from inception to March 2012[105] and January 1950 to April 2015.[106] The Population Approaches to Improve Diet, Physical Activity, and Smoking Habits. A Scientific Statement from the American Heart Association (AHA Scientific Statement) covered January 1, 2007 to publication.[107] The PAG Midcourse Report included a review of reviews of physical activity intervention studies focused on youth ages 3 to 17 years that were published January 2001 through July 2012; a total of 31 reviews containing 910 studies (not mutually exclusive) were included.[26]

The included reviews examined the effects of physical activity interventions carried out in school settings. Four reviews[26, 101-103] assessed interventions to increase physical activity during school recess. Lonsdale et al[105] and the PAG Midcourse Report[26] examined interventions aimed at increasing moderate-to-vigorous physical activity in physical education (PE) lessons. Mears and Jago[106] examined physical activity interventions in after-school programs.

All of the reviews addressed changes in physical activity levels. Five reviews[26, 101, 105-107] examined individual-level time spent in vigorous-intensity physical activity and/or moderate-to-vigorous physical activity. Saraf et al[104] also assessed changes in sedentary activity.

Evidence on the Overall Relationship

Evidence on multi-component interventions: The PAG Midcourse Report found sufficient evidence that multi-component school-based interventions—those in which two or more intervention strategies are concurrently implemented—increase physical activity levels during school hours.[26] Effective combination of strategies include the following: 1) providing enhanced PE that increases lesson time, is delivered by well-trained specialists, and emphasizes instructional practices that provide substantial moderate-to-vigorous physical activity; 2) providing classroom activity breaks; 3) developing activity sessions before and/or after school, including active transportation; 4) building behavioral skills related to physical activity participation; and 5) providing after-school activity space and equipment.

Two prominent multi-component school-based intervention trials—the Child and Adolescent Trial for Cardiovascular Health (CATCH) and Sports, Play, and Active Recreation for Kids (SPARK)—provide examples of programs that were effective and have been disseminated into communities. CATCH involved a large number of schools, a multi-component behavioral intervention over three grades, and children of diverse backgrounds. The CATCH interventions include school-based (school food service, PE, classroom curricula) and home-based (home curricula, family-fun activities) components.[108] Results showed that vigorous physical activity was significantly higher among intervention students (Mean (M)=58.6 minutes) compared to controls (M=46.5 minutes) ($P<0.003$).[109]

The SPARK interventions include a physical education component (including dedicated time for health-fitness and skill-fitness activities) and a self-management program to promote physical activity outside of school. SPARK also provides on-site staff development, and extensive follow-up support.[110] Among its findings are that students spent more minutes per week being physically active in teacher- and specialist-led classes compared to controls (33 minutes, 40 minutes, and 18 minutes, respectively, $P<0.001$), although PA did not increase outside of school.[110]

Evidence on physical education interventions: The PAG Midcourse Report found sufficient evidence that PE interventions increase physical activity levels during PE classes.[26] Important strategies include the following: 1) developing and implementing a well-designed PE curriculum; 2) enhancing instructional practices to provide substantial moderate-to-vigorous physical activity; and 3) providing teachers with appropriate training.

A meta-analysis[105] evaluating the evidence on PE classes found moderate evidence that interventions that modified the structure of PE classes can be effective for increasing youth physical activity levels during PE. The meta-analysis indicated an absolute difference of 10.37 percent (95% CI: 6.33-14.41) of lesson time spent in moderate-to-vigorous physical activity in favor of the interventions over controls. This estimated difference of 10.37 percent of lesson time corresponds to 24 percent more active learning time in the intervention groups compared with the control condition (SMD=0.62; 95% CI: 0.39-0.84). Age, sex, and intervention duration did not moderate intervention effects.

Effective intervention strategies included teacher learning focused on class organization, management and instruction and supplementing standard PE classes with high-intensity activity (i.e., fitness infusion). Additional strategies included in some studies were cognitive components (e.g., knowledge, motivation), adding more PE lessons in addition to modifying or enriching PE, and changing elements of the PE environment to promote more activity.

Demetriou and Honer[100] conducted a systematic review of the effectiveness of school-based interventions with a physical activity component by measuring changes in total physical activity. Forty-two of 74 studies (56.8%) reported positive results in favor of the intervention group, whereas five studies (6.8%) reported a negative effect. One study by Lubans and Sylva[111] found a significant effect on moderate-to-vigorous (minutes per week) in favor of the intervention group with a small effect size of d=0.12.

The AHA Scientific Statement concluded that, with few exceptions, school-based interventions that focused on improving PE curriculum, often in combination with other school- or home-based physical activity components, showed improvements in objectively measured school-based and total physical activity.[107]

Evidence on school recess interventions: Studies on school recess interventions included pre-school and school-aged youth (typically ages 3 or 4 to 11 years, although the PAG Midcourse Report[26] included age groups up to 17 years). The literature available consists of a small number of studies that often lack rigor (i.e., relatively few RCTs demonstrating between group differences) or adequate reporting of study methods. Studies typically employed interventions of short duration (e.g., 4 weeks) and/or included small sample sizes. This has led to a high risk of bias and heterogeneity of results. Escalante et al[101] reported on only one pre-school intervention study,[112] and it did not significantly increase physical activity. In school-aged children, Escalante et al,[101] Parrish et al,[103] and Ickes et al[102] reviewed many of the same articles. They found in several studies that playground markings,[113, 114] playground redesign[115] and, in some instances, game equipment[116] significantly increased children's recess and lunchtime moderate-intensity physical activity, vigorous-intensity physical activity, and/or moderate-to-vigorous physical activity compared with controls. However, overall a small magnitude of effect was seen (no effect sizes reported). For example, Stratton and Mullan[113] found that playground markings encouraged greater moderate-to-vigorous physical activity within the intervention group (2.4% and 6.9% in early and late primary school, respectively) and vigorous-intensity physical activity (1.6% and 4.1% in early and late primary school, respectively). Game equipment increased girls', but not boys', moderate-to-vigorous physical activity within the experimental group by 3.9 percent.[116] This work is supported by the AHA Scientific Statement, which concluded that effective school-based approaches to improve physical activity include increasing the availability and types of playground spaces and equipment.[107]

Features of physical activity intervention targets and measures: Physical activity outcomes varied, but were often reported as light-intensity physical activity, moderate-to-vigorous physical activity, or steps per day. Assessment approaches used to capture physical activity varied considerably and included estimated physical activity from heart rate,[113] or use of accelerometers[115-117] or pedometers.[118] Descriptions of specific physical activity frequency, intensity, duration, and/or type were generally lacking in the reviews.

Evidence on Specific Factors

Evidence in the reviews evaluating different racial/ethnic groups, adverse events, and cost-effectiveness is currently lacking or infrequently reported. Although in some cases participant ethnicity or income distributions were reported, the results typically were not reported by ethnic/racial or income subgroups.[117, 119] Some studies reported recruiting children within low-income areas,[113, 115] but results were not reported by income stratification.

For additional details on this body of evidence, visit: https://health.gov/paguidelines/second-edition/report/supplementary-material.aspx for the Evidence Portfolio.

Public Health Impact

Schools represent a universal setting for reaching youth across different locales, age subgroups, and sociodemographic strata, making them a potentially powerful venue for implementing physical activity promotion interventions. This is particularly the case given emerging evidence linking physical activity interventions to positive behavioral and academic outcomes in children.[120] However, different types of school-based interventions exhibit a significant degree of heterogeneity in intervention effectiveness. Strong evidence demonstrates that multi-component school-based interventions are effective for increasing physical activity. Of relevance to this conclusion, the new Comprehensive School Physical Activity Program framework outlines a multi-component approach that provides opportunities for children to engage in physical activity throughout the school day. The approach includes physical activity before and after school, physical activity during the school day, a comprehensive and required physical education curriculum, family and community engagement, and staff involvement.[121] Given that each state has compulsory school attendance laws and most states require 180 days of instruction, opportunities to intervene on physical activity for nearly 50 percent of each year are available.[122]

PE classes have been one of the most common modes for delivering physical activity interventions in school-based settings. Given the prevalence of PE classes in primary and secondary education districts across the United States, the promise of PE-based interventions that actively promote movement and physical activity during the PE class period is substantial. The *2016 Shape of the Nation* report indicated that nearly all states have adopted their own standards for PE programs.[121]

Effective and sustainable strategies for delivering physical activity interventions through PE classes that meet national physical activity guidelines for children could be beneficial for achieving adherence to guidelines. Studies of PE that have included teacher education focused on class organization, management, and instruction and on supplementing PE classes with high-intensity activity have shown particular promise. Evidenced-based programs, such as SPARK[110] and CATCH,[108] offer curricula, training, equipment, certification, and technical support for teachers and recreation leaders serving students from Pre-K through 12th grade.

Strategies for before- and after-school physical activities or informal physical activity during the school day (e.g., recess, activity breaks) have been relatively understudied and warrant attention. SHAPE America recommends schools provide at least one 20-minute recess period daily.[123] Data suggest that children who are least likely to get daily recess include those from urban areas, children who live below the poverty line, and children who are struggling academically.[124] Additionally, some studies have highlighted the benefits of classroom activity breaks, which could be a particularly beneficial strategy in low income and/or under-resourced schools, or schools in urban or congested areas without dedicated playgrounds.[125, 126]

Worksite Interventions

Source of evidence: Systematic reviews

Conclusion Statement

Limited evidence suggests overall that worksite interventions are effective for increasing physical activity in adults, particularly over medium (i.e., 6 to 11 months) and longer periods (i.e., 12 or more months). **PAGAC Grade: Limited.**

Review of the Evidence

Six systematic reviews[127-132] were included. The systematic reviews, which included a range of 9[131] to 58[127] studies, covered an extensive timeframe, including from inception,[130, 131] from 1950,[127] and through 2014.[131] The majority of studies examined interventions delivered broadly across workplaces among generally healthy adults,[127-129] while others focused exclusively on men,[130] nurses,[131] and university and college staff.[132]

Evidence on the Overall Relationship

Studies included reviews of worksite-based physical activity interventions delivered alone or combined with other behaviors (e.g., nutrition), or that were part of broader wellness interventions. The general methodological quality of the evidence varied considerably and included randomized and cluster-randomized designs as well as quasi-experimental and demonstration project (e.g., pretest-posttest) designs. The studies reviewed focused on walking programs to increase overall levels of physical activity as well as programs aimed at increasing structured exercise (e.g., aerobic classes, strength training). Interventions that included actual physical activity participation (e.g., active travel, stair walking interventions, exercise classes) as well as those featuring counseling, health promotion, or information messaging approaches (e.g., health checks, signage in the workplace, education classes) demonstrated moderate levels of efficacy across a wide range of intervention lengths (i.e., 6 weeks to 4 years).[127] Approaches that focused broadly on wellness (with physical activity elements included) and those that included onsite exercise classes demonstrated more limited efficacy.[127, 128] Walking-based programs, where the primary outcomes were either steps or overall physical activity, were generally more efficacious than structured exercise classes.[127] The length of the interventions was typically short in duration (less than 6 months), with longer-term interventions (12 months or more) demonstrating mixed efficacy. Although the systematic reviews included a sufficient number of studies from which to draw conclusions, most studies did not provide precise information regarding the magnitude of the effects of the intervention strategies on physical activity behavior change.

Features of physical activity intervention targets and measures: The worksite interventions varied in intervention delivery mode, intensity, and duration. The most common intervention strategies used were goal setting, action planning, and prompted self-monitoring of behavior. Physical activity was largely measured by self-reported activity (i.e., minutes per week of moderate-to-vigorous physical activity, MET-hours per week, and activity kilocalories per week).

Evidence on Specific Factors

Evidence in the reviews evaluating different racial/ethnic groups and adverse events is currently lacking or infrequently reported. The cost-effectiveness of worksite physical activity interventions, when reported, was mixed.[128] The evidence for specific employee groups such as men,[130] nurses,[131] and university and college staff[132] all showed limited efficacy.

For additional details on this body of evidence, visit: https://health.gov/paguidelines/second-edition/report/supplementary-material.aspx for the Evidence Portfolio.

Public Health Impact

Worksites represent a pervasive setting for reaching a broad segment of the adult population, particularly given the amount of time many people spend at their place of work. However, identifying the most effective ways of leveraging workplace environments to promote discernable and sustainable increases in physical activity in response to worksite interventions remains challenging. Promising strategies include counseling-based approaches, health promotion messaging in the workplace, and worksite-based walking programs,[127] whereas interventions focused on other forms of structured exercise during work time have had more limited efficacy.[127-129]

COMMUNICATION ENVIRONMENT LEVEL

The communication environment encompasses a broad array of information and communication technologies (ICT) that have the potential to span locations and sociodemographic conditions. ICT are generally defined as those technologies that use computerized information or communication interfaces and/or that allow people and organizations to interact in the digital world.[133] They include remote (as opposed to in-person) communication channels, such as telephone or computer-tailored print; wearable sensors and activity monitoring devices; interventions delivered over the Internet (i.e., the networking infrastructure connecting computers worldwide) or the web (i.e., information-sharing models that are built on top of the Internet); mobile phone applications (apps); text-messaging (i.e., short message service); social media (e.g., social network platforms); and interactive video games promoting active play or exercise.

The diverse types of ICTs currently available coupled with their accessibility and reach across increasingly representative segments of the U.S. youth and adult populations, have made them an attractive platform upon which to evaluate physical activity interventions. Despite this growing interest among the scientific community, the current evidence base in this area remains constrained in terms of less rigorous study designs of short duration and small and often highly selected samples that lack heterogeneity. Evidence related to different population segments will be discussed to the extent possible when available.

The evidence that was reviewed fell within seven broad technology intervention domains: 1) wearable activity monitors; 2) telephone-assisted interventions; 3) web-based or Internet-delivered interventions; 4) computer-tailored print; 5) mobile phone programs; 6) social media; and 7) interactive video games promoting active play or exercise.

As noted earlier, the categories were not identified a priori and were not specifically included as search terms, but rather emerged during the broad 2011-2016 evidence search that was undertaken. Such a condensed approach necessarily limits the size and, potentially, the types of evidence considered at this level.

Wearable Activity Monitors

Sources of evidence: Meta-analyses, systematic reviews

Conclusion Statements

Strong evidence demonstrates that wearable activity monitors, including step counters (pedometers) and accelerometers, when used in conjunction with goal-setting and other behavioral strategies, can help increase physical activity in the general population of adults as well as in those who have type 2 diabetes. **PAGAC Grade: Strong.**

Moderate evidence indicates that these monitors can help increase physical activity in adults with overweight or obesity. **PAGAC Grade: Moderate.**

Limited evidence suggests that wearable activity monitors may help increase physical activity in adults with musculoskeletal disorders. **PAGAC Grade: Limited.**

Review of the Evidence

A total of seven reviews, including four systematic reviews[134-137] and three meta-analyses,[138-140] were included. The systematic reviews included a range of 5 to 14 studies. Reviews covered the following timeframes: from inception of the database to February 2014,[136] inception to August 2016,[137] and 2000 to January 2015.[135] Funk and Taylor[134] did not report the timeframe searched. However, the included studies were published between 2004 and 2011. Each of the included meta-analyses examined 11 studies. All meta-analyses covered an extensive timeframe: from inception to July 2015[138] and 1994 to June 2013.[139, 140] All of the included reviews examined interventions using activity monitors. Four reviews[134, 136, 139, 140] specifically examined pedometer-based interventions, while Goode et al[135] examined the use of accelerometers.

Evidence on the Overall Relationship

All included reviews addressed changes in physical activity. Five reviews[134, 136, 137, 139, 140] specifically examined changes in the number of steps per day. de Vries et al[138] examined steps per day, total moderate-to-vigorous physical activity minutes per time unit, walking MET-minutes per week, and kilocalories expended in physical activity per week. Across this area, study durations were usually short (i.e., less than 6 months).

Data indicate that, in **general adult populations***,* interventions that include step-counters or accelerometers within a structured program (e.g., individually-based interventions, coaching, group-based interventions) can have a small but positive effect on physical activity levels when compared with usual care or minimal-attention control arms. For example, in one systematic review and meta-analysis,[135] accelerometry interventions across 12 trials resulted in a small but significant increase in physical activity levels (SMD=0.26; 95% CI: 0.04-0.49). The effects of these wearable activity monitors may be accentuated when specific physical activity goals are provided. The type of goal (e.g., self-identified goals versus a 10,000-step goal) may make little difference with respect to effectiveness in helping to promote physical activity change. The additional benefit of activity monitors (step-counters or accelerometers) when compared with an active comparison arm (e.g., a physical activity intervention without activity monitors) is less clear (SMD in accelerometer intervention studies using an active comparison arm=0.17; 97% CI: -1.09 to 1.43).[135] This review reported that they could find no head-to-head comparison of the use of accelerometers versus step-counters in promoting regular physical activity.

In a meta-analysis of patients with **type 2 diabetes**,[139] step-counter use significantly increased physical activity by a mean of 1,822 steps per day (7 studies, 861 participants; 95% CI: 751-2,894 steps per day). In this patient population, use of a step-counter in combination with setting a specific physical activity goal resulted in significantly more steps per day compared to control arms (weighted mean difference (WMD) of 3,200 steps per day; 95% CI: 2,053-4,347 steps per day), whereas step-counter use without a goal did not significantly increase physical activity relative to control arms (WMD of 598 steps per day; 95% CI: -65 to 1,260 steps per day). Use of a step diary or log also was related to a statistically significant increase in physical activity (WMD=2,816 steps per day), whereas when a step diary was not used, physical activity did not increase significantly (WMD=115 steps per day). This meta-analysis of step counter use in type 2 diabetes looked at heterogeneity between studies and found that setting physical activity goals explained the heterogeneity between study results, whereas sample size, intervention duration, and intervention quality did not.

In a somewhat smaller meta-analysis of adults with **overweight or obesity**,[138] a significant positive intervention effect for steps per day was found for behavioral physical activity interventions that included an activity monitor when compared with wait-list or usual care interventions (N=4) (SMD=0.90; 95% CI: 0.61-1.19, $P<0.0001$). A similar intervention comparison also found a significant positive effect for total moderate-to-vigorous physical activity minutes per time unit (N=3) (SMD=0.50; 95% CI: 0.11-0.88, $P=0.01$). Meanwhile, although a positive trend was found for total moderate-to-vigorous physical activity minutes per time unit when an activity monitor was added to existing interventions relative to when it was not, the failure to reach statistical significance obtained in the latter analysis, which included three studies, renders conclusions less certain (SMD for total moderate-to-vigorous physical activity minutes per time unit=0.43; 95% CI: 0.00-0.87). In a meta-analysis of a similar intervention comparison (i.e., the addition of an activity monitor to an existing intervention versus when it was not added) using the mean difference for walking MET-minutes per week as the outcome and involving only two studies (both of which included women only), a statistically significant positive effect was found (mean difference for walking MET-minutes per week=282; 95% CI: 103.82-460.18, *P*=0.002). The authors reported that no adverse events related to the interventions were noted, and no statistically significant negative effects on physical activity outcomes were found. The somewhat more variable results and fewer studies reported with overweight or obese adults led to the evidence grade of "Moderate" as opposed to "Strong."

In a systematic review of seven RCTs of step-counter-based walking interventions in **patients with musculoskeletal disorders**,[136] five of the seven study interventions reported a significant increase in steps over baseline averaging 1,950 steps per day, but the magnitude of the change varied markedly across studies (range=818-2,829 steps per day), and only two studies reported significant improvements relative to the control arm.

Features of physical activity intervention targets and measures: The major physical activity outcomes reported were steps (based on step-counters) and/or accelerometry-based minutes per day or week of moderate-to-vigorous physical activity, with little mention of frequency or duration. Physical activity intervention targets focused mostly on step counts, with step targets often set at 10,000 steps per day or as a percent increase in steps per day. In studies that used accelerometers, intervention targets often focused on moderate-to-vigorous physical activity, with behavioral targets ranging from 120-250 minutes per week.

Evidence on Specific Factors

Evidence in the reviews evaluating different racial/ethnic groups, adverse events, and cost-effectiveness is currently lacking or infrequently reported. Many of the studies in this area consist of reasonably short intervention periods, with the impacts of activity monitor use over longer time periods less clear.

For additional details on this body of evidence, visit: https://health.gov/paguidelines/second-edition/report/supplementary-material.aspx for the Evidence Portfolio.

Public Health Impact

In adults, step-counters and other wearable activity monitors represent a useful adjunct to physical activity programs that include other behavioral strategies (e.g., goal-setting, coaching). The daily feedback that activity monitors provide can enhance efforts to increase walking and other types of physical activity. The increasing availability of a diverse range of activity monitors, a growing number of which have been shown to have good reliability and validity, makes them a promising intervention tool for population-wide physical activity promotion. Figure F11-2 illustrates by showing how a pedometer can be used to track walking.

Figure F11-2. Using a Pedometer to Track Walking

For adults who prefer walking as a form of aerobic activity, pedometers or step counters are useful in tracking progress toward personal goals. Popular advice, such as walking 10,000 steps a day, is not a guideline *per se*, but a way people may choose to meet the *Physical Activity Guidelines*. The key to using a pedometer to meet the Guidelines is to first set a time goal (minutes of walking a day) and then calculate how many steps are needed each day to reach that goal.

Episodes of brisk walking that last at least 10 minutes count toward meeting the Guidelines. However, just counting steps using a pedometer doesn't ensure that a person will achieve those episodes. People generally need to plan episodes of walking if they are to use pedometer step goals appropriately.

As a basis for setting step goals, it's preferable that people know how many steps they take per minute of a brisk walk. A person with a lower fitness level, who takes fewer steps per minute than a fit adult will need fewer steps to achieve the same time of walking.

One way to set a step goal is the following:

1. To determine usual daily steps from baseline activity, a person wears a pedometer to observe the number of steps taken on several ordinary days with no episodes of walking for exercise. Suppose the average is about 5,000 steps a day.

2. While wearing the pedometer, the person measures the number of steps taken during a walk of 10 minutes. For this person, suppose this is 1,000 steps. For a goal of 40 minutes of walking, the goal would total 4,000 steps (1,000 X 4).

3. To calculate a daily step goal, add the usual daily steps (5,000) to the steps required for a 40 minute walk (4,000), to get the total steps per day (5,000 + 4,000 = 9,000).

Then, each week, the person gradually increases the number of total steps a day until the step goal is reached. Rate of progression should be individualized. Some people who start out at 5,000 steps a day can add 500 steps per day each week. Others, who are less fit and starting out at a lower number of steps, should add a smaller number of steps each week.

Source: 2008 Physical Activity Guidelines for Americans.[2]

Telephone-assisted Interventions

Sources of evidence: Systematic review, meta-analysis

Conclusion Statement

Strong evidence demonstrates that telephone-assisted interventions, including those lasting 1 year or longer, are a safe and effective means for increasing physical activity in general adult populations, including older adults. **PAGAC Grade: Strong.**

Review of the Evidence

Two systematic reviews were included.[141, 142] The systematic reviews included a range of 11 to 27 studies that examined the effects of telephone-based interventions on levels of physical activity. Foster et al[141] covered an extensive timeframe, from inception to October 2012, while Goode et al[142] covered 2006 to April 2010.

Evidence on the Overall Relationship

The majority of high-quality studies in this area produced effect sizes indicating a moderate or better intervention effect (i.e., d>0.5). The evidence indicates that longer-duration interventions (i.e., 12 months or more) are associated with greater effectiveness. At least two large-scale dissemination studies of mid-life and older adults have been conducted, with results from these studies showing pre-post intervention increases in regular physical activity levels across a year commensurate with those obtained in RCTs. The majority of participants in the study samples have been Caucasian and well-educated,[141] although the two large-scale dissemination studies included more ethnically and regionally diverse groups of mid-life and older adults.[142] In the small number of telephone-assisted interventions that have combined physical activity and dietary interventions, the evidence suggests that including a focus on dietary changes (e.g., increasing fruit and vegetable intake, decreasing dietary fat) may in some circumstances hinder physical activity changes in the adult and older adult populations that have been studied.[142]

Features of physical activity intervention targets and measures: The physical activity outcome measures varied across studies, and included self-reported continuous physical activity variables (e.g., estimated energy expenditure in kilocalories per day, mean minutes per week of moderate-to-vigorous physical activity, mean number of physical activity episodes in the past 4 weeks), percentage of the sample meeting national physical activity guidelines, and accelerometry-derived physical activity variables. Types of physical activity included walking as well as other participant-chosen forms of moderate-to-vigorous physical activity. A large proportion of interventions were at least 6 months in duration, with a number that were 12 months or more.

Evidence on Specific Factors

The Cochrane review,[141] which included nine RCTs involving telephone support lasting at least a year in generally healthy adults, reported no evidence of an increased risk of adverse events. Evidence evaluating intervention cost-effectiveness is limited, but in two studies in which cost analyses were conducted, results supported the cost effectiveness of telephone-delivered interventions.[142]

For additional details on this body of evidence, visit: https://health.gov/paguidelines/second-edition/report/supplementary-material.aspx for the Evidence Portfolio.

Public Health Impact

Given the pervasiveness of phone ownership across the U.S. population as well as globally, phone-based interventions represent an effective strategy for increasing physical activity in adult populations that can be broadly disseminated. Promising methods for dissemination include automated telephone interventions (e.g., interactive voice response systems) and trained peer advising by phone.

