Evidence Portfolio – Chronic Conditions Subcommittee, Question 1

Among cancer survivors, what is the relationship between physical activity and (1) all-cause mortality; (2) cancer-specific mortality; or (3) risk of cancer recurrence or second primary cancer?

a. Is there a dose-response relationship? If yes, what is the shape of the relationship?
b. Does the relationship vary by age, sex, race/ethnicity, socio-economic status, or weight status?
c. Does the relationship vary based on: frequency, duration, intensity, type (mode), or how physical activity is measured?

Sources of Evidence: Existing Systematic Reviews, Meta-Analyses, and Pooled Analyses

Conclusion Statements and Grades

BREAST CANCER

Moderate evidence indicates that greater amounts of physical activity after diagnosis are associated with lower risks of breast cancer-specific mortality and all-cause mortality in female breast cancer survivors. **PAGAC Grade: Moderate.**

Insufficient evidence is available to determine whether physical activity after diagnosis is associated with risk of breast cancer recurrence or second primary breast cancer. **PAGAC Grade: Not assignable.**

Moderate evidence indicates that a dose-response relationship exists; as levels of physical activity increase, risks of breast cancer-specific mortality and all-cause mortality decrease in female breast cancer survivors. **PAGAC Grade: Moderate.**

Moderate evidence indicates that greater amounts of physical activity after diagnosis are associated with lower risks of breast-cancer-specific mortality in both pre- and postmenopausal breast cancer survivors, with menopause as a proxy for age, while greater amounts of physical activity are associated with lower risks for all-cause mortality in only postmenopausal breast cancer survivors. **PAGAC Grade: Moderate.**

Moderate evidence indicates that greater amounts of physical activity after diagnosis are associated with lower risks of all-cause mortality in breast cancer survivors with both normal weight and overweight or obesity, while greater amounts of physical activity after diagnosis are associated with lower risks of breast cancer-specific mortality only in breast cancer survivors with overweight or obesity. **PAGAC Grade: Moderate.**

Insufficient evidence is available to determine whether the relationship between physical activity and all-cause mortality or breast cancer-specific mortality differs by sex, race/ethnicity or socioeconomic status in breast cancer survivors. **PAGAC Grade: Not assignable.**

Insufficient evidence is available to determine whether the frequency, duration, intensity, or type (mode) of physical activity is related to all-cause mortality or breast cancer-specific mortality in breast cancer survivors. **PAGAC Grade: Not assignable.**

COLORECTAL CANCER

Moderate evidence indicates that greater amounts of physical activity after diagnosis are associated with lower risks of colorectal cancer-specific mortality and all-cause mortality in colorectal cancer survivors. **PAGAC Grade: Moderate.**

Insufficient evidence is available to determine whether physical activity after diagnosis is associated with risk of colorectal cancer recurrence or second primary colorectal cancer. **PAGAC Grade: Not assignable.**

Moderate evidence indicates that a dose-response relationship exists; as levels of physical activity increase, risks of colorectal cancer-specific mortality and all-cause mortality decrease in colorectal cancer survivors. **PAGAC Grade: Moderate.**

Moderate evidence indicates that the association between physical activity and both colorectal cancer-specific mortality and all-cause mortality does not vary across age groups from middle to older ages. **PAGAC Grade: Moderate**.

Moderate evidence indicates that the association between physical activity and both colorectal cancer-specific mortality and all-cause mortality does not vary between men and women. **PAGAC Grade**: **Moderate.**

Insufficient evidence is available to determine whether the relationship between physical activity and all-cause mortality or colorectal cancer-specific mortality differs by race/ethnicity, socioeconomic status, or weight status in colorectal cancer survivors. **PAGAC Grade: Not assignable.**

Insufficient evidence is available to determine whether the frequency, duration, intensity, or type (mode) of physical activity is related to all-cause mortality or colorectal cancer-specific mortality in colorectal cancer survivors. **PAGAC Grade: Not assignable.**

PROSTATE CANCER

Limited evidence suggests an inverse association between highest versus lowest levels of physical activity after diagnosis and all-cause mortality in prostate cancer survivors. **PAGAC Grade: Limited.**

Moderate evidence indicates an inverse association between highest versus lowest levels of physical activity after diagnosis and prostate cancer-specific mortality in prostate cancer survivors. **PAGAC Grade: Moderate.**

Insufficient evidence is available on the association between physical activity level and prostate cancer recurrence or progression. **PAGAC Grade: Not assignable.**

Limited evidence suggests that a dose-response relationship exists; as levels of physical activity increase, risks of prostate cancer-specific mortality and all-cause mortality decrease in prostate cancer survivors. **PAGAC Grade: Limited.**

Insufficient evidence is available on the association between physical activity and prostate cancer survival or recurrence by age, race/ethnicity, socioeconomic status, or weight status. **PAGAC Grade: Not assignable.**

Limited evidence suggests that increased frequency, duration, and intensity of physical activity may be associated with decreased risks for all-cause mortality and prostate cancer-specific mortality in prostate cancer survivors. **PAGAC Grade: Limited.**

Description of the Evidence

The Chronic Conditions Subcommittee chose to rely exclusively on existing reviews including systematic reviews, meta-analyses, pooled analyses, and reports for this question. The subcommittee reviewed the evidence to determine which cancer types and which components of the research question [(1) all-cause mortality; (2) cancer-specific mortality; or (3) risk of cancer recurrence or second primary cancer)] could be answered. As determined by the subcommittee, the search for existing reviews provided sufficient evidence to answer some of the components of the question for breast, colorectal, and prostate cancer. Additional searches for original research were not conducted based on the a-priori decision to focus on existing reviews.

BREAST CANCER

Existing Systematic Reviews, Meta-Analyses, and Pooled Analyses

Overview

A total of 11 existing reviews examining breast cancer survivors were included: 3 systematic reviews,[1-3] 5 meta-analyses,[4-8] and 3 pooled analyses from one pooling project.[9-11] The reviews were published between 2011 and 2016.

The systematic reviews included a range of 17 to 213 studies and covered the following timeframes: 1950 to 2011,[1] inception to 2012,[2] and 1980 to 2012.[3]

The meta-analyses included a range of 6–26 studies and covered the following timeframes: 1966 to 2014,[6] inception to 2013 and 2016,[4, 7] and 1965 to 2014.[8] Ibrahim and Al-Homaidh[5] did not report a timeframe.

The pooled analyses included data from 3[11] and 4[9, 10] studies.

Exposures

All of the included reviews examined self-reported total physical activity. Four meta-analyses examined the highest vs. lowest levels of pre- and post-diagnosis physical activity.[5-8] Friedenreich et al,[4] Beasley et al,[9] and Nelson et al[11] focused on post-diagnosis physical activity. Beasley et al[9] examined adherence to the U.S. Department of Health and Human Services' *2008 Physical Activity Guidelines for Americans* of 2.5 hours (10 metabolic equivalent hours per week) of moderate-intensity physical activity per week. Nelson et al[11] assessed the impact of very low levels of physical activity. Ballard-Barbash et al[1] examined all types of pre- and post-diagnosis physical activity for observational studies and physical activity interventions defined as aerobic, endurance, or strength training exercise performed for recreational, household, commuting, or work-related purposes for randomized trials.

Outcomes

The included reviews examined all-cause and cancer-specific mortality among breast cancer survivors. Some reviews also examined breast cancer recurrence and new primary cancer.

COLORECTAL CANCER

Existing Systematic Reviews and Meta-Analyses

Overview

A total of 8 existing reviews examining colorectal cancer survivors were included: 2 systematic reviews[1, 12] and 6 meta-analyses.[4, 7, 13-16] The reviews were published between 2010 and 2016.

The systematic reviews included 39[1] and 10[12] studies and covered a timeframe from 1950 to 2011 and 1950 to 2008, respectively.

The meta-analyses included a range of 7–26 studies and covered the following timeframes: inception to 2013,[7, 13, 15] 1970 to 2013,[14] and inception to 2016.[4, 16]

Exposures

All of the included reviews examined self-reported total physical activity. The majority of included reviews examined the highest vs. lowest levels of pre- and post-diagnosis total physical activity. Ballard-Barbash et al[1] examined all types of pre- and post-diagnosis physical activity for observational studies and physical activity interventions defined as aerobic, endurance, or strength training exercise performed for recreational, household, commuting, or work-related purposes for randomized trials. Friedenreich et al[4] focused on post-diagnosis physical activity.

Outcomes

The included reviews examined all-cause and cancer-specific mortality among colorectal cancer survivors. Some reviews also examined colorectal cancer recurrence.

PROSTATE CANCER

Existing Systematic Review and Meta-Analyses

Overview

Two existing reviews examining prostate cancer survivors were included: 1 systematic review[1] and 1 meta-analysis.[4] The reviews were published in 2012 and 2016.

The systematic review[1] included 39 studies and covered a timeframe from 1950 to 2011.

The meta-analysis[4] included 26 studies and covered a timeframe from inception to 2016.

Exposures

All of the included reviews examined self-reported total physical activity. Ballard-Barbash et al[1] examined all types of pre- and post-diagnosis physical activity for observational studies and physical activity interventions defined as aerobic, endurance, or strength training exercise performed for recreational, household, commuting, or work-related purposes for randomized trials. Friedenreich et al[4] focused on post-diagnosis physical activity.

Outcomes

Both included reviews examined cancer-specific mortality. The Ballard-Barbash et al[1] review addressed all-cause mortality, and the Friedenreich et al[4] review examined recurrence. The Committee reviewed the source papers from the Friedenreich et al[4] review for information on all-cause mortality.

Populations Analyzed

The table below lists the populations analyzed in each article.

Table 1. Populations Analyzed by All Sources of Evidence

	Sex	Age	Weight Status	Chronic Conditions	Other
Ballard-Barbash, 2012		Adults >18		Mixed cancer, Breast cancer	
Barbaric, 2010		Adults >18		Breast cancer, Colorectal cancer	
Beasley, 2012	Female	Adults >18	Overweight (BMI: 25–29.9), Obese (BMI: ≥30)	Breast cancer	BMI < 25. Menopausal status, Hormone receptor status
Des Guetz, 2013		Adults 21–84		Colorectal cancer	
Fontein, 2013	Female	Adults		Breast cancer	
Friedenreich, 2016		Adults		Breast cancer, Colorectal cancer, Prostate cancer	
Ibrahim, 2011	Female			Breast cancer	
Je, 2013				Colorectal cancer	
Lahart, 2015		Adults		Breast cancer	
Nechuta, 2016	Female	Adults 20–83		Breast cancer	
Nelson, 2016	Female	Adults		Breast cancer	
Otto, 2015		Adults		Colorectal cancer	
Schmid, 2014	Female	Adults	Underweight (BMI: below 18.5), Normal/healthy weight (BMI: 18.5–24.9), Overweight and Obese	Breast cancer, Colorectal cancer	Menopausal status, Estrogen receptor status
World Cancer Research Fund International, 2014	Female	Adults		Breast cancer	Menopausal status
Wu, 2016		Adults		Colorectal cancer	
Zhong, 2014	Female	All ages	Underweight (BMI: below 18.5), Normal/healthy weight (BMI: 18.5–24.9), Overweight and Obese	Breast cancer	Menopausal

Supporting Evidence

Existing Systematic Reviews, Meta-Analyses, and Pooled Analyses

Table 2. Existing Systematic Reviews, Meta-Analyses, and Pooled Analyses Individual Evidence Summary Tables

