Evidence Portfolio – Sedentary Subcommittee, Question 3

Q3. What is the relationship between sedentary behavior and cancer mortality?

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

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

Conclusion Statements and Grades

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

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

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

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

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

Description of the Evidence

An initial search for systematic reviews, meta-analyses, pooled analyses, and reports did not identify sufficient literature to fully answer the research question as determined by the Sedentary Subcommittee. A supplementary search for original research was conducted to capture the most recent literature.

Existing Systematic Reviews and Meta-Analyses

Overview

A total of 5 existing reviews were included: 2 meta-analyses[1, 2] and 3 systematic reviews.[3-5] The reviews were published from 2010 to 2016.

The meta-analyses included 8[1] and 10[2] studies that addressed cancer mortality. Both meta-analyses covered an extensive timeframe: from inception to one year before publication.

The systematic reviews included a range of 2 to 4 studies that addressed cancer mortality. Reviews covered the following timeframes: from 1980 to June 2010,[3] from 1989 to February 2010,[4] and from 1996 to January 2011.[5]

Exposures

All of the included reviews examined sedentary behavior. All of the reviews used a comprehensive definition of sedentary behavior that included any activities requiring low levels of energy expenditure (≤1.5 metabolic equivalents), such as sitting time, television viewing, or screen time.

Outcomes

All included reviews addressed cancer mortality as an outcome.

Original Research

Overview

Five original research studies were included.[6-10] All of the included studies were prospective cohort studies and were published between 2014 and 2016.

The majority of the studies (n=4) were conducted in the United States,[6, 8-10] one was in Australia.[7] The analytic sample size ranged from 2,918 to 154,614.

Exposures

Three of the studies used self-reported data to measure sedentary behavior. Of these studies, two assessed participants' sitting per day,[8, 9] while the other study[7] assessed participants' television viewing time.

The two studies used objective devices to measure sedentary behaviors. One studies used accelerometers,[10] while the one study[6] used an activity monitor.

Outcomes

All included studies addressed cancer mortality as an outcome.

Populations Analyzed

The table below lists the populations analyzed in each article.

Table 1. Populations Analyzed by All Sources of Evidence

	Sex	Age	Chronic Conditions	Other
Biswas, 2015		Adults		
Ekelund, 2016		Adults		
Ensrud, 2014	Male	Adults ≥71		
Grace, 2016		Adults ≥25		
Lee, 2016		Adults 50–79	Diabetes, Congestive Heart Failure	Post-menopausal, Smoking
Lynch, 2010		Adults		
Matthews, 2015	Male	Adults 59–82		
Proper, 2011		Adults		
Schmid, 2016	Male	Adults 50–85		
Thorp, 2011		Adults		

Supporting Evidence

Existing Systematic Reviews and Meta-Analyses

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

<table>
<tr><td colspan="2">Meta-Analysis
Citation: 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.</td></tr>
<tr><td>Purpose: To quantify the association between sedentary time and hospitalizations, all-cause mortality, cardiovascular disease (CVD), diabetes, and cancer in adults independent of PA.</td><td rowspan="4">Abstract: BACKGROUND: The magnitude, consistency, and manner of association between sedentary time and outcomes independent of physical activity remain unclear. PURPOSE: To quantify the association between sedentary time and hospitalizations, all-cause mortality, cardiovascular disease, diabetes, and cancer in adults independent of physical activity. DATA SOURCES: English-language studies in MEDLINE, PubMed, EMBASE, CINAHL, Cochrane Library, Web of Knowledge, and Google Scholar databases were searched through August 2014 with hand-searching of in-text citations and no publication date limitations. STUDY SELECTION: Studies assessing sedentary behavior in adults, adjusted for physical activity and correlated to at least 1 outcome. DATA EXTRACTION: Two independent reviewers performed data abstraction and quality assessment, and a third reviewer resolved inconsistencies. DATA SYNTHESIS: Forty-seven articles met our eligibility criteria. Meta-analyses were performed on outcomes for cardiovascular disease and diabetes (14 studies), cancer (14 studies), and all-cause mortality (13 studies). Prospective cohort designs were used in all but 3 studies; sedentary times were quantified using self-report in all but 1 study. Significant hazard ratio (HR) associations were found with all-cause mortality (HR, 1.240 [95% CI, 1.090 to 1.410]), cardiovascular disease mortality (HR, 1.179 [CI, 1.106 to 1.257]), cardiovascular disease incidence (HR, 1.143 [CI, 1.002 to 1.729]), cancer mortality (HR, 1.173 [CI, 1.108 to 1.242]), cancer incidence (HR, 1.130 [CI, 1.053 to 1.213]), and type 2 diabetes incidence (HR, 1.910 [CI, 1.642 to 2.222]). Hazard ratios associated with sedentary time and outcomes were generally more pronounced at lower levels of physical activity than at higher levels. LIMITATION: There was marked heterogeneity in research designs and the assessment of sedentary time and physical activity. CONCLUSION: Prolonged sedentary time was independently associated with deleterious health outcomes regardless of physical activity.</td></tr>
<tr><td>Timeframe: Inception–2014</td></tr>
<tr><td>Total # of Studies: 41</td></tr>
<tr><td>Author's Definition of Sedentary:
A distinct class of waking behaviors characterized by little physical movement and low energy expenditure (≤1.5 metabolic equivalents), including sitting, television watching, and reclined posture.</td></tr>
<tr><td>Outcomes Addressed:
All-cause mortality, CVD mortality, cancer mortality.</td><td></td></tr>
<tr><td>Populations Analyzed:
Adults</td><td>Author-Stated Funding Source: No funding source used</td></tr>
</table>