Web-based or Internet-delivered Interventions

Sources of evidence: Meta-analysis, systematic reviews

Conclusion Statements

Strong evidence demonstrates that Internet-delivered interventions that include educational components have a small but consistently positive effect in increasing physical activity levels in the general adult population, particularly in the shorter-term (i.e., less than 6 months), when compared with interventions that do not include Internet-delivered materials. **PAGAC Grade: Strong.**

Limited, early evidence suggests that web-based or Internet-delivered interventions may have some efficacy in increasing short-term physical activity levels in individuals with type 2 diabetes. **PAGAC Grade: Limited.**

Review of the Evidence

A total of four reviews, including three systematic reviews[141, 143, 144] and one meta-analysis,[145] were included. The systematic reviews included a range of 7 to 15 studies and covered an extensive timeframe: from inception to October 2012,[141] 1966 to April 2011,[143] and 1991 to March 2013.[144] The meta-analysis[145] included 34 studies published between 1990 and June 2011. The included reviews examined interventions delivered remotely over the Internet or a web page. One systematic review[145] assessed studies that used the Internet, email communication, or a combination. Foster et al[141] assessed web 2.0 and remote interventions that at times used the Internet in combination with other types of mediated interventions.

The majority of studies have been conducted in the general adult population, and most did not screen for initial physical activity status as one of the study enrollment criteria. Participants have been primarily Caucasian, well-educated, and middle-aged, and the majority of participants have been female.

For individuals with type 2 diabetes, the overall quality of studies for this subpopulation has been mixed. The impacts of web-based or Internet-delivered interventions on population subgroups with chronic diseases other than type 2 diabetes are currently unclear,[143] given that available studies often report high participant attrition levels and relatively short intervention time periods (often less than 6 months).

Evidence on the Overall Relationship

Overall effect size estimates indicate a small but positive intervention effect on physical activity in the **general adult population** (d=0.14).[145] Studies that initially screened participants and enrolled only those classified as sedentary or insufficiently active produced larger effects (d=0.37) relative to studies that did not screen participants for physical activity level (d=0.12).[145] The Davies et al[145] meta-analysis, which targeted either physical activity only (N=21) or physical activity and additional health-related behaviors, such as nutrition or weight management behaviors (N=13), found that the two different types of interventions produced similar effect sizes.

In a systematic review of nine web-based physical activity interventions in individuals with **type 2 diabetes**,[144] six studies reported significant short-term increases (less than 6 months, typically) in physical activity when compared with a control arm. The overall magnitude of the physical activity increases reported in this review ranged from 3 percent to 125 percent. In a systematic review of seven self-guided web-based physical activity intervention trials among patients with a range of chronic disease conditions (e.g., multiple sclerosis, heart failure, type 2 diabetes mellitus, physical disabilities, metabolic syndrome),[143] three studies reported significant physical activity improvements relative to controls, while four studies reported nonsignificant differences between groups.[143] Effect sizes ranged from 0.13-0.56, with wide variability in physical activity change across studies.

Features of physical activity intervention targets and measures: Physical activity outcome variables consisted mainly of self-reported total (overall) physical activity or leisure time physical activity. Physical activity intervention targets were in general not specified.

Evidence on Specific Factors

Evidence in the reviews evaluating different racial/ethnic groups, adverse events, and cost-effectiveness is currently lacking or infrequently reported. One article of remote and web 2.0 interventions[141] noted that the seven studies reviewed, which totaled 2,892 participants, showed no evidence of an increased risk of adverse events.

For additional details on this body of evidence, visit: https://health.gov/paguidelines/second-edition/report/supplementary-material.aspx for the Evidence Portfolio.

Public Health Impact

Given the increasing access to and reach of the Internet as well as web-based programs and tools across diverse populations, these modes of intervention delivery have the potential for affecting a sizeable portion of the population. Thus, the small but significant physical activity increases that can occur from widely accessible interventions like these can have a potentially meaningful public health impact at the population level. Finding ways to continue to engage users over the longer term (i.e., beyond 3 to 6 months) is strongly indicated.

Computer-tailored Print Interventions

Source of evidence: Systematic reviews

Conclusion Statement

Moderate evidence indicates that computer-tailored print interventions, which collect user information through mailed surveys that is then used to generate computer-tailored mailings containing personalized physical activity advice and support, have a small but positive effect in increasing physical activity in general populations of adults when compared with minimal or no-treatment controls, particularly over short time periods (e.g., less than 6 months). **PAGAC Grade: Moderate.**

Review of the Evidence

Two systematic reviews were included.[141, 146] The systematic reviews included a range of 11 to 26 studies and covered an extensive timeframe: from inception to October 2012[141] and inception to May 2010.[146] The included reviews examined interventions using computer-tailored printed materials. Short et al[146] also assessed the effectiveness of materials constructed using different health behavior theories. Studies typically tailored the intervention materials on psychosocial variables (e.g., perceived barriers, motivational readiness to change physical activity), with a few tailoring on behavioral, demographic, and environmental variables. Many studies did not adequately define their tailoring variables. The majority of studies delivered the tailored print materials through the mail using either a standard letter or newsletter.

Evidence on the Overall Relationship

The majority of studies in this area produced effect sizes that were small (i.e., Cohen's *d* ranging from 0.12 to 0.35) when compared to minimal or no-intervention control arms. Effects of computer-tailored print interventions have been more variable when compared with other active interventions (e.g., targeted print, tailored websites), although no clear evidence currently indicates that more intensive web-based interventions are generally better than tailored print. One factor that is common among successful computer-tailored print interventions is that they entail multiple contacts with users (as opposed to single-contact interventions). The impacts of intervention factors other than multiple contacts (e.g., inclusion of action plans or environmental information) are less clear. Some evidence suggests that participants' pre-intervention physical activity levels may not greatly influence responses to computer-tailored print interventions, although this participant characteristic deserves further evaluation. Interventions that were explicitly derived from theory were reported to be more effective generally than those in which use of theory was not explicitly described. The most frequently used tailoring variables were psychosocial and behavioral variables (e.g., perceived barriers). Most studies in this area were of short (less than 6 months) to medium (between 6 to 11 months) duration.

Features of physical activity intervention targets and measures: Physical activity outcome variables consisted primarily of either self-reported or accelerometry-derived minutes per week of primarily moderate-to-vigorous physical activities, as well as the proportion of the sample reaching national physical activity guidelines. For single-contact interventions, a variety of physical activity types were targeted as part of the intervention, including leisure time, transport, sport activities, and moderate-to-vigorous physical activity more broadly. For multiple-contact interventions, the general type of physical activity targeted in the interventions consisted predominately of moderate-to-vigorous physical activity, with participants allowed to choose specific activities.

Evidence on Specific Factors

Evidence in the reviews evaluating different racial/ethnic groups and adverse events is currently lacking or infrequently reported. In the few studies that have compared the cost-effectiveness of computer-tailored print to other tailored interventions (e.g., tailored Internet, computer-tailored phone delivery of information), the delivery of the computer-tailored print intervention was reported to be more cost-efficient at 12 months compared to these other modalities. Some studies evaluated interventions that included both physical activity and another health behaviors (e.g., dietary change), with mixed results. The mixed results may be due in part to the use of single-contact only print interventions in most of the multiple-health behavior studies, which was found to be linked with weaker intervention effects overall.

For additional details on this body of evidence, visit: https://health.gov/paguidelines/second-edition/report/supplementary-material.aspx for the Evidence Portfolio.

Public Health Impact

Computer-tailored print interventions represent a potentially useful strategy for delivering tailored physical activity information to population segments with sufficient reading skills, particularly those who may not be able to or be interested in accessing personalized information through other technology-based or mediated platforms, such as the Internet, mobile phone applications, or phone-assisted interventions. Such subpopulations may include individuals with lower computer or technology literacy and those living in remote areas where other communication channels are lacking or unreliable. Based on the evidence, a more contact-intensive print interaction schedule may result in increased effectiveness over time, depending upon the target audience, relative to a less dense interaction schedule (e.g., one or two tailored print interactions only). The lag time typically experienced between users mailing back their informational surveys for physical activity tailoring purposes and their subsequent receipt of the print-based advice (which was, in some cases, 4 weeks) needs to be taken into account when using this intervention delivery mode.

Mobile Phone Programs

Sources of evidence: Meta-analyses, systematic reviews

Conclusion Statements

Moderate evidence indicates that mobile phone programs consisting of or including text-messaging have a small to moderate positive effect on physical activity levels in general adult populations. **PAGAC Grade: Moderate.**

Strong evidence demonstrates that the use of smartphone applications increases regular physical activity in children and adolescents. **PAGAC Grade: Strong.**

Limited evidence suggests that smartphone applications increase regular physical activity in the general populations of adults. **PAGAC Grade: Limited.**

Review of the Evidence

A total of eight reviews, including five systematic reviews[147-151] and three meta-analyses,[152-154] were included. The systematic reviews included a range of 9 to 30 studies. Reviews covered the following timeframes: from inception to October 2011,[147] inception to September 2013,[148] inception to March 2015,[149] 2000 to 2012,[150] and 2006 to October 2016.[151] The meta-analyses included a range of 11 to 74 studies. One analysis[154] covered from inception to October 2011, and Fanning et al[153] covered 2000 to July 2012. Brannon and Cushing[152] did not report the timeframe searched. The included reviews examined the effects of mobile phone interventions. The interventions used smartphones, mobile wireless devices, or personal digital assistants in a variety of ways to promote health behavior change. Two reviews[151, 152] specifically examined the use of smartphone applications (apps), while Buchholz et al[147] and Head et al[154] assessed text messaging interventions. Almost all of the studies reviewed were of short duration (i.e., less than 6 months).

Evidence on the Overall Relationship

Features of physical activity intervention targets and measures: In most studies, physical activity was measured by wearable devices (accelerometers or step-counters), or with a combination of device-based and self-reported measurement instruments. Physical activity intervention targets were focused mostly on increasing steps per day of walking, with some studies using more general forms of moderate-to-vigorous physical activity as an intervention target.

Evidence on Specific Factors

Evidence on text-messaging interventions: A systematic review[147] as well as two meta-analyses[153, 154] that examined text messaging interventions aimed at **general adult populations** found significant positive effect sizes, relative to controls, that were on average 0.40 or greater, with a median effect size in one systematic review of 0.50.[147] Studies ranged in duration from 4 to 52 weeks. However, a relatively small number of RCTs of text-messaging have been conducted to date. Although successful studies in this area have been conducted on four continents, the populations that have been studied have been primarily young to middle-aged women who were well-educated. In a number of these studies, text-messaging was used primarily to provide cues or simple messages for becoming more active, either as a primary target or as part of a weight loss program. Only a modest number of studies have occurred to date involving text-messaging interventions in persons with chronic diseases (e.g., cardiovascular disease) and no systematic reviews were found during the 2011-2016 evidence review period evaluating text-messaging interventions in youth.

Evidence on smartphone app interventions: Strong evidence exists for the efficacy of smartphone apps in **youth***.* Interventions in youth have occurred in school settings as well as in other community settings, and have studied diverse populations, including Caucasian, African American, Hispanic, southeast Indian, Moroccan, Turkish, and European samples. Interventions have been reported to have small to moderate effects in both girls and boys, with one systematic review reporting Cohen's *d* coefficients ranging from -0.36 to 0.86.[152] When the effects of different behavior change strategies that comprise the smartphone apps have been investigated systematically (i.e., through meta-analysis and meta-regression techniques), different types and combinations of strategies were found to be particularly effective in increasing physical activity levels in children versus adolescents.[152] In children, general encouragement and modeling of appropriate behavior have been found to be significant predictors of positive physical activity effects. In adolescents, providing consequences for behavior change, providing information related to others' approval, self-monitoring, and the use of behavioral contracts have been found to be significant predictors of positive physical activity effects. Of note, providing adolescents with specific instruction has been reported to diminish the effects of the intervention.[152] As part of these meta-regression analyses, investigators were able to explain 45 percent of the variability in physical activity effect size among children and 62 percent of the variability in physical activity effect size among adolescents.[152]

In contrast, relatively few rigorously controlled studies have been reported evaluating the use of smartphone applications (apps) to promote regular physical activity in **adult populations***.* Although a recent systematic review did not provide effect size estimates,[151] 11 of 21 RCTs or comparison arm studies that included a smartphone app intervention aimed at physical activity promotion reported a significant positive effect on at least one physical activity variable relative to a control or comparison arm. However, the average study duration was short (i.e., typically less than 6 months). Studies that combined the use of a smartphone app with other intervention strategies (e.g., telephone coaching, short message service (SMS), motivational emails) were more likely in general to report significant improvements on behavioral outcomes than those studies using stand-alone apps.

For additional details on this body of evidence, visit: https://health.gov/paguidelines/second-edition/report/supplementary-material.aspx for the Evidence Portfolio.

Public Health Impact

In light of their accessibility across diverse mobile phone platforms and their ability to generate moderate to strong increases in physical activity among at least some segments of the population, text-messaging and smartphone applications represent promising public health strategies that should be targeted further for investigation and intervention translation. In addition to being used alone in some population subgroups, they may serve as potentially useful adjuncts to other physical activity interventions.

Social Media

Sources of evidence: Meta-analyses; systematic reviews

Conclusion Statement

Limited evidence suggests that physical activity interventions based on or including social media are effective for increasing physical activity in adults or youth. **PAGAC Grade: Limited.**

Review of the Evidence

A total of three reviews, including one systematic review[155] and two meta-analyses,[156, 157] and a governmental report[26] were included. The systematic review[155] included 10 studies published between 2000 and December 2012. The meta-analyses included a range of 16 to 22 studies. Mita et al[156] covered 2000 to June 2014 and Williams et al[157] covered 2000 to May 2013. All of the included reviews examined health behavior interventions using web-based social media or social networking platforms. The reviews addressed changes in physical activity levels, including exercise behaviors. One review[155] also addressed physical inactivity and mediators of behavior changes, such as physical activity self-efficacy. The PAG Midcourse Report included a review of reviews of physical activity intervention studies focused on youth ages 3 to 17 years that were published January 2001 through July 2012; a total of 31 reviews containing 910 studies (not mutually exclusive) were included.[26]

Evidence on the Overall Relationship

In two meta-analyses,[156, 157] the reported SMD did not reach statistical significance (SMD=0.07; 95% CI: -0.25 to 0.38, 8 studies; SMD=0.13; 95% CI: -0.04 to 0.30, 12 studies, respectively), although the overall pattern of results for the studies targeting physical activity generally favored the intervention arm.

The available literature consists of a small number of studies that often lack rigor or the adequate reporting of study methods. This has led to a high risk of bias due to incomplete reporting of outcome data as well as study attrition rates. When reported, study attrition rates were frequently high despite often short intervention periods (i.e., less than 6 months). Study interventions were highly variable and the populations studied consisted primarily of Caucasian women of higher socioeconomic status. To date, many of the available studies have used social media platforms with relatively low levels of media richness and social presence (e.g., bulletin boards, discussion boards, message forums), as opposed to richer social media platforms (e.g., social networking sites).

The literature to date suggests that intervention effectiveness may be enhanced through focusing on social media features with stronger social presence and media richness (e.g., media content that people can share through social networking sites).

In contrast to the above web-based social media or social networking platforms, a national multi-cultural, 5-year social media/social marketing campaign called VERB™,[59] described in the PAG Midcourse Report,[26] delivered educational and motivational messages about physical activity aimed at U.S. youth ages 9 to 13 years ("tweens") and their parents through a diverse range of social communication channels. Media messages were delivered through television, radio, Internet, print media, and through school and community promotions. Among the successes of the VERB campaign were high levels of campaign awareness—approximately three-quarters of tweens surveyed were aware of the campaign, and that awareness was associated with increased likelihood of reporting being physically active relative to those who were unaware of the campaign. A significant dose-response effect was found in that greater reported exposure to campaign messages was associated with a greater percentage of children reporting physical activity on the day before the assessment interview (gamma statistic=0.19, CI 0.11-0.26, $P<0.05$), and a greater median number of weekly physical activity sessions during free-time (gamma statistic=0.09, CI 0.04-0.13, $P<0.05$).[59] At the 2004 assessment time point, there was a 22 percent difference in median number of weekly physical activity sessions during free-time among those children reporting an awareness of VERB relative to children reporting no awareness of VERB.[59] Effect sizes for the VERB awareness effect on physical activity behavior ranged from 0.06 to 0.12.[59] In addition, exposure to the VERB campaign during the tween years had carry-over value into adolescence (ages 13 to17 years).[26]

Features of physical activity intervention targets and measures: Physical activity was measured using a variety of largely self-reported variables, including estimated energy expenditure per week, moderate-intensity physical activity per week, moderate-to-vigorous physical activity per week, and total minutes of physical activity per week. Relatively few studies specified physical activity intensity targets as part of the intervention. When they were noted, they consisted of either moderate or moderate-to-vigorous physical activities.

Evidence on Specific Factors

Evidence in the reviews evaluating different racial/ethnic groups, adverse events, and cost-effectiveness is generally lacking or infrequently reported.

For additional details on this body of evidence, visit: https://health.gov/paguidelines/second-edition/report/supplementary-material.aspx for the Evidence Portfolio.

Public Health Impact

Given the growing popularity of social media, it is likely that additional rigorously designed and longer-term intervention studies will emerge over the coming years, which will provide much needed scientific information on this increasingly prevalent communication platform. Given the diversity of uses and the substantial population reach of social media platforms across broad age ranges and socioeconomic groups, this technology has the potential to affect population levels of physical activity. Intervention effectiveness may be enhanced by considering additional social media platforms (e.g., Twitter, Snapchat, Instagram) that could increase population reach. In addition, using multiple, complementary social media and communication channels, as was done in the VERB campaign, may increase the overall penetrance and impact of physical activity messages and programs for specific population groups.

Interactive Video Games Promoting Active Play or Exercise

Source of evidence: Systematic reviews

Conclusion Statements

Limited evidence suggests that active video game interventions used in structured community-based programs are effective for increasing physical activity in healthy children. **PAGAC Grade: Limited.**

Limited evidence suggests that technology-based exercise programs (i.e., “exergames”) are a potentially acceptable and safe approach for use in programs aimed at increasing physical activity levels in adults ages 60 years and older. **PAGAC Grade: Limited.**

Review of the Evidence

A total of three systematic reviews were included.[158-160] The systematic reviews included a range of 22 to 54 studies. Two systematic reviews covered an extensive timeframe: from inception to May 2015,[158, 159] while the third review covered 2000 to August 2013.[160] Two of the included reviews examined the effects of active video game interventions among children.[158, 160] Valenzuela et al[159] examined technology-based interventions among older adults, with the majority of studies using a gaming console. Included reviews addressed changes in physical activity levels. Liang and Lau[160] assessed the immediate physical activity effects (energy expenditure or physical activity levels during active video game play) as well as the habitual physical activity or change in physical activity levels. No systematic reviews dating from 2011 to 2016 were found for interactive video game interventions in general populations of adults.

Evidence on the Overall Relationship

In one systematic review of school-based active video game use to increase physical activity in **youth younger than age 18 years**,[158] 9 of 14 studies reporting physical activity outcomes found some increases in light-intensity physical activity and/or moderate-to-vigorous physical activity assessed primarily through activity monitors or questionnaires. However, several of these studies did not report significance testing or used uncontrolled pre-posttest designs. In at least five studies, higher levels of physical activity in the school setting were found in the control arm relative to the intervention arm. Two studies found that the significant increases in moderate-to-vigorous physical activity during the school-based active video game sessions did not extend to the rest of the school day or to home activity. This latter finding is supported in a second systematic review of 21 physical activity promotion studies,[160] which reported no overall effects of active video game play alone on physical activity levels in the home setting. In this systematic review, the explicit use of behavioral theory in intervention development was associated with reported improvements in physical activity in four of the five studies reporting their use.

A systematic review of 22 studies evaluated the use and acceptability of active video games among **older adults** (mean age range from 67 to 86 years) living at home or in independent living units, retirement settings, or low-care residential care facilities.[159] Active video game participation rates across the relatively short intervention periods (i.e., 3 to 20 weeks) were reported as high across delivery sites, delivery modes, and levels of supervision (median=91.3%). However, these studies have rarely reported overall physical activity behavior change as an outcome. They have been focused primarily on physical function outcomes (i.e., balance, strength, endurance, fitness). Studies in this area have been constrained by weak designs, limited reporting of study attrition, and short intervention periods.

Features of physical activity intervention targets and measures: Physical activity outcome variables included time spent during the active video game in light-intensity and/or moderate-to-vigorous physical activity, assessed primarily through either activity monitors or questionnaires. The physical activities used in the active video games were designed to mimic dance, sports (e.g., tennis, boxing, bowling), or aerobic fitness classes.

Evidence on Specific Factors

Evidence in the reviews evaluating different racial/ethnic groups and cost-effectiveness is currently lacking or infrequently reported. With respect to safety, in a systematic review of 22 studies of older adults,[159] only one study reported minor adverse events.

For additional details on this body of evidence, visit: https://health.gov/paguidelines/second-edition/report/supplementary-material.aspx for the Evidence Portfolio.

Public Health Impact

For youth, even though study quality to date generally has been poor, this work provides some indication that the use of active video games that involve structured physical activity programming in some community settings (e.g., schools) could potentially be useful in increasing physical activity levels during the in-school period. Such observations require more rigorous evaluation, including assessment of potential compensation effects (e.g., increased sedentary behavior) during post-school home and leisure time.

For older adults, even though initial short-term evaluations of active video games have reported them to be a potentially acceptable, feasible, and safe exercise modality in suitably screened and supervised groups of older adults, few data currently exist related to their effectiveness in increasing overall physical activity levels.

PHYSICAL ENVIRONMENT AND POLICY LEVEL

Environmental- and policy-level interventions broadly include those that focus on features of a locale that relate directly to the built environment (e.g., access to parks, trails, or recreational facilities; pedestrian or bicycling infrastructure), or to laws, local ordinances, organizational policies, and institutional practices that can influence physical activity levels. Relevant types of interventions or physical activity-inducing features typically have included point-of-decision prompts to promote stair use, as well as features of land use or design (e.g., proximity and access to parks, trails, and natural spaces; mixed land use and infrastructure to promote active commuting; levels of street connectivity and residential density).[161-163] Other neighborhood characteristics, including perceptions of neighborhood walkability, aesthetics, and perceptions of safety or crime, also have been studied.[107, 161-163] Some physical activity interventions that could be included at the environmental and policy level have been reviewed elsewhere in this report, most notably those occurring in school-based settings, such as the availability of outdoor playground spaces and equipment, and environmental features supporting active recess.

In contrast to other levels of impact, environmental and policy approaches are, by their nature, constrained by the inherent difficulties and challenges in conducting this type of contextually complex research. Because of this, the Subcommittee weighed size and consistency of results along with the use of longitudinal and quasi-experimental designs more heavily in this evidence area relative to the other evidence areas where experimental designs are more feasible. Notably, although a large amount of the evidence to date has used cross-sectional designs, investigators have made a concerted effort in recent years to advance the field through employing stronger longitudinal, quasi-experimental, and natural experimental designs such as the Residential Environments Project (RESIDE) conducted in Australia.[164] These combinations of evidence have brought increased scientific rigor to the evaluation of the field.

For each of the types of environmental- and policy-level interventions reviewed here, evidence evaluating differences in exposure to environmental interventions by different racial/ethnic groups or intervention strategies tailored to specific racial or ethnic populations was generally scarce or absent. Individual studies cited in the review for point-of-decision prompts did at times focus on culturally relevant messaging or signage, although not consistently.[107, 165]

As noted earlier, the categories were not identified a priori and were not specifically included as search terms, but rather emerged during the broad 2011-2016 evidence search that was undertaken. Such a condensed approach necessarily limits the size and, potentially, the types of evidence considered at this level.

Point-of-Decision Prompts to Promote Stair Use

Sources of evidence: Systematic reviews and reports

Conclusion Statement

Strong evidence demonstrates that interventions that target point-of-decision prompts to use stairs versus escalators or elevators are effective over the short term in increasing stair use among adults. **PAGAC Grade: Strong.**

Review of the Evidence

Two systematic reviews[165, 166] and the AHA Scientific Statement[107] were included. The systematic reviews included a range of 6 to 67 studies. The following timeframes were covered in the systematic reviews: inception to July 2015,[166] 1970 to 2012.[165] The American Heart Association Scientific Statement covered January 1, 2007 through publication.[107]

The included reviews examined different approaches to increasing stair use as a means of promoting physical activity behavior. Most studies used a single strategy of signage, placed at the decision point for choosing to take the stairs or an escalator or elevator. The signage messages typically included health and weight control benefits, such as the amount of calorie expenditure accompanying stair use, or distance traveled. Other strategies included music, artwork, or other methods for improving stairwell attractiveness.

Outcomes focused on stair use or stair climbing assessed largely through behavioral observation methods. A few studies used technology-based methods, such as counting machines or videotaping.