<table>
<tr><th colspan="2">Breast Cancer, Colorectal Cancer, and Prostate Cancer</th></tr>
<tr><td colspan="2">Systematic Review
Citation: Ballard-Barbash R, Friedenreich CM, Courneya KS, Siddiqi SM, McTiernan A, Alfano CM. Physical activity, biomarkers, and disease outcomes in cancer survivors: a systematic review. J Natl Cancer Inst. 2012;104(11):815-840. doi:10.1093/jnci/djs207.</td></tr>
<tr><td>Purpose: To systematically examine results in two areas of research involving cancer survivors: PA and cancer-specific and all-cause mortality, and PA and relevant cancer biomarkers.</td><td rowspan="5">Abstract: BACKGROUND: Cancer survivors often seek information about how lifestyle factors, such as physical activity, may influence their prognosis. We systematically reviewed studies that examined relationships between physical activity and mortality (cancer-specific and all-cause) and/or cancer biomarkers. METHODS: We identified 45 articles published from January 1950 to August 2011 through MEDLINE database searches that were related to physical activity, cancer survival, and biomarkers potentially relevant to cancer survival. We used the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Statement to guide this review. Study characteristics, mortality outcomes, and biomarker-relevant and subgroup results were abstracted for each article that met the inclusion criteria (ie, research articles that included participants with a cancer diagnosis, mortality outcomes, and an assessment of physical activity). RESULTS: There was consistent evidence from 27 observational studies that physical activity is associated with reduced all-cause, breast cancer-specific, and colon cancer-specific mortality. There is currently insufficient evidence regarding the association between physical activity and mortality for survivors of other cancers. Randomized controlled trials of exercise that included biomarker endpoints suggest that exercise may result in beneficial changes in the circulating level of insulin, insulin-related pathways, inflammation, and, possibly, immunity; however, the evidence is still preliminary. CONCLUSIONS: Future research directions identified include the need for more observational studies on additional types of cancer with larger sample sizes; the need to examine whether the association between physical activity and mortality varies by tumor, clinical, or risk factor characteristics; and the need for research on the biological mechanisms involved in the association between physical activity and survival after a cancer diagnosis. Future randomized controlled trials of exercise with biomarker and cancer-specific disease endpoints, such as recurrence, new primary cancers, and cancer-specific mortality in cancer survivors, are warranted.</td></tr>
<tr><td>Timeframe: January 1950–August 2011</td></tr>
<tr><td>Total # of Studies: 39</td></tr>
<tr><td>Exposure Definition: For randomized controlled trial PA exposure: aerobic, endurance, or strength training exercise performed for recreational, household, commuting, or work-related purposes. Other types of conditioning or stretching exercise (e.g., yoga, pilates, tai chi, nonpurposive movement) were excluded. These restrictions were not applied to PA reported in observational studies. Many studies reported metabolic equivalents. One study used high-intensity activities (competitive sports, running) during years after menses.
Measures Steps: No
Measures Bouts: No
Examines HIIT: No</td></tr>
<tr><td>Outcomes Addressed: All-cause mortality, cancer-specific outcomes, recurrence, new primary cancer or cancer-specific deaths, or deaths from any cause or biomarkers in cancer survivors. Subgroup for breast cancer survivors.
Examine Cardiorespiratory Fitness as Outcome: No</td></tr>
</table>

Populations Analyzed: Adults >18, Breast cancer	**Author-Stated Funding Source:** Alberta Heritage Foundation for Medication Research and Canada Research Chairs program.

<table>
<tr><th colspan="2">Colorectal Cancer</th></tr>
<tr><td colspan="2">Systematic Review
Citation: Barbaric M, Brooks E, Moore L, Cheifetz O. Effects of physical activity on cancer survival: a systematic review. Physiother Can. 2010;62(1):25-34. doi:10.3138/physio.62.1.25.</td></tr>
<tr><td>Purpose: To systematically evaluate and summarize the available evidence investigating the effect of PA on the survival of individuals with cancer.</td><td rowspan="4">Abstract: PURPOSE: Physical activity (PA) has been suggested to help increase the survival of individuals with cancer. The objective of this review was to systematically evaluate and summarize the available evidence investigating the effect of PA on the survival of individuals with cancer. METHODS: Electronic databases (CINAHL, EMBASE, and MEDLINE) were systematically searched for randomized controlled trials and cohort studies. Selected studies were assessed by two independent investigators for methodological quality, using the PEDro scale. RESULTS: Ten prospective cohort studies met the inclusion criteria. Quality-assessment scores averaged 5/10 on the PEDro scale, with two articles obtaining a score of 6/10. The majority of studies found that individuals participating in higher levels of physical activity had a reduced risk of cancer-related mortality. This trend was observed specifically for breast, colon, and colorectal cancers. On average, it appears that engaging in higher levels of metabolic equivalent hours per week may help to improve survival rates among individuals diagnosed with cancer. CONCLUSION: Patients diagnosed with cancer demonstrated a trend toward increased survival with greater levels of PA. However, because only prospective cohort studies were included in the study, the conclusions drawn should be regarded with caution.</td></tr>
<tr><td>Timeframe: 1950–2008</td></tr>
<tr><td>Total # of Studies: 10</td></tr>
<tr><td>Exposure Definition: PA defined as ‘‘bodily movement produced by skeletal muscles that results in energy expenditure,’’ including conditioning exercises, sports, occupational activities, and household activities. Exposure data presented in metabolic equivalent hours/week. Level of PA was assessed based on at least 1 of 3 timeframes: (1) activity level at least 1 year prior to diagnosis; (2) lifetime level of PA; and (3) level of PA post-diagnosis and throughout follow-up.
Measures Steps: No
Measures Bouts: No
Examines HIIT: No</td></tr>
<tr><td>Outcomes Addressed: Survival: assessed by vital status at the end of the study period. Other outcomes: survival probability, disease-free survival, and cancer-specific and overall mortality.
Examine Cardiorespiratory Fitness as Outcome: No</td></tr>
<tr><td>Populations Analyzed: Adults >18, Breast cancer, Colorectal cancer</td><td>Author-Stated Funding Source: Not reported.</td></tr>
</table>

<table>
<tr><th colspan="2">Breast Cancer</th></tr>
<tr><td colspan="2">Pool Analysis
Citation: Beasley JM, Kwan ML, Chen WY, et al. Meeting the physical activity guidelines and survival after breast cancer: findings from the after breast cancer pooling project. Breast Cancer Res Treat. 2012;131(2):637-643. doi:10.1007/s10549-011-1770-1.</td></tr>
<tr><td>Purpose: To investigate whether the 2008 PA Guidelines recommendation of at least 2.5 hours (10 metabolic equivalent [MET] hours/week) of moderate intensity PA per week to reduce risk of morbidity and mortality (all-cause and breast cancer) extends to breast cancer survivors.</td><td rowspan="4">Abstract: The 2008 Physical Activity (PA) Guidelines recommend engaging in at least 2.5 h (10 MET-hours/week) of moderate intensity PA per week (defined as 4 METs) to reduce risk of morbidity and mortality. This analysis was conducted to investigate whether this recommendation can be extended to breast cancer survivors. Data from four studies of breast cancer survivors measuring recreational PA from semi-quantitative questionnaires a median of 23 months post-diagnosis (interquartile range 18-32 months) were pooled in the After Breast Cancer Pooling Project (n = 13,302). Delayed entry Cox proportional hazards models were applied in data analysis with adjustment for age, post-diagnosis body mass index, race/ethnicity, menopausal status, TNM stage, cancer treatment, and smoking history. Engaging in at least 10 MET-hours/week of PA was associated with a 27% reduction in all-cause mortality (n = 1,468 events, Hazard Ratio (HR) = 0.73, 95% CI, 0.66-0.82) and a 25% reduction in breast cancer mortality (n = 971 events, HR = 0.75, 95% CI 0.65-0.85) compared with women who did not meet the PA Guidelines (<10 MET-hours/week). Risk of breast cancer recurrence (n = 1,421 events) was not associated with meeting the PA Guidelines (HR = 0.96, 95% CI, 0.86-1.06). These data suggest that adhering to the PA guidelines may be an important intervention target for reducing mortality among breast cancer survivors.</td></tr>
<tr><td>Total # of Studies: 4</td></tr>
<tr><td>Exposure Definition: PA: questionnaire adopted from the Arizona Activity Frequency Questionnaire (only recreational activities), in-person interviews (recreational exercise), self report, and Women's Health Initiative PA questionnaire. Meeting PA guidelines: engaging in ≥10 MET hours/week, equivalent to 2.5 hours of moderate PA per week (4 METs) or to 1.25 hours of vigorous PA (8 METs) per week. Created PA quintiles from MET hours/week.
Measures Steps: No
Measures Bouts: No
Examines HIIT: No</td></tr>
<tr><td>Outcomes Addressed: All-cause mortality, breast cancer-specific mortality, and breast cancer recurrence, defined as a local/regional recurrence, distant recurrence/metastasis, or development of a new breast primary.
Examine Cardiorespiratory Fitness as Outcome: No</td></tr>
<tr><td>Populations Analyzed: Female, Adults >18, BMI <25; Overweight (BMI: 25–29.9), Obese (BMI: ≥30), Breast cancer, Menopausal status, Hormone receptor status</td><td>Author-Stated Funding Source: National Institutes of Health National Cancer Institute.</td></tr>
</table>

<table>
<tr><th colspan="2">Colorectal Cancer</th></tr>
<tr><td colspan="2">Meta-Analysis
Citation: Des Guetz G, Uzzan B, Bouillet T, et al. Impact of physical activity on cancer-specific and overall survival of patients with colorectal cancer. Gastroenterol Res Pract. October 2013:340851. doi:10.1155/2013/340851.</td></tr>
<tr><td>Purpose: To assess the influence of pre- and post-diagnosis levels of PA in cancer-specific survival and overall survival for colorectal cancer.</td><td rowspan="5">Abstract: Background. Physical activity (PA) reduces incidence of colorectal cancer (CRC). Its influence on cancer-specific (CSS) and overall survival (OS) is controversial. Methods. We performed a literature-based meta-analysis (MA) of observational studies, using keywords "colorectal cancer, physical activity, and survival" in PubMed and EMBASE. No dedicated MA was found in the Cochrane Library. References were cross-checked. Pre- and postdiagnosis PA levels were assessed by MET. Usually, "high" PA was higher than 17 MET hour/week. Hazard ratios (HRs) for OS and CSS were calculated, with their 95% confidence interval. We used more conservative adjusted HRs, since variables of adjustment were similar between studies. When higher PA was associated with improved survival, HRs for detrimental events were set to <1. We used EasyMA software and fixed effect model whenever possible. Results. Seven studies (8056 participants) were included, representing 3762 men and 4256 women, 5210 colon and 1745 rectum cancers. Mean age was 67 years. HR CSS for postdiagnosis PA (higher PA versus lower) was 0.61 (0.44-0.86). The corresponding HR OS was 0.62 (0.54-0.71). HR CSS for prediagnosis PA was 0.75 (0.62-0.91). The corresponding HR OS was 0.74 (0.62-0.89). Conclusion. Higher PA predicted a better CSS. Sustained PA should be advised for CRC. OS also improved (reduced cardiovascular risk).</td></tr>
<tr><td>Timeframe: Inception–February 2013</td></tr>
<tr><td>Total # of Studies: 7</td></tr>
<tr><td>Exposure Definition: Metabolic equivalents (METs); high PA defined as more than 17 MET hours/week. Stratified analyses on the outcome provided on pre-diagnosis and post-diagnosis PA.
Measures Steps: No
Measures Bouts: No
Examines HIIT: No</td></tr>
<tr><td>Outcomes Addressed: Cancer-specific survival: cancer-specific deaths. Overall survival: overall death. Cancer-specific survival and overall survival by pre- and post-diagnosis of cancer.
Examine Cardiorespiratory Fitness as Outcome: No</td></tr>
<tr><td>Populations Analyzed: Adults 21–84; Colorectal cancer</td><td>Author-Stated Funding Source: Not reported.</td></tr>
</table>