Meta-Analysis

Citation: Ekelund U, Steene-Johannessen J, Brown WJ, et al. Does physical activity attenuate, or even eliminate, the detrimental association of sitting time with mortality? A harmonised meta-analysis of data from more than 1 million men and women. *Lancet.* 2016;388(10051):1302-1310. doi:10.1016/S0140-6736(16)30370-1.

Purpose: To examine the joint and stratified associations of sedentary behavior and physical activity with all-cause mortality.	**Abstract:** BACKGROUND: High amounts of sedentary behaviour have been associated with increased risks of several chronic conditions and mortality. However, it is unclear whether physical activity attenuates or even eliminates the detrimental effects of prolonged sitting. We examined the associations of sedentary behaviour and physical activity with all-cause mortality. METHODS: We did a systematic review, searching six databases (PubMed, PsycINFO, Embase, Web of Science, Sport Discus, and Scopus) from database inception until October, 2015, for prospective cohort studies that had individual level exposure and outcome data, provided data on both daily sitting or TV-viewing time and physical activity, and reported effect estimates for all-cause mortality, cardiovascular disease mortality, or breast, colon, and colorectal cancer mortality. We included data from 16 studies, of which 14 were identified through a systematic review and two were additional unpublished studies where pertinent data were available. All study data were analysed according to a harmonised protocol, which categorised reported daily sitting time and TV-viewing time into four standardised groups each, and physical activity into quartiles (in metabolic equivalent of task [MET]-hours per week). We then combined data across all studies to analyse the association of daily sitting time and physical activity with all-cause mortality, and estimated summary hazard ratios using Cox regression. We repeated these analyses using TV-viewing time instead of daily sitting time. FINDINGS: Of the 16 studies included in the meta-analysis, 13 studies provided data on sitting time and all-cause mortality. These studies included 1 005 791 individuals who were followed up for 2-18·1 years, during which 84 609 (8·4%) died. Compared with the referent group (ie, those sitting <4 h/day and in the most active quartile [>35·5 MET-h per week]), mortality rates during follow-up were 12-59% higher in the two lowest quartiles of physical activity (from HR=1·12, 95% CI 1·08-1·16, for the second lowest quartile of physical activity [<16 MET-h per week] and sitting <4 h/day; to HR=1·59, 1·52-1·66, for the lowest quartile of physical activity [<2·5 MET-h per week] and sitting >8 h/day). Daily sitting time was not associated with increased all-cause mortality in those in the most active quartile of physical activity. Compared with the referent (<4 h of sitting per day and highest quartile of physical activity [>35·5 MET-h per week]), there was no increased risk of mortality during follow-up in those who sat for more than 8 h/day but who also reported >35·5 MET-h per week of activity (HR=1·04; 95% CI 0·99-1·10). By contrast, those who sat the least (<4 h/day) and were in the lowest activity quartile (<2·5 MET-h per week) had a significantly increased risk of dying during follow-up (HR=1·27, 95% CI 1·22-1·31). Six studies had data on TV-viewing time (N=465 450; 43 740 deaths). Watching TV for 3 h or more per day was associated with increased mortality regardless of physical activity, except in the most active quartile, where mortality was significantly increased only in people who watched TV for 5 h/day or more (HR=1·16, 1·05-1·28). INTERPRETATION: High levels of moderate intensity physical activity (ie, about 60-75 min per day) seem to eliminate the increased risk of death associated with high sitting time. However, this high activity level
Timeframe: Inception–2015	
Total # of Studies: 16	
Author's Definition of Sedentary: Daily sitting or TV-viewing time.	
Outcomes Addressed: All-cause mortality, cardiovascular disease mortality, and cancer mortality.	