Evidence on the Overall Relationship

Evidence for this category comes largely from quasi-experimental studies, with controlled before-and-after studies or interrupted time series designs.[107, 166] Few RCTs have been conducted.[107] Studies were conducted in different community settings (e.g., transit hubs, worksites, hospitals, shopping malls). Most studies were short term, with one systematic review finding that most ranged from 4 to 12 weeks.[165] In another review,[166] two of three studies had durations of 12 or fewer weeks. In one systematic review of 67 studies, 77 percent reported increases in stair use.[166] For those studies with significant effects (N=55 studies), the percent stair use increase ranged from 0.3 percent to 34.7 percent. When odds ratios were reported, they ranged from 1.05 (95% CI: 1.01-1.10) to 2.90 (95% CI: 2.55-3.29).[166] According to Jennings et al,[166] a variety of intervention characteristics (i.e., single versus multiple intervention strategies; single versus multiple messages; poster size) yielded similar effects. Other characteristics (i.e., inclusion of text and images [89%] versus text-based only [75%]; a focus on time [88%] and fitness [85%] versus health [78%] messages) appear to be promising areas to explore further. Improvements in stair use were found across different settings, such as public (80% reported significant improvements) and worksite settings (67% reported significant improvements). Several studies have reported that positive point-of-decision prompt effects were observed across population subgroups varying in different characteristics, such as age, sex, and weight status. One study included in the reviews[167] found a stronger positive effect for participants estimated to have overweight than those having normal weight status. Two studies that were reviewed found an interaction between sex and age such that older women were the least likely to use the stairs.[168, 169]

Built Environment Characteristics That Support Active Transport

Sources of evidence: Systematic reviews, reports

Conclusion Statement

Moderate evidence indicates that built environment characteristics and infrastructure that support active transport to destinations (e.g., Safe Routes to School programs, street connectivity, a mix of residential, commercial, and public land uses) are positively associated with greater walking and cycling for transport among children, adults, and older adults compared to environments that do not have these features. **PAGAC Grade: Moderate.**

Review of the Evidence

Three systematic reviews,[165, 170, 171] one meta-analysis,[172] and two reports[107, 161] were included. The systematic reviews and reports included a range of 12 to 42 studies. *The Guide to Community Preventive Services*[161] included seven studies that reported on transportation-related walking and cycling. The following timeframes were covered in the systematic reviews: inception to December 2016,[161] January 2000 to September 2016,[172] inception to June 2009,[170] inception to November 2014,[171] and 1970 to 2012.[165] The AHA Scientific Statement covered January 1, 2007 through publication.[107]

Environmental characteristics being evaluated consisted of geographical information systems (GIS)-assessed or self-reported environmental factors, including land-use mix, pedestrian and cycle routes, road design, and urban planning policies (e.g., provision of parks, trails, or open space). The studies represented a mix of cross-sectional and longitudinal study designs. Two studies examined interventions to promote active transport. Examples included a walking school bus program (i.e., a group of children walking to school with one or more adults), Safe Routes to School programs,[165] RCTs evaluating support for active commuting,[171] pre-post designs examining polices such as Ride to Work Day, and changes in cycle infrastructure.[171]

Outcomes included self-reported transport physical activity (e.g., total walking for transport, within-neighborhood walking for transport, cycling for transport, total active travel). Outcomes also included changes at an aggregate population level (e.g., percent cycling to work, number of days cycling, percent walking or cycling to school, overall physical activity).

Evidence on the Overall Relationship

Longitudinal evidence described in The Community Guide highlights the results of a large natural experiment (RESIDE)[164] and multiple smaller prospective quasi-experimental studies finding significant increases in active transport over time in response to supportive environmental characteristics (e.g., walkability, land-use mix or destinations). The RESIDE study examined changes in physical activity based on built environment characteristics among those who moved to new neighborhoods compared with those who did not. Longer-term follow-up (i.e., 7 years) of this natural experiment indicated increases in active transportation, with perceptions of safety and the environment related to physical activity change. These results indicated, for example, that each unit increase in perceived safety from crime was associated with 3.2 minutes per week more of transport physical activity. In addition, the association remained similar (3.6 minutes per week increases with unit increases in perceived safety from crime) when also controlling for built environmental characteristics such as residential density, streets connectivity, and number of local destinations, which together comprise many walkability indices.

The above experimental and quasi-experimental studies notwithstanding, a large proportion of the evidence in this area comes from cross-sectional studies. A number of such studies also support the relationship between environmental characteristics and active transport behavior in general adult populations. Of the cross-sectional studies reported in The Community Guide, 18 out of 27 studies (66.6%) found higher transport walking or cycling to be associated with more favorable walkability indices.[161] In addition, of 11 cross-sectional studies that compared residents in more versus less activity-supportive environments, the Community Guide found that those living in more activity-supportive environments had higher transport-related walking (median=37.8 minutes) and recreational walking (median=13.7 minutes) per week.

The AHA Scientific Statement found evidence in favor of land-use mix, identifying at least 18 cross-sectional observational studies finding a relationship with physical activity in adults.[107] Those studies that included specific outcomes for active transport found a similar pattern. For example, one study[173] found that adults reporting more destinations (i.e., 7 to 13) within a 5-minute walking distance were more likely to walk for transport than those who did not report any destinations within a 5-minute walking distance (OR=2.4; 95% CI: 1.3-4.3). A similar pattern emerged when number of destinations was captured using environmental audit tools. Those data indicated that persons living in neighborhoods with more non-residential destinations had higher transport-related walking than those living in neighborhoods with fewer such destinations (OR=3.5; 95% CI: 2.3-5.5). For youth, eight systematic reviews were included, with positive associations found between land-use mix and children's physical activity (OR ranged from 1.8 (95% CI: 1.05-3.42) to 3.46 (95% CI: 1.6-7.47)), particularly when active commuting to school was included. Some studies examined safety (i.e., traffic and crime) and its associations with walking to school or other neighborhood destinations among children or adolescents. Across two individual systematic reviews[174, 175] that were included in the AHA Scientific Statement,[107] six of nine studies that examined traffic safety found a significant association between road safety and active travel. These systematic reviews[174, 175] also included 12 studies that examined crime-related safety assessed through parental perception and active transport. Four out of 12 studies found a significant inverse association. One such study found that lower parent safety concerns were associated with a 5.2 higher odds of active commuting to school.

Among older adults, consistent links have been found between both perceived and objectively assessed neighborhood characteristics and active transport.[172] A meta-analysis of 42 quantitative studies found significant positive associations among a number of environmental variables and active transport behaviors, including residential density and urbanization, walkability, easy access to building entrances, and access to and availability of services and destinations. A weak, negative association was found between neighborhood disorder (e.g., litter, vandalism and decay) and total walking for transport.

Fraser and Lock[170] examined relationships among active transport policies, such as those relating to cycle paths or routes and other urban planning features (e.g., road design, provision of parks or trails), as well as policies supporting Safe Routes to School programs. Twenty-one studies were reviewed, of which 16 were cross-sectional surveys (with 8 of those using GIS), 3 included some longitudinal information, 1 was observational and examined cycle routes, and 1 was a secondary analysis of census information. Eleven of the 21 studies found a positive association between environmental factors and cycling. Fraser and Lock[170] included seven studies examining active transport patterns and environmental factors associated with active commuting to school programs among children. An example of one such program was the California Safe Routes to School program. A cross-sectional evaluation of this program reported that when the program was part of children's normal routes to school, 15.4 percent of children walked or cycled versus 4.3 percent of children for whom it was not present.

Two reviews examined specific policy or environmental interventions to promote active transport. Stewart et al[171] reviewed 12 studies from six countries, including two RCTs and 10 pre-intervention or post-intervention designs. Seven of the studies examined individual or group-based interventions conducted through community and workplace settings (e.g., cycle training, ride to work days, materials such as maps, activity diaries), and five involved environmental interventions, such as construction of a bridge or changes in cycling infrastructure. Of the seven individual or group interventions, six of seven found increases in cycling for transport; however, only three of six of those studies reached statistical significance. The environmental interventions were found to have small positive effects. Reynolds et al[165] specifically examined 10 active transport interventions (e.g., Safe Routes to School, walking school buses, workplace-based active transport interventions) and reported support for an increased prevalence of walking to school and distance walking to school across the interventions.

Community Design and Characteristics That Support Recreational Physical Activity

Sources of evidence: Systematic review, reports

Conclusion Statement

Moderate evidence indicates that community design and characteristics that support physical activity, such as having safe and readily usable walking and cycling infrastructure and other favorable built environment elements are positively associated with greater recreational forms of physical activity among children and adults compared to environments that do not have these features. **PAGAC Grade: Moderate.**

Review of the Evidence

One systematic review,[162] one scientific statement,[107] and one report[161] were included. Brennan et al[162] reviewed 396 study groupings (i.e., articles reporting on the same type of intervention were collapsed) (N=600 total studies). The AHA Scientific Statement included 19 studies (15 systematic reviews/meta analyses that included 7 for children and 8 for adults) and 7 original articles (4 for children and 3 for adults) that focused on sidewalk and street design.[107] The Community Guide included 11 studies that assessed the effects of changes to characteristics of the built environment ("construction projects"), 6 studies related to sprawl and activity supportive environments, 7 studies of pre-defined neighborhood types (i.e., ones that are more versus less supportive of physical activity), and 66 studies of summary scores of existing built environments or comparisons across communities.[161] The following timeframes were covered: inception to December 2016,[161] 2000-2009,[162] and January 1, 2007 through publication.[107]

The included reviews examined the relationships between recreational physical activity and a number of different environmental features, including pedestrian infrastructure (e.g., sidewalk availability) street design (e.g., street connectivity), GIS-measured characteristics of the environment, self-report of various environmental characteristics, construction or other changes to the built environment, and neighborhood walkability indices.

Outcomes included associations with measured total physical activity, recreational walking and cycling, moderate-to-vigorous physical activity, and, in some instances, change in physical activity over time.

Evidence on the Overall Relationship

The Community Guide summarized the results of larger and smaller scale longitudinal studies.[161] Longitudinal evidence from these investigations, including the large RESIDE study,[164] has provided valuable information concerning the impacts of environmental characteristics on recreational physical activity over time. The results from RESIDE indicated that each unit increase in perceived safety from crime was associated with 13.5 minutes per week more of recreational physical activity over a 7-year follow-up period. This amount of increase remained similar (13.7 minutes per week) when also controlling for additional built environmental characteristics (i.e., residential density, streets connectivity, and mix of local destinations).

In addition to RESIDE, the Community Guide reviewed 10 smaller-scale longitudinal studies that focused on neighborhood or community projects.[161] For recreation-related walking and cycling, two of two studies showed favorable results. For moderate-to-vigorous physical activity overall, including recreational activity, two of two studies showed favorable results.

Additionally, The Community Guide reviewed 11 cross-sectional studies comparing environments that were more versus less supportive of physical activity, finding that adults in neighborhoods that were more environmentally supportive of physical activity reported a median of 50.4 more minutes per week of moderate-to-vigorous physical activity and averaged about 13.7 minutes more of recreational walking compared with neighborhoods that were less supportive.[161]

Walkability indices (i.e., summary scores reflecting a combination of built environment characteristics, such as street connectivity, residential density, and land-use mix) also have been used in a number of cross-sectional studies to evaluate recreation-related walking and cycling. Based on a review of 16 such studies in The Community Guide that used walkability indices to capture the built environment, 10 of 16

(62.5%) showed favorable associations, such that higher levels of recreation-related walking and cycling were associated with higher walkability indices. This finding was consistent when moderate-to-vigorous physical activity was used as the physical activity outcome, with 12 of 19 (63.2%) studies finding higher levels of moderate-to-vigorous physical activity to be associated with higher walkability indices.

In addition to studies that specifically measured recreational physical activity, some studies reported on more general categories of physical activity that included recreational physical activity. Studies included in the AHA Scientific Statement examined such outcomes separately for children and adults.[107] Of the seven systematic reviews focusing on children or adolescents, all seven included outcomes related to pedestrian infrastructure and all reported evidence to support significant associations. Characteristics of the pedestrian infrastructure and type of outcome varied, with some examining presence of sidewalks, while others examined sidewalk improvements or bicycle and walking trails. Outcomes included walking or cycling for transport or recreation. Of the seven systematic reviews, four included outcomes related to street design, and found street connectivity to be positively associated with general physical activity levels. Among adults, of the nine systematic reviews/meta analyses, eight focused on pedestrian infrastructure, with mixed results. For example, the presence of sidewalks was significantly associated with physical activity behavior (i.e., walking, meeting physical activity guidelines) in about half.

Similarly, Brennan et al[162] reviewed 396 study groupings (N=600 studies) for 24 policy or environmental intervention strategies for physical activity and obesity. Their review provided an additional assessment related to neighborhood design and infrastructure, from which they positively categorized activity-supportive community design (i.e., land use, commercial or residential proximity that supports physical activity) and street design (i.e., pedestrian, bicycle or transit oriented design to support physical activity).

In the Community Guide,[161] of the 18 studies that reported on total walking, assessed through questions which typically included leisure time or recreational physical activity, 12 (66.6%) reported positive associations with walkability indices. Among those assessing total physical activity, 4 of 14 studies (28.6%) were reported as significant. Five studies examined the percentage of individuals reaching recommended levels of moderate-to-vigorous physical activity, with three out of five studies (60%) reporting significant associations with walkability indices.

In addition, for adults, the largely cross-sectional studies reviewed by the AHA Scientific Statement generally indicated a significant relationship between neighborhood aesthetics and leisure-time physical activity, walking, or meeting physical activity recommendations (ORs ranged from 1.13 to 2.6).[107]

Neighborhood safety and crime are environmental factors that have been explored in several different ways. These include the associations between parent perceptions of neighborhood safety and child physical activity, and associations between personal- and crime-related safety as well as traffic-related safety among adults. For children, the findings generally support a positive association between parental perceptions of safety and child recreational physical activity. For adults, in one meta-analysis[176] cited by the AHA Scientific Statement,[107] absence of heavy traffic was associated with more walking and leisure-time physical activity (OR=1.22; 95% CI: 1.08-1.37). No effect sizes were provided for crime-related safety.

Access to Indoor and/or Outdoor Recreation Facilities or Outlets

Sources of evidence: Systematic reviews, report

Conclusion Statement

Moderate evidence indicates that having access to indoor (e.g., gyms) and/or outdoor recreation facilities or outlets, including parks, trails, and natural or green spaces, is positively associated with greater physical activity among adults and children compared to environments that do not have these features. **PAGAC Grade: Moderate.**

Review of the Evidence

Three systematic reviews,[177-179] and one report[107] were included. The systematic reviews and reports included a range of 12 to 90 studies. The following timeframes were covered in the systematic reviews: inception to October 2013,[178] inception to July 2014,[179] and 1990 to June 2013.[177] The AHA Scientific Statement covered January 1, 2007 through publication in 2012.[107] The variables included in this section were exposure to indoor and outdoor facilities in which to participate in physical activity. Access measures included objective (e.g., number of facilities, distance from park) and perceived measures of access. Outcomes included primarily walking, cycling, and total physical activity.

Evidence on the Overall Relationship

The AHA Scientific Statement found evidence to support improved accessibility to indoor and outdoor recreational facilities for physical activity promotion.[107] Greater access generally was shown to be related to more physical activity among adults (OR 1.20; 95% CI: 1.06-1.34).[176] Among children, 9 of 13 cross-sectional studies supported the relationship between accessibility and youth physical activity, particularly for girls.

For the specific case of access to parks and trails, some evidence (four of nine studies) supported the implementation of built environment interventions for encouraging use specifically of urban green space. More promising evidence (three of three studies) exists for a combined approach (i.e., changes to the built environment such as building a new footpath and a physical activity promotion campaign or skills development program).[179] Other studies indicated more mixed associations between exposure to parks and green space and physical activity levels.[177, 178] In one review of 20 studies, 5 (25%) reported a positive association between parks and physical activity.[177] Some factors noted by Bancroft et al[177] for the inconsistency of effects across these studies were heterogeneity in reporting standards, including variations in the distances used to categorize density of and proximity to parks, and a mix of objective and self-reported physical activity measures.

Evidence on Specific Factors

Evidence in the reviews evaluating different racial/ethnic groups and adverse events is currently lacking or infrequently reported. One systematic review[180] examined 27 studies to summarize the cost-benefit or cost-effectiveness of environmental and policy-related interventions. Of the 27 studies, 8 focused on community and built environments for physical activity. Some of the types of interventions related to physical activity included physical activity equipment in parks, access to recreation and fitness centers, bicycle or trail networks and infrastructure, and Open Streets programs (i.e., urban streets and pathways made more accessible for walking, cycling, and other forms of physical activity through temporarily reducing motor vehicle access). Most of the studies reported economic benefit for these types of interventions. For example, the cost-benefit ratio of the Open Streets program in four international cities ranged from 1.02 to 1.23 in Guadalajara, Mexico, to 2.23 to 4.26 in Bogotá, Colombia.[181] Another study included in the McKinnon et al[180] systematic review calculated a cost-benefit ratio of 2.94, such that every $1 of investment in bicycle or pedestrian trail development resulted in a calculated $2.94 direct medical or health benefit (i.e., estimation of direct medical cost difference for active versus inactive).[182]

For additional details on this body of evidence, visit: https://health.gov/paguidelines/second-edition/report/supplementary-material.aspx for the Evidence Portfolio.

Public Health Impact of All Physical Environment and Policy Level Interventions Reviewed

Given the ubiquitous nature of the environmental contexts surrounding "place-based" behaviors, such as physical activity, the ramifications of identifying and promoting the types of environments that are most conducive to supporting and facilitating regular physical activity across the population are immense. The evidence indicates that a diverse array of environmental factors and features can influence physical activity levels across different age groups and community settings, including schools, worksites, transit hubs, parks, neighborhoods, and residential settings. Most of this evidence, however, has focused on urban environments, with relatively little information currently available related to environmental features that may influence physical activity behavior in rural settings.

In addition, because environmental and policy level approaches are often inextricably intertwined, systematic reviews of these two approaches were considered together. Relatively little systematic evidence was found during the 2011 to 2016 evidence search period evaluating the effects of specific policies related to urban sprawl, land-use mix, and other factors on different types of physical activity and for different population segments. Only one review was located during this time period that focused specifically on policy approaches for physical activity promotion.[162] This review was primarily descriptive in nature, and characterized land use policies and school physical activity policies as among the most promising of those policy domains that have been studied.[162] A few other policy-specific studies were described briefly as part of other reviews, including one prospective study using a time-series analysis, described in The Community Guide,[161] which reported positive impacts of urban sprawl curtailment policies on physical activity levels.[183] The Community Guide also reviewed five cross-sectional studies that used sprawl indices to examine the relationship between urban sprawl and physical activity behavior. Four of the five studies (80%) found a relationship between less sprawl and higher physical activity across various physical activity domains (transport, recreation, total physical activity, and walking). In contrast, the AHA Scientific Statement[107] reported finding little evidence evaluating the effectiveness of such regulatory approaches for promoting physical activity. Taken together, these reviews suggest that while the policy intervention literature does not currently have sufficient evidence to receive an evidence grade, their potentially far-reaching impacts, both alone and in combination with environmental and related interventions, merit further systematic investigation.

Question 2. What interventions are effective for reducing sedentary behavior?

As described in *Part F. Chapter 2. Sedentary Behavior,* a sufficient body of evidence now exists to substantiate the role of sedentary behavior patterns on an array of health outcomes. In light of the detrimental effects of extended patterns of daily sedentary behavior on the public's health, a growing evidence base is aimed at developing and evaluating interventions targeted specifically at reducing prolonged sitting and related sedentary behaviors in youth and adults. Sedentary behavior interventions are defined as those strategies that target reductions in sedentary behavior outcomes, which may include self-reported or context-specific forms of sedentary behavior (e.g., television viewing), accelerometer- or movement-based outcomes, or posture-based outcomes (e.g., lying or seated behaviors at less than 1.5 METs). These behaviors are ubiquitous, habitual, and socially-reinforced in modern societies. In addition, a number of the environmental, social, and individual-level determinants of sedentary behavior appear to be distinct from those associated with physical activity. The presence of unique determinants that influence sedentary behavior supports the development and testing of specific intervention strategies and approaches to reducing sedentary time—a number of which may be separate from methods aimed directly at increasing physical activity.

The 2011 to 2016 evidence review yielded three primary domains of evidence about interventions aimed at reducing sedentary behavior. These domains include youth interventions (i.e., interventions targeting populations ages 3 to 18 years with the primary goal of reducing television and other screen-based behaviors), adult interventions (i.e., interventions aimed at adult populations with the primary goal of reducing overall and context-specific forms of sedentary behavior such as television viewing or transport-related sedentary time), and worksite interventions (i.e., interventions targeting sedentary behavior in the work place).

As noted earlier, the categories were not identified a priori and were not specifically included as search terms, but rather emerged during the broad 2011 to 2016 evidence search that was undertaken. Such a condensed approach necessarily limits the size and, potentially, the types of evidence considered for this question. It should be noted that, given the relative newness of the sedentary behavior interventions field, the overall evidence base was smaller for this field compared to the physical activity promotion field. However, this newer evidence base tended toward more rigorous methods (i.e., meta-analysis of RCTs).

YOUTH INTERVENTIONS

Sources of evidence: Meta-analyses, systematic reviews

Conclusion Statement

Moderate evidence indicates that interventions targeting youth, primarily through reductions in television viewing and other screen-time behaviors in primarily school-based settings, have small but consistent effects on reducing sedentary behavior. **PAGAC Grade: Moderate.**

Review of the Evidence

Four meta-analyses[184-187] and five systematic reviews[158, 188-191] were included. The meta-analyses included a range of 13 to 34 studies. The systematic reviews included a range of 10 to 22 studies. Studies overall covered an extensive timeframe, including a number from inception through 2015. The majority of studies reviewed focused on youth ages 3 to 18 years. Although most reviewed studies focused primarily on the school setting,[158, 184, 186-188, 190] some included other clinical, community, or home settings.[185-187, 189, 190] The majority of studies reviewed were at least 6 months in duration, although study duration ranged from 3 weeks to 4 years. The majority of studies targeted television and other screen-time behaviors as the primary outcome of interest, while some quantified changes in overall[158] and school-based sedentary time.[191] Interventions were delivered by educators, parents or families, healthcare providers, and researchers.

Evidence on the Overall Relationship

Studies varied in intervention targets—some interventions focused on sedentary behavior exclusively and others targeted multiple health behaviors simultaneously. As a whole, the studies reviewed showed small but consistent effects on sedentary behavior reduction (e.g., mean difference was −20.44 minutes per day; 95% CI: -30.69 to -10.20),[185] with no trends evident for greater efficacy from either multiple behavior change interventions (i.e., sedentary behavior plus physical activity and/or dietary interventions) or sedentary behavior-only interventions. The studies had a small trend for community- or home-based interventions to show somewhat greater efficacy compared to interventions in other settings (e.g., school settings), as well as a trend for accelerometer-based studies to show somewhat greater efficacy than studies with self-reported outcomes.[187] School-based interventions focused primarily on reducing screen time in children through in-class or after-school curricula, and typically included messages targeting screen time as well as other health behaviors (e.g., exercise, diet). Such interventions had small but consistent effects in reducing sedentary time, particularly for those lasting longer than 6 months (e.g., mean difference was −0.25 hours per day; 95% CI: -0.37 to -0.13).[184] Accelerometer-based studies generally showed greater reductions in sedentary behavior than did studies with self-reported outcomes. It was not clear from the evidence reviewed, given the general lack of health outcomes assessed in a number of the intervention studies, whether the small but consistent reductions in sedentary behavior were large enough to produce or maintain positive health outcomes. In addition, although the studies suggested that longer-term interventions were able to maintain their efficacy, few studies measured or demonstrated sustainability of sedentary reductions once the intervention ended.

Evidence on Specific Factors

Evidence in the reviews evaluating effects in different racial/ethnic groups, adverse events, and cost-effectiveness is currently lacking or infrequently reported.

Features of sedentary behavior intervention targets and measures: Interventions commonly employed school-based counseling or tailored feedback to reduce screen time behaviors. Parental involvement also was often implemented, including sending newsletters home or inviting parents to attend workshops. Most school-based programs were integrated into existing curricula and were delivered over extended time periods. Less common strategies included the installation of sit-stand desks in classrooms. The most commonly reported outcome was self-reported screen time behaviors (e.g., watching television, DVD or video viewing, electronic gaming, computer-based activities, and small screen activities) in minutes per day. Other less commonly reported outcomes were steps per day (pedometer) and accelerometer-based energy expenditure changes.

For additional details on this body of evidence, visit: https://health.gov/paguidelines/second-edition/report/supplementary-material.aspx for the Evidence Portfolio.

Public Health Impact

Given the rapid growth of new and varied platforms for media consumption and growing concerns about prolonged sedentary time and sitting among youth, interventions targeting reductions in screen time are appealing and have the potential for widespread and substantive decreases in overall sedentary time across the day. The overall conclusion that these types of approaches have small but consistent effects suggests opportunities for increasing the intensity and/or robustness of the intervention approaches to enhance overall efficacy. Although the vast majority of studies focused primarily on school-based settings, a small number of studies suggested potentially promising effects on screen time using home-based interventions. Also of note was the extended length of the interventions (i.e., 6 months or more) and the similar efficacy found for interventions that targeted screen time solely versus those focused on multiple behaviors. These findings support the feasibility of carrying out these types of interventions over sustained periods of time, either alone or in combination with other important health behavior intervention targets (e.g., physical activity, diet).

ADULT INTERVENTIONS

Sources of evidence: Meta-analyses, systematic reviews

Conclusion Statement

Limited evidence suggests that sedentary behavior interventions targeting decreases in overall sedentary time in general adult populations are effective. **PAGAC Grade: Limited.**

Review of Evidence

Four meta-analyses[154, 192-194] and one systematic review[151] were included. The meta-analyses included a range of 19 to 36 studies. The systematic review included 30 studies. Studies overall covered an extensive timeframe, with most including studies from inception through 2015. The studies reviewed included adults ages 18 to 94 years, and focused on general behavioral change approaches for reducing sedentary time[192, 193] or technology-mediated interventions.[151, 154, 194] Most interventions reviewed were of short duration (less than 3 months).

Evidence on the Overall Relationship

Behavior interventions targeting some combination of physical activity, diet, and/or sedentary behavior had small and variable effects in adults for reducing sedentary time (e.g., in one review only 6 of 20 studies showed significant effects, with a mean difference of -24.18 minutes per day [95% CI: -40.66 to -7.70]).[193] Interventions targeting sedentary behavior exclusively had the most promising effects (e.g., mean difference= -41.76 minutes per day [95% CI: -78.92 to -4.60]). However, these studies were of short duration (less than 3 months), had limited follow-up, and were of poor scientific quality due to lack of blinding and large effect variability.[193] Interventions targeting physical activity exclusively had limited to no effect on overall sedentary behavior (e.g., only 6 of 19 studies showed significant effects, with a mean difference of -0.22 hour per day [95% CI: -0.35 to -0.10]).[192] Evidence on the use of technology-mediated approaches to reduce sedentary behavior in adults (e.g., smartphone apps, text messages) was reported to be scarce.[151, 154, 194]

Evidence on Specific Factors

Evidence in the reviews evaluating different racial/ethnic groups, adverse events, and cost-effectiveness is currently lacking or infrequently reported.