<table>
<tr><th colspan="2">Breast Cancer</th></tr>
<tr><td colspan="2">Systematic Review
Citation: Fontein DB, de Glas NA, Duijm M, et al. Age and the effect of physical activity on breast cancer survival: a systematic review. Cancer Treat Rev. 2013;39(8):958-965. doi:10.1016/j.ctrv.2013.03.008.</td></tr>
<tr><td>Purpose: To review the current literature in relation to the effect of PA on survival in breast cancer patients, with a focus on the elderly breast cancer patient in particular.</td><td rowspan="5">Abstract: The effect of physical activity (PA) on cancer survival is still the topic of debate in oncology research focusing on survivorship, and has been investigated retrospectively in several large clinical trials. PA has been shown to improve quality of life, fitness and strength, and to reduce depression and fatigue. At present, there is a growing body of evidence on the effects of PA interventions for cancer survivors on health outcomes. PA and functional limitations are interrelated in the elderly. However the relationship between breast cancer survival and PA in older breast cancer patients has not yet been fully investigated. Our systematic review of the existing literature on this topic yielded seventeen studies. Most reports demonstrated an improved overall and breast cancer-specific survival. Furthermore, in studies that compared younger women with older or postmenopausal women, it was suggested that the beneficial effect of PA may be even greater in older women. Understanding the interaction between physical functioning and cancer survival in older breast cancer patients is key, and may contribute to successful treatment and survival. In this population of cancer survivors it is therefore imperative to embark on research focused on improving physical functioning in the context of comorbidities and functional limitations.</td></tr>
<tr><td>Timeframe: Inception–2012</td></tr>
<tr><td>Total # of Studies: 17</td></tr>
<tr><td>Exposure Definition: PA was defined as any PA relating to aerobic, endurance, or strength training for the purposes of recreation, household, commuting, or work. Only studies investigating leisure or total activity (occupational and/or non-occupational) were selected. For most studies, metabolic equivalent (MET) hours were used (or calculated) to assess PA in relation to survival outcomes.
Measures Steps: No
Measures Bouts: No
Examines HIIT: No</td></tr>
<tr><td>Outcomes Addressed: Hazard ratios of all-cause mortality, breast cancer-specific mortality, and breast cancer recurrence.
Examine Cardiorespiratory Fitness as Outcome: No</td></tr>
<tr><td>Populations Analyzed: Female, Adults, Breast cancer</td><td>Author-Stated Funding Source: None.</td></tr>
</table>

Breast Cancer, Colorectal Cancer, and Prostate Cancer	
Meta-Analysis **Citation:** Friedenreich CM, Neilson HK, Farris MS, Courneya KS. Physical activity and cancer outcomes: a precision medicine approach. *Clin Cancer Res.* 2016;22(19):4766-4775.	
Purpose: To lay a foundation for this exciting new area of precision oncology by appraising the current observational epidemiological evidence overall and from a precision exercise perspective.	**Abstract:** There is increasing interest in applying a precision medicine approach to understanding exercise as a potential treatment for cancer. We aimed to inform this new approach by appraising epidemiologic literature relating postdiagnosis physical activity to cancer outcomes overall and by molecular/genetic subgroups. Across 26 studies of breast, colorectal, and prostate cancer patients, a 37% reduction was seen in risk of cancer-specific mortality, comparing the most versus the least active patients (pooled relative risk = 0.63; 95% confidence interval: 0.54-0.73). Risks of recurrence or recurrence/cancer-specific death (combined outcome) were also reduced based on fewer studies. We identified ten studies of associations between physical activity and cancer outcomes by molecular or genetic markers. Two studies showed statistically significant risk reductions in breast cancer mortality/recurrence for the most (versus least) physically active estrogen receptor-positive/progesterone receptor-positive (ER+/PR+) patients, while others showed risk reductions among ER-PR- and triple-negative patients. In colorectal cancer, four studies showed statistically significant risk reductions in cancer-specific mortality for patients with high (versus low) physical activity and P21 expression, P27 expression, nuclear CTNNB1-, PTGS2 (COX-2)+, or IRS1 low/negative status. One prostate cancer study showed effect modification by Gleason score. As a means to enhance this evidence, future observational studies are needed that will measure physical activity objectively before and after diagnosis, use standardized definitions for outcomes, control for competing risks, assess nonlinear dose-response relations, and consider reverse causality. Ultimately, randomized controlled trials with clinical cancer outcomes and a correlative component will provide the best evidence of causality, relating exercise to cancer outcomes, overall and for molecular and genetic subgroups.
Timeframe: Inception–March 2016	
Total # of Studies: 26	
Exposure Definition: Highest versus lowest levels of post-diagnosis PA (interviewer-administered questionnaires, self-administered questionnaires, or a combination). Dose-response (metabolic equivalent [MET] hours/week). **Measures Steps:** No **Measures Bouts:** No **Examines HIIT:** No	
Outcomes Addressed: Cancer-specific mortality (breast cancer, colorectal cancer, prostate cancer, mixed). Breast cancer recurrence. **Examine Cardiorespiratory Fitness as Outcome:** No	
Populations Analyzed: Adults, Breast cancer, Colorectal cancer, Prostate cancer	**Author-Stated Funding Source:** Not reported.

<table>
<tr><th colspan="2">Breast Cancer</th></tr>
<tr><td colspan="2">Meta-Analysis
Citation: Ibrahim EM, Al-Homaidh A. Physical activity and survival after breast cancer diagnosis: meta-analysis of published studies. Med Oncol. 2011;28(3):753-765. doi:10.1007/s12032-010-9536-x.</td></tr>
<tr><td>Purpose: To better understand the role of PA on breast cancer outcomes.</td><td rowspan="5">Abstract: Published data have shown that physical activity (PA) has a positive role on the primary prevention of breast cancer risk. However, the role of PA on breast cancer outcome has been controversial with inconsistent data. The lack of a meta-analysis that addresses that issue prompted the current report. A comprehensive literature search identified eight studies, of which two studies were excluded. The remaining six studies (12,108 patients with breast cancer) were included in this meta-analysis. Pre-diagnosis PA reduced all causes mortality by 18% but had no effect on breast cancer deaths. Post-diagnosis PA reduced breast cancer deaths by 34% (HR=0.66, 95% CI, 0.57-0.77, P<0.00001), all causes mortality by 41% (HR=0.59, 95% CI, 0.53-0.65, P<0.00001), and disease recurrence by 24% (HR=0.76, 95% CI, 0.66-0.87, P=0.00001). Breast cancer mortality was reduced by pre-diagnosis PA in women with body mass index (BMI)<25 kg/m2, while post-diagnosis PA reduced that risk among those with BMI>/=25 kg/m2. On the other hand, post-diagnosis PA reduced all causes mortality regardless of the BMI. The analysis showed that post-diagnosis PA reduced breast cancer deaths (HR=0.50, 95% CI, 0.34-0.74, P=0.0005), and all causes mortality (HR=0.36, 95% CI, 0.12-1.03, P=0.06) among patients with estrogen receptor (ER)-positive tumor, while women with ER-negative disease showed no gain. The current meta-analysis provides evidence for an inverse relationship between PA and mortality in patients with breast cancer and supports the notion that appropriate PA should be embraced by breast cancer survivors.</td></tr>
<tr><td>Timeframe: Not reported</td></tr>
<tr><td>Total # of Studies: 6</td></tr>
<tr><td>Exposure Definition: Different types of PA as measured in metabolic equivalent (MET) hours per week. The different categories that were analyzed are: low-level PA, 0 to 3 MET hours/week; intermediate PA, 2.8 to 8.9 MET hours/week; intermediate to high-level PA, >8 MET hours/week; and high-level PA, >15 MET hours/week. Stratified analysis on the outcome provided by pre-diagnosis and post-diagnosis PA .
Measures Steps: No
Measures Bouts: No
Examines HIIT: No</td></tr>
<tr><td>Outcomes Addressed: Hazard ratios of breast cancer deaths, all-cause mortality, and breast cancer recurrence.
Examine Cardiorespiratory Fitness as Outcome: No</td></tr>
<tr><td>Populations Analyzed: Female, Breast cancer</td><td>Author-Stated Funding Source: Not reported.</td></tr>
</table>

<table>
<tr><th colspan="2">Colorectal Cancer</th></tr>
<tr><td colspan="2">Meta-Analysis
Citation: Je Y, Jeon JY, Giovannucci EL, Meyerhardt JA. Association between physical activity and mortality in colorectal cancer: a meta-analysis of prospective cohort studies. Int J Cancer. 2013;133(8):1905-1913. doi:10.1002/ijc.28208.</td></tr>
<tr><td>Purpose: To understand the association between PA and colorectal cancer outcomes, colorectal cancer-specific mortality, and overall mortality in colorectal cancer survivors.</td><td rowspan="5">Abstract: Several prospective cohort studies have examined the association between prediagnosis and/or postdiagnosis physical activity (PA) on colorectal cancer outcomes and reported conflicting results. To quantitatively assess this association, we have conducted a meta-analysis of prospective studies. Databases and reference lists of relevant studies were searched using MEDLINE and EMBASE up to January 2013. Pooled relative risks (RRs) with 95% confidence intervals (CIs) were calculated using random-effects models. For this meta-analysis, a total of seven prospective cohort studies were included. The analysis included 5,299 patients for prediagnosis PA and 6,348 patients for postdiagnosis PA, followed up over a period ranging from 3.8 to 11.9 years. The analyses showed that patients who participated in any amount of PA before diagnosis had a RR of 0.75 (95% CI: 0.65-0.87, p < 0.001) for colorectal cancer-specific mortality compared to patients who did not participate in any PA. Those who participated in high PA before diagnosis (vs. low PA) had a RR of 0.70 (95% CI: 0.56-0.87, p = 0.002). Similarly, patients who participated in any PA after diagnosis had a RR of 0.74 (95% CI: 0.58-0.95, p = 0.02) for colorectal cancer-specific mortality compared to patients who did not participate in any PA. Those who participated in high PA after diagnosis (vs. low PA) had a RR of 0.65 (95% CI: 0.47-0.92, p = 0.01). Similar inverse associations of prediagnosis or postdiagnosis PA were found for all-cause mortality. In conclusion, both prediagnosis and postdiagnosis PA were associated with reduced colorectal cancer-specific mortality and all-cause mortality.</td></tr>
<tr><td>Timeframe: 1970–2013</td></tr>
<tr><td>Total # of Studies: 7</td></tr>
<tr><td>Exposure Definition: PA in metabolic equivalent (MET) hours per week. Separate analyses for exerciser versus non-exerciser, moderate level of PA versus low PA, and high level of PA versus low PA. The lowest category was defined as low-level PA (0, <3, and <3.5 MET hours per week or sedentary: reference group); the highest category was defined as high-level PA (18 and 8.75 MET hours per week or sufficiently active).
Measures Steps: No
Measures Bouts: No
Examines HIIT: No</td></tr>
<tr><td>Outcomes Addressed: Relative risk of colorectal cancer-specific mortality, all-cause mortality, or disease-free survival.
Examine Cardiorespiratory Fitness as Outcome: No</td></tr>
<tr><td>Populations Analyzed: Colorectal cancer</td><td>Author-Stated Funding Source: National Research Foundation of Korea.</td></tr>
</table>