	attenuates, but does not eliminate the increased risk associated with high TV-viewing time. These results provide further evidence on the benefits of physical activity, particularly in societies where increasing numbers of people have to sit for long hours for work and may also inform future public health recommendations.
Populations Analyzed: Adults	**Author-Stated Funding Source:** No funding source used

<table>
<tr><td colspan="2">Systematic Review
Citation: Lynch BM. Sedentary behavior and cancer: a systematic review of the literature and proposed biological mechanisms. Cancer Epidemiol Biomarkers Prev. 2010. 19:2691-709</td></tr>
<tr><td>Purpose: To evaluate the research on sedentary behavior and cancer, to summarize possible biological pathways that may underlie these associations, and to propose an agenda for future research.</td><td rowspan="5">Abstract: BACKGROUND: Sedentary behavior (prolonged sitting or reclining characterized by low energy expenditure) is associated with adverse cardiometabolic profiles and premature cardiovascular mortality. Less is known for cancer risk. The purpose of this review is to evaluate the research on sedentary behavior and cancer, to summarize possible biological pathways that may underlie these associations, and to propose an agenda for future research. METHODS: Articles pertaining to sedentary behavior and (a) cancer outcomes and (b) mechanisms that may underlie the associations between sedentary behavior and cancer were retrieved using Ovid and Web of Science databases. RESULTS: The literature review identified 18 articles pertaining to sedentary behavior and cancer risk, or to sedentary behavior and health outcomes in cancer survivors. Ten of these studies found statistically significant, positive associations between sedentary behavior and cancer outcomes. Sedentary behavior was associated with increased colorectal, endometrial, ovarian, and prostate cancer risk; cancer mortality in women; and weight gain in colorectal cancer survivors. The review of the literature on sedentary behavior and biological pathways supported the hypothesized role of adiposity and metabolic dysfunction as mechanisms operant in the association between sedentary behavior and cancer. CONCLUSIONS: Sedentary behavior is ubiquitous in contemporary society; its role in relation to cancer risk should be a research priority. Improving conceptualization and measurement of sedentary behavior is necessary to enhance validity of future work. IMPACT: Reducing sedentary behavior may be a viable new cancer control strategy.</td></tr>
<tr><td>Timeframe: 1980–June 2010</td></tr>
<tr><td>Total # of Studies: 18</td></tr>
<tr><td>Author's Definition of Sedentary: Prolonged sitting or reclining characterized by low energy expenditure.</td></tr>
<tr><td>Outcomes Addressed: Cancer mortality</td></tr>
<tr><td>Populations Analyzed: Adults</td><td>Author-Stated Funding Source: National Health and Medical Research Council Public Health Training Fellowship and an Alberta Innovates-Health Solutions Fellowship</td></tr>
</table>