Features of sedentary behavior intervention targets and measures: Interventions included education/behavioral approaches to reducing sedentary time, either alone or in combination with interventions aimed at increasing physical activity and/or changing dietary intake. Sedentary behavior reduction strategies included the use of television-limiting devices, smartphone apps, and text messaging services that delivered sedentary behavior reduction advice and education, and behavioral strategies such as goal setting and action planning. Sedentary behavior was measured using a variety of objective and self-report methods. Most studies used a self-reported estimate of total sedentary time, and expressed reductions in sedentary time in minutes per day or hours per day. Some studies also reported context-specific reductions in sedentary time (i.e., television viewing, transport-related sedentary behavior). Few studies used accelerometer-measured reductions in energy expenditure, number of sitting breaks, and number of prolonged sitting events.

For additional details on this body of evidence, visit: https://health.gov/paguidelines/second-edition/report/supplementary-material.aspx for the Evidence Portfolio.

Public Health Impact

The evidence is currently limited for approaches that target overall sedentary time in adults. This is due largely to variability in the number of behaviors being targeted in interventions that report outcomes on sedentary time and the varied approaches implemented. Substantial evidence shows strategies targeting solely increases in physical activity are not effective at reducing sedentary time. Multiple behavior change approaches showed mixed and inconsistent results, while the most promising approaches were those that targeted sedentary behavior exclusively.

WORKSITE INTERVENTIONS

Source of evidence. Meta-analyses, systematic reviews

Conclusion Statement

Moderate evidence indicates that interventions targeting sedentary behavior in worksites—particularly among workers who perform their job duties primarily while seated—have moderate to large short-term effects in reducing sedentary behavior. **PAGAC Grade: Moderate.**

Review of Evidence

Two meta-analyses[195, 196] and two systematic reviews[197, 198] were included. The meta-analyses included a range of 8[196] to 21[195] studies. The systematic reviews included 15[198] and 40[197] studies. Studies reviewed were from inception through 2015. The ages of the individuals in the studies were primarily 18 to 64 years, and most were office workers who performed their job duties primarily while seated. The interventions reviewed included educational or behavioral and environmental strategies (e.g., motivational or educational signage placed in public locations, moving printers and/or waste bins to more central locations farther away), physical changes to work stations (e.g., sit-stand workstations, treadmill desks, portable pedal machines), stair use promotion, and worksite-supported policy changes (e.g., walking meetings). Most interventions reported lasted 3 to 6 months.

Evidence on the Overall Relationship

Interventions that focused on providing educational or motivational support showed only small and inconsistent effects on sedentary behavior (e.g., mean difference was -15.52 minutes per 8-hour workday [95% CI: -22.88 to -8.16]).[195] Interventions that targeted physical changes to work stations (i.e., predominantly the addition of sit-stand workstations, with a few that used treadmill desks or portable pedal machines) had consistently medium to large effects (e.g., mean difference was -72.78 minutes per 8-hour workday [95% CI: -104.92 to -40.64]). Additionally, these effects were stronger when these types of work station changes were combined with educational and behavioral support (e.g., mean difference was -88.80 minutes per 8-hour workday [95% CI: -132.69 to -44.61]).[195] A number of these studies used less rigorous nonrandomized designs, shorter-term follow-ups (3 to 6 months), and small sample sizes.[196] Walking workstations and cycle ergometers appeared to have more limited efficacy compared to sit-stand workstations in reducing sedentary time (i.e., sitting) in the workplace.[196]

Evidence on Specific Factors

Evidence in the reviews evaluating different racial/ethnic groups, adverse events, and cost-effectiveness is currently lacking or infrequently reported.

Features of sedentary behavior intervention targets and measures: Intervention strategies were varied, with the most prominent intervention strategy being the addition of a sit-stand workstation at the employee's primary work location. Other strategies, tested singly or in combination, were education or behavioral approaches, computer prompts, mindfulness instructions related to sedentary time, e-newsletters, walking strategies, and environmental or policy changes in the workplace. The primary measure of sedentary behavior was device-measured sedentary or sitting time during work hours, typically expressed in 8-hour units for comparability across varying work times. Fewer studies included self-reported total sedentary time and reported sitting time, with some of these studies using a text message-based experience sampling methodology.

For additional details on this body of evidence, visit: https://health.gov/paguidelines/second-edition/report/supplementary-material.aspx for the Evidence Portfolio.

Public Health Impact

Given that working adults—particularly those who perform their job functions while seated—spend a substantial portion of their overall day sitting at work, a strong rationale exists for targeting reductions in sedentary time through the workplace. These workplace interventions also are appealing because they may complement physical activity interventions and can be implemented during times when physical activity is generally not feasible. The evidence suggests moderate to large short-term effects for some sedentary behavior intervention approaches. More specifically, it appears that environmental supports (e.g., sit-stand workstations) may be needed to achieve substantive changes in sedentary time in work settings, particularly among office workers and those with similar job types. Educational and behavioral support approaches alone do not appear robust enough to produce substantive impacts on workplace sedentary behavior. However, combining environmental, education or behavioral, and policy changes aimed at reducing prolonged sedentary behavior in the workplace yielded the strongest effects. The quality of the reported evidence (i.e., short duration interventions, nonrandomized designs) prevented a stronger evidence grade. However, it should be noted that two recent large-scale cluster RCTs of 3-month[199] and 12-month durations[200] that were not able to be included in this evidence review demonstrated similar efficacy to the studies reviewed here.

NEEDS FOR FUTURE RESEARCH

The evidence review in this chapter highlights a number of research needs across the different intervention areas highlighted in the review. It should be noted, however, that given that the evidence review was not comprehensive, a number of other intervention areas were not captured in this evidence review that also undoubtedly merit further research.

In light of some unique aspects of scientific intervention development specific to the Information and Communication Technologies area, the research needs that are broadly applicable to all topic areas contained in this chapter are presented first, followed by an additional set of research needs specific to the fast-growing information and communication technologies intervention arena.

Research Needs that are Broadly Applicable to All Topic Areas Presented in this Chapter

1. Broaden enrollee targets in randomized controlled trials and other research in this area to incorporate diverse population subgroups, including broader age groups, men as well as women, diverse racial/ethnic groups, and vulnerable and underrepresented population groups (e.g., lower-income residents, patient subgroups).
   Rationale: In order to develop interventions that have the potential for having a public health impact at the population level, it is critical to ensure that diverse age, sex, racial/ethnic, cultural, geographic, and income groups are included in the experimental research designs that can most effectively advance the field. Data collected across these various subgroups of the population will inform how to adapt interventions to subgroup needs through formative and iterative intervention design methods, and can help strengthen interventions through ensuring that they are targeted effectively for specific subgroups as well as tailored to individual preferences and requirements.
2. Test physical activity and sedentary behavior interventions over longer time periods (i.e., more than 12 months) to better understand how to sustain their positive effects.
   Rationale: Because many of the positive health effects of regular physical activity and reduced sedentary time can accumulate over time and require regular engagement across time, methods for maintaining regular physical activity and reduced sedentary patterns are critical. Yet, as pointed out in this chapter, relatively few interventions have been systematically tested across time periods lasting several years, and knowledge concerning how best to foster sustained physical activity maintenance in different subgroups over time remains inadequate.

3. Report, in experimental and quasi-experimental investigations of physical activity interventions, intervention-related dose-response relations and adverse events to aid intervention evaluation, translation, and dissemination.

   Rationale: Experimental investigations in this area can benefit from consistent inclusion of information related to intervention dose-response (e.g., how does the intensity of the intervention, in terms of the type of communication delivery channel being used [e.g., in-person, mediated], as well as number, length, or schedule of contacts, affect the amount of physical activity change?). In addition, adverse events related to the intervention are important for determining intervention safety and appropriateness for various population subgroups, but are rarely reported in a systematic fashion.

4. Develop efficient methods for collecting cost data on all interventions being tested to inform cost-benefit and cost-effectiveness comparisons across the physical activity intervention field as a whole. For those intervention areas that are further developed, use comparative effectiveness designs to more efficiently advance the study and translation of interventions to promote physical activity and reduce sedentary behavior.

   Rationale: In an increasingly cost-conscious health environment, it is important for the public and decision-makers alike to gain a better understanding of the costs of different interventions relative to their effectiveness to make more informed decisions in relation to intervention choice. In those intervention areas with evidence grades of Moderate or Strong, the use of comparative effectiveness experimental designs, in which interventions that have been shown to have merit are tested "head-to-head," will advance knowledge more rapidly than designs that continue to use weaker controls or comparisons (e.g., minimal or no intervention, wait-list controls). In addition, further systematic evaluation of potentially cost-efficient intervention delivery sources (e.g., peer-led interventions) and delivery channels (e.g., automated behavioral counseling systems, virtual advisors), either as adjuncts to or replacements for more staff-intensive interventions, is warranted.

5. Develop standards in the field for choosing the most appropriate comparator arms with which to compare emerging physical activity interventions when evaluating their efficacy and effectiveness.

   Rationale: Similar to other health behavior fields, advancing the physical activity promotion field along the continuum of science, from discovery of promising interventions through dissemination of interventions that work, will require investigators to employ the most relevant comparator arms to answer the specific questions of interest that are being pursued. Relatively little consensus currently exists, however, concerning the most appropriate comparators to use to answer the various types of questions reflected across the different levels of impact described in this chapter. The field as a whole would benefit from building general consensus concerning the most appropriate types of comparators, along with design parameters, to be considered, based on the current state of the evidence and the most critical questions emanating from it.

6. For those intervention topic areas receiving a Strong or Moderate evidence grade, develop and systematically test methods for effectively implementing such physical activity promotion and sedentary behavior change approaches in real-world settings.

   Rationale: Although the current evidence review identified a number of physical activity promotion approaches and strategies that are effective in increasing physical activity behavior, few such approaches have been systematically disseminated across the U.S. population. In light of the sizable portion of the population that could benefit from increasing their regular physical activity levels, the development and systematic testing of potentially effective implementation methods and strategies are critical.

7. Develop and systematically test multi-component interventions that span multiple levels of influence to increase intervention impact and potential sustainability of behavior change.

   Rationale: It is clear that health behaviors such as physical activity and sedentary behavior are influenced by an array of individual, sociocultural, community, and environmental factors, yet many of the interventions that have been tested contain elements centered primarily on one level of impact (e.g., personal factors; institutional factors; built environment factors). Increasing the effectiveness and robustness of interventions likely could occur through targeting people within their environmental and social contexts (i.e., person-environment interactions). An example of such multi-level interventions includes combining individual-level behavioral skill-building strategies with neighborhood-level built environmental interventions to promote increased walkability.

8. Test, using experimental methods, strategies for promoting regular physical activity and reduced sedentary behavior across key life-course transitions, when such health behaviors potentially result in deleterious outcomes.

   Rationale. Common life-course transitions and the changes in role expectations and social and environmental contexts that often accompany them, can lead to negative impacts on physical activity levels and other health behaviors. Such transitions include changes from school to the workforce; changes in marital status and family roles and configurations; and physical transitions occurring at puberty, menopause, or with the onset of a chronic conditions. Systematic testing of methods and approaches for facilitating regular physical activity and reduced sedentary behavior during and following such common transitions could have significant, population level impacts.

9. Conduct experimental research aimed at testing systematically how best to combine physical activity interventions with other health behavior interventions, such as sedentary behavior, sleep quality, or dietary change interventions, to promote optimal physical activity change within the context of such multi-behavioral interventions.

   Rationale: Given the potential health-related synergies that can accrue when both physical activity and sedentary behavior change, or physical activity and dietary changes are implemented, systematic investigations of how best to combine these important health behaviors in different population subgroups are strongly indicated. Currently, little is known concerning the best approaches for combining health-enhancing physical activity with sedentary behavior change or dietary interventions, regardless of intervention modality, to facilitate sustainable behavior changes in both health behaviors. The few randomized controlled trials in this area are intriguing, however.[10] For example, some evidence exists suggesting that, in some population subgroups, introducing dietary interventions along with physical activity interventions may reduce the amount of physical activity change observed.[11] Further systematic evaluation of potential behavioral compensation effects between physical activity and sedentary behaviors is also warranted to ensure that physical activity increases during one portion of the day do not result in increased sedentary behavior in other portions of the day.

10. Increase the scientific utility of systematic reviews and meta-analyses to inform future research directions in the physical activity promotion and sedentary behavior reduction fields.

    Rationale: Although the number of systematic reviews has exploded across virtually all physical activity promotion and sedentary behavior areas, a number of such reviews lack specific types of quantitative information that can be useful in obtaining an accurate summation of a research area upon which future research can be applied. Such information includes the following:

    - Inclusion, whenever possible, of quantitative estimates of effect sizes or other magnitude of effect statistics for the articles included in the review, as opposed to simply *P* values;

- Clear descriptions of statistical outcomes for between-arm comparisons for all controlled or comparison arm studies along with specific notations when authors did not report such between-arm comparisons;
- Inclusion in each study, whenever possible, of the net physical activity differences achieved between intervention and control arms (e.g., with respect to mean step increases per day or mean minutes per week of moderate-to-vigorous physical activity achieved) over the specific time period under investigation;
- Inclusion of subgroup analyses based on key sociodemographic characteristics (e.g., sex, socioeconomic status, race/ethnicity, age) to identify which interventions might require specific targeting to be effective in different population subgroups.
- Reporting of adverse events and any unintended consequences of the interventions.

Research Needs Specific to Information and Communication Technologies Level Evidence

1. Employ additional types of experimental designs and methods that will allow for more rapid testing of information and communication technology interventions.

   Rationale: In light of the rapid evolution of the information and communication technologies interventions discussed in this chapter, traditional 2-arm parallel-arm trial designs may not easily allow researchers to keep up with the technology innovations that are occurring in this area. Further use of more advanced experimental designs, such as fractional or multi-level factorial designs and just-in-time adaptive interventions, is warranted.

2. Further explore methods and pathways for systematically exploiting the vast amounts of commercially available physical activity-relevant data and interventions that already reside in this area.

   Rationale: Millions of people representing a diverse and growing segment of the population are currently using commercial technologies aimed at physical activity behavior. Such databases have vast potential for accelerating our knowledge concerning the most effective ways of promoting physical activity among different population groups, yet remain relatively untouched. Exploring appropriate avenues for using these naturally-occurring databases provides a potentially paradigm-shifting approach to accelerate scientific advances in this area and the attendant public health benefits that can be gained.[201]

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PART G. NEEDS FOR FUTURE RESEARCH

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OVERARCHING RESEARCH NEEDS

Following are a set of questions the Committee believes are most important and critical for informing the scientific foundation for the next set of physical activity guidelines.

- Determine the independent and interactive effects of physical activity and sedentary behavior on multiple health outcomes in youth, adults, and older adults.

  Rationale: Preliminary evidence from one 2016 review and meta-analysis indicates a significant interaction among physical activity (measured as moderate-to-vigorous physical activity) and sedentary time on all-cause mortality.[1] The extent to which physical activity, at the workplace or during leisure time, can compensate for increases in sedentary time—for individuals of all ages—is a timely, important and popular question.

- Determine the role and contribution of light-intensity activity alone or in combination with moderate-to-vigorous physical activity to health outcomes.

  Rationale: The importance of light physical activities to health outcomes has been an interest for a long time. However, the scientific community has been limited by survey tools that poorly quantify physical activity. The development and wide use of wearable monitors that permit quantification of light physical activity and total physical activity now permit and promote a new series of investigations critical to the understanding of the role of total range of physical activity on health. The role of steps and step counting to measurement of physical activity exposure and promotion derives from this issue.

- Identify effective intervention strategies for increasing physical activity through actions in multiple settings in youth, adults, and older adults. How does the effectiveness of interventions differ by sex, age, race/ethnicity, socioeconomic, and other factors?

  Rationale: Once guidelines are established, developing effective strategies to help individuals achieve the goals remains a most critical step in improving the general health of our communities. However, effective intervention strategies necessarily vary by an individual’s personality, culture, environment, socioeconomic status, medical condition, fitness level, and other personal factors.

Understanding these intervention modifiers will be critical to developing strategies for effective means to increase physical activity for communities.

- Strengthen the understanding of dose-response relationships between physical activity and multiple health outcomes in youth, adults, and older adults, and especially during the life transitions between these categories.

  Rationale: Before the widespread adoption of device-based measures of physical activity, it was almost impossible to obtain reliable data on the various components of physical activity contributing to health effects in large populations. Most of the relevant information on dose-response with respect to intensity, frequency, duration, and longevity of physical activity interventions on health effects comes from small controlled training trials that can carefully control the exposure parameters of interest. To understand the effects of the frequency, intensity, time, and type (FITT) exposure parameters at the population level will require use of devised-based measures of physical activity incorporated into longitudinal study designs, whether they be controlled randomized trials or longitudinal cohort studies.

- Expand knowledge of the extent to which the relationships between physical activity and health outcomes are modified by demographic factors including sex and race/ethnicity.

  Rationale: The health effects of physical activity have been conducted in samples that were not fully representative of the population (e.g., only females or males; mostly non-Hispanic white race/ethnicity). Very significant health disparities have been linked to race, ethnicity, and socioeconomic status. Studying whether (and how) physical activity mitigates race-based health disparities in a number of conditions—heart disease, cancer, obesity, type 2 diabetes, Alzheimer's disease, and many others—could have far-reaching public health implications. In the future, more studies should be designed specifically to consider differential effects across demographic sub-groups.

- Develop instrumentation and data collection systems that will enhance physical activity surveillance systems in the United States.

  Rationale: Based on the information and evidence described in this report, bouts of moderate-to-vigorous physical activity of less than 10-minutes have value and may be included in the accumulated total, and light-intensity physical activity is a beneficial behavior for individuals who are highly sedentary and perform no or little moderate-to-vigorous physical activity. Therefore, these aspects of physical activity, which are most accurately measured by devices, are important to capture across the U.S. population. Information relevant to physical activity promotion, such as the presence of supportive programs (community or site-specific), policies, or environmental supports, are also important to monitor. Instrumentation and data collection systems are needed to enhance the collection of this information. Research is needed to determine the most appropriate metrics and data collection methods to capture this information for surveillance or for large-scale surveys.

CHAPTER 1. PHYSICAL ACTIVITY BEHAVIORS: STEPS, BOUTS, AND HIGH INTENSITY TRAINING

Question 1. Step Count Per Day and Question 2. Bout Duration

1. Conduct additional longitudinal research, either in the form of prospective studies or randomized controlled trials, to examine the dose-response relationship between:

    a) Steps per day and health outcomes, and

    b) Whether physical activity accumulated in bouts of less than 10 minutes in duration enhances health outcomes.

    Rationale: This information is critical for setting target volumes of physical activity using steps per day as the metric and for firmly establishing that steps per day predicts the incidence of future disease outcomes. In this review, only one randomized controlled trial was identified and it did not include multiple arms to examine the effects of various doses of steps per day on outcomes.

    The majority of studies reviewed supporting the health benefits of physical activity accumulated in bouts of less than 10 minutes in duration used a cross-sectional design, with none of the randomized studies reporting on the effects of physical activity accumulated in bouts of less than 10 minutes. Having this knowledge will inform potential cause and effect rather than simply associations.

2. Include measurement methods in prospective and randomized controlled studies that will examine:

a) Whether the rate of stepping and the length (bouts) of continuous steps influence the relationship between steps per day and disease outcomes

b) Whether physical activity performed in a variety of bout lengths has differential effects on health outcomes

Rationale: The studies reviewed used simple pedometers providing accumulated steps and could neither address patterns nor intensity of steps per day. Additional physical activity assessment methods collecting these data should provide a better target for recommending physical activity volume. Based on the studies reviewed, randomized studies did not report on physical activity accumulated in bouts less than 10 minutes in duration, and only two prospective studies were identified that reported on physical activity accumulated in bouts less than 10 minutes. This may be a result of the methods used to assess physical activity in randomized and prospective studies, and suggests the need to include physical activity assessment methods that allow for these data to be available for analysis.

Question 3. High Intensity Interval Training

1. Conduct longer-term randomized controlled trials to assess the adherence to and the effects of high intensity interval training, compared to other types of physical activity programs, on physiological, morphological, and cardiometabolic health outcomes. They should address issues of dose-response and be of at least 6 months in duration. These randomized controlled trials should include diverse groups of adults who have overweight or obesity and/or who are at high risk of cardiovascular disease or type 2 diabetes. They should systematically assess adverse events, including musculoskeletal injuries, attributable to high intensity interval training, compared to other types of exercise training, among adults with a wide variety of health and disease characteristics.

   Rationale: Most high intensity interval training intervention periods are less than 12 weeks, which may be insufficient time to assess the magnitude and sustainability of clinically-important changes in some physiological, morphological, and cardiometabolic health outcomes. The willingness and ability of individuals to adhere to high intensity interval training programs is currently unknown. Prescriptively designing these studies to include participants who have overweight or obesity and/or who are at high risk of cardiovascular disease or type 2 diabetes is important to inform health promotion practitioners and policy leaders on the utility of recommending high intensity interval training for health among a large proportion of the U.S. adult population. At present, evaluation of the safety of high intensity interval training among adults with varied health and disease characteristics is compromised by the limited data available, in part, due to the low proportion of studies reporting adverse events.

CHAPTER 2. SEDENTARY BEHAVIOR

1. Conduct research using prospective cohorts on the interactive effects of physical activity and sedentary behavior on all-cause and cardiovascular disease mortality and incident cardiovascular disease, especially on the role of light-intensity physical activity on attenuating the relationship between sitting and mortality.

   Rationale: Evidence on the role of physical activity in displacing the mortality risks associated with sedentary behavior is limited. A better understanding of these interactive effects will allow for more specific recommendations regarding the amount and intensity of physical activity required to maximize health benefits among people with higher or lower levels of sedentary behavior. Given that associations between specific risk factors and cancer mortality are affected by cancer screening and treatment availability and efficacy, studies of the associations between sedentary behavior and all-cancer mortality are not a priority.

2. Conduct research using prospective cohorts on the role of bouts and breaks in sedentary behavior in relation to all-cause and cardiovascular disease mortality.

   Rationale: The preponderance of the existing evidence on prospective associations between sedentary behavior and health is based on the association between daily or weekly duration of sedentary behavior. More research is needed on the relationship between patterns of sedentary behavior and mortality and other health outcomes, especially the role of sedentary bouts and breaks. This information will contribute to the development of recommendations on how sedentary behavior patterns should be modified to maximize related health benefits. Given that associations between specific risk factors and cancer mortality are affected by cancer screening and treatment availability and efficacy, studies of the associations between sedentary behavior and all-cancer mortality are not a priority.

3. Conduct research on how factors such as sex, age, race/ethnicity, socioeconomic status, and weight status relate to the association between sedentary behavior and cardiovascular disease incidence and cardiovascular disease mortality.

   Rationale: Compared to the evidence base for all-cause mortality, fewer studies have addressed issues of effect modification by these factors on the relationship between sedentary behavior and cardiovascular disease incidence and mortality. This information will help determine how generalizable the potential benefits of reducing sedentary behavior are in preventing cardiovascular disease and whether different recommendations are required based one's sex, age, race/ethnicity, socioeconomic status, or weight status. Given that associations between specific risk factors and cancer mortality are affected by cancer screening and treatment availability and efficacy, studies of the associations between sedentary behavior and all-cancer mortality are not a priority.

4. Conduct research using prospective cohorts to disentangle the independent effects of sedentary behavior and adiposity on risk of type 2 diabetes.

   Rationale: Given that the association between sedentary behavior and type 2 diabetes is attenuated when body mass index is a covariate in the statistical models, this suggests that body mass index may be in the causal pathway between sedentary behavior and risk of type 2 diabetes. However, further research is required to understand the nature and direction of this relationship to better understand whether the relationship between sedentary behavior and type 2 diabetes is truly causal.

5. Conduct randomized controlled trials to test the health effects of interventions to replace time spent in sedentary behaviors with standing and light-, moderate-, and vigorous-intensity physical activity.

   Rationale: The preponderance of the evidence on the health effects of sedentary behavior has come from observational epidemiological studies. To develop public health guidelines and develop effective intervention strategies, more evidence is required on the positive and negative consequences associated with replacing sedentary behavior with greater intensity activities for short or long durations.

CHAPTER 3. BRAIN HEALTH

1. Conduct randomized controlled trials of moderate-to-vigorous physical activity across the lifespan, including in youth, to better understand its effects on cognitive development, quality of life and health-related quality of life, state and trait anxiety, and sleep outcomes.

   Rationale: Despite considerable research focused on the importance of physical activity on brain health in adults and older adults, the paucity of knowledge during other periods of the lifespan should be addressed to better understand physical activity effects on cognition, quality of life, affect, anxiety and depression, and sleep outcomes, and how they may change, across the entire lifespan. Physical activity may beneficially affect measures of brain health in common childhood disorders such as attention deficit hyperactivity disorder and autism spectrum disorder, but the impact on these conditions, or the long-term impact of physical activity during childhood on adult outcomes are largely unknown.

2. Conduct randomized controlled trials that manipulate the physical activity dose in a systematic fashion to improve the understanding of the dose-response relationship and durability of physical activity effects on brain health. Conduct these studies in healthy children and adults, and also in populations with conditions and impairments of brain health (e.g., dementia, sleep disorders, mood disorders).