Breast Cancer	
Meta-Analysis **Citation:** Lahart IM, Metsios GS, Nevill AM, Carmichael AR. Physical activity, risk of death and recurrence in breast cancer survivors: a systematic review and meta-analysis of epidemiological studies. *Acta Oncol.* 2015;54(5):635-654. doi:10.3109/0284186X.2014.998275.	
Purpose: To evaluate the available literature pertaining to the effects of PA on all-cause and breast cancer-related deaths as well as recurrence in women diagnosed with breast cancer.	**Abstract:** Strong evidence exists supporting the effect of lack of physical activity on the risk of developing breast cancer. However, studies examining the effects of physical activity on breast cancer outcomes, including survival and prognosis have been inconclusive. Therefore, the aim of the current study was to provide a systematic review and meta-analysis of studies investigating the association between physical activity and breast cancer recurrence and death. METHODS: PubMed, EMBASE, and CENTRAL databases were searched up to 18 October 2014. Reference lists of retrieved articles and relevant previous reviews were also searched. Observational studies that reported risk estimates for all-cause and/or breast cancer-related death and/or breast cancer recurrences by levels of physical activity, were included in the review. Random effects models were used to calculate pooled hazard ratios (HR) and 95% confidence intervals (CI) and to incorporate variation between studies. The Newcastle-Ottawa scale was used to critically appraise the risk of bias across studies. RESULTS: Twenty-two prospective cohort studies were eligible in this meta-analysis. During average follow-up periods ranging from 4.3 to 12.7 years there were 123 574 participants, 6898 all-cause deaths and 5462 breast cancer outcomes (i.e. breast cancer-related deaths or recurrences). The average Newcastle-Ottawa score was six stars (range 4-8). Compared to those who reported low/no lifetime recreational pre-diagnosis physical activity, participants who reported high lifetime recreational pre-diagnosis physical activity levels had a significantly lower risk of all-cause (HR = 0.82, 95% CI 0.70-0.96, $p < 0.05$) and breast cancer-related death (HR = 0.73, 95% CI 0.54-0.98, $p < 0.05$). Significant risk reductions for all-cause and breast cancer-related death was also demonstrated for more recent pre-diagnosis recreational physical activity (HR = 0.73, 95% CI 0.65-0.82, $p < 0.001$; and HR = 0.84, 95% CI 0.73-0.97, $p < 0.05$, respectively), post-diagnosis physical activity (HR = 0.52, 95% CI 0.43-0.64, $p < 0.01$; and HR = 0.59, 95% CI 0.45-0.78, $p < 0.05$, respectively) and meeting recommended physical activity guidelines (i.e. >/= 8 MET-h/wk) post-diagnosis (HR = 0.54, 95% CI 0.38-0.76, $p < 0.01$; and HR = 0.67, 95% CI 0.50-0.90, $p < 0.01$, respectively). However, there was evidence of heterogeneity across lifetime recreational pre- and post-diagnosis physical activity analyses. Both pre-diagnosis (lifetime and more recent combined) and post-diagnosis physical activity were also associated with reduced risk of breast cancer events (breast cancer progression, new primaries and recurrence combined) (HR = 0.72 95% CI 0.56-0.91, $p < 0.01$; and HR = 0.79, 95% CI 0.63-0.98, $p < 0.05$, respectively). CONCLUSION: There is an inverse relationship between physical activity and all-cause, breast cancer-related death and breast cancer events. The current meta-
Timeframe: 1966–2014	
Total # of Studies: 22	
Exposure Definition: PA levels were assessed via self-administered questionnaires. PA exposure: group 1, reference group of those who perform no/low levels of PA; group 2, sufficiently active (i.e., performing at least 150 minutes/week of moderate or 75 minutes/week of vigorous PA). Comparisons between: 1) lifetime pre-diagnosis PA; 2) more recent (≤12 years) pre-diagnosis total PA; 3) post-diagnosis recreational PA; and 4) meeting recommended PA guidelines post-diagnosis (defined as 8 metabolic equivalent [MET] hours/week). **Measures Steps:** No **Measures Bouts:** No **Examines HIIT:** No	
Outcomes Addressed: Hazard ratios of all-cause mortality and breast cancer mortality. Risk of breast cancer recurrence. **Examine Cardiorespiratory Fitness as Outcome:** No	

	analysis supports the notion that appropriate physical activity may be an important intervention for reducing death and breast cancer events among breast cancer survivors.
Populations Analyzed: Adults, Breast cancer	**Author-Stated Funding Source:** Not reported.

<table>
<tr><th colspan="2">Breast Cancer</th></tr>
<tr><td colspan="2">Pool Analysis
Citation: Nechuta S, Chen WY, Cai H, et al. A pooled analysis of post-diagnosis lifestyle factors in association with late estrogen-receptor-positive breast cancer prognosis. Int J Cancer. 2016;138(9):2088-2097. doi:10.1002/ijc.29940.</td></tr>
<tr><td>Purpose: To evaluate the associations of post-diagnosis lifestyle factors with breast cancer prognosis overall, and to evaluate the associations of lifestyle factors with late breast cancer outcomes among estrogen receptor-positive breast cancer survivors.</td><td rowspan="4">Abstract: Lifestyle factors have been well studied in relation to breast cancer prognosis overall; however, associations of lifestyle and late outcomes (>5 years after diagnosis) have been much less studied, and no studies have focused on estrogen receptor-positive (ER+) breast cancer survivors, who may have high risk of late recurrence and mortality. We utilized a large prospective pooling study to evaluate the associations of lifestyle factors with late recurrence and all-cause mortality among 6,295 5-year ER+ Stage I-III breast cancer survivors. Pooled and harmonized data were available on clinical factors and lifestyle factors (pre- to post-diagnosis weight change, body mass index (BMI) (kg/m(2)), recreational physical activity, alcohol intake and smoking history), measured on average 2.1 years after diagnosis. Updated information for weight only was available. Study heterogeneity was evaluated by the Q-statistic. Multivariable Cox regression models were stratified by study. Adjusting for clinical factors and potential confounders, >/= 10% weight gain and obesity (BMI, 30-34.99 and >/= 35) were associated with increased risk of late recurrence (hazard ratios (95% confidence intervals): 1.24 (1.00-1.53), 1.40 (1.05-1.86) and 1.41 (1.02-1.93), respectively). Daily alcohol intake was associated with late recurrence, 1.28 (1.01-1.62). Physical activity was inversely associated with late all-cause mortality (0.81 (0.71-0.93) and 0.71 (0.61-0.82) for 4.9 to <17.4 and >/= 17.4 metabolic equivalent-hr/week). A U-shaped association was observed for late all-cause mortality and BMI using updated weight (1.42 (1.15-1.74) and 1.40 (1.09-1.81), <21.5 and >/= 35, respectively). Smoking was associated with increased risk of late outcomes. In this large prospective pooling project, modifiable lifestyle factors were associated with late outcomes among long-term ER+ breast cancer survivors.</td></tr>
<tr><td>Total # of Studies: 4</td></tr>
<tr><td>Exposure Definition: Self-reported information on recreational PA was converted into metabolic equivalent (MET) hours/week (all activities combined). PA was classified based on tertiles (0 to <4.9, 4.9–17.4, and ≥17.4) and as meeting (yes or no) the U.S. 2008 recommendations (≥10 MET hours/week, equivalent to about 2.5 hours of moderate intensity activity per week).
Measures Steps: No
Measures Bouts: No
Examines HIIT: No</td></tr>
<tr><td>Outcomes Addressed: Hazard ratios for post-diagnosis lifestyle factors in association with late all-cause mortality.
Examine Cardiorespiratory Fitness as Outcome: No</td></tr>
<tr><td>Populations Analyzed: Female, Adults 20–83, Breast cancer</td><td>Author-Stated Funding Source: National Cancer Institute at the National Institutes of Health.</td></tr>
</table>

<table>
<tr><th colspan="2">Breast Cancer</th></tr>
<tr><td colspan="2">Pool Analysis
Citation: Nelson SH, Marinac CR, Patterson RE, et al. Impact of very low physical activity, BMI, and comorbidities on mortality among breast cancer survivors. Breast Cancer Res Treat. 2016;155(3):551-557. doi:10.1007/s10549-016-3694-2.</td></tr>
<tr><td>Purpose: To examine associations of post-diagnosis body mass index (BMI), very low PA, and comorbidities with breast cancer-specific and all-cause mortality.</td><td rowspan="4">Abstract: The purpose of this study was to examine post-diagnosis BMI, very low physical activity, and comorbidities, as predictors of breast cancer-specific and all-cause mortality. Data from three female US breast cancer survivor cohorts were harmonized in the After Breast Cancer Pooling Project (n = 9513). Delayed entry Cox proportional hazards models were used to examine the impact of three post-diagnosis lifestyle factors: body mass index (BMI), select comorbidities (diabetes only, hypertension only, or both), and very low physical activity (defined as physical activity <1.5 MET h/week) in individual models and together in multivariate models for breast cancer and all-cause mortality. For breast cancer mortality, the individual lifestyle models demonstrated a significant association with very low physical activity but not with the selected comorbidities or BMI. In the model that included all three lifestyle variables, very low physical activity was associated with a 22 % increased risk of breast cancer mortality (HR 1.22, 95 % CI 1.05, 1.42). For all-cause mortality, the three individual models demonstrated significant associations for all three lifestyle predictors. In the combined model, the strength and significance of the association of comorbidities (both hypertension and diabetes versus neither: HR 2.16, 95 % CI 1.79, 2.60) and very low physical activity (HR 1.35, 95 % CI 1.22, 1.51) remained unchanged, but the association with obesity was completely attenuated. These data indicate that after active treatment, very low physical activity, consistent with a sedentary lifestyle (and comorbidities for all-cause mortality), may account for the increased risk of mortality, with higher BMI, that is seen in other studies.</td></tr>
<tr><td>Total # of Studies: 3</td></tr>
<tr><td>Exposure Definition: PA levels were ascertained by study-specific questionnaires and were converted to metabolic equivalent (MET) hours per week. PA levels were low (<1.5) and not low (>1.5).
Measures Steps: No
Measures Bouts: No
Examines HIIT: No</td></tr>
<tr><td>Outcomes Addressed: All-cause and breast cancer mortality: % mortality, hazard ratios.
Examine Cardiorespiratory Fitness as Outcome: No</td></tr>
<tr><td>Populations Analyzed: Female, Adults, Breast cancer</td><td>Author-Stated Funding Source: National Cancer Institute at the National Institutes of Health, Susan G. Komen Foundation, Nurses' Health Study, Life After Cancer Epidemiology Study.</td></tr>
</table>

<table>
<tr><th colspan="2">Colorectal Cancer</th></tr>
<tr><td colspan="2">Meta-Analysis
Citation: Otto SJ, Korfage IJ, Polinder S, et al. Association of change in physical activity and body weight with quality of life and mortality in colorectal cancer: a systematic review and meta-analysis. Support Care Cancer. 2015;23(5):1237-1250. doi:10.1007/s00520-014-2480-0.</td></tr>
<tr><td>Purpose: To systematically review the literature reporting on longitudinal changes in PA and weight on quality of life and mortality in colorectal cancer survivors.</td><td rowspan="5">Abstract: PURPOSE: A systematic review and a meta-analysis were performed to assess the associations between change over time in physical activity and weight and quality of life and mortality in colorectal cancer patients. METHODS: The PubMed, Embase, and Cochrane Central Register of Controlled Trials databases were searched for English language articles published between January 1, 1990 and October 7, 2013. These articles reported results for changes in physical activity and body weight, assessed at pre- to post-diagnosis or at post-diagnosis only. A random effects model was used to analyze pooled quality of life and mortality estimates. RESULTS: Seven eligible studies were identified and analyzed. Increased physical activity was associated with higher overall quality of life scores (N = 3 studies; standardized mean difference (SMD) = 0.74, 95 % confidence interval (CI) = 0.66-0.82), reduced disease-specific mortality risk (hazard ratio (HRpooled) = 0.70, 95 % CI = 0.55-0.85), and reduced overall mortality (HRpooled = 0.75, CI = 0.62-0.87) (N = 2 studies). Weight gain was not associated with disease-specific (HRpooled = 1.02, CI = 0.84-1.20) or overall (HRpooled = 1.03, CI = 0.86-1.19) mortality (N = 3 studies). CONCLUSIONS: Increased physical activity was associated with improved quality of life, a reduced risk of colorectal cancer, and overall mortality rate. Given the paucity of the literature published on this topic, this finding should be interpreted with caution.</td></tr>
<tr><td>Timeframe: Inception–October 2013</td></tr>
<tr><td>Total # of Studies: 7</td></tr>
<tr><td>Exposure Definition: Self-reported PA measures were quantified as the number of metabolic equivalents (METs) per week, the number of minutes of PA per week, and meeting or not meeting a guideline for frequency of moderate- to strenuous-intensity exercise per week.
Measures Steps: No
Measures Bouts: No
Examines HIIT: No</td></tr>
<tr><td>Outcomes Addressed: Hazard ratios between PA and colorectal cancer, all-cause mortality, and colorectal cancer-specific mortality.
Examine Cardiorespiratory Fitness as Outcome: No</td></tr>
<tr><td>Populations Analyzed: Adults, Colorectal cancer</td><td>Author-Stated Funding Source: Department of Public Health of the Erasmus MC, University Medical Center Rotterdam.</td></tr>
</table>