<table>
<tr><td colspan="2">Systematic Review
Citation: Proper KI, Singh AS, van Mechelen W, Chinapaw MJ. Sedentary behaviors and health outcomes among adults: A systematic review of prospective studies. Am J Prev Med. 2011;40(2):174-182. doi:10.1016/j.amepre.2010.10.015.</td></tr>
<tr><td>Purpose: To systematically review the literature with respect to the relationship between diverse sedentary behaviors and health outcomes among adults, taking into account the methodologic quality of the studies.</td><td rowspan="5">Abstract: CONTEXT: Nowadays, people spend a substantial amount of time per day on sedentary behaviors and it is likely that the time spent sedentary will continue to rise. To date, there is no review of prospective studies that systematically examined the relationship between diverse sedentary behaviors and various health outcomes among adults. PURPOSE: This review aimed to systematically review the literature as to the relationship between sedentary behaviors and health outcomes considering the methodologic quality of the studies. EVIDENCE ACQUISITION: In February 2010, a search for prospective studies was performed in diverse electronic databases. After inclusion, in 2010, the methodologic quality of each study was assessed. A best-evidence synthesis was applied to draw conclusions. EVIDENCE SYNTHESIS: 19 studies were included, of which 14 were of high methodologic quality. Based on inconsistency in findings among the studies and lack of high-quality prospective studies, insufficient evidence was concluded for body weight-related measures, CVD risk, and endometrial cancer. Further, moderate evidence for a positive relationship between the time spent sitting and the risk for type 2 diabetes was concluded. Based on three high-quality studies, there was no evidence for a relationship between sedentary behavior and mortality from cancer, but strong evidence for all-cause and CVD mortality. CONCLUSIONS: Given the trend toward increased time in sedentary behaviors, additional prospective studies of high methodologic quality are recommended to clarify the causal relationships between sedentary behavior and health outcomes. Meanwhile, evidence to date suggests that interventions aimed at reducing sedentary behavior are needed.</td></tr>
<tr><td>Timeframe: 1989–February 2010</td></tr>
<tr><td>Total # of Studies: 19</td></tr>
<tr><td>Author's Definition of Sedentary: Activities that do not increase energy expenditure substantially above the resting level (1.0–1.5 metabolic equivalents); includes activities such as sleeping, sitting, lying down, watching TV, and engaging in other forms of screen-based entertainment.</td></tr>
<tr><td>Outcomes Addressed: All-cause mortality, cardiovascular disease mortality, cancer mortality.</td></tr>
<tr><td>Populations Analyzed: Adults</td><td>Author-Stated Funding Source: Not Reported</td></tr>
</table>

<table>
<tr><td colspan="2">Systematic Review
Citation: Thorp AA, Owen N, Neuhaus M, Dunstan DW. Sedentary behaviors and subsequent health outcomes in adults a systematic review of longitudinal studies, 1996-2011. Am J Prev Med. 2011;41(2):207-215. doi:10.1016/j.amepre.2011.05.004.</td></tr>
<tr><td>Purpose: To systematically review and provide an informative synthesis of findings from longitudinal studies published since 1996 reporting on relationships between self-reported sedentary behavior and device-based measures of sedentary time with health-related outcomes in adults.</td><td rowspan="5">Abstract: CONTEXT: To systematically review and provide an informative synthesis of findings from longitudinal studies published since 1996 reporting on relationships between self-reported sedentary behavior and device-based measures of sedentary time with health-related outcomes in adults. EVIDENCE ACQUISITION: Studies published between 1996 and January 2011 were identified by examining existing literature reviews and by systematic searches in Web of Science, MEDLINE, PubMed, and PsycINFO. English-written articles were selected according to study design, targeted behavior, and health outcome. EVIDENCE SYNTHESIS: Forty-eight articles met the inclusion criteria; of these, 46 incorporated self-reported measures including total sitting time; TV viewing time only; TV viewing time and other screen-time behaviors; and TV viewing time plus other sedentary behaviors. Findings indicate a consistent relationship of self-reported sedentary behavior with mortality and with weight gain from childhood to the adult years. However, findings were mixed for associations with disease incidence, weight gain during adulthood, and cardiometabolic risk. Of the three studies that used device-based measures of sedentary time, one showed that markers of obesity predicted sedentary time, whereas inconclusive findings have been observed for markers of insulin resistance. CONCLUSIONS: There is a growing body of evidence that sedentary behavior may be a distinct risk factor, independent of physical activity, for multiple adverse health outcomes in adults. Prospective studies using device-based measures are required to provide a clearer understanding of the impact of sedentary time on health outcomes.</td></tr>
<tr><td>Timeframe: 1996–January 2011</td></tr>
<tr><td>Total # of Studies: 48</td></tr>
<tr><td>Author's Definition of Sedentary: A distinct class of activities that require low levels of energy expenditure in the range of 1.0–1.5 metabolic equivalents and involve sitting during commuting and leisure time and sitting in the workplace and the domestic environment.</td></tr>
<tr><td>Outcomes Addressed: All-cause mortality, cardiovascular disease mortality, cancer mortality.</td></tr>
<tr><td>Populations Analyzed: Adults</td><td>Author-Stated Funding Source: Australian National Health and Medical Research Council, Healthy Lifestyle Research Centre, Queensland Health, Victorian Health Promotion Foundation</td></tr>
</table>