   Rationale: To date, little evidence exists to draw strong conclusions about the optimal intensity, duration, and frequency of physical activity to enhance brain health (i.e., cognition, quality of life, anxiety, depression, sleep). This work is critically needed to better inform the public and practitioners about the amount of activity needed to observe changes in brain health outcomes in healthy individuals and in individuals with cognitive, sleep, or mood disorders. Although the current literature base does not allow for a firm understanding of a dose-response relationship between either acute or chronic physical activity on brain health, recommended doses of physical activity (e.g., moderate-to vigorous-intensity) have demonstrated positive effects on brain health across the lifespan.

3. Conduct randomized controlled trials of both light and moderate-to-vigorous physical activity in individuals with cognitive (e.g., dementia), mood (e.g., anxiety, depression), sleep (e.g., insomnia), and other mental health disorders (e.g., schizophrenia) to better understand its effects on brain

health in these conditions, including aspects of quality of life and health-related quality of life. Further, conduct randomized controlled trials and observational studies in individuals at different stages or severity of impairment, including studies in individuals at risk of disease (e.g., genetic risk) as well as individual with comorbid conditions (e.g., anxiety and depression) to examine whether physical activity delays or prevents disease onset and progression, or interacts with common treatments used by individuals with disorders and diseases.

Rationale: Knowledge of this area varies across impairments, with some diseases and disorders having significantly more research than others (e.g., depression). Yet, even in the context of some of these more common conditions, there is a paucity of research on some outcomes that are highly relevant for optimal functioning, such as the impact of physical activity on sleep, cognitive, and quality of life in individuals with depression. In addition, little is known about the effects of physical activity on conditions that often co-occur, like anxiety and depression. Other conditions that are also associated with impaired brain health (e.g., autism spectrum disorder, cancer, traumatic brain injury) have received little focus to date. Research in this area would contribute to a better understanding of etiologic subcategories of cognitive, sleep, mood, and other mental health conditions such as Alzheimer's disease and related dementias, and Lewy Body, Vascular, and Mixed Dementias, which are increasingly recognized and diagnosed within the domains of impaired mental and neurological health in aging.

4. Conduct randomized controlled trials of physical activity that examine brain imaging and other biomarker metrics across the lifespan and in conditions characterized by cognitive, mood, and sleep impairments.

   Rationale: These studies could yield a better understanding of circulating biomarkers (e.g., neurotrophins) associated with brain health, and the relative roles of genetic (e.g., *ApoE4* gene) and environmental risk factors (e.g., stroke risk factors, traumatic brain injury) as covariates influencing the response to physical activity. To date, although candidate biomarkers and environmental risk factors have been identified, little systematic study in humans has emerged in the literature especially in relation to markers associated with affect, anxiety, depression, and sleep.

5. Conduct studies to monitor sedentary time and conduct randomized controlled trials that systematically reduce sedentary behaviors to improve the understanding of the impact of varying contexts, patterns, and durations of sedentary behavior on brain health outcomes (e.g., depression symptoms) throughout the lifespan and in populations with brain health disorders and diseases.

   Rationale: The understanding of the effects of sedentary behavior on brain health is in its infancy. Given that recent evidence indicates that sedentary behavior is distinct from physical inactivity, a greater understanding of the effect of sedentary behavior on brain health may inform and target interventions aimed at improving brain health across a variety of populations, including school-aged children, middle-aged adults, and older adults, as these populations spend considerable time during their day engaged in sitting and other sedentary behaviors. In addition, portable health technologies that continuously measure physical activity, estimate its intensity, and characterize sleep behavior, may offer inroads to better understand such relationships, and perhaps test novel interventions using connected health approaches.

6. Conduct appropriate analyses to examine effect modification by demographic factors. Such analytical approaches require studies that include large samples and substantial variation in sample characteristics (i.e., race/ethnicity, socioeconomic status).

   Rationale: Although some understanding of the effects of physical activity during the developing years and in aging has emerged, evidence for other demographic factors has not been demonstrated in a systematic fashion, affording little opportunity to form strong conclusions about any potential effect of these factors. Findings that incorporate other demographic factors stand to generalize the physical activity-brain health literature, improving understanding of this relationship more broadly across the U.S. population, deepening understanding of health disparities, and informing interventions aimed at improving brain health.

7. Conduct randomized controlled trials and prospective observational studies that will improve understanding of the latency and persistence of the improvements in brain health following both acute and regular physical activity. These studies should have larger sample sizes, longer follow-up periods, and a broader range of instruments and outcomes relevant for brain health (e.g., mental subdomain of health-related quality of life, affect).

Rationale: To date, the temporal dynamics of the effects of physical activity on brain health are poorly understood. Yet, it is known that individuals start and stop exercise regimens on a regular basis and such variability in the consistency of physical activity may differentially influence the impact of physical activity on brain health outcomes. It is possible that the persistence of the effects might also depend on the dose of activity (frequency, intensity, time, type), the age of the individual, the presence of a disorder or disease, or other factors. Enrolling samples of sufficient size to support mediator analyses (i.e., exploration of putative mechanisms through which the interventions operate) will provide useful information for adapting the interventions to optimize uptake among different subgroups as well as to identify key elements that are essential to improving brain health.

8. Conduct randomized controlled trials and prospective observational research on the impact of muscle-strengthening exercises (often referred to in the literature as resistance training) and other forms of physical activity (e.g., yoga, tai chi), and other modes of activity on brain health outcomes.

   Rationale: Most research in this area has been conducted using aerobic exercise approaches (e.g., brisk walking). Given the effects of muscle-strengthening exercises and the increased popularity of many other forms of physical activity (e.g., yoga, tai chi) and the evolving evidence of their influence on multiple health outcomes, it will be important to understand how these different modalities differentially influence cognition, quality of life, affective, anxiety, depression, and sleep outcomes.

CHAPTER 4. CANCER PREVENTION

1. Conduct epidemiologic studies of effects of physical activity on risk of cancer for specific cancer sites that have not been adequately studied, preferably large prospective cohort studies.

   Rationale: Very little evidence exists on the relationship between physical activity and the risk of cancer at several sites, particularly the rare cancers. Therefore additional pooled datasets and meta-analyses may be needed. Additional studies would provide the data necessary for the useful insights that would be possible through analyses of pooled datasets and meta-analyses.

2. Conduct epidemiologic studies of effects of physical activity on risk of cancer in specific race, ethnic, and socioeconomic groups.

Rationale: Few studies have had sufficiently large numbers of participants from specific racial, ethnic, or socioeconomic subgroups to assess the effects of physical activity on risk of developing cancer. This additional research is particularly important, as many groups are at high risk of cancer (i.e., African Americans are at increased risk for colon, prostate, and breast cancers), are typically diagnosed with more advanced disease (i.e. individuals from low socioeconomic groups or others without access to medical care), and are often insufficiently active.

3. Conduct studies to test effect modification by age on the associations between physical activity and cancer risk.

Rationale: Some evidence suggests that risk for some cancers such as colon and breast is increasing in younger age groups, who are also less active today than in previous generations. It would be important to know whether physical activity can be protective in this younger age group.

4. Conduct epidemiologic studies, preferably prospective cohort studies, to determine effects of specific types of physical activity on cancer risk.

Rationale: Few data are available on the associations of specific activities on cancer risk. It would be useful to know whether moderate-intensity activities such as walking are sufficient to provide protection. Also, insufficient data exist on associations of other activities such as muscle-strengthening activity on cancer risk.

Conduct epidemiologic studies, preferably prospective cohort studies, to more precisely determine dose-response effect of physical activity on cancer risk.

Rationale: All data in available studies have been from self-reported recall of usual activities. Collecting data with device-based measures of activity will be important, as will determining precise measures of dose of activity.

5. Conduct randomized controlled clinical trials testing exercise effects on cancer incidence.

Rationale: All available data are from observational studies, which could suffer from confounding effects of other variables. Randomized trials in high risk individuals could be more cost-effective, as trials with smaller sample sizes or shorter follow-up durations might be feasible.

CHAPTER 5. CARDIOMETABOLIC HEALTH AND PREVENTION OF WEIGHT GAIN

1. Conduct longitudinal research on lower exposure levels of physical activity to allow for an enhanced understanding of the dose-response associations between physical activity and weight gain, hypertension, and type 2 diabetes across a wider spectrum of exposure.

   Rationale: Only limited evidence is currently available on the effect of physical activity less than 150 minutes per week on prevention of weight gain, hypertension, and type 2 diabetes. Thus, limited data are currently available to inform whether lower amounts of physical activity can be effective for preventing these conditions. Having this knowledge is important and will inform public health recommendations regarding the minimum physical activity exposure that can be effective for preventing weight gain or the development of obesity, hypertension, and type 2 diabetes.

2. Conduct large research trials with ample sample sizes to allow for stratum-specific analyses to determine whether the influence of physical activity on the prevention of weight gain, hypertension, and type 2 diabetes varies by age, sex, race/ethnicity, socioeconomic status, or initial weight status.

   Rationale: Only limited evidence is currently available on whether the influence of physical activity on weight gain or risk of hypertension or type 2 diabetes varies by age, sex, race/ethnicity, socioeconomic status, weight status. Moreover, little is known about whether the influence of physical activity varies when the exposure to physical activity is consistent across individuals with different demographic characteristics. Having this information will inform public health recommendations regarding whether physical activity exposure to prevent weight gain needs to vary by age, sex, race/ethnicity, socioeconomic status, weight status, and other demographic characteristics, and may allow for more precise individual-level physical activity recommendations. Thus, adequately designed and statistically powered studies are needed to allow for comparisons across the various strata of demographic characteristics to examine whether the influence of physical activity varies by these factors.

3. Conduct experimental research on varying intensities (light, moderate, and vigorous) of physical activity, while holding energy expenditure constant, to determine the independent effects of physical activity intensity on weight gain, hypertension, and type 2 diabetes.

Rationale: Limited evidence is available on whether the influence of physical activity on weight gain, hypertension, or type 2 diabetes is consistent across intensities (light, moderate, vigorous) when total energy expenditure is held constant, and only limited evidence is available on the influence of light-intensity physical activity on weight gain. This information will inform public health recommendations regarding whether the emphasis to prevent weight gain, hypertension, or type 2 diabetes should be on total volume of physical activity regardless of intensity, or whether the emphasis needs to be on volume of physical activity that is performed at a specific intensity.

4. Conduct observational and experimental research that quantifies energy intake and eating behavior to determine whether these factors influence the association between physical activity and weight gain.

   Rationale: The majority of the studies examined regarding weight gain either did not report that diet and eating behavior were measured or considered in the analysis. Given that both dietary factors, primarily energy intake, and energy expenditure from physical activity can influence body weight regulation, it is important to understand whether the physical activity exposure necessary to limit weight gain will vary based on diet or eating behavior patterns.

5. Within research that is conducted, disclose the standard criteria and methods that were used to determine the blood pressure status of the study sample to better isolate samples with hypertension from those with normal blood pressure and prehypertension, and report results separately by blood pressure classification.

   Rationale: Strong evidence demonstrates the magnitude of the blood pressure response to physical activity varies by resting blood pressure, with greater benefits occurring among adults with prehypertension than normal blood pressure. However, study samples often include mixed samples of adults with hypertension, prehypertension, and normal blood pressure, and findings are frequently not reported separately by blood pressure classification. Consistent with the law of initial values, this practice underestimates the blood pressure benefits of physical activity. In addition, samples with prehypertension are underrepresented as they are often mixed with samples with hypertension. Reporting findings by blood pressure classification will inform public health recommendations on the magnitude and precision of the blood pressure reductions that result from physical activity among adults with normal blood pressure and prehypertension.

6. Conduct randomized controlled trials to examine the influence of types of physical activity other than aerobic, dynamic resistance, or combined aerobic and dynamic resistance physical activity on blood pressure and other health outcomes among adults with normal blood pressure and prehypertension.

   Rationale: Limited evidence on these topics is available among adults with normal blood pressure and prehypertension. Gaining this information will inform the public health recommendations on the types of physical activity that optimize blood pressure benefit.

7. Conduct experimental research that examines both the acute (i.e., short-term or immediate, referred to as postexercise hypotension) and the chronic (i.e., long-term or training) blood pressure response to physical activity among adults with prehypertension and normal blood pressure.

   Rationale: Insufficient evidence exists on the acute blood pressure response to physical activity despite primary-level reports suggesting a close relationship between the blood pressure response to acute and chronic exercise. Developing a better understanding of acute blood pressure responses will inform public health recommendations on possible behavioral strategies to increase adherence to physical activity for blood pressure benefit.

8. Conduct observational and experimental research examining the relationship between physical activity and blood pressure using the 2017 *Guideline for the Prevention, Detection, Evaluation and Management of High Blood Pressure in Adults* new blood pressure classification scheme.[2]

   Rationale: The literature that was reviewed to answer this question was based upon The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7)[3] blood pressure classification scheme. The new guideline increases the number of people with hypertension, eliminates the category of prehypertension, and adds the category of elevated blood pressure. The relationship between physical activity and blood pressure according to this new blood pressure classification scheme remains to be determined.

CHAPTER 6. ALL-CAUSE MORTALITY AND CARDIOVASCULAR DISEASE

Several advances in our understanding of the relationships among physical activity and these outcomes have occurred since the Physical Activity Guidelines Advisory Committee Report, 2008.[4] Most of the literature upon which the conclusions were based used survey data and questionnaire data; physical activity exposures were assessed using self-reported estimates of time spent in aerobic continuous moderate-to-vigorous physical activity accumulated in bouts of at least ten minutes. Therefore, all other components across the physical activity spectrum—sedentary behavior, light-intensity physical activity, and any moderate-to-vigorous physical activity in bouts less than 10 minutes –was considered "baseline" physical activity. Researchers have begun to incorporate device-based measures of physical activity into their measurement armamentarium. This has permitted assessments of the relationship of activity of less than moderate-to-vigorous intensity with health outcomes; it has permitted the assessment of the effects of episodes of moderate-to-vigorous physical activity of less than 10 minutes on health outcomes. These issues are addressed in *Part F. Chapter 1. Physical Activity Behaviors: Steps, Bouts, and High Intensity Training*.

More research is needed in these areas:

1. Conduct research on the role of light intensity physical activities in risk reduction for all-cause mortality, cardiovascular disease mortality, and incident cardiovascular disease (coronary heart disease, stroke and heart failure). This can most economically and efficiently be accomplished by incorporating devices (pedometers or wearables) to measure physical activity into all clinical drug trials with all-cause mortality, cardiovascular disease mortality, or incident cardiovascular disease as outcomes.

   Rationale: As reported in this chapter, the benefits of moderate-to-vigorous physical activity on all-cause mortality, cardiovascular disease mortality, and incident cardiovascular disease (coronary heart disease, stroke and heart failure) are well-documented and strong. However, these studies ignore the effects of physical activity that are not characterized as moderate-to-vigorous in intensity (i.e., light intensity). The development of device-based measures of physical activity (pedometers, accelerometers, and other wearables) provides the scientific imperative to begin to explore the relations of all intensities and amounts of physical activity—light- to vigorous-intensity; small to large total amounts. These studies are beginning to appear.[5-9] Unfortunately, there are not enough studies on the relation of light-intensity physical activity, total physical activity, or step counts per day to provide enough information for meta-analyses to be performed in these areas for the outcomes of interest here. Therefore, this is a major future research need in this area.

2. Conduct research on the possibility of increased risk associated with high amounts of physical activity.

   Rationale: Whether high amounts (volumes) of aerobic physical exercise lead to increased cardiac morbidity or mortality is an important, yet open question. As discussed in this chapter, there is a hint in some studies of an increase in cardiovascular risk in high-volume aerobic athletes. Recent reports document increased coronary calcium scores in masters athletes[10, 11]; however, there seems to be a U-shaped relationship with life-long volume of training.[11] These findings may explain the hint of an increased cardiovascular risk in long-term athletes. Clearly, this issue demands more study in athletic populations.

3. Conduct research on the relative importance of the various characteristics of physical activity exposure (total volume, intensity, frequency and mode) on all-cause mortality, cardiovascular disease mortality, and incident cardiovascular disease (coronary heart disease, stroke and heart failure).

   Rationale: The second edition of the Scientific Report continues to rely on studies of aerobic ambulatory moderate-to-vigorous physical activity, primarily collected via survey, to understand the relationship of physical activity to all-cause mortality, cardiovascular disease mortality, and incident cardiovascular disease. Underexplored are the importance of frequency and intensity relative to volume of aerobic exercise; the importance of muscle strengthening to these clinical outcomes; whether swimming, biking, and rowing contribute to cardiovascular health equally to aerobic ambulatory exercise; and what the energy expenditures and programs are for these aerobic activities for equivalent clinical outcomes. If we are going to prescribe exercise of all modalities as options for individuals who want to exercise for health, we need better understanding of the relative contributions of a general range of options.

CHAPTER 7. YOUTH

1. Conduct randomized controlled trials and prospective observational studies to elucidate the dose-response relationships for physical activity and health outcomes, including adiposity, cardiometabolic health, and bone health in children and adolescents at each developmental stage.

   Rationale: Few studies have been designed to directly examine dose-response relationships between physical activity and health outcomes in young persons. This gap constitutes a major limitation in the process of identifying the types and amounts of physical activity needed to produce health benefits at each developmental stage.

2. Undertake randomized controlled trials and prospective observational studies to determine whether the health effects of physical activity during childhood and adolescence differ across groups based on sex, age, maturational status, race/ethnicity, and socioeconomic status.

   Rationale: Few studies have been designed to directly examine the extent to which the health effects of physical activity may differ across demographic subgroups. This gap substantially limits the ability to determine whether the dose of physical activity needed to produce health benefits varies across population sub-groups. Studies aimed at elucidating the extent to which race/ethnicity modifies the effects of physical activity on health outcomes should consider social, cultural, and biological factors that may influence an effect modifying role of race/ethnicity.

3. Conduct experimental and prospective observational studies to examine the health effects of physical activity in children and adolescents with elevated risk status based on adiposity, cardiometabolic health, and bone health.

   Rationale: Most children and adolescents fall within the normal, healthy range on key health indicators, and consequently increased physical activity is unlikely to enhance their already normal status. However, children at elevated risk may manifest improved status with increased physical activity. A considerable volume of research has been conducted in children and adolescents with overweight and obesity, but more research is needed with young persons who have elevated cardiometabolic and bone health risk.

4. Examine the effects of novel forms of physical activity, including high intensity interval training and exergaming, on health outcomes in youth. Both experimental and prospective observational studies should be conducted.

   Rationale: Certain forms of physical activity are particularly prevalent among children and adolescents, and more research is needed to determine the extent to which these forms of physical activity affect key health outcomes.

5. Develop valid instruments for measuring physical activity and examine the health effects of physical activity in very young children between birth and 2 years.

   Rationale: In part because of a lack of validated measures of physical activity in very young children, knowledge of the relationship between physical activity and health outcomes in children between birth and age 2 years is very limited.

6. Undertake studies, using longitudinal research designs, to examine the relationship between specific forms of sedentary behavior (e.g., sitting time, screen time) and health outcomes in children and adolescents using both self-report and device-based assessment of sedentary behavior.

   Rationale: Current research on the relationship between sedentary behavior and health is limited by a dearth of studies using device-based measures of time spent in sedentary behavior. Many studies have focused on television viewing as an indicator of sedentary behavior, but television viewing is confounded by exposures other than sedentary time. Research is needed to differentiate between the health effects of time spent sedentary and time spent in specific behaviors that typically include sedentary time.

7. Conduct intervention studies to test the effects of reducing sedentary behavior on health outcomes in children and adolescents.

   Rationale: Very few studies have examined the health effects associated with reduction of time spent in sedentary behavior among children and adolescents. The findings of such studies would inform the process of identifying the levels of time spent in sedentary behavior that may be associated with negative health outcomes. Further, these studies would determine the extent to which reduction of time spent in sedentary behavior influences time spent in moderate-to-vigorous and light-intensity physical activity.

8. Examine the interactive effects of sedentary behavior and physical activity of varying intensities on health outcomes in children and youth.

   Rationale: The relationship between physical activity and health outcomes in children and adolescents may be modified by amount of time spent in sedentary behavior. That is, youth who spend large amounts of time in sedentary behavior may require higher levels of physical activity to produce a particular health outcome. Studies should be undertaken to directly examine this issue.

9. Undertake prospective observational studies to examine the effects of physical activity during childhood and adolescence on health outcomes later in life.

   Rationale: Large-scale cohort studies that have followed children into adulthood and have used state-of-the-art measures of physical activity are rare, particularly in the United States. Accordingly, knowledge of the long-term impact of physical activity status early in life on health outcomes later in life is very limited. Further, the findings of such studies could inform development of physical activity guidelines for individuals in transitional periods, such as early adulthood.

10. Determine in children and adolescents the impact of genetic profiles on behavioral and physiological responses to physical activity and on the health effects of physical activity.

    Rationale: Studies in adults have shown that the health effects of physical activity are moderated by genetic profile such that a given dose of physical activity produces widely varying effects on indicators of health. Our knowledge of the relationship between physical activity and health in children and adolescents would be enriched by undertaking similar studies in young persons. Such studies could expand knowledge of how genes and the environment may interact in influencing indicators of health in young persons.

CHAPTER 8. WOMEN WHO ARE PREGNANT OR POSTPARTUM

1. Conduct observational and experimental studies of the effects of vigorous-intensity physical activity before and during pregnancy on maternal and fetal outcomes.

   Rationale: The safety and benefits of moderate-intensity physical activity during pregnancy and the postpartum period are now generally accepted. The safety and benefits of vigorous-intensity (absolute and perceived) physical activity are less well-documented and this type of activity may be discouraged by some health care providers. For women who have not been physically active, a program of moderate-intensity physical activity would be recommended. On the other hand, substantial numbers of women participate regularly in vigorous physical activity (e.g., running, stationary cycling, rowing) before pregnancy and may want to continue such activity for as long as possible throughout pregnancy. Information from such studies would provide valuable information on minimal effective levels of vigorous activity and maximal threshold levels for safety.

2. Continue to conduct large-scale observational studies to investigate longitudinally the relationship between various types and volumes of physical activity before and during pregnancy and during the postpartum period on short- and long-term weight status.

   Rationale: Although it is established that habitual moderate-intensity physical activity of a volume in the recommended target zone is associated with reduced weight gain during pregnancy, information about the relationship between various types and volumes of physical activity and weight change during pregnancy and the postpartum period would help guide the development of clinical and public health recommendations.

3. Conduct experimental and observational studies to investigate the effects of various types, intensities, and volumes of regular physical activity on quality of life and symptoms of anxiety and depression and during pregnancy, and quality of life and symptoms of anxiety during the postpartum period.

   Rationale: Although strong evidence demonstrates that regular moderate-intensity physical activity reduces depressive symptoms during the postpartum period, little information exists about the role of physical activity on perceived quality of life and symptoms of anxiety and depression symptoms during pregnancy and quality of life and symptoms of anxiety during the postpartum period.

Emerging evidence suggests that maternal mental health affects the health of the developing fetus. Knowledge about the benefits of even low doses of physical activity, as well as about the benefits of various modes of physical activity for women with anxiety or depression can help to promote a healthy pregnancy for both mother and fetus.

4. Conduct experimental and observational studies to determine the influence of regular physical activity on quality of sleep during pregnancy and the postpartum period.

   Rationale: Although regular physical activity is known to improve sleep and feelings of quality of life in the general population, little is known about the effect of regular physical activity on quality of sleep during pregnancy and the postpartum period. Getting enough sleep, especially during the postpartum period, is a common problem for new mothers. If women during pregnancy and postpartum benefit from acute episodes and regular participation in physical activity as do those in the general population, it could improve overall level of energy and quality of life.

5. Conduct large observational studies to determine whether specific types, intensities, and doses of physical activity affect maternal and fetal outcomes, such as preterm birth, low birth weight, and preeclampsia differentially.

   Rationale: Most of the experimental research on physical activity during pregnancy relies on the 2008 Physical Activity Guidelines[12] or the 2015 American College of Obstetricians and Gynecologists[13] recommendations of 150 minutes per week of moderate-intensity activity. Limited evidence suggests that certain types of physical activity, such as prolonged standing or lifting heavy loads performed in an occupational setting, may have different health effects for pregnant women than when performed during leisure time. The veracity of the observation needs to be determined, and, if confirmed, it will be important to determine whether the results are caused by the nature of the activities or the setting or perhaps other confounding factors (socioeconomic status, education level, age). Observing the impact of varying types, intensities, and doses of physical activity in varying domains (leisure-time, occupational, household, transportation) on a range of maternal and fetal outcomes would significantly advance current knowledge and inform both clinical and public health practice.

6. Conduct observational and/or experimental research that has adequate statistical power to determine whether the associations between physical activity and maternal or fetal outcomes vary by age, race/ethnicity, socioeconomic status, or weight status.

   Rationale: Most of the studies reviewed in this report were not designed or powered to test for effect modification by various sociodemographic factors or by body weight. Such information is important for making more specific physical activity recommendations for various population sub-groups in efforts to reduce health disparities among pregnant women.

CHAPTER 9. OLDER ADULTS

1. Conduct large-scale randomized controlled trials of older adults at high risk of falls designed with fall-related injuries and bone fractures as the primary outcomes of interest.

   Rationale: The incidence of fall-related injury or bone fracture is typically a secondary outcome of interest for randomized controlled trials designed to assess the effect of physical activity on the rate of falling. This issue results in insufficient sample sizes across studies to assess injurious falls and fractures, increases the potential for selection or information bias, and results in inadequate collection of pertinent injury-related data.

2. Conduct large observational and experimental studies to investigate further the dose-response relationships between physical activity (aerobic, muscle-strengthening, balance, and multicomponent) and fall-related injuries and bone fractures.

   Rationale: Currently, little information is available regarding the dose-response relationship between physical activity and fall-related injuries in older adults. Such information in necessary for setting minimum activity thresholds for effectiveness and maximum thresholds for safety.