<table>
<tr><th colspan="2">Breast and Colorectal Cancers</th></tr>
<tr><td colspan="2">Meta-Analysis
Citation: Schmid D, Leitzmann MF. Association between physical activity and mortality among breast cancer and colorectal cancer survivors: a systematic review and meta-analysis. Ann Oncol. 2014;25(7):1293-1311. doi:10.1093/annonc/mdu012.</td></tr>
<tr><td>Purpose: To quantify the evidence from prospective studies of PA in relation to total mortality and cancer mortality among survivors of breast cancer or colorectal cancer.</td><td rowspan="4">Abstract: BACKGROUND: Physical activity improves physical function during and after cancer treatment, but whether physical activity imparts survival benefit remains uncertain. DESIGN: Using prospective studies published through June 2013, we conducted a systematic review and random-effects meta-analysis of pre- and post-diagnosis physical activity in relation to total and cancer mortality among breast or colorectal cancer survivors. RESULTS: Sixteen studies of breast cancer survivors and seven studies of colorectal cancer survivors yielded 49095 total cancer survivors, including 8129 total mortality cases and 4826 cancer mortality cases. Comparing the highest versus lowest levels of pre-diagnosis physical activity among breast cancer survivors, the summary relative risks (RRs) of total and breast cancer mortality were 0.77 [95% confidence interval (CI) = 0.69-0.88] and 0.77 (95% CI = 0.66-0.90, respectively. For post-diagnosis physical activity, the summary RRs of total and breast cancer mortality were 0.52 (95% CI = 0.42-0.64) and 0.72 (95% CI = 0.60-0.85), respectively. For pre-diagnosis physical activity among colorectal cancer survivors, the summary RRs of total and colorectal cancer mortality were 0.74 (95% CI = 0.63-0.86) and 0.75 (95% CI = 0.62-0.91), respectively. For post-diagnosis physical activity, the summary RRs of total and colorectal cancer mortality were 0.58 (95% CI = 0.48-0.70) and 0.61 (95% CI = 0.40-0.92), respectively. Each 10 metabolic equivalent task-hour/week increase in post-diagnosis physical activity (equivalent to current recommendations of 150 min/week of at least moderate intensity activity) was associated with 24% (95% CI = 11-36%) decreased total mortality risk among breast cancer survivors and 28% (95% CI = 20-35%) decreased total mortality risk among colorectal cancer survivors. Breast or colorectal cancer survivors who increased their physical activity by any level from pre- to post-diagnosis showed decreased total mortality risk (RR = 0.61; 95% CI = 0.46-0.80) compared with those who did not change their physical activity level or were inactive/insufficiently active before diagnosis. CONCLUSION: Physical activity performed before or after cancer diagnosis is related to reduced mortality risk among breast and colorectal cancer survivors.</td></tr>
<tr><td>Timeframe: Inception–June 2013</td></tr>
<tr><td>Total # of Studies: 23</td></tr>
<tr><td>Exposure Definition: Metabolic equivalent (MET) hours/week.
Measures Steps: No
Measures Bouts: No
Examines HIIT: No</td></tr>
<tr><td>Outcomes Addressed: Relative risk of breast cancer and colorectal cancer mortality.
Examine Cardiorespiratory Fitness as Outcome: No</td><td></td></tr>
<tr><td>Populations Analyzed: Female, Adults, Underweight (BMI: below 18.5), Normal/healthy weight (BMI: 18.5–24.9), Overweight and obese, Breast cancer, Colorectal cancer, Menopausal status, Estrogen receptor status</td><td>Author-Stated Funding Source: Not reported.</td></tr>
</table>

<table>
<tr><th colspan="2">Breast Cancer</th></tr>
<tr><td colspan="2">Meta-Analysis
Citation: World Cancer Research Fund International. Continuous update project report: systematic review on diet, nutrition, physical activity and survival and second cancers in breast cancer survivors. www.wcrf.org/sites/default/files/Breast-Cancer-Survivors-SLR-2014-Report.pdf. Published June 2014. Accessed September 22, 2017.</td></tr>
<tr><td>Purpose: To identify and summarize the available information from published epidemiologic research on lifestyle and several health outcomes among women with a history of breast cancer.</td><td rowspan="5">Abstract: None available.</td></tr>
<tr><td>Timeframe: 1980–June 2012</td></tr>
<tr><td>Total # of Studies: 213</td></tr>
<tr><td>Exposure Definition: Total PA was defined as the physical activities involved in different types of activities; e.g., occupational, recreational, and household activities; or recreational and household activities; or non-occupational activity when it includes walking time, stair climbing, and city block walking, since these activities are not considered as recreational activity but are part of daily routine activities. Recreational PA was defined as PA in leisure time. Vigorous PA was any type of vigorous activity in recreational and non-recreational activities.
Measures Steps: No
Measures Bouts: No
Examines HIIT: No</td></tr>
<tr><td>Outcomes Addressed: Total mortality, breast cancer mortality.
Examine Cardiorespiratory Fitness as Outcome: No</td></tr>
<tr><td>Populations Analyzed: Female, Adults, Breast cancer, Menopausal status</td><td>Author-Stated Funding Source: World Cancer Research Fund International.</td></tr>
</table>

<table>
<tr><th colspan="2">Colorectal Cancer</th></tr>
<tr><td colspan="2">Meta-Analysis
Citation: Wu W, Guo F, Ye J, et al. Pre- and post-diagnosis physical activity is associated with survival benefits of colorectal cancer patients: a systematic review and meta-analysis. Oncotarget. 2016;7(32):52095-52103. doi:10.18632/oncotarget.10603.</td></tr>
<tr><td>Purpose: To test and determine whether pre- or post-diagnosis PA could influence cancer-specific and total mortality, in order to better understand the effects of PA interventions on prognosis of colorectal cancer survivors.</td><td rowspan="5">Abstract: OBJECTIVE: Physical activity is associated with reduced risk of colorectal cancer. However, whether physical activity could impart cancer patients' survival benefits remains uncertain. The aim of this study is to systematically evaluate the relationship between physical activity and colorectal cancer mortality. RESULTS: Our meta-analysis included 11 studies involving 17,295 patients with a follow-up period ranging from 3.8 to 11.9 years. Results indicated that physical activity was inversely associated with overall (RR = 0.81, 95% CI = 0.72-0.91) and colorectal cancer-specific mortality (RR = 0.79, 95% CI = 0.71-0.89) before the diagnosis of cancer, respectively. For physical activity after diagnosis, the pooled RRs of colorectal cancer-specific and total mortality were 0.77 (95% CI, 0.63-0.94) and 0.71 (95% CI, 0.63-0.81), respectively. Similar inverse associations between exercise and prognosis were found among colorectal cancer survivors who had high-level exercise compared with those who had low-level exercise or were inactive. There was no obvious evidence for publication bias among studies. MATERIALS AND METHODS: We performed a systematic data search in PubMed, Cochrane Library databases and Web of Science for relevant articles before Jan 2016. We adopted adjusted estimates to calculate pooled relative risks (RRs) with 95% confidence intervals (CI) by the random-effects model. The publication bias was assessed by Begg's test. CONCLUSIONS: Our meta-analysis provides comprehensive evidence that physical activity, whether before or after the diagnosis of colorectal cancer, is related to reduced overall and cancer-specific mortality. Our findings may have significant public health implications and more prospective randomized clinical trials should be warranted to certify this protective association.</td></tr>
<tr><td>Timeframe: Inception–January 2016</td></tr>
<tr><td>Total # of Studies: 11</td></tr>
<tr><td>Exposure Definition: The level of PA was accessed as metabolic equivalent (MET) hours or hours per week of PA based on questionnaires.
Measures Steps: No
Measures Bouts: No
Examines HIIT: No</td></tr>
<tr><td>Outcomes Addressed: Relative risk for the association between PA and survival among high-level vs. low-level PA.
Examine Cardiorespiratory Fitness as Outcome: No</td></tr>
<tr><td>Populations Analyzed: Adults, Colorectal cancer</td><td>Author-Stated Funding Source: Not reported.</td></tr>
</table>

<table>
<tr><th colspan="2">Breast Cancer</th></tr>
<tr><td colspan="2">Meta-Analysis
Citation: Zhong S, Jiang T, Ma T, et al. Association between physical activity and mortality in breast cancer: a meta-analysis of cohort studies. Eur J Epidemiol. 2014;29(6):391-404. doi:10.1007/s10654-014-9916-1.</td></tr>
<tr><td>Purpose: To investigate the association between PA and mortality in breast cancer.</td><td rowspan="5">Abstract: Previous studies concerning the association between physical activity (PA) and mortality in breast cancer yielded mixed results. We investigated the association by performing a meta-analysis of all available studies. Relevant studies were identified by searching PubMed and EMBASE to January 2014. We calculated the summary relative risk (RR) and 95 % confidence intervals (CIs) using random-effects models. The dose-response relationship was assessed by restricted cubic spline model and multivariate random-effect meta-regression. Sixteen cohort studies involving 42,602 patients of breast cancer were selected for meta-analysis. The analyses showed that patients who participated in any amount of PA before diagnosis had a RR of 0.82 (95 % CI 0.74-0.91) for breast cancer-specific mortality (vs. low PA). Those who participated in high PA and moderate PA before diagnosis had a RR of breast cancer-specific mortality of 0.81 (95 % CI 0.72-0.90) and 0.83 (95 % CI 0.73-0.94), respectively. Similar inverse associations of prediagnosis PA were found for all-cause mortality. Postdiagnosis PA on breast cancer-specific and all-cause mortality also showed the same results. Stratifying by body mass index (<25 vs. >/=25) or menopausal status, all the subgroups experienced benefits with PA, with a stronger mortality reduction among overweight women than normal weight women and among postmenopausal women than premenopausal women. A linear and significant dose-response association was only found for breast cancer-specific or all-cause mortality and prediagnosis PA (P for nonlinearity = 0.07 and 0.10, respectively). In conclusion, both prediagnosis and postdiagnosis PA were associated with reduced breast cancer-specific mortality and all-cause mortality.</td></tr>
<tr><td>Timeframe: 1965–January 2014</td></tr>
<tr><td>Total # of Studies: 16</td></tr>
<tr><td>Exposure Definition: Metabolic equivalent (MET) hours per week and kilocalories (kcal) per week were used to measure the levels of PA (low-level PA=reference category; high-level PA=highest category; moderate level PA=in-between; and moderate-high level of PA=low- and moderate-level PA).
Measures Steps: No
Measures Bouts: No
Examines HIIT: No</td></tr>
<tr><td>Outcomes Addressed: Relative risk between PA and breast cancer-specific and all-cause mortality in breast cancer patients.
Examine Cardiorespiratory Fitness as Outcome: No</td></tr>
<tr><td>Populations Analyzed: Female, All ages, Underweight (BMI: below 18.5), Normal/healthy weight (BMI: 18.5–24.9), Overweight and Obese, Breast cancer, Menopausal</td><td>Author-Stated Funding Source: National Natural Science Foundation of China.</td></tr>
</table>