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

Nutrition Evidence Library (NEL) Bias Assessment Tool (BAT): Original Research					
	Biswas, 2015	Ekelund, 2016	Lynch, 2010	Proper, 2011	Thorp, 2011
(???) = Can't Determine					
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	No	Yes
Comprehensive literature search performed.	Yes	Yes	Yes	Yes	Yes
Duplicate study selection and data extraction performed.	Yes	Yes	No	Yes	No
Search strategy clearly described.	Yes	Yes	Yes	Yes	Yes
Relevant grey literature included in review.	No	Yes	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.	Yes	Yes	N/A	N/A	N/A
Scientific quality (risk of bias) of included studies assessed and documented.	Yes	Yes	No	Yes	No
Results depended on study quality, either overall, or in interaction with moderators.	Yes	Yes	N/A	Yes	N/A
Scientific quality used appropriately in formulating conclusions.	Yes	Yes	N/A	Yes	N/A
Data appropriately synthesized and if applicable, heterogeneity assessed.	Yes	Yes	N/A	N/A	N/A
Effect size index chosen justified, statistically.	Yes	Yes	N/A	N/A	N/A
Individual-level meta-analysis used.	No	Yes	N/A	N/A	N/A
Practical recommendations clearly addressed.	Yes	Yes	Yes	Yes	Yes
Likelihood of publication bias assessed.	Yes	Yes	No	No	No
Conflict of interest disclosed.	Yes	Yes	Yes	No	No

Original Research

Table 4. Original Research Individual Evidence Summary Tables

<table>
<tr><td colspan="2">Original Research
Citation: Ensrud KE, Blackwell TL, Cauley JA, et al. Objective measures of activity level and mortality in older men. J Am Geriatr Soc. 2014;62(11):2079-2087. doi:10.1111/jgs.13101.</td></tr>
<tr><td colspan="2">Purpose: To comprehensively assess associations of objective measures of activity level with mortality risk in older men.</td></tr>
<tr><td>Study Design: Prospective cohort study</td><td rowspan="4">Abstract: OBJECTIVES: To examine associations between objective measures of activity level and mortality risk in older men. DESIGN: Prospective cohort study. SETTING: Six U.S. sites. PARTICIPANTS: Men aged 71 and older followed an average of 4.5 years (N = 2,918). MEASUREMENTS: Time awake spent in sedentary behavior (metabolic equivalent (MET) level </=1.50), light activity (MET level 1.51-2.99), and at least moderate activity (MET level >/=3.00) measured using an activity monitor worn for 5 days or longer and expressed as quartiles. Deaths were confirmed with death certificates; cause of death was adjudicated by review of certificates and records. RESULTS: During follow-up, 409 (14%) men died. After multivariable adjustment, comparing Q4 with Q1, more time spent in sedentary behavior (Q4 vs Q1, hazard ratio (HR) = 1.51, 95% confidence interval (CI) = 1.10-2.08), less time spent in light activity (Q1 vs Q4, HR = 1.54, 95% CI = 1.06-2.24), and less time spent in at least moderate activity (Q1 vs Q4, HR = 1.56, 95% CI = 1.09-2.25) were similarly associated with greater mortality risk primarily due to higher risks of cardiovascular and noncardiovascular, noncancer death. The association between time spent in sedentary behavior and mortality varied according to time spent at higher activity level. More time spent in sedentary behavior was associated with greater risk of death in men spending 1.2 (median) h/d or more in at least moderate activity (Q4 vs Q1, HR = 2.09, 95% CI = 1.26-3.49) but not in those spending less time (Q4 vs Q1, HR = 1.02, 95% CI = 0.62-1.66) (P = .005 for interaction). CONCLUSION: In older men exceeding current guidelines on physical activity, more time spent in sedentary behavior is