3. Conduct large-scale randomized controlled trials comparing various doses of balance training and muscle-strengthening training on physical function in the general population of older people.

   Rationale: Little information is currently available on the amount of balance and muscle-strengthening training necessary to maintain or to improve physical function among generally healthy older people. Such information is important for attenuating the aging-related decline in physical function, thereby delaying the onset of frailty and maintaining physical independence in aging.

4. Conduct large-scale randomized controlled trials to determine the effects of tai chi, qigong, dance, active video gaming, and yoga on physical function in healthy older adults, as well as those with different chronic conditions.

   Rationale: These activities have only recently been considered as effective strategies for maintaining and improving physical function in older people. These forms of physical activity may be especially beneficial for those with already-existing chronic disease and/or limitations to mobility. Such research should address: 1) the types or modes of such activity that are most effective for specific chronic conditions; and 2) the minimal effective doses of these activities for improving physical function.

5. Conduct prospective cohort studies of physical activity and physical function in older adults that include objective measures (e.g., heart rate monitors) of relative intensity of activity.

   Rationale: The relationship of relative versus absolute intensity to the health benefits of regular physical activity remains unclear. Epidemiologic (i.e., observational) studies using objective monitoring would: 1) allow for more robust analyses of how intensity affects health benefits, and 2) facilitate integration of findings from observational studies (which typically measure intensity of activity using absolute intensity) with those from randomized controlled trials (which typically measure intensity of activity using relative intensity).

6. Conduct more meta-analyses with meta-regressions to determine the extent to which the heterogeneity of results often observed among different studies of physical activity and physical function can be explained by variation in the tests used to measure physical function.

   Rationale: Composite measures of physical function (such as the combination of measures resulting in a single score used in the Diong et al[14, 15] paper) tend to result in stronger effect sizes with physical activity, compared with single measures. This may be due to the fact that physical function comprises a constellation of attributes that may not be adequately captured by a single measure. Moreover, comparison among studies is difficult due to differences in how physical function is characterized and assessed (performance measures versus self-reported activities of daily living function or quality of life). Such meta-analyses would allow investigators to derive a single best composite measure to be used consistently in future studies of physical function.

7. Conduct more experimental research on dual-task training that clearly describe the dual-task training procedures and the parameters of the secondary task. In addition, these studies should provide evidence of whether dual-task costs were reduced by training and whether dual-task training transfers to untrained tasks.

   Rationale: Dual-task training is a relatively new area of research in aging, and the methodologic quality of the studies reviewed for this report ranged from poor to moderate. To ensure internal validity and reproducibility, future research in this area should provide as much detail as possible in describing the methods and should consider multiple outcome tasks (trained and untrained) in the analysis.

8. Conduct large-scale randomized controlled trials and/or meta-regression analyses to establish dose-response effects of aerobic and resistance training on physical function for people with chronic obstructive pulmonary disease, frailty, osteoporosis, cognitive impairment, Parkinson's disease, visual impairments, and following hip fracture or stroke.

   Rationale: Currently, little information is available regarding the dose-response relationship between aerobic and strengthening activities and physical function in specific vulnerable subgroups of older adults. These modes of activity are proven effective in minimizing the age-related decline in physiological reserve and function among the general aging population, and thus may be especially important for older people with chronic conditions that limited their mobility. Such information in necessary for setting minimum activity thresholds for effectiveness and maximum thresholds for safety.

9. Conduct large-scale randomized controlled trials to investigate the optimal dose and mode of physical activity necessary to improve and maintain balance function and reduce injury-related falls and fractures in persons with frailty, hip fracture, osteoporosis, Parkinson's disease, visual impairments, and stroke.

Rationale: Balance is essential for maintaining physical function and mobility, particularly among people with existing functional and mobility limitations due to frailty, osteoporosis, Parkinson's disease, visual impairments, or following hip fracture or a stroke. Currently, little information is available regarding the types or optimal dose of exercise for improving balance function. Such information in necessary for setting minimum activity thresholds for effectiveness and maximum thresholds for safety.

10. Conduct large-scale randomized controlled trials with 6- and 12-month post-intervention follow-up assessments to determine the effects of physical activity on activities of daily living mobility, instrumental activities of daily living, free-living physical or ambulatory activity and social participation for older individuals with chronic disease. These individuals are at accelerated risk of functional decline, disability, and social isolation.

    Rationale: Little evidence currently exists on how improvements in strength, balance, and endurance following a physical activity intervention to improve physical function translate into everyday improvements in activities of daily living function and social participation, especially after the formal intervention period is over. Such knowledge would provide important information on how improvements in physiologic function can contribute to and sustain certain behavioral aspects of healthy aging (such as self-care, independence, social engagement) and quality of life.

11. Conduct large cohort and experimental studies to determine the dose-intensity and timing of physical activity necessary to prevent functional decline or to improve physical function across the spectrum of cognitive dysfunction and dementia.

    Rationale: Limited evidence currently exists about the impact of physical activity training on physical function limitations that often co-occur with cognitive dysfunction and dementia. Cognition and mobility are intimately linked, and improving physical function through physical activity in a cognitively impaired population might have broad effects for independence and activities of daily living.

12. Conduct large-scale observational or experimental studies with adequate statistical power to determine whether the relationship between physical activity and risk of fall-related injuries or loss of physical function in older people varies by race/ethnicity, sex, socioeconomic status, or level of existing impairments across the aging spectrum.

    Rationale: The vast majority of available research has been conducted on older white women, thereby limiting the generalizability of the findings to this demographic subgroup alone. Moreover, the potential impact of these influential factors often is not considered in statistical analyses, thus limiting the ability to determine whether effect modification exists at all. Results from this type of research would provide stronger scientific foundations for local, state, and national government, medical, and community wellness entities committed to reducing possible health disparities among various demographic sectors. This research would also support public and private partners in developing effective physical activity programs and policies to help individuals maintain their health and function through older age.

CHAPTER 10. INDIVIDUALS WITH CHRONIC CONDITIONS

This section is organized into two parts. First, five cross-cutting needs for research are discussed that integrate similar research needs relevant to more than one chronic condition (involving conditions reviewed by this chapter or chronic conditions generally). Then, research needs specific to each chronic condition are listed. Research needs within each topic area are listed in order of priority. .

Priority Research Needs on Preventive Effects of Physical Activity in Individuals with Chronic Conditions

For the five research priorities in this section, research designs should generally include and compare self-report and device-based measures of physical activity. All the questions in this chapter found insufficient evidence to determine whether method of measurement of physical activity influences reported relationships between physical activity and health outcomes.

1. Conduct research on how characteristics of aerobic activity, muscle-strengthening activity, balance training, and combined activity (e.g., dose, duration, intensity, frequency, and type) influence the relationship between physical activity and health outcomes in individuals with chronic conditions.

Rationale: A basic element of public health recommendations in physical activity is to specify the frequency, duration, intensity, types, and amounts of physical activity that provide health benefits. Hence, it is remarkable that the reviews of this chapter provided so few data on how these characteristics of physical activity influence health effects. For example, in osteoarthritis, no reviews were located comparing the relative effects of different types of physical activity or of different amounts of physical activity. Yet this chapter has some provocative findings illustrating the importance of research in this area. For example, in type 2 diabetes, research indicated: (1) muscle-strengthening activity and aerobic activity have independent effects on hemoglobin A1C (indicating the importance of combined activity), and (2) vigorous-intensity activity is more efficient in lowering hemoglobin A1C (larger effect on hemoglobin A1C for a given volume of aerobic activity) than moderate-intensity activity. The increased interest in health benefits of light-intensity activity makes it an even higher priority to conduct randomized trials comparing different intensities and types of physical activity, and to conduct long-term cohort studies that provide dose-response data. For uncommonly performed types of activity (e.g., balance training), cohort studies are not feasible, so dose-response randomized trials are needed. To some extent, such as in individuals with hypertension, studies are needed to understand how characteristics of physical activity influence acute physiologic and health effects of activity.

2. Conduct research in individuals with chronic conditions on the effects of physical activity in reducing risk of developing additional chronic conditions (co-morbidities).

Rationale: The introduction of this chapter explains the public health importance of preventing multiple chronic conditions. In essence, as the number of chronic conditions afflicting a person increases, generally physical function worsens, health-related quality of life decreases, and cost of medical care increases. Despite a broad search for preventive effects of physical activity on reduced risk of any co-morbid condition, this chapter could make only a few conclusions related to prevention of co-morbidity. This lack of evidence is despite higher risk of co-morbid conditions in some chronic diseases, as illustrated by the higher risk of cardiovascular disease in individuals with spinal cord injury. Whereas the incidence of a few chronic conditions may be high enough to study in randomized controlled trials, generally prospective cohort studies are needed of long-term effects of physical activity on risk of common co-morbidities.

3. Conduct research on the secondary prevention effects of physical activity in individuals with chronic conditions, that is, research on how physical activity reduces risk of progression of the chronic condition and mitigates the effects of the chronic condition on physical function and health-related quality of life.

   Rationale: The amount of information located on secondary prevention by the evidence reviews varied substantially by chronic condition. Except for osteoarthritis, in individuals affected by the chronic conditions of this chapter, high-quality randomized controlled trials of effects of exercise on physical function and health-related quality of life are needed, including longer term studies (e.g., 4-6 months) that have adequate statistical power. For effects of physical activity on progression, generally prospective cohort studies are needed. For example, cohort studies are needed on effects of physical activity in type 2 diabetes on risk of neuropathy, nephropathy, retinopathy, and foot disorders.

4. Conduct systematic and coordinated randomized controlled trials on the health effects of tai chi, qigong, and yoga in individuals with chronic conditions.

   Rationale: With one exception (osteoarthritis), the evidence for health benefits of tai chi, qigong, and yoga was rated as insufficient by the evidence reviews of this chapter. Although randomized controlled trials of these forms of physical activity were located, often they were few in number, small, and/or of low methodologic quality. Although higher quality randomized controlled trials of these types of physical activity are a priority, it is important that such trials be conducted in a systematic and coordinated fashion. Currently, the types and forms of these physical activity types studied in trials vary substantially, as do reported effects. Public health guidelines need to specify details about physical activity—in this case for each exercise type, to specify the specific movements and minimal dose that are effective in improving health. Such information is not currently available, and systematic and coordinated randomized controlled trials are necessarily to provide this information.

5. Conduct research on whether or not individual characteristics influence the effects of physical activity interventions on health outcomes in individuals with chronic conditions.

Rationale: The evidence reviews of this chapter found little information on whether or not the effects of physical activity vary by individual characteristics, such as age, sex, race/ethnicity, body weight, socioeconomic status, and severity of the chronic condition. The importance of such information is illustrated by findings in type 2 diabetes. The evidence suggested effects of physical activity on hemoglobin A1C were larger in individuals with the highest levels of hemoglobin A1C, thus emphasizing those at higher risk of progression with more severe disease were not less likely to benefit from physical activity. From the standpoint of evidence needed for public health guidelines, this is a lower priority need for research because beneficial effects of physical activity have been demonstrated across a wide variety of populations. However, it is desirable for prevention guidelines be appropriately tailored to individuals. Thus, this topic remains a research priority.

Priority Research Needs on Preventive Effects of Physical Activity in Individuals with a Specific Chronic Condition

Question 1: Cancer Survivors

6. Continue long-term follow-up of cohorts of cancer survivors, with repeated self-report and device-based measures of physical activity, to determine long-term effects of physical activity on recurrence and survival.

   Rationale: Although survival from breast cancer is improving, the risk of mortality continues for 20 years or more, especially for women with hormone receptor positive tumors. Survival from prostate cancer tends to be long-term for most men, but for some, progression occurs in spite of optimal treatment. Furthermore, many men with prostate cancer have increased risk for cardiovascular disease, and the primary cause of death in these patients is cardiovascular disease. Therefore, the effect of physical activity on long-term all-cause mortality in prostate cancer survivors will need to be assessed. Colorectal cancer survival is increased with lower stage at diagnosis, and many individuals survive long-term. However, little is known about effects of physical activity on long-term colorectal cancer survival. Continued follow-up of large cohorts will allow for identification of individuals with less common cancers, who can then be followed to determine associations between physical activity level and survival from these other cancers.

7. Conduct randomized controlled trials and cohort studies of physical activity and cancer survival, recurrence, and second primary cancer, aimed at eliminating effects of possible confounders.

Rationale: Treatment type, adherence, and completion are strong predictors of cancer outcomes and can reduce physical activity levels. Fatigue from the cancer and its treatments can reflect adverse clinical processes, and can also reduce physical activity interest and ability. Therefore, randomized controlled trials to test the effect of physical activity on survival, recurrence, and second primary cancer are needed. In addition, cohort studies with appropriate adjustment for clinical sources of confounding can provide additional information, especially if randomized controlled trials are not feasible.

8. Conduct prospective cohort studies and randomized controlled trials to determine effects of physical activity on cancer survival, recurrence, and second primary cancer in understudied groups, such as survivors from diverse races, ethnicities, and socioeconomic groups; individuals with metastatic cancer; men with breast cancer; individuals with cancers other than breast, colorectal, and prostate cancer; and patients treated with cardiotoxic drugs (such as doxorubicin and trastuzumab), radiotherapy, and hormonal treatments.

    Rationale: Few studies have investigated the effects of physical activity on cancer prognosis and survival within specific race, ethnic, or socioeconomic groups. Some of these groups have high risk for poor survival, and are also less likely to meet recommended levels of physical activity. Therefore, determining whether physical activity can improve survival and reduce recurrence and second primary cancers in specific groups is important. Patients treated with cardiotoxic drugs, radiotherapy, or hormonal therapies may have increased risk for cardiac events; it is not known whether physical activity could be cardioprotective in such patients, or whether some forms of physical activity could increase risk of cardiac events.

Question 2: Osteoarthritis

9. Conduct prospective cohort and longer-term randomized controlled trials on osteoarthritis disease progression, with device-based measures used to quantify physical activity exposures and with molecular and imaging disease status biomarkers as outcomes.

    Rationale: There is great confusion in the field on whether physical activity and exercise causes osteoarthritis in the absence of underlying injury and whether specific physical activity and exercise exposure amounts and intensities lead to disease progression. Studies are needed to address these critical issues. Because it takes years for disease activity to result in structural, detectable radiographic changes in the joint, sophisticated imaging modalities, such as magnetic resonance imaging, and biological biomarkers of disease activity (circulating systemic or intra-articular) are required to measure the outcomes.

10. Conduct research to clarify how osteoarthritis progression is modified by baseline demographic and disease characteristics**.**

    Rationale: For the outcome of disease progression induced by physical activity, some evidence suggests that baseline disease status plays a role in modifying the effect of physical activity, but this role has not yet been fully explained. In addition, although a relationship between body mass index and osteoarthritis is generally recognized, no studies have investigated through meta-analyses whether body mass index modifies the physical activity-osteoarthritis relationship.

11. Conduct direct head-to-head comparisons of the relative effectiveness of physical activity and analgesics for pain control in individuals with osteoarthritis.

    Rationale: The current review of the literature revealed that the effect sizes of pain control for exercise therapy is very similar to that of analgesics, including narcotic analgesics.[16] If true, this would be a critical observation with profound implications for patient care, especially as the effects of physical activity on osteoarthritis-related pain seem to be durable for up to six months following cessation of an intervention. Determining the comparative effects of physical activity and analgesics on osteoarthritis pain could contribute greatly to effective clinical management of osteoarthritis.

Question 3: Hypertension

12. Conduct research in people with hypertension on the relationships among physical activity and risk of co-morbid conditions, physical function, health-related quality of life, and cardiovascular disease progression and mortality, which compares effects of physical activity in African Americans to effects in other racial/ethnic groups.

    Rationale: Due to the disproportionate burden of hypertension among African Americans, large trials are needed that are sufficiently powered to perform stratified analyses between African Americans and other racial/ethnic groups. Gaining this information will inform public health recommendations about demographic characteristics that influence the relationship between physical activity and blood pressure, and provide insight into the populations that will experience the greatest cardiovascular health benefits from physical activity.

13. Conduct research that discloses the standard criteria and methods that were used to determine the blood pressure status of the study sample to better isolate samples with hypertension from those with normal blood pressure and prehypertension.

    Rationale: Limited evidence suggests the magnitude of the blood pressure response to physical activity varies by resting blood pressure level, with the greatest blood pressure reductions occurring among adults with hypertension that have the highest resting blood pressure levels. Study sample often include mixed samples of adults with hypertension, prehypertension, and normal blood pressure, and findings are frequently not reported separately by blood pressure classification. Consistent with the law of initial values, this practice underestimates the antihypertensive benefits of physical activity. Reporting findings by blood pressure classification will inform public health recommendations on the magnitude and precision of the blood pressure reductions that result from physical activity among adults with hypertension.

14. Conduct research that discloses and quantifies medication use, particularly antihypertensive medication use among samples with hypertension.

    Rationale: Medication use is poorly reported and is a significant confounder in interpreting the clinical significance of the blood pressure response to physical activity. In addition, evidence is lacking on the interactive effects of physical activity and antihypertensive medication use, another important clinical outcome on that has insufficient evidence. Gaining this information is important to determine whether the influence of physical activity on blood pressure varies by antihypertensive medication use.

Question 4: Type 2 Diabetes

15. Conduct randomized controlled trials comparing the effects of shifting time from sedentary behavior to low-intensity aerobic activity, moderate-intensity aerobic activity, low-intensity muscle-strengthening activity, and moderate-intensity muscle-strengthening activity on indicators of risk of progression of type 2 diabetes.

Rationale: Evidence is growing of the benefits of reducing sedentary behavior, particularly in individuals with chronic conditions affecting metabolic health. Research is needed on whether shifting sedentary time to light-intensity activities affects progression of type 2 diabetes. If light-intensity activities are beneficial, it is important to compare the efficiency and effectiveness of light-intensity versus moderate-intensity activity. Given the well-documented health benefits of shifting time to moderate-intensity aerobic and muscle-strengthening activities, randomized controlled trials are needed that answer questions such as: Does it require shifting, say, 2 to 3 hours from sedentary to light-intensity activity to obtain the same benefits? Or does it take more like 6 to 8 hours?

16. Conduct randomized controlled trials of fall prevention exercise in adults with type 2 diabetes who are at increased risk of falls and fall injuries.

Rationale: A major finding in the Older Adults chapter (see *Part F. Chapter 9. Older Adults*) is that fall prevention exercise programs can substantially reduce risk of serious fall injuries in the general aging population. However, the risk factor profile for falls in adults with type 2 diabetes may differ substantially from the profile in the general population, due to effects specific to type 2 diabetes-related on fall risk factors (e.g., neuropathy, myopathy, impaired vision, and foot disorders). The search for evidence located one small review of fall prevention programs in type 2 diabetes. Thus, RCTs are needed on effects of fall prevention exercise in individuals with type 2 diabetes at increased fall risk.

Question 5: Multiple Sclerosis

17. Conduct randomized controlled trials to determine the effects of physical activity on basic and instrumental activities of daily living, participation, and community engagement for individuals with multiple sclerosis.

Rationale: Strong evidence now exists that greater physical activity can improve walking function, strength, and fitness for individuals with multiple sclerosis. This supports a rationale for further research to determine whether this translates into improved basic and instrumental activities of daily living, increased free-living physical activity, and improved safety in mobility.

18. Conduct longitudinal cohort studies to determine the potential for physical activity to serve as a moderator of disease progression and changes in brain health in individuals with multiple sclerosis.

Rationale: Systematic reviews of controlled studies find no evidence that physical activity alters disease progression, in contrast to epidemiological studies that indicate possible disease-modifying effects.[17] However, these controlled studies are limited by relatively brief intervention lengths, small sample sizes, and lack of measures of brain disease activity; factors that multi-site studies of disease-modifying medications show are needed to fully explore the natural history of multiple sclerosis. This discrepancy between epidemiological and controlled studies, and bench neuroscience findings that physical activity can provide neuroprotective effects and stimulate neuroplasticity, including for brain white matter, support a rationale for further research into disease modification.

Question 6: Spinal Cord Injury

19. Conduct randomized controlled trials in children and adolescents with spinal cord injury to determine effects of physical activity on psychosocial and social environmental development and participation.

    Rationale: A knowledge gap exists regarding health benefits in this population, which differs from adults in terms of mechanisms for injury and greater potential for neuroplasticity and recovery. Future research in pediatric spinal cord injury is needed to determine age-appropriate modalities and prescriptions for physical activity to facilitate recovery of mobility, optimize functional recovery and independence in daily activities, prevent or reduce comorbid and secondary complications, and optimize psychosocial and psychological development across the formative childhood and adolescent years.

20. Conduct research in individuals with spinal cord injury to determine effects of physical activity on basic and instrumental activities of daily living, free-living physical activity, social participation and engagement, balance and risk for injurious falls and fractures.

    Rationale: The evidence in this report that selected modes of physical activity can produce clinically significant improvements in physical function supports a rationale for randomized studies to determine whether such gains translate into improved daily function, participation, and engagement in activities in the living space and social environment. Systematic analyses of relationships between age, race/ethnicity, socioeconomic status, and weight status need to be built into all such research recommendations. Generally, randomized controlled trials are necessary to address the research need.

Question 7: Intellectual Disabilities

21. Conduct randomized controlled trials to determine the effects of physical activity on cognitive function, neurodevelopmental profiles, instrumental activities of daily living, and adaptive functioning that are related to neuropsychological status in individuals with intellectual disabilities.

    Rationale: Only limited evidence is available on the effects of physical activity on four important outcomes in people with intellectual disabilities: cognitive function, neurodevelopmental profiles, instrumental activities of daily living, and adaptive functioning. Randomized studies are needed to determine whether physical activity can improve cognition for individuals with intellectual disabilities across the age spectrum. Likewise, future research is needed to investigate effects of greater physical activity on neurodevelopment and adaptive functioning. In addition, research should also consider these broader outcomes in an age- and intellectual disability-specific fashion.

22. Conduct randomized controlled trials and cohort studies on effects of physical activity in individuals with a variety of etiologies for intellectual disabilities, and determine whether health effects vary by age, race/ethnicity, socioeconomic status, and weight status.

    Rationale. As the most common genetic cause of intellectual disability in the United States, Down syndrome has received the most research attention. Major gaps exist on the potential health benefits of physical activity in most other conditions, including autism spectrum disorder and autistic traits, Fragile X syndrome, tuberous sclerosis, neurologic sequelae of toxins (e.g., alcohol, lead), maternal and fetal infections, and nutritional deficiencies (e.g., iodine, protein-calorie malnutrition), and neurological sequelae associated with prematurity. Future research is needed to address race/ethnicity, socioeconomic status, and weight status as factors that influence relationships between physical activity and health outcomes for individuals with disabilities.

CHAPTER 11. PROMOTING REGULAR PHYSICAL ACTIVITY

The evidence review in this chapter highlights a number of research needs across the different intervention areas highlighted in the review. It should be noted, however, that given that the evidence review was not comprehensive, a number of other intervention areas were not captured in this evidence review that also undoubtedly merit further research.

In light of some unique aspects of scientific intervention development specific to the Information and Communication Technologies area, the research needs that are broadly applicable to all topic areas contained in this chapter are presented first, followed by an additional set of research needs specific to the fast-growing information and communication technologies intervention arena.

Research Needs that are Broadly Applicable to All Topic Areas Presented in this Chapter

1. Broaden enrollee targets in randomized controlled trials and other research in this area to incorporate diverse population subgroups, including broader age groups, men as well as women, diverse racial/ethnic groups, and vulnerable and underrepresented population groups (e.g., lower-income residents, patient subgroups).

   Rationale: In order to develop interventions that have the potential for having a public health impact at the population level, it is critical to ensure that diverse age, sex, racial/ethnic, cultural, geographic, and income groups are included in the experimental research designs that can most effectively advance the field. Data collected across these various subgroups of the population will inform how to adapt interventions to subgroup needs through formative and iterative intervention design methods, and can help strengthen interventions through ensuring that they are targeted effectively for specific subgroups as well as tailored to individual preferences and requirements.

2 Test physical activity and sedentary behavior interventions over longer time periods (i.e., more than 12 months) to better understand how to sustain their positive effects.

   Rationale: Because many of the positive health effects of regular physical activity and reduced sedentary time can accumulate over time and require regular engagement across time, methods for maintaining regular physical activity and reduced sedentary patterns are critical. Yet, as pointed out in this chapter, relatively few interventions have been systematically tested across time periods lasting several years, and knowledge concerning how best to foster sustained physical activity maintenance in different subgroups over time remains inadequate.

3. Report, in experimental and quasi-experimental investigations of physical activity interventions, intervention-related dose-response relations and adverse events to aid intervention evaluation, translation, and dissemination.

Rationale: Experimental investigations in this area can benefit from consistent inclusion of information related to intervention dose-response (e.g., how does the intensity of the intervention, in terms of the type of communication delivery channel being used (e.g., in-person, mediated), as well as number, length, or schedule of contacts, affect the amount of physical activity change?). In addition, adverse events related to the intervention are important for determining intervention safety and appropriateness for various population subgroups, but are rarely reported in a systematic fashion.

4. Develop efficient methods for collecting cost data on all interventions being tested to inform cost-benefit and cost-effectiveness comparisons across the physical activity intervention field as a whole. For those intervention areas that are further developed, use comparative effectiveness designs to more efficiently advance the study and translation of interventions to promote physical activity and reduce sedentary behavior.

   Rationale: In an increasingly cost-conscious health environment, it is important for the public and decision-makers alike to gain a better understanding of the costs of different interventions relative to their effectiveness to make more informed decisions in relation to intervention choice. In those intervention areas with evidence grades of Moderate or Strong, the use of comparative effectiveness experimental designs, in which interventions that have been shown to have merit are tested "head-to-head," will advance knowledge more rapidly than designs that continue to use weaker controls or comparisons (e.g., minimal or no intervention, wait-list controls). In addition, further systematic evaluation of potentially cost-efficient intervention delivery sources (e.g., peer-led interventions) and delivery channels (e.g., automated behavioral counseling systems, virtual advisors), either as adjuncts to or replacements for more staff-intensive interventions, is warranted.