Table 3. Existing Systematic Reviews, Meta-Analyses, and Pooled Analyses Quality Assessment Chart

	Ballard-Barbash, 2012	Barbaric, 2010	Beasley, 2012	Des Guetz, 2013	Fontein, 2013	Friedenreich, 2016
Review questions and inclusion/exclusion criteria delineated prior to executing search strategy.	Yes	Yes	No	Yes	Yes	Yes
Population variables defined and considered in methods.	Yes	No	Yes	Yes	Yes	No
Comprehensive literature search performed.	Partially Yes	Partially Yes	N/A	Yes	Yes	No
Duplicate study selection and data extraction performed.	Yes	Yes	N/A	No	Yes	No
Search strategy clearly described.	Yes	Yes	N/A	Yes	Yes	Yes
Relevant grey literature included in review.	No	No	N/A	No	No	No
List of studies (included and excluded) provided.	No	Yes	N/A	No	No	No
Characteristics of included studies provided.	Yes	Yes	No	Yes	Yes	No
FITT defined and examined in relation to outcome effect sizes.	N/A	No	Yes	Yes	N/A	Yes
Scientific quality (risk of bias) of included studies assessed and documented.	No	Yes	No	No	No	No
Results depended on study quality, either overall, or in interaction with moderators.	N/A	No	N/A	N/A	N/A	N/A
Scientific quality used appropriately in formulating conclusions.	N/A	Yes	N/A	N/A	N/A	N/A
Data appropriately synthesized and if applicable, heterogeneity assessed.	N/A	N/A	Yes	Yes	N/A	No
Effect size index chosen justified, statistically.	N/A	No	No	No	N/A	Partially Yes
Individual-level meta-analysis used.	N/A	N/A	Yes	Partially Yes	N/A	No
Practical recommendations clearly addressed.	Yes	Yes	Yes	Yes	Yes	Yes
Likelihood of publication bias assessed.	No	No	N/A	No	No	No
Conflict of interest disclosed.	No	No	Yes	No	Yes	No

	Ibrahim, 2011	Je, 2013	Lahart, 2015	Nechuta, 2016	Nelson, 2016
Review questions and inclusion/exclusion criteria delineated prior to executing search strategy.	Yes	Yes	Yes	Yes	Yes
Population variables defined and considered in methods.	Yes	Yes	Yes	Yes	Yes
Comprehensive literature search performed.	Yes	Partially Yes	Yes	N/A	N/A
Duplicate study selection and data extraction performed.	No	Yes	Yes	N/A	N/A
Search strategy clearly described.	Yes	Yes	Yes	N/A	N/A
Relevant grey literature included in review.	No	No	No	N/A	N/A
List of studies (included and excluded) provided.	Yes	No	No	N/A	N/A
Characteristics of included studies provided.	Yes	Yes	Yes	Yes	Yes
FITT defined and examined in relation to outcome effect sizes.	Yes	Yes	No	Yes	Yes
Scientific quality (risk of bias) of included studies assessed and documented.	No	Yes	Yes	No	No
Results depended on study quality, either overall, or in interaction with moderators.	N/A	Yes	Yes	N/A	N/A
Scientific quality used appropriately in formulating conclusions.	N/A	Yes	Yes	N/A	N/A
Data appropriately synthesized and if applicable, heterogeneity assessed.	Yes	Yes	Yes	Yes	Yes
Effect size index chosen justified, statistically.	Yes	Yes	Yes	Yes	Yes
Individual-level meta-analysis used.	No	No	No	Yes	Yes
Practical recommendations clearly addressed.	Yes	Yes	Yes	Yes	Yes
Likelihood of publication bias assessed.	Yes	Yes	Yes	N/A	N/A
Conflict of interest disclosed.	No	No	No	Yes	Yes

	Otto, 2015	Schmid, 2014	World Cancer Research Fund International, 2014	Wu, 2016	Zhong, 2014
Review questions and inclusion/exclusion criteria delineated prior to executing search strategy.	Yes	Yes	Yes	Yes	Yes
Population variables defined and considered in methods.	Yes	Yes	No	Yes	Yes
Comprehensive literature search performed.	Partially Yes	Partially Yes	Yes	Yes	Yes
Duplicate study selection and data extraction performed.	Yes	Yes	No	Yes	Yes
Search strategy clearly described.	Yes	Yes	Yes	Yes	Yes
Relevant grey literature included in review.	No	No	No	No	No
List of studies (included and excluded) provided.	No	No	No	No	No
Characteristics of included studies provided.	Yes	Yes	Yes	Yes	Yes
FITT defined and examined in relation to outcome effect sizes.	No	Yes	Yes	Yes	Yes
Scientific quality (risk of bias) of included studies assessed and documented.	Yes	No	Yes	Yes	Yes
Results depended on study quality, either overall, or in interaction with moderators.	No	N/A	No	Yes	Yes
Scientific quality used appropriately in formulating conclusions.	Yes	N/A	No	No	Yes
Data appropriately synthesized and if applicable, heterogeneity assessed.	Yes	Yes	Yes	Yes	Yes
Effect size index chosen justified, statistically.	Yes	Yes	Yes	Yes	Yes
Individual-level meta-analysis used.	No	No	No	No	No
Practical recommendations clearly addressed.	Yes	Yes	No	Yes	Yes
Likelihood of publication bias assessed.	Yes	Yes	Yes	Yes	Yes
Conflict of interest disclosed.	Yes	No	No	No	Yes

Appendices

Appendix A: Analytical Framework

Topic Area
Chronic Conditions

Systematic Review Questions

Among cancer survivors, what is the relationship between physical activity and (1) all-cause mortality; (2) cancer-specific mortality; or (3) risk of cancer recurrence or second primary cancer?

a. Is there a dose-response relationship? If yes, what is the shape of the relationship?
b. Does the relationship vary by age, sex, race/ethnicity, socio-economic status, or weight status?
c. Does the relationship vary based on: frequency, duration, intensity, type (mode), or how physical activity is measured?

Population
Cancer survivors of a single type of cancer of all ages

Intervention/Exposure
All types and intensities of physical activity

Comparison
Cancer survivors who participate in varying levels of physical activity

Key Definitions

- Cancer survivor: A person who has been diagnosed with, is undergoing treatment for, or has received treatment for any type of cancer.
- Cancer recurrence: Original primary cancer is detected after a remission (when cancer was not detectable).
- Second primary cancer: A new cancer that occurs sometime after diagnosis of original primary cancer.

Endpoint Health Outcomes

All-cause mortality
Cancer-specific mortality
Cancer recurrence
Second primary cancer
Adverse events related to physical activity

Appendix B: Final Search Strategy

Search Strategy: PubMed (Systematic Reviews, Meta-Analyses, Pooled Analyses, and High-Quality Reports)

Database: PubMed; Date of Search: 12/13/2016; 151 results

Set	Search Terms
Limit: Language	(English[lang])
Limit: Exclude animal only	NOT ("Animals"[Mesh] NOT ("Animals"[Mesh] AND "Humans"[Mesh]))
Limit: Publication Date (Systematic Reviews/Meta-Analyses)	AND ("2006/01/01"[PDAT] : "3000/12/31"[PDAT])
Limit: Publication Type Include (Systematic Reviews/Meta-Analyses)	AND (systematic[sb] OR meta-analysis[pt] OR "systematic review"[tiab] OR "systematic literature review"[tiab] OR metaanalysis[tiab] OR "meta analysis"[tiab] OR metanalyses[tiab] OR "meta analyses"[tiab] OR "pooled analysis"[tiab] OR "pooled analyses"[tiab] OR "pooled data"[tiab])
Limit: Publication Type Exclude (Systematic Reviews/Meta-Analyses)	NOT ("comment"[Publication Type] OR "editorial"[Publication Type])
Outcomes	AND ((Death[mh] OR Mortalit*[tiab] OR Mortality[mh] OR "Neoplasm Recurrence, Local"[mh] OR Recurrence[mh] OR "Neoplasms, Second Primary"[mh] OR Survival[tiab]) OR ((Death[tiab] OR Dying[tiab] OR Fatal*[tiab] OR Postmortem[tiab] OR Recurrence[tiab] OR "Second cancer"[tiab] OR "Second primary cancer"[tiab] OR "Second neoplasm"[tiab] OR "Second primary neoplasm"[tiab]) NOT medline[sb]))
Cancer	AND ((neoplasms[mh] OR "cancer Survivors"[tiab] OR "cancer survivor"[tiab]) OR (("Cancer"[tiab] OR "Neoplasm"[tiab] OR "Tumor"[tiab] OR "Carcinogenesis"[tiab] OR "Leukemia"[tiab] OR "Lymphoma"[tiab] OR "Malignancy"[tiab] OR Blastoma[tiab] OR "Tumour"[tiab] OR "Melanoma"[tiab] OR "Myeloma"[tiab] OR "Carcinoma"[tiab] OR "Neoplasia"[tiab] OR "Sarcoma"[tiab] OR Tumors[tiab] OR Tumours[tiab] OR Neoplasms[tiab] OR Adenosarcoma[tiab] OR Angiosarcoma[tiab] OR Astrocytoma[tiab] OR Cholangiocarcinoma[tiab] OR Chondrosarcoma[tiab] OR Craniopharyngioma[tiab] OR Ependymoma[tiab] OR Fibrosarcoma[tiab] OR Glioma[tiab] OR Langerhans Cell Histiocytosis[tiab] OR Hodgkin's Disease[tiab] OR Leiomyosarcoma[tiab] OR Medulloblastoma[tiab] OR Mesothelioma[tiab] OR Neuroblastoma[tiab] OR

Set	Search Terms
	Rhabdomyosarcoma[tiab] OR Osteosarcoma[tiab]) NOT medline[sb]))
Physical Activity	AND (("Aerobic activities"[tiab] OR "Aerobic activity"[tiab] OR "Cardiovascular activities"[tiab] OR "Cardiovascular activity"[tiab] OR "Endurance activities"[tiab] OR "Endurance activity"[tiab] OR "Exercise"[mh] OR "Functional training"[tiab] OR "leisure-time physical activity"[tiab] OR "Lifestyle activities"[tiab] OR "Lifestyle activity"[tiab] OR "muscle stretching exercises"[mh] OR "Physical activity"[tiab] OR "Physical conditioning"[tiab] OR "Qi gong"[tiab] OR "Recreational activities"[tiab] OR "Recreational activity"[tiab] OR "Resistance training"[tiab] OR "strength training"[tiab] OR "Tai ji"[mh] OR "Yoga"[mh] OR “Free living activities”[tiab] OR “Free living activity”[tiab] OR “Sedentary”[tiab] OR "Sedentary lifestyle"[mh]) OR (("Exercise"[tiab] OR "Tai chi"[tiab] OR "Tai ji"[tiab] OR "Walk"[tiab] OR "Walking"[tiab] OR "Yoga"[tiab]) NOT medline[sb]))

Search Strategy: CINAHL (Systematic Reviews, Meta-Analyses, Pooled Analyses, and High-Quality Reports)

Database: CINAHL; Date of Search: 12/22/16; 1 result
All terms searched in title or abstract

