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.**

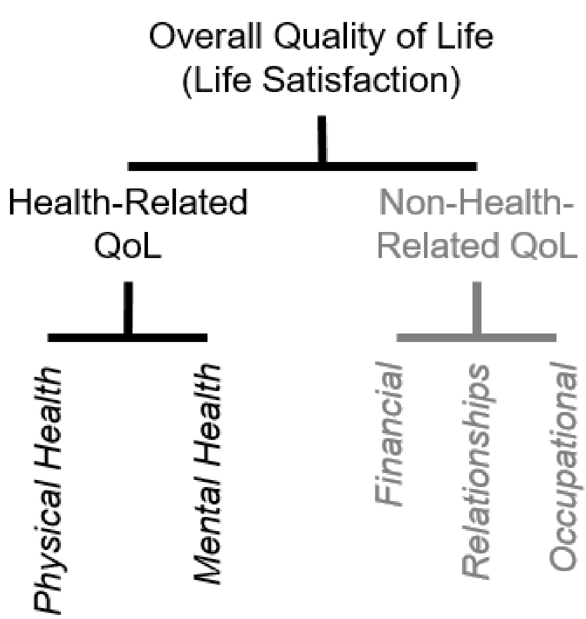
Insufficient evidence is available to determine whether the association between physical activity and quality of life varies as a function of race/ethnicity, socioeconomic status, or body mass index. **PAGAC Grade: Not assignable.**

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.**

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

Insufficient evidence is available to determine the dose-response of physical activity on depression in youth. **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: Limited.**

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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