5. Develop standards in the field for choosing the most appropriate comparator arms with which to compare emerging physical activity interventions when evaluating their efficacy and effectiveness.

   Rationale: Similar to other health behavior fields, advancing the physical activity promotion field along the continuum of science, from discovery of promising interventions through dissemination of interventions that work, will require investigators to employ the most relevant comparator arms to answer the specific questions of interest that are being pursued. Relatively little consensus currently exists, however, concerning the most appropriate comparators to use to answer the various types of questions reflected across the different levels of impact described in this chapter. The field as a whole would benefit from building general consensus concerning the most appropriate types of comparators, along with design parameters, to be considered, based on the current state of the evidence and the most critical questions emanating from it.

6. For those intervention topic areas receiving a Strong or Moderate evidence grade, develop and systematically test methods for effectively implementing such physical activity promotion and sedentary behavior change approaches in real-world settings.

   Rationale: Although the current evidence review identified a number of physical activity promotion approaches and strategies that are effective in increasing physical activity behavior, few such approaches have been systematically disseminated across the U.S. population. In light of the sizable portion of the population that could benefit from increasing their regular physical activity levels, the development and systematic testing of potentially effective implementation methods and strategies are critical.

7. Develop and systematically test multi-component interventions that span multiple levels of influence to increase intervention impact and potential sustainability of behavior change.

   Rationale: It is clear that health behaviors such as physical activity and sedentary behavior are influenced by an array of individual, sociocultural, community, and environmental factors, yet many of the interventions that have been tested contain elements centered primarily on one level of impact (e.g., personal factors; institutional factors; built environment factors). Increasing the effectiveness and robustness of interventions likely could occur through targeting people within their environmental and social contexts (i.e., person-environment interactions). An example of such multi-level interventions includes combining individual-level behavioral skill-building strategies with neighborhood-level built environmental interventions to promote increased walkability.

8. Test, using experimental methods, strategies for promoting regular physical activity and reduced sedentary behavior across key life-course transitions, when such health behaviors potentially result in deleterious outcomes.

Rationale: Common life-course transitions and the changes in role expectations and social and environmental contexts that often accompany them, can lead to negative impacts on physical activity levels and other health behaviors. Such transitions include changes from school to the workforce; changes in marital status and family roles and configurations; and physical transitions occurring at puberty, menopause, or with the onset of a chronic conditions. Systematic testing of methods and approaches for facilitating regular physical activity and reduced sedentary behavior during and following such common transitions could have significant, population level impacts.

9. Conduct experimental research aimed at testing systematically how best to combine physical activity interventions with other health behavior interventions, such as sedentary behavior, sleep quality, or dietary change interventions, to promote optimal physical activity change within the context of such multi-behavioral interventions.

   Rationale: Given the potential health-related synergies that can accrue when both physical activity and sedentary behavior change, or physical activity and dietary changes are implemented, systematic investigations of how best to combine these important health behaviors in different population subgroups are strongly indicated. Currently, little is known concerning the best approaches for combining health-enhancing physical activity with sedentary behavior change or dietary interventions, regardless of intervention modality, to facilitate sustainable behavior changes in both health behaviors. The few randomized controlled trials in this area are intriguing, however.[18] For example, some evidence exists suggesting that, in some population subgroups, introducing dietary interventions along with physical activity interventions may reduce the amount of physical activity change observed.[19] Further systematic evaluation of potential behavioral compensation effects between physical activity and sedentary behaviors is also warranted to ensure that physical activity increases during one portion of the day do not result in increased sedentary behavior in other portions of the day.

10. Increase the scientific utility of systematic reviews and meta-analyses to inform future research directions in the physical activity promotion and sedentary behavior reduction fields.

Rationale: Although the number of systematic reviews has exploded across virtually all physical activity promotion and sedentary behavior areas, a number of such reviews lack specific types of quantitative information that can be useful in obtaining an accurate summation of a research area upon which future research can be applied. Such information includes the following:

- Inclusion, whenever possible, of quantitative estimates of effect sizes or other magnitude of effect statistics for the articles included in the review, as opposed to simply *P* values;
- Clear descriptions of statistical outcomes for between-arm comparisons for all controlled or comparison arm studies along with specific notations when authors did not report such between-arm comparisons;
- Inclusion in each study, whenever possible, of the net physical activity differences achieved between intervention and control arms (e.g., with respect to mean step increases per day or mean minutes per week of moderate-to-vigorous physical activity achieved) over the specific time period under investigation;
- Inclusion of subgroup analyses based on key sociodemographic characteristics (e.g., sex, socioeconomic status, race/ethnicity, age) to identify which interventions might require specific targeting to be effective in different population subgroups.
- Reporting of adverse events and any unintended consequences of the interventions.

Research Needs Specific to Information and Communication Technologies-Level Evidence

1. Employ additional types of experimental designs and methods that will allow for more rapid testing of information and communication technology interventions.

   Rationale: In light of the rapid evolution of the information and communication technologies interventions discussed in this chapter, traditional 2-arm parallel-arm trial designs may not easily allow researchers to keep up with the technology innovations that are occurring in this area. Further use of more advanced experimental designs, such as fractional or multi-level factorial designs and just-in-time adaptive interventions, is warranted.

2. Further explore methods and pathways for systematically exploiting the vast amounts of commercially available physical activity-relevant data and interventions that already reside in this area.

   Rationale: Millions of people representing a diverse and growing segment of the population are currently using commercial technologies aimed at physical activity behavior. Such databases have vast potential for accelerating our knowledge concerning the most effective ways of promoting physical activity among different population groups, yet remain relatively untouched. Exploring appropriate avenues for using these naturally-occurring databases provides a potentially paradigm-shifting approach to accelerate scientific advances in this area and the attendant public health benefits that can be gained.[20]

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Part H. Appendices

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PART H. APPENDIX 1. GLOSSARY OF TERMS

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This section provides definitions for many of the key terms used in this report, and the definitions reflect those commonly used in the scientific literature as well as in major reports and recommendations for physical activity and health. The Committee recognizes that as research continues and the evidence base for physical activity and health grows and evolves, new terms will emerge and definitions may change. Also, please see *Part C. Background and Key Physical Activity Concepts* for additional discussion of selected terms in this glossary and their related concepts.

Physical Activity and Exercise

Physical activity. Bodily movement produced by skeletal muscles that results in energy expenditure. The term does not require or imply any specific aspect or quality of movement and encompasses all types, intensities, and domains.

Exercise. Physical activity that is planned, structured, repetitive, and designed to improve or maintain physical fitness, physical performance, or health. Exercise encompasses all intensities.

Non-exercise physical activity. All physical activity that is not exercise.

Sedentary behavior. Any waking behavior characterized by an energy expenditure of 1.5 or fewer METs while sitting, reclining, or lying. Most office work, driving a car, and sitting while watching television are examples of sedentary behaviors. Sedentary behavior and sedentary activity (see definition below) are similar but not synonymous; both are limited to energy expenditures 1.5 or fewer METs, but sedentary activity includes standing.

Types of Physical Activity

Aerobic physical activity. Forms of activity that are intense enough and performed long enough to maintain or improve an individual's cardiorespiratory fitness. Aerobic activities commonly require the use of large muscle groups. Examples of aerobic activities include walking, basketball, soccer, wheelchair rolling, or dancing.

Anaerobic physical activity. High-intensity activity that exceeds the capacity of the cardiovascular system to provide oxygen to muscle cells for the usual oxygen-consuming metabolic pathways. Anaerobic activity can be maintained for only a short period of time, about 2 to 3 minutes. Sprinting and power lifting are examples of anaerobic physical activity.

Balance training. Movements that safely challenge postural control. If practiced regularly, they improve the ability to resist intrinsic or environmental forces that cause falls whether walking, standing, or sitting. Walking backward, standing on one leg, or using a wobble board are examples of balance training. Strengthening muscles of the core and legs also improves balance.

Bone-strengthening activities. Movements that create impact- and muscle-loading forces on bone. These forces stress the bone, which adapts by modifying its structure (shape) or mass (mineral content), thereby increasing its resistance to fracture. Jumping, hopping, skipping, and dancing are activities that strengthen bones, as are high-resistance muscle-strengthening activities.

Flexibility training (stretching). Activity that improves the range and ease of movement around a joint. Static stretching, various poses of yoga, and some movements of tai chi are examples of flexibility training.

High-intensity interval training (**HIIT**) is a form of interval training consisting of alternating short periods of intense anaerobic exercise with less intense aerobic recovery periods. There are no universally accepted lengths for either the anaerobic period, the recovery period, nor the ratio of the two; no universally accepted number of cycles for any HIIT session or the entire duration of the training bout;

and no universally accepted relative intensity at which the intense anaerobic component should be performed.

Muscle-strengthening activities. Physical activities that maintain or improve muscular strength (how much resistance can be overcome), endurance (how many times or for how long can resistance be overcome), or power (how fast can the resistance be overcome). Muscle-strengthening activities include everyday behaviors, such as carrying heavy groceries, shoveling snow, lifting children, or climbing stairs, as well as the use of exercise equipment, such as weight machines, free weights, or elastic bands.

Resistance training. A method of muscle-strengthening activity or conditioning that involves the progressive use of resistance to increase one's ability to exert or resist force.

- **Isometric resistance exercise (iso meaning equal and metric meaning length).** A type of muscle contraction during which the muscle generates force without lengthening and movement of the object.
- **Dynamic resistance exercise.** A type of contraction during which the muscle generates force by changing length to move an object. Contractions that produce a lengthening of the muscle are termed eccentric, whereas those involving shortening are termed concentric.

Domains of Physical Activity

Activities of daily living: Activities required for everyday living, including eating, bathing, toileting, dressing, getting into or out of a bed or chair, and basic mobility.

Instrumental activities of daily living. Activities related to independent living, including preparing meals, managing money, shopping for groceries or personal items, and performing housework.

Household physical activity. Activity done in or around the home, such as cooking, cleaning, home repair, yardwork, or gardening.

Leisure-time physical activity. Discretionary activity performed when one is not working, transporting oneself to a different location, or doing household chores. Sports or exercise, going for a walk, and playing games (hopscotch, basketball), are examples of leisure-time physical activity.

Occupational physical activity. Activity performed at work, such as stocking shelves in a store, delivering packages in an office, preparing or serving food in restaurant, or carrying tools in a garage are examples of occupational physical activity.

Transportation physical activity. Activity performed to get from one place to another, such as walking to and from work, school, or shopping.

Absolute and Relative Intensity

Absolute intensity. The rate of energy expenditure required to perform any given physical activity. It can be measured in metabolic equivalents, kilocalories, joules, or milliliters of oxygen consumption.

- **Metabolic equivalent of task (MET).** A unit that represents the metabolic cost of physical activity. One MET is the rate of energy expenditure while sitting at rest, which, for most people approximates an oxygen uptake of 3.5 ml per kg per min. The energy expenditure of other activities is expressed in multiples of METs. For example, for the average adult, sitting and reading requires about 1.3 METs, strolling or walking slowly requires about 2.0 METs, and running at 5 miles per hour requires about 8.3 METS.

Absolute rates of energy expenditure are commonly divided into four categories:

- **Sedentary activity.** Activity requiring 1.0 to 1.5 METs, such as sitting and reading or watching television, or standing quietly.
- **Light intensity.** Activity requiring 1.6 to less than 3.0 METs, such as walking at a slow pace (2 mph or less) or cooking.
- **Moderate intensity.** Activity requiring 3.0 to less than 6.0 METs, such as walking briskly (3 to 4 mph), mopping or vacuuming, or raking a yard.
- **Vigorous intensity.** Activity requiring 6.0 or greater METs, such as walking very fast (4.5 to 5 mph), running, mowing grass with a hand-push mower, or participating in an aerobics class.

Relative intensity. Relative intensity refers to the ease or difficulty with which an individual performs any given physical activity. It has a physiologic basis and can be described using physiologic parameters, such as percent of aerobic capacity (VO_2max) or percent of maximal heart rate. Relative intensity can also be estimated by self-report of level of perceived exertion during an activity.

Dose, Volume, and Dose-response for Aerobic Activities

Dose. The amount of physical activity performed or prescribed. Dose is commonly calculated for a specific period of time, such as per day or per week, and has been limited to moderate-to-vigorous physical activity. Aerobic physical activity dose commonly has three components:

- **Frequency.** The number of sessions or bouts of physical activity performed per day or per week.
- **Duration.** The length of time for each session or bout.
- **Intensity.** The rate of energy expended during the physical activity session or bout, usually in METs.

Dose-response. The relationship between the dose or volume of physical activity and the magnitude of its effect on a health outcome (e.g., mortality) or physiologic measure (e.g., aerobic fitness). A graduated response—small dose with small response, large dose with large response—is evidence of the truth of the relationship. For ordinal data, a dose-response relationship requires at least three levels of exposure.

Volume. The quantification of the dose of activity accumulated over a specified length of time. Volume is usually expressed in MET-minutes or MET-hours per day or week, which involves multiplying the physical activity frequency and duration by the MET values corresponding to that physical activity.

Physical Fitness and Physical Function

Physical fitness. The ability to carry out daily tasks with vigor and alertness, without undue fatigue and with ample energy to enjoy leisure-time pursuits and meet unforeseen emergencies. It has been defined by the World Health Organization as "the ability to perform muscular work satisfactorily." Physical fitness includes a number of components consisting of cardiorespiratory endurance (aerobic power), skeletal muscle endurance, skeletal muscle strength, skeletal muscle power, flexibility, balance, speed of movement, reaction time, and body composition.

- **Agility**. Ability to change position of the entire body in space with speed and accuracy.
- **Balance**. Ability to maintain the body's equilibrium while stationary or moving.
- **Cardiorespiratory endurance**. Ability to perform large muscle, whole-body exercise at moderate to high intensities for extended periods of time.
- **Coordination**. Ability to carry out motor tasks smoothly and accurately.
- **Flexibility**. The range of motion possible at a joint.

- **Musculoskeletal fitness.** The integrated function of muscle strength, muscle endurance, and muscle power to enable the performance of work.
- **Power**. The rate at which work can be performed.
- **Strength**. Ability of a muscle or muscle group to exert force.

Physical function. The ability of a person to move around and to perform types of physical activity. Measures of physical function include measures of ability to walk (e.g., usually gait speed), run, climb stairs, carry groceries, sweep the floor, stand up, and bathe.

Related Physical Fitness Terms

Accumulation/Accumulate The concept of meeting a specific physical activity dose or goal by performing activity in several bouts, then adding together the time spent during each of these bouts. For example, a 30-minute per day goal could be met by performing several bouts of moderate-to-vigorous physical activity throughout the day.

Adaptation. The body's response to exercise or activity. Some of the body's structures and functions favorably adjust to the increase in demands placed on them whenever physical activity of a greater amount or higher intensity is performed than what is usual for the individual. It is these adaptations that are the basis for much of the improved health and fitness associated with increases in physical activity.

Adverse event. In the context of physical activity, a negative health event. Examples of adverse events as a result of physical activity include musculoskeletal injuries (injury to bone, muscles, or joints), heat-related conditions (e.g., heat exhaustion), and cardiovascular (e.g., heart attack or stroke) events.

Maximal oxygen uptake (VO_2max). The body's capacity to transport and use oxygen during a maximal exertion involving dynamic contraction of large muscle groups, such as during running or cycling. It is also known as maximal aerobic power. Peak oxygen consumption (VO_{2peak}) is the highest rate of oxygen consumption observed during an exhaustive exercise test.

Overload. The amount of new activity added to a person's usual level of activity. The risk of injury to bones, muscles, and joints is directly related to the size of the overload.

Progression. The process of increasing the intensity, duration, frequency, or amount of activity or exercise as the body adapts to a given activity pattern.

Repetitions. The number of times a person lifts a weight in muscle-strengthening activities.

Specificity. A principle of exercise physiology that indicates that physiologic changes in the human body in response to physical activity are highly dependent on the type of physical activity. For example, the physiologic effects of walking are largely specific to the lower body and the cardiovascular system.

Health and Health Conditions

Health. A human condition with physical, social, and psychological dimensions, each characterized on a continuum with positive and negative poles. Positive health is associated with a capacity to enjoy life and to withstand challenges; it is not merely the absence of disease. Negative health is associated with morbidity, and in the extreme, with premature mortality.

Quality of life. A concept that reflects how individuals perceive and react to their health status and to other, non-medical aspects of their lives.

- **Health-related quality of life.** A multi-dimensional concept that reflects the way that individuals perceive and react to their health status. It includes domains related to physical, mental, emotional, and social functioning.

Body weight status. A concept encompassing issues related to weight gain, loss, and maintenance.

- **Clinically significant weight loss.** A change in body weight of 5 percent or greater.

- **Excessive weight gain.** A change in body weight of more than 2 kg per year or 10 kg per decade; or, a weight increase of more than 3 percent.

Brain health. The optimal functioning of behavioral and biological measures of the brain and the subjective experiences arising from brain function (e.g., mood).

- **Affect.** Subjective experience of feeling states defined by independent dimensions of valence (pleasure) and activation.

- **Anxiety.** An unpleasant high activation feeling state characterized by feelings of apprehension, worry, and physical sensations arising from activation of the autonomic nervous system. In the extreme, these feelings can become a clinical disorder.

- **Cognition.** The set of mental processes that contribute to perception, memory, intellect, and action. Cognitive function can be assessed using a variety of techniques including paper-pencil based tests, neuropsychological testing, and computerized testing methods. Cognitive functions are divided into different domains that capture both the type of process as well as the brain areas and circuits that support those functions. Working memory, visual attention, and long-term memory are all examples of different cognitive domains that are thought to be dependent on overlapping yet largely separate neural systems.

- **Depression.** An unpleasant low activation feeling state characterized by sadness, or feelings of hopelessness or guilt. In the extreme, these feelings can become a clinical disorder.

- **Sleep.** A reversible behavioral state of perceptual disengagement from and unresponsiveness to the environment, which consists of two separate states that are as different from one another as they are from wakefulness: Rapid Eye Movement (REM) and Non-REM.

Cancer. A collection of related diseases in which some of the body's cells begin to divide without stopping and spread into surrounding tissues.

- **Cancer survivor.** A person who has been diagnosed with, is undergoing treatment for, or has received treatment for any type of cancer.

- **Cancer recurrence.** An event in which the original primary cancer is detected after a remission (the period during which cancer was no longer detected).

- **Second primary cancer.** A new cancer that occurs sometime after diagnosis of original primary cancer.

Cardiovascular disease. Diseases of the heart, brain, and blood vessel system (arteries, capillaries, veins) within the entire body. Cardiovascular disease encompasses coronary heart disease/ischemic heart disease, coronary artery disease, stroke, and heart failure. It does not include congenital heart disease.

Diabetes. A disease characterized by high blood glucose levels caused by either a lack of insulin or the body's inability to use insulin efficiently. The extent that blood glucose is persistently elevated is commonly assessed by measuring glycated hemoglobin, abbreviated as HbA1C. The current criteria used to diagnose diabetes are an HbA1C of 6.5% or higher, fasting blood glucose of 126 mg per dL or higher, and/or a 2-hour oral glucose tolerance test (OGTT) blood glucose of 200 mg per dL or higher.

- **Prediabetes.** Having an HbA1C of 5.7% to 6.4%, fasting blood glucose of 100 to 125 mg per dl, and/or an OGTT 2-hour blood glucose of 140 mg per dL to 199 mg per dL with fasting blood glucose of less than 126 mg per dL.

- **Normal blood glucose.** Having an HbA1C below 5.7%, fasting blood glucose less than 100 mg per dL, and an OGTT 2-hour blood glucose lower than 140 mg per dL.

Disease progression. A change or worsening of a disease over time.

Fall. The act of moving without control from being upright to not being upright.

Hypertension. A condition in which blood pressure remains elevated over time.

- **Current blood pressure classification scheme.** According to the 2017 *Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults,* hypertension is defined as a resting systolic blood pressure of 130 mmHg or greater and/or a resting diastolic blood pressure 80 mmHg or greater, or taking antihypertensive medication, regardless of the resting blood pressure level. Normal blood pressure is defined as having resting systolic blood pressure less than 120 mmHg and a diastolic blood pressure less than 80 mmHg. These Guidelines eliminate the term "prehypertension" and add "elevated blood pressure," which is defined as a resting systolic blood pressure between 120 to 129 mmHg and a diastolic blood pressure less than 80 mmHg.
- **Blood pressure classification scheme used by the Committee.** Because the literature reviewed by the Committee was based upon the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) blood pressure classification scheme, these classifications were used to answer the Committee's blood pressure questions. The JNC 7 defines hypertension as having a resting systolic blood pressure of 140 mmHg or greater and/or a resting diastolic blood pressure 90 mmHg or greater, or taking antihypertensive medication, regardless of the resting blood pressure level. Prehypertension is defined as a systolic blood pressure from 120 to 139 mmHg and /or diastolic blood pressure from 80 to 89 mmHg. Normal blood pressure is defined as having a systolic blood pressure less than 120 mmHg and diastolic blood pressure less than 80 mmHg.

Intellectual disability. Significant limitation in both intellectual function and adaptive behavior, defined as the collection of conceptual, social, and practical skills that are learned and performed within everyday life, that manifests before the age of 18 years.

Multiple sclerosis. An immune-mediated process in which an abnormal response of the body's immune system is directed against the central nervous system, which consists of the brain, spinal cord, and optic nerves. It is marked by symptoms such as fatigue, gait disturbances, and spasticity and is typically characterized by evidence of damage in at least two separate areas of the central nervous system that occurred at least 1 month apart.

Osteoarthritis. A disorder of movable joints occurring idiopathically in characteristic locations and increasing with age. Osteoarthritis can occur secondarily in any joint in response to a joint insult (e.g., injury, infection). Osteoarthritis involves anatomic, and/or physiologic derangements of all joint tissues (characterized by cartilage degradation, bone remodeling, osteophyte formation, joint inflammation, muscle weakness and loss of normal joint function), that can culminate in illness (pain, stiffness, or loss of quality of life).

Postpartum period. A period of time for a woman that encompasses the date of birth through 1 year after birth.

Risk of co-morbid conditions. The chance of having one or more additional conditions.

Spinal cord injury. Damage incurred to the spinal cord resulting from trauma, disease, or degeneration and marked by symptoms that vary according to the level (location) and severity of the injury.

Study Design and Synthesis

Case-control study. A type of epidemiologic study design in which participants are selected based on the presence or absence of a specific outcome of interest, such as cancer or diabetes. The participant's past physical activity practices are assessed, and the association between past physical activity and presence of the outcome is determined.

Cross-sectional study. A type of epidemiologic study that compares and evaluates specific groups or populations at a single point in time.

Intervention. Any kind of planned activity or group of activities (including programs, policies, and laws) designed to prevent disease or injury or promote health in a group of people, about which a single summary conclusion can be drawn.

Meta-analysis. A review of a focused question that follows rigorous methodological criteria and uses statistical techniques to combine data from studies on that question.

Observational study. A study in which outcomes are measured but no attempt is made to change the outcome. The two most commonly used designs for observational studies are case-control studies and prospective cohort studies.

Prospective cohort study. A type of epidemiologic study in which the practices of the enrolled subjects are determined and the subjects are followed (or observed) for the development of selected outcomes. It differs from randomized controlled trials in that the exposure is not assigned by the researchers.

Randomized controlled trial. A type of study design in which participants are randomly grouped on the basis of an investigator-assigned exposure of interest, such as physical activity. For example, among a group of eligible participants, investigators may randomly assign them to exercise at three levels: no activity, moderate-intensity activity, and vigorous-intensity activity. The participants are then followed over time to assess the outcome of interest, such as change in abdominal fat.

Retrospective study. A study in which the outcomes have occurred before the study data collection has begun.

Systematic review. A review of a clearly defined question that uses systematic and explicit methods to identify, select, and critically evaluate relevant research, and to collect and analyze data from the studies included in the review.

Measurement

Effect size. The difference in mean outcomes of the treatment (exposed) and control (unexposed) groups, divided by the standard deviation of the outcome in the control group or the pooled standard deviation.

Hazard ratio. A measure of how often a particular event happens in one group compared to how often it happens in another group, over time. A hazard ratio of 1.0 means that there is no difference in survival or time to event between the two groups. A hazard ratio of greater than 1.0 or less than 1.0 means that survival or time to event was better in one of the groups. For example, a hazard ratio of 0.5 for mortality in people who participate in physical activity, compared with people who are inactive, indicates that active persons are 0.5 times (50%) less likely to have died at any particular point in time, compared with those who are inactive.

Odds ratio. A measure of association used in epidemiologic studies. It measures the chances of an event (or disease) occurring in one group of people as compared to another group with different characteristics. For example, an odds ratio of 0.5 for high blood pressure in people who participate in physical activity, compared with people who are inactive, indicates that active persons have 50% lower odds of having high blood pressure, compared with those who are inactive.

Relative risk. A measure of association used in epidemiologic studies. It measures the magnitude of association between an exposure (such as physical activity) and a disease (such as colon cancer). In physical activity, relative risk is typically the ratio of the risk of a disease or disorder when comparing groups of people who vary in their amount of physical activity. A relative risk of 0.5 for colon cancer associated with physical activity, compared with inactivity, indicates that active persons have 0.5 times (or 50%) the risk of developing colon cancer compared to inactive persons.