Set	Search Terms
Limits	2006-present English language Peer reviewed Exclude Medline records Human
Limit: Publication Type Include (Systematic Reviews/Meta-Analyses)	AND (“systematic review” OR “systematic literature review” OR "metaanalysis" OR "meta analysis" OR metanalyses OR "meta analyses" OR "pooled analysis" OR “pooled analyses” OR "pooled data")
Physical Activity	AND ("Aerobic activities" OR "Aerobic activity" OR "Cardiovascular activities" OR "Cardiovascular activity" OR "Endurance activities" OR "Endurance activity" OR "Exercise" OR "Functional training" OR "leisure-time physical activity" OR "Lifestyle activities" OR "Lifestyle activity" OR "Physical activity" OR "Physical conditioning" OR "Qi gong" OR "Recreational activities" OR "Recreational activity" OR "Resistance training" OR "strength training" OR "Tai chi" OR "Tai ji" OR "Walk" OR "Walking" OR "Yoga" OR “Free living activities” OR “Free living activity” OR “Sedentary”)
Cancer	AND ("Cancer" OR "Neoplasm" OR "Tumor" OR "Carcinogenesis" OR "Leukemia" OR "Lymphoma" OR "Malignancy" OR "Blastoma" OR "Tumour" OR "Melanoma" OR "Myeloma" OR "Carcinoma" OR "Neoplasia" OR "Sarcoma" OR "Tumors" OR "Tumours" OR "Neoplasms" OR "Adenosarcoma" OR "Angiosarcoma" OR "Astrocytoma" OR "Cholangiocarcinoma" OR "Chondrosarcoma" OR "Craniopharyngioma" OR "Ependymoma" OR "Fibrosarcoma" OR "Glioma" OR "Langerhans Cell Histiocytosis" OR "Hodgkin's Disease" OR "Leiomyosarcoma" OR "Medulloblastoma" OR "Mesothelioma" OR "Neuroblastoma" OR "Rhabdomyosarcoma" OR "Osteosarcoma" OR "cancer Survivors" OR "cancer survivor")
Outcomes	AND ("Death" OR "Dying" OR Fatal* OR Mortalit* OR "Postmortem" OR "Recurrence" OR "Second cancer" OR "Second primary cancer" OR "Second neoplasm" OR "Second primary neoplasm" OR "Survival")

Search Strategy: Cochrane (Systematic Reviews, Meta-Analyses, Pooled Analyses, and High-Quality Reports)

Database: Cochrane; Date of Search: 12/22/16; 14 results

All terms searched in title, abstract, or keywords

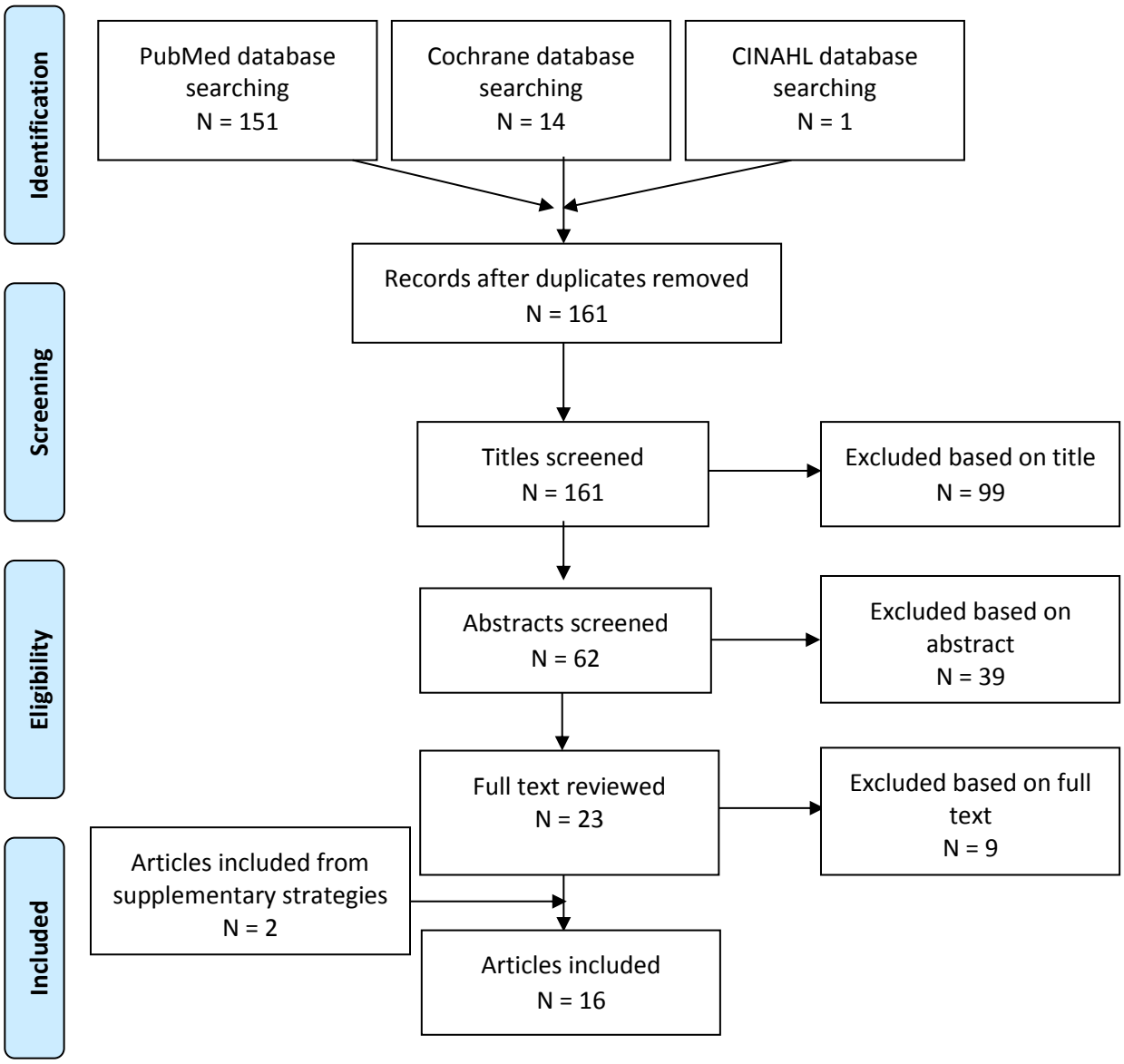
Set	Search Terms
Limits	2006-present Word variations not searched Cochrane Reviews (Reviews) and Other Reviews
Physical Activity	AND ("Aerobic activities" OR "Aerobic activity" OR "Cardiovascular activities" OR "Cardiovascular activity" OR "Endurance activities" OR "Endurance activity" OR "Exercise" OR "Functional training" OR "leisure-time physical activity" OR "Lifestyle activities" OR "Lifestyle activity" OR "Physical activity" OR "Physical conditioning" OR "Qi gong" OR "Recreational activities" OR "Recreational activity" OR "Resistance training" OR "strength training" OR "Tai chi" OR "Tai ji" OR "Walk" OR "Walking" OR "Yoga" OR "Free living activities" OR "Free living activity" OR "Sedentary")
Cancer	AND ("Cancer" OR "Neoplasm" OR "Tumor" OR "Carcinogenesis" OR "Leukemia" OR "Lymphoma" OR "Malignancy" OR "Blastoma" OR "Tumour" OR "Melanoma" OR "Myeloma" OR "Carcinoma" OR "Neoplasia" OR "Sarcoma" OR "Tumors" OR "Tumours" OR "Neoplasms" OR "Adenosarcoma" OR "Angiosarcoma" OR "Astrocytoma" OR "Cholangiocarcinoma" OR "Chondrosarcoma" OR "Craniopharyngioma" OR "Ependymoma" OR "Fibrosarcoma" OR "Glioma" OR "Langerhans Cell Histiocytosis" OR "Hodgkin's Disease" OR "Leiomyosarcoma" OR "Medulloblastoma" OR "Mesothelioma" OR "Neuroblastoma" OR "Rhabdomyosarcoma" OR "Osteosarcoma" OR "cancer Survivors" OR "cancer survivor")
Outcomes	AND ("Death" OR "Dying" OR Fatal* OR Mortalit* OR "Postmortem" OR "Recurrence" OR "Second cancer" OR "Second primary cancer" OR "Second neoplasm" OR "Second primary neoplasm" OR "Survival")

Supplementary Strategies

At full-text review members of the Physical Activity Guidelines Chronic Conditions Subcommittee identified two relevant articles[3, 4] that were not captured by the search strategies.

Appendix C: Literature Tree

Existing Systematic Reviews, Meta-Analyses, Pooled Analyses, and Reports Literature Tree



Appendix D: Inclusion/Exclusion Criteria

Chronic Conditions Subcommittee

Among cancer survivors, what is the relationship between physical activity and (1) all-cause mortality, (2) cancer-specific mortality, or (3) risk of cancer recurrence or second primary cancer?

a. Is there a dose-response relationship? If yes, what is the shape of the relationship?
b. Does the relationship vary by age, sex, race/ethnicity, socio-economic status, or weight status?
c. Does the relationship vary based on: frequency, duration, intensity, type (mode), or how physical activity is measured?

Category	Inclusion/Exclusion Criteria	Notes/Rationale
Publication Language	**Include:** • Studies published with full text in English	
Publication Status	**Include:** • Studies published in peer-reviewed journals • Reports determined to have appropriate suitability and quality by PAGAC **Exclude:** • Grey literature, including unpublished data, manuscripts, abstracts, conference proceedings	
Research Type	**Include:** • Original research • Meta-analyses • Systematic reviews • Reports determined to have appropriate suitability and quality by PAGAC	
Study Subjects	**Include:** • Human subjects	
Age of Study Subjects	**Include:** • People of all ages	
Health Status of Study Subjects	**Include:** • Studies of cancer survivors of a single cancer type **Exclude:** • Studies that include cancer survivors as part of the study sample but do not analyze results separately for cancer survivors only.	Cancer survivor: A person who has been diagnosed with, is undergoing treatment for, or has received treatment for any type of cancer.
Date of Publication	**Include:** • Original research published from 2006 to 2016 • Systematic reviews and meta-analyses published from 2006 to 2016	
Study Design	**Include:** • Randomized controlled trials • Prospective cohort studies • Systematic reviews	

	• Meta-analyses • Pooled analyses • PAGAC-approved reports **Exclude:** • Narrative reviews • Commentaries • Editorials • Non-randomized controlled trials • Retrospective cohort studies • Case-control studies • Cross-sectional studies • Before-and-after studies	
Intervention/ Exposure	**Include studies in which the exposure or intervention is:** • All types and intensities of physical activity, including sedentary behavior **Exclude:** • Studies that do not include physical activity • Studies of multimodal interventions that do not present data on physical activity alone • Studies of a single, acute session of exercise • Studies of a disease-specific therapeutic exercise delivered by a medical professional (e.g., physical therapist) • Studies with measures of physical fitness as the exposure	
Outcome	**Include studies in which the outcome is:** • All-cause mortality • Cancer-specific mortality • Cancer recurrence • Second primary cancer • Adverse events related to physical activity **Exclude:** • Studies of cancer survivors that study only the relationship of physical activity with physiologic measurements of cancer biomarkers.	

Appendix E: Rationale for Exclusion at Abstract or Full-Text Triage for Existing Systematic Reviews, Meta-Analyses, Pooled Analyses, and Reports

The table below lists the excluded articles with at least one reason for exclusion, but may not reflect all possible reasons.