Confidence interval. When a measure of association, such as relative risk or hazard ratio, is calculated, one can also calculate a confidence interval, or a band of uncertainty, around the estimate. Typically, 95% confidence intervals are used in epidemiologic studies. For example, if the estimated relative risk for colon cancer associated with physical activity, compared with inactivity, is 0.5 with a 95% confidence interval of 0.3 to 0.8, this means that if the study were repeated over and over, in at least 95% of the repetitions the true estimate of the relative risk would be between 0.3 and 0.8.

Standardized mean difference. A summary statistic used in meta-analyses when the studies all assess the same outcome but measure it in a variety of ways (for example, all studies measure depression but they use different psychometric scales). In this circumstance, it is necessary to standardize the results of the studies to a uniform scale before they can be combined. The standardized mean difference expresses the size of the intervention effect in each study relative to the variability observed in that study, usually the standard deviation of the measures.

PART H. APPENDIX 2. SUBCOMMITTEE AND WORK GROUP MEMBERSHIP

Subcommittee or Work Group	Chair	Members	Consultants	HHS Federal Liaison
Subcommittee 1: Aging	Loretta DiPietro	David Buchner Wayne Campbell Kirk I. Erickson Kenneth E. Powell		Richard D. Olson
Subcommittee 2: Brain Health	Kirk I. Erickson	Charles H. Hillman Richard F. Macko David X. Marquez Kenneth E. Powell	David E. Conroy Steven J. Petruzzello	Rachel M. Ballard
Subcommittee 3: Cancer – Primary Prevention	Anne McTiernan	Peter T. Katzmarzyk Kenneth E. Powell	Christine M. Friedenreich	Alison Vaux-Bjerke
Subcommittee 4: Cardiometabolic Health and Weight Management	John M. Jakicic	Wayne Campbell Loretta DiPietro Russell R. Pate Linda S. Pescatello Kenneth E. Powell	Ronald J. Sigal	Katrina L. Piercy
Subcommittee 5: Exposure	William E. Kraus	Wayne Campbell Kathleen F. Janz John M. Jakicic Kenneth E. Powell	William L. Haskell	Richard P. Troiano
Subcommittee 6: Individuals with Chronic Conditions	David Buchner	William E. Kraus Richard F. Macko Anne McTiernan Linda S. Pescatello Kenneth E. Powell	Christine M. Friedenreich Virginia Byers Kraus Ronald J. Sigal	Stephanie M. George
Subcommittee 7: Promotion of Physical Activity	Abby C. King	John M. Jakicic David X. Marquez Melicia C. Whitt-Glover	Matthew P. Buman Melissa A. Napolitano	Janet E. Fulton

Subcommittee or Work Group	Chair	Members	Consultants	HHS Federal Liaison
Subcommittee 8: Sedentary Behavior	Peter T. Katzmarzyk	John M. Jakicic Kenneth E. Powell		Richard P. Troiano
Subcommittee 9: Youth	Russell R. Pate	Charles H. Hillman Kathleen F. Janz Peter T. Katzmarzyk Kenneth E. Powell Melicia C. Whitt-Glover		Deborah A. Galuska
Physical Fitness Work Group	William E. Kraus	Kirk I. Erickson Kathleen F. Janz Russell R. Pate	William L. Haskell	Richard P. Troiano
Pregnancy and Postpartum Work Group	Kenneth E. Powell	Loretta DiPietro	Kelly Evenson	Katrina L. Piercy
Young Adult Transition Work Group	Kathleen F. Janz	David Buchner Wayne Campbell Peter T. Katzmarzyk Russell R. Pate Kenneth E. Powell		Katrina L. Piercy Richard P. Troiano

PART H. APPENDIX 3. BIOGRAPHICAL SKETCHES OF THE COMMITTEE MEMBERS

Abby C. King, PhD, Co-Chair

Dr. King is Professor of Health Research & Policy and Medicine at Stanford School of Medicine. Recipient of the Outstanding Scientific Contributions in Health Psychology Award from the American Psychological Association, her research focuses on the development, evaluation, and translation of public health interventions to reduce chronic disease and its key risk factors, including physical inactivity and sedentary behavior. She has developed and evaluated the effectiveness of state-of-the-art communication technologies and community-based participatory research perspectives to address health disparities among disadvantaged populations worldwide. She has served on a number of government taskforces in the U.S. and abroad, including membership on the HHS Scientific Advisory Committee on National Health Promotion and Disease Prevention Objectives for 2020, and the Science Board of the President's Council on Fitness, Sports & Nutrition. An elected member of the Academy of Behavioral Medicine Research and Past President of the Society of Behavioral Medicine, Dr. King was one of 10 U.S. scientists honored by the Association of American Medical Colleges in 2014 for outstanding research targeting health inequities. Her research on citizen science engagement to promote healthful living environments for all has been honored with an international excellence award.

Kenneth E. Powell, MD, MPH, Co-Chair

Dr. Powell is a public health and epidemiologic consultant. He was an epidemiologist with the CDC for 25 years and with the Georgia Department of Human Resources for nearly 8 years. The relationship between physical activity and health has been an important theme during his career. He planned, chaired, and edited the papers from the first national workshop on the epidemiologic and public health aspects of physical activity and exercise in 1985. He has authored more than 50 scientific articles on a wide range of aspects of physical activity. Dr. Powell is a member of the Coordinating Team on Physical Activity for the Task Force on Community Preventive Services, Guide to Community Preventive Services. He has served on the Institute of Medicine Committee on Physical Activity, Health, Transportation, and Land Use (2005); Committee on Progress in Preventing Childhood Obesity (2008); and Committee on Physical Activity and Physical Education in the School Setting (2013). He was also a member of the 2008 Physical Activity Guidelines Advisory Committee.

David Buchner, MD, MPH

Dr. Buchner received his BA degree from Harvard University and his MD from the University of Kansas. After a residency in general internal medicine, he was a fellow in the Robert Wood Johnson Clinical Scholars Program at University of Washington, where he received his M.P.H. degree and training in geriatric medicine. Dr. Buchner joined the University of Washington faculty in 1982 and rose to the ranks of Professor of Health Services in the School of Public Health and Adjunct Professor of Medicine. While in Seattle, he also worked in the Health Services Research and Development unit of the Seattle VA Medical Center (now the VA Puget Sound Health Care System). In 1999, Dr. Buchner joined the US Centers for Disease Control and Prevention as Chief of the Physical Activity and Health Branch. In 2008, Dr. Buchner joined the faculty of the Department of Kinesiology and Community Health at the University of Illinois as a Shahid and Ann Carlson Khan Professor in Applied Health Sciences. He has published extensively in the area of physical activity and health, with an emphasis on physical activity in older adults and the role of physical activity in preventing fall injuries. Dr. Buchner retired from the University of Illinois in Summer 2017.

Wayne Campbell, PhD

Dr. Campbell is a Professor in the Department of Nutrition Science and Adjunct Faculty in the Department of Health and Kinesiology at Purdue University. Dr. Campbell's expertise integrates human nutrition, exercise physiology, and geriatrics. His research interests include assessing the effects of dietary energy and macronutrient intakes, especially protein, and exercise training on human body composition, skeletal muscle composition and function, and indexes of cardio-metabolic health. Dr. Campbell also studies the effects of dietary patterning, nutritional supplementation, and exercise on appetite, ingestive behaviors, insulin mediated glucose control and body weight management across the life course. Dr. Campbell has served on research advisory panels for NIH, USDA, NASA, USARIEM, and FAA, and was a member of the HHS/USDA 2015 Dietary Guidelines Advisory Committee.

Loretta DiPietro, PhD, MPH

Dr. DiPietro is Professor and Chair of the Department of Exercise and Nutrition Sciences, the Milken Institute School of Public Health at The George Washington University (GW). She received her training in epidemiology at Yale University. For nearly three decades, her research has focused on physical activity, and she has worked very hard to combine the two disciplines of epidemiology and physiology to better understand the mechanistic underpinnings of the benefits of exercise. Dr. DiPietro is recognized internationally as a leader in the field of physical activity and aging. An accomplished and widely published researcher, she has been awarded numerous grants from the NIH and the American Cancer Society, and has been invited to lecture around the world. She is a current fellow of the American College of Sports Medicine and the Editor-in-Chief of the Journal of Physical Activity and Health. Dr. DiPietro is a former Epidemic Intelligence Service (EIS) Officer in the Commissioned Corps of the United States Public Health Service. She joined GW in 2008 from Yale University School of Medicine, where she was associate professor of epidemiology and public health and a fellow at the John B. Pierce Laboratory.

Kirk I. Erickson, PhD

Dr. Erickson received his PhD in Psychology from the University of Illinois. He is a Professor in the Departments of Psychology and Geriatric Medicine at the University of Pittsburgh, working in the Center for the Neural Basis of Cognition within the Center for Neuroscience. His research examines cognitive and brain changes which occur as a function of physical health and aging as well as in the development of training and physical activity and exercise trials. Additionally, Dr. Erickson investigates the effects of obesity and physical activity on brain health in elderly with mild cognitive impairment and Parkinson’s disease. Dr. Erickson is the recipient of the 2015 Chancellor’s Distinguished Research Award from the University of Pittsburgh and currently serves on several editorial boards, external advisory boards, and the University of Pittsburgh Senate on Research Activities.

Charles H. Hillman, PhD

Dr. Hillman received his doctorate from the University of Maryland in 2000, and then began his career on the faculty at the University of Illinois, where he was a Professor in the Department of Kinesiology and Community Health for 16 years. He continued his career at Northeastern University in Boston, Massachusetts in 2016, where he currently holds appointments in the Department of Psychology and the Department of Physical Therapy, Movement, & Rehabilitation Sciences. He directs the Center for Cognitive and Brain Health, which has the mission of understanding the role of health behaviors on brain and cognition to maximize health and well-being, and promote the effective functioning of individuals across the lifespan. Dr. Hillman has published 170 refereed journal articles, 10 book chapters, and co-edited a text entitled Functional Neuroimaging in Exercise and Sport Sciences. He has served on an Institute of Medicine of the National Academies committee entitled Educating the Student Body: Taking Physical Activity and Physical Education to School. His work has been funded by the National Institutes of Health (NIH), Intelligence Advanced Research Projects Activity (IARPA), and several private sponsors. Finally, his work has been featured in the media including: CNN, National Public Radio, Good Morning America, Time, Newsweek, and the New York Times.

John M. Jakicic, PhD

Dr. Jakicic is a Distinguished Professor in the Department of Health and Physical Activity, and is also the Director of the Healthy Lifestyle Institute and the Director of the Physical Activity and Weight Management Research Center at the University of Pittsburgh. Dr. Jakicic has an international reputation as a leading scholar in the area of physical activity and weight control, and this builds on a line of research to determine the appropriate dose of physical activity for long-term body weight regulation. He studies the interaction between energy expenditure and energy intake, and the influence of these factors on body weight regulation. Dr. Jakicic's research was key to the public health recommendation that physical activity can be beneficial when separated into multiple 10-minute sessions per day. He is an expert in the implementation of strategies to improve long-term adherence to physical activity, and the understanding of behavioral and physiological mechanisms that are involved with linking physical activity to body weight regulation. Dr. Jakicic has served on various national and international committees to develop physical activity guidelines for the prevention and treatment of obesity and other chronic conditions. Dr. Jakicic has been influential in the heightened awareness of physical activity as a key lifestyle behavior to improve health.

Kathleen F. Janz, EdD

Dr. Janz is a physical activity epidemiologist at the University of Iowa in the Department of Health and Human Physiology and the Department of Epidemiology. She conducts population- and clinically-based research addressing the effect of physical activity and physical fitness to health outcomes. Her work seeks to understand type, dose, and pattern of physical activity associated with metabolic and musculoskeletal health. Her secondary area of research is physical activity measurement, specifically the modeling of objective measures using group-based trajectory and multi-level growth models, to better understand the effects of physical activity in prospective observational and intervention studies. As an 18-year investigator with the Iowa Bone Development Study, she has worked with colleagues to quantify physical activity dose associated with bone mass, density, and geometry. She recently led the physical activity and exercise section for the National Osteoporosis Foundation's *Position Statement on Peak Bone Mass Development and Lifestyle Factors*. This statement includes public health recommendations for bone-healthy physical activity for youth. Dr. Janz is an active fellow in the American College of Sports Medicine and the National Academy of Kinesiology. She is on the editorial boards of *JAMA Pediatrics*, *Frontiers in Endocrinology*, and *Pediatric Exercise Science*.

Peter T. Katzmarzyk, PhD

Dr. Katzmarzyk is Professor and Associate Executive Director for Population and Public Health Sciences at the Pennington Biomedical Research Center where he holds the Marie Edana Corcoran Endowed Chair in Pediatric Obesity and Diabetes. He is an internationally recognized leader in the field of physical activity and obesity epidemiology, with a special emphasis on pediatrics and ethnic health disparities. He has over two decades of experience in conducting large clinical and population-based studies in children and adults. Dr. Katzmarzyk has a special interest in global health, and has a record of building research capacity in physical activity and obesity research in developing countries. He has published his research in more than 400 scholarly journals and books, and has delivered over 160 invited lectures in 15 countries. He is an Associate Editor for Medicine and Science in Sports and Exercise and an editorial board member for the International Journal of Obesity, Pediatric Obesity, and Metabolic Syndrome and Related Disorders. In addition to his research, Dr. Katzmarzyk plays a leading role in national health advocacy initiatives chairing the Research Advisory Committee for the U.S. Report Card on Physical Activity for Children and Youth for the National Physical Activity Plan Alliance.

William E. Kraus, MD

Dr. Kraus is a physician scientist and Professor in the Division of Cardiology, Department of Medicine at Duke University. He is director of translational research at the Duke Molecular Physiology Institute and the Duke Center for Living, a multidisciplinary treatment and research facility dedicated to the primary and secondary prevention of cardiovascular disease. Dr. Kraus is Director for Clinical Research. He has been Medical Director of the Duke Cardiac Rehabilitation Program since 1994. His undergraduate degree was in Astronomy and Astrophysics (1977) from Harvard College and his Medical degree (1983) and training (Internal Medicine Residency and Cardiology Fellowship) all at Duke University School of Medicine. Dr. Kraus' research interests span from basic science in the cellular signaling processes underlying the plasticity of skeletal muscle gene expression and mechanisms of skeletal myocyte development and differentiation to the human physiology underlying exercise training benefits on cardiovascular health to the human genetics of cardiometabolic diseases. He has been principal investigator for STRRIDE—a series of three NIH-sponsored human studies focusing on the dose-response effects of exercise training on cardiometabolic health. He served on the 2008 Physical Activity Guidelines Advisory Committee.

Richard F. Macko, MD

Dr. Macko is a Professor of Neurology, Medicine, Physical Therapy and Rehabilitation Science at University of Maryland, School of Medicine, where he leads Exercise and Robotics Research to improve health and function for persons disabled by stroke and other neurological conditions. He is an enthusiastic ambassador representing the science and practice of exercise rehabilitation from many collaborators in many cultures, focused on improving multiple physiological and functional systems for persons with neurological and other disability conditions linked to aging. He has 16 years of service as Research Director for Veterans Affairs Maryland, Geriatrics Research, Educational, and Clinical Center, developing personalized exercise programs for persons with chronic disability conditions associated with aging. He received the Paul B. Magnuson Award in 2010, the highest Veterans Affairs Rehabilitation Research Award for developing task-oriented exercise for Veterans with chronic disability from stroke. Dr. Macko's exercise research is culturally enriched by global collaborations, including current endeavors targeting sub-Saharan Africa. Dr. Macko has extensive service on consensus and review committees including NIH, VA, Canadian National Centers, American Stroke Association and American College of Sports Medicine recommendations for exercise after stroke. He contributed at the 2008 National Academies of Science, Adequacy of Evidence for Physical Activity Guidelines.

David X. Marquez, PhD

Dr. Marquez directs the Exercise Psychology Laboratory at the University of Illinois at Chicago, specializing in Exercise Psychology/Behavioral Medicine. He received his PhD in Kinesiology from the University of Illinois at Urbana-Champaign. His research agenda focuses on disparities in physical activity and disease/disability among Latinos. Dr. Marquez has been Chair of the Minority Health and Research Special Interest Group of the American College of Sports Medicine (ACSM) and Chair of the Physical Activity SIG of the Society of Behavioral Medicine (SBM). He is a fellow of the ACSM, SBM, and the Gerontological Society of America. He was Principal Investigator (PI) of an RCT funded by the Alzheimer's Association; and he is currently funded with an NIH R01, a large-scale RCT of the impact of the BAILAMOS© dance program on cognitive and physical function of older Latinos. In related work he is the Leader of the Latino Core of the Rush Alzheimer's Disease Center (3P30AG010161-25S1), a prospective study that is recruiting and enrolling older Latinos without dementia who agree to annual, detailed clinical evaluations.

Anne McTiernan, MD, PhD

Dr. McTiernan is a Full Member at the Fred Hutchinson Cancer Research Center and Research Professor at the University of Washington Schools of Medicine and Public Health. Her research focuses on associations among exercise, diet, obesity, and risk for cancer development and prognosis. She was Principal Investigator of the National Cancer Institute funded Seattle Transdisciplinary Research on Energetics and Cancer program that investigated mechanisms linking obesity and sedentary lifestyles with cancer. She has received research funding from the National Institutes of Health, the Breast Cancer Research Foundation, and Susan G. Komen. She is an elected Fellow in the American College of Sports Medicine and the Obesity Society. She has published more than 390 scientific manuscripts in major medical journal, is lead author of the book, Breast Fitness (St. Martin's Press, 2000), and Editor of Cancer Prevention and Management through Exercise and Weight Control (CRC Press LLL, 2005) and Physical Activity, Dietary Calorie Restriction, and Cancer (Springer; 2010). Her committee service related to physical activity includes the 2008 U.S. Department of Health and Human Services Physical Activity Guidelines Advisory Committee, the International Agency for Research on Cancer, the American Cancer Society, and the World Cancer Research Fund.

Russell R. Pate, PhD

Dr. Pate is a Professor in the Department of Exercise Science in the Arnold School of Public Health at the University of South Carolina. He has held several administrative positions including Chair, Department of Exercise Science; Associate Dean for Research, Arnold School of Public Health; and Vice Provost for Health Sciences. Dr. Pate is an exercise physiologist with interests in physical activity and physical fitness in children and the health implications of physical activity. His research has been supported by the NIH, the CDC, the American Heart Association, and several private foundations and corporations. He coordinated the effort that led to the development of the recommendation on Physical Activity and Public Health of the CDC and the American College of Sports Medicine (1995). He served on the 2005 Dietary Guidelines Advisory Committee, the 2008 Physical Activity Guidelines Advisory Committee, and an Institute of Medicine panel that developed guidelines on prevention of childhood obesity. He currently serves as Chair of the National Physical Activity Plan Alliance. In 2012 he received the Honor Award from the American College of Sports Medicine.

Linda S. Pescatello, PhD

Dr. Pescatello is a Distinguished Professor of Kinesiology at the University of Connecticut (UConn). She holds joint appointments in the Departments of Allied Health Sciences, Nutritional Sciences, and Physiology and Neurobiology at UConn, and the Department of Community Medicine and Health Care at the UConn School of Medicine. Her research focuses on exercise prescription to optimize health benefits, particularly among adults with hypertension and overweight and obesity; and on genetic and clinical determinants of the response of health-related phenotypes to exercise, particularly blood pressure and muscle strength. Dr. Pescatello was an associate editor of the American College of Sports Medicine (ACSM) Guidelines for Exercise Testing and Prescription the eighth edition, was the senior editor of ACSM's Guidelines for Exercise Testing and Prescription (9th edition), and recently she served as an expert panel and writing team member on an update of the ACSM's exercise preparticipation health screening recommendations. She has authored more than 150 manuscripts, four books, and 16 book chapters, and has had numerous UConn, American Heart Association, National Dairy Council, National Institutes of Health, and Unites States Department of Agriculture-funded grants. Dr. Pescatello has served in multiple leadership roles for ACSM.

Melicia C. Whitt-Glover, PhD

Dr. Whitt-Glover is President and CEO of Gramercy Research Group in Winston-Salem, NC. Gramercy Research Group's mission is to positively influence and improve the lives of individuals and communities by addressing health and related issues. Dr. Whitt-Glover is currently involved in research studies designed to identify effective strategies to increase weight loss and weight gain prevention among underserved communities, and to promote adherence to national recommendations for diet and physical activity. Dr. Whitt-Glover received her BA (Exercise Physiology, 1993) and MA (Exercise Physiology, 1996) from the University of North Carolina at Chapel Hill. She received her Ph.D. (Epidemiology, 1999) from the University of South Carolina. Dr. Whitt-Glover completed a postdoctoral fellowship at the University of Pennsylvania School of Medicine (2000-2002) and served on the faculty at the University of Pennsylvania School of Medicine (2002-2003) and Wake Forest University School of Medicine (2003-2009) before starting Gramercy Research Group in 2009.

PART H. APPENDIX 4. PUBLIC COMMENT PROCESS

As a government advisory committee, the Physical Activity Guidelines Advisory Committee (Committee) is required by the Federal Advisory Committee Act to function with an open process in which the public may participate. This was accomplished through public submission of written comments and oral testimony given to the Committee.

Federal Register notices alerted the public to Committee meetings held in-person and/or by videocast. In these notices and at the meetings, the public was invited and reminded to submit their comments to an online database at https://health.gov/paguidelines. The public comments process opened on June 28, 2016 and closed on November 10, 2017.

A public comments database was developed for the 2018 Committee process based on the structure and content used for the 2015 Dietary Guidelines Advisory Committee.

Topics for Comments

When submitting comments, the public selected one or more topic areas to categorize their comment. Initially, these topic areas were:

- PA prescription: dose/volume/intensity/frequency
- All-cause mortality
- Cardiorespiratory health (CVD, asthma, stroke, etc.)
- Metabolic health (metabolic syndrome and diabetes)
- Energy balance (weight management)
- Musculoskeletal health (arthritis, scoliosis, back pain, delayed-onset muscle soreness, etc.)
- Functional health (ability to perform activities of daily living; prevention of disability with aging)
- Cancer
- Mental Health (diagnosed)
- Youth: ages 6-17
- Youth: ages 3-6
- Adverse Events (injury, air quality, etc.)
- Older adults
- Pregnant women
- Individuals with disabilities
- Racial/ethnic diversity
- Sedentary behavior
- Cognition across the lifespan (youth and older adults)

After the Committee's first public meeting, during which they formed topic-specific Subcommittees, the topic areas were amended to align with these Subcommittees. The new list included:

- Aging
- Brain Health (mental health, cognition, etc.)
- Cancer – Primary Prevention
- Cardiometabolic Health and Weight Management
- Exposure/Dose Response of Physical Activity
- Individuals with Chronic Conditions
- Promotion of Physical Activity (behavior change)
- Sedentary Behavior
- Youth: ages 3-6
- Youth: ages 6-17
- Individuals with Disabilities
- Pregnant Women
- Racial/Ethnic Diversity
- Miscellaneous

Guidelines for Submissions

The Committee requested that submitted comments define terms as specifically as possible. For example, when referring to physical activity, the Committee asked that the comment specify the type (e.g., walking, jumping rope, or biking) and intensity (e.g., light, moderate, or vigorous) of activity to ensure the comment was accurately interpreted.

Individual submissions were allowed to include up to five attachments, such as journal articles, reports, and other scientific material for the Committee to consider.

Additional guidelines were provided for public comments:

1. **Comments must be related to the stated purpose of the request.** Public comments are requested for specific purposes, which are stated at the top of online comment collection forms. Comments unrelated to the stated purpose will not be published.
2. **Comments must be suitable for online publication**. Comments that contain profanity, inappropriate images, copyrighted materials, or that are intended to defame specific individuals (i.e., slander or libel) or groups of individuals (i.e., derogatory or discriminatory remarks) will not be published.
3. **Comments must not contain information that is exempt from public disclosure**. Public availability of comments is subject to the Freedom of Information Act (FOIA). FOIA exempts certain types of information from public disclosure. Comments that contain information that is exempt under FOIA will not be published. For more information about FOIA exemptions, visit: https://www.foia.gov/faq.html#exemptions.

For all public comments, submitters were required to provide the following information: topic area(s), the comment itself (5,000 character limit), any accompanying attachments, full name (with option to make it public), affiliation, and organization. They also were required to provide their email address, phone number, and zip code, but this information was not included when the comment was posted on the public comments page at https://health.gov/paguidelines. Submitters were given the option to provide their business or academic credentials and postal address, including country. This information was not posted on the public website. After the comment was submitted, confirmation was provided to the submitter by e-mail.

Federal staff reviewed each submitted comment. Comments not posted were either: (1) duplicate submission of another comment posted by the same submitter, or (2) comments that did not pertain to the Committee.

All submitted comments that pertained to the Committee were provided to the Committee members and published online. Copies of all submitted comments were retained by the coordinating federal office, the Office of Disease Prevention and Health Promotion. With the exception of comments that are subject to FOIA exemptions, comments that were not published online because they did not meet the stated guidelines are available for public inspection upon request by contacting odphpinfo@hhs.gov.

A total of 131 comments were submitted and 109 were relevant to the Committee's work.

The majority of comments submitted fell into these topic areas: Promotion of Physical Activity and Youth (ages 3-6 and 6-17). However, comments were received in all 14 topic areas and covered a wide range of issues.

In addition to written comments, oral comments from two individuals were presented at the October 2016 public meeting. These individuals each provided 3 minutes or less of testimony before the Committee, and they submitted a brief outline of their comments when they registered to participate in the comment session.

The oral and written comments provided by the public were valuable in that they helped the Committee gather background information and understand public and professional perceptions. Comments from the public brought new issues to light, as well as new approaches to current issues and emerging evidence. They also highlighted and ensured consideration of topics deemed to be important by the submitters, who represented a variety of backgrounds and focus areas. The public comments will remain archived at https://health.gov/paguidelines.