Citation	Outcome	Population	Study Design	Exposure	Not ideal fit for replacement of de novo search	Other
Allott EH, Masko EM, Freedland SJ. Obesity and prostate cancer: weighing the evidence. *Eur Urol.* 2013;63(5):800-809. doi:10.1016/j.eururo.2012.11.013.				X		
Arem H, Irwin ML. Obesity and endometrial cancer survival: a systematic review. *Int J Obes (Lond).* 2013;37(5):634-639. doi:10.1038/ijo.2012.94.				X		
Battaglini CL. Physical activity and hematological cancer survivorship. *Recent Results Cancer Res.* 2011;186:275-304. doi:10.1007/978-3-642-04231-7_12.					X	
Bergenthal N, Will A, Streckmann F, et al. Aerobic physical exercise for adult patients with haematological malignancies. *Cochrane Database Syst Rev.* 2014;(11):Cd009075. doi:10.1002/14651858.CD009075.pub2.	X					
Berrino F. Life style prevention of cancer recurrence: the yin and the yang. *Cancer Treat Res.* 2014;159:341-351. doi:10.1007/978-3-642-38007-5_20.			X			
Biswas A, Oh PI, Faulkner GE, et al. Sedentary time and its association with risk for disease incidence, mortality, and hospitalization in adults: a systematic review and meta-analysis. *Ann Intern Med.* 2015;162(2):123-132. doi:10.7326/M14-1651.		X				
Bouillet T, Bigard X, Brami C, et al. Role of physical activity and sport in oncology: scientific commission of the National Federation Sport and Cancer CAMI. *Crit Rev Oncol Hematol.* 2015;94(1):74-86. doi:10.1016/j.critrevonc.2014.12.012.			X			
Cannioto RA, LaMonte MJ, Kelemen LE, et al. Recreational physical inactivity and mortality in women with invasive epithelial ovarian cancer: evidence from the Ovarian Cancer Association Consortium. *Br J Cancer.* 2016;115(1):95-101. doi:10.1038/bjc.2016.153.						X

Citation	Outcome	Population	Study Design	Exposure	Not ideal fit for replacement of de novo search	Other
Carmichael AR, Daley AJ, Rea DW, Bowden SJ. Physical activity and breast cancer outcome: a brief review of evidence, current practice and future directions. *Eur J Surg Oncol.* 2010;36(12):1139-1148. doi:10.1016/j.ejso.2010.09.011.			X			
Davies NJ, Batehup L, Thomas R. The role of diet and physical activity in breast, colorectal, and prostate cancer survivorship: a review of the literature. *Br J Cancer.* 2011;105(suppl 1):S52-S73. doi:10.1038/bjc.2011.423.			X			
Fahey PP, Mallitt KA, Astell-Burt T, Stone G, Whiteman DC. Impact of pre-diagnosis behavior on risk of death from esophageal cancer: a systematic review and meta-analysis. *Cancer Causes Control.* 2015;26(10):1365-1373. doi:10.1007/s10552-015-0635-z.						X
Felbel S, Meerpohl JJ, Monsef I, Engert A, Skoetz N. Yoga in addition to standard care for patients with haematological malignancies. *Cochrane Database Syst Rev.* 2014;(6):Cd010146. doi:10.1002/14651858.CD010146.pub2.	X				X	
Furmaniak AC, Menig M, Markes MH. Exercise for women receiving adjuvant therapy for breast cancer. *Cochrane Database Syst Rev.* 2016;9:Cd005001.	X					
Ganz PA, Yip CH, Gralow JR, et al. Supportive care after curative treatment for breast cancer (survivorship care): resource allocations in low- and middle-income countries. A Breast Health Global Initiative 2013 consensus statement. *Breast.* 2013;22(5):606-615. doi:10.1016/j.breast.2013.07.049.			X			
Hackshaw-McGeagh LE, Perry RE, Leach VA, et al. A systematic review of dietary, nutritional, and physical activity interventions for the prevention of prostate cancer progression and mortality. *Cancer Causes Control.* 2015;26(11):1521-1550. doi:10.1007/s10552-015-0659-4.				X		
Hall-Alston, J. Exercise and the breast cancer survivor: the role of the nurse practitioner. *Clin J Oncol Nurs.* 2015;19(5):E98-E102. doi:10.1188/15.CJON.E98-E102.	X					

Citation	Outcome	Population	Study Design	Exposure	Not ideal fit for replacement of de novo search	Other
Halle M, Schoenberg MH. Physical activity in the prevention and treatment of colorectal carcinoma. *Dtsch Arztebl Int.* 2009;106(44):722-727. doi:10.3238/arztebl.2009.0722.			X			
Hanson ED, Wagoner CW, Anderson T, Battaglini CL. The Independent effects of strength training in cancer survivors: a systematic review. *Curr Oncol Rep.* 2016;18(5):31. doi:10.1007/s11912-016-0511-3.	X					
Haydon AM, MacInnis RJ, English DR, Giles GG. Effect of physical activity and body size on survival after diagnosis with colorectal cancer. *Gut.* 2006;55(1):62-67. doi:10.1136/gut.2005.068189.			X			
Haydon AM, MacInnis RJ, English DR, Morris H, Giles GG. Physical activity, insulin-like growth factor 1, insulin-like growth factor binding protein 3, and survival from colorectal cancer. *Gut.* 2006;55(5):689-694. doi:10.1136/gut.2005.081547.			X			
Hayes SC, Spence RR, Galvão DA, Newton RU. Australian Association for Exercise and Sport Science position stand: optimising cancer outcomes through exercise. *J Sci Med Sport.* 2009;12(4):428-434. doi:10.1016/j.jsams.2009.03.002.			X			
Kohler LN, Garcia DO, Harris RB, Oren E, Roe DJ, Jacobs ET. Adherence to diet and physical activity cancer prevention guidelines and cancer outcomes: a systematic review. *Cancer Epidemiol Biomarkers Prev.* 2016;25(7):1018-1028. doi:10.1158/1055-9965.EPI-16-0121.				X		
Koutsokera A, Kiagia M, Saif MW, Souliotis K, Syrigos KN. Nutrition habits, physical activity, and lung cancer: an authoritative review. *Clin Lung Cancer.* 2013;14(4):342-350. doi:10.1016/j.cllc.2012.12.002.	X					
Kroenke CH, Michael YL, Shu XO, et al. Post-diagnosis social networks, and lifestyle and treatment factors in the After Breast Cancer Pooling Project. *Psychooncology.* 2016;26(4):544-552. doi:10.1002/pon.4059.				X		

Citation	Outcome	Population	Study Design	Exposure	Not ideal fit for replacement of de novo search	Other
Li T, Wei S, Shi Y, et al. The dose-response effect of physical activity on cancer mortality: findings from 71 prospective cohort studies. *Br J Sports Med.* 2016;50(6):339-345. doi:10.1136/bjsports-2015-094927.						X
Li Y, Gu M, Jing F, et al. Association between physical activity and all cancer mortality: dose-response meta-analysis of cohort studies. *Int J Cancer.* 2016;138(4):818-832. doi:10.1002/ijc.29828.						X
Loprinzi PD, Lee H. Rationale for promoting physical activity among cancer survivors: literature review and epidemiologic examination. *Oncol Nurs Forum.* 2014;41(2):117-125. doi:10.1188/14.ONF.117-125.	X					
Lu Y, John EM, Sullivan-Halley J, et al. History of recreational physical activity and survival after breast cancer: the California Breast Cancer Survivorship Consortium. *Am J Epidemiol.* 2015;181(12):944-955. doi:10.1093/aje/kwu466.						X
Lynch BM. Sedentary behavior and cancer: a systematic review of the literature and proposed biological mechanisms. *Cancer Epidemiol Biomarkers Prev.* 2010;19(11):2691-2709.	X					
Markes M, Brockow T, Resch KL. Exercise for women receiving adjuvant therapy for breast cancer. *Cochrane Database Syst Rev.* 2006;(4):Cd005001.	X					
Molmenti CL, Hibler EA, Ashbeck EA, et al. Sedentary behavior is associated with colorectal adenoma recurrence in men. *Cancer Causes Control.* 2014;25(10):1387-1395. doi:10.1007/s10552-014-0444-9.		X				
Monninkhof EM, Elias SG, Vlems FA, et al; TFPAC. Physical activity and breast cancer: a systematic review. *Epidemiology*. 2007;18(1):137-157.	X					
Morales-Oyarvide V, Meyerhardt JA. Vitamin D and physical activity in patients with colorectal cancer: epidemiological evidence and therapeutic implications. *Cancer J.* 2016;22(3):223-231. doi:10.1097/PPO.0000000000000197.			X			

Citation	Outcome	Population	Study Design	Exposure	Not ideal fit for replacement of de novo search	Other
National Collaborating Centre for Cancer, National Institute for Health and Care Excellence. *Metastatic Spinal Cord Compression: Diagnosis and Management of Patients at Risk of or With Metastatic Spinal Cord Compression*. Cardiff, Wales: National Collaborating Centre for Cancer; 2008.	X					
Pekmezi DW, Demark-Wahnefried W. Updated evidence in support of diet and exercise interventions in cancer survivors. *Acta Oncol.* 2011;50(2):167-178. doi:10.3109/0284186X.2010.529822.	X					
Perreault K, Bauman A, Johnson N, Britton A, Rangul V, Stamatakis E. Does physical activity moderate the association between alcohol drinking and all-cause, cancer and cardiovascular diseases mortality? A pooled analysis of eight British population cohorts. *Br J Sports Med.* 2016; August 31. doi10.1136/bjsports-2016-096194.			X			
Rajarajeswaran P, Vishnupriya R. Exercise in cancer. *Indian J Med Paediatr Oncol.* 2009;30(2):61-70. doi:10.4103/0971-5851.60050.	X					
Reimers CD, Knapp G, Reimers AK. Does physical activity increase life expectancy? A review of the literature. *J Aging Res.* 2012;2012:243958. doi.10.1155/2012/243958.		X				
Rhea DJ, Lockwood S. Adults surviving lung cancer two or more years: a systematic review. *JBI Libr Syst Rev.* 2012;10(34):2297-2349.	X					
Schmitz KH, Courneya KSH, Matthews C, et al; American College of Sports Medicine. American College of Sports Medicine roundtable on exercise guidelines for cancer survivors. *Med Sci Sports Exerc.* 2010;42(7):1409-1426. doi:10.1249/MSS.0b013e3181e0c112.			X			
Schwartz AL. Physical activity. *Semin Oncol Nurs.* 2008;24(3):164-170.			X			
Sebio Garcia R, Yáñez Brage MI, Giménez Moolhuyzen E, Granger CL, Denehy L. Functional and postoperative outcomes after preoperative exercise training in patients with lung cancer: a systematic review and meta-analysis. *Interact Cardiovasc Thorac Surg.* 2016;23(3):486-497. doi:10.1093/icvts/ivw152.	X					

Citation	Outcome	Population	Study Design	Exposure	Not ideal fit for replacement of de novo search	Other
Speed-Andrews AE, Courneya KS. Effects of exercise on quality of life and prognosis in cancer survivors. *Curr Sports Med Rep.* 2009;8(4):176-181. doi:10.1249/JSR.0b013e3181ae98f3.	X					
Stamatakis E, Chau JY, Pedisic Z, et al. Are sitting occupations associated with increased all-cause, cancer, and cardiovascular disease mortality risk? A pooled analysis of seven British population cohorts. *PLoS One.* 2013;8(9):e73753. doi.10.1371/journal.pone.0073753.				X		
Van Blarigan EL, Meyerhardt JA. Role of physical activity and diet after colorectal cancer diagnosis. *J Clin Oncol.* 2015;33(16):1825-1834.			X			
Wang D, Zheng W, Wang SM, et al. Estimation of cancer incidence and mortality attributable to overweight, obesity, and physical inactivity in China. *Nutr Cancer.* 2012;64(1):48-56.			X			
Warburton DE, Charlesworth S, Ivey A, Nettlefold L, Bredin SS. A systematic review of the evidence for Canada's Physical Activity Guidelines for Adults. *Int J Behav Nutr Phys Act.* 2010;7:39. doi:10.1186/1479-5868-7-39.	X					
Zhang FF, Saltzman E, Must A, Parsons SK. Do childhood cancer survivors meet the diet and physical activity guidelines? A review of guidelines and literature. *Int J Child Health Nutr.* 2012;1(1):44-58.	X					

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11. Nelson SH, Marinac CR, Patterson RE, et al. Impact of very low physical activity, BMI, and comorbidities on mortality among breast cancer survivors. *Breast Cancer Res Treat*. 2016;155(3):551-557. doi:10.1007/s10549-016-3694-2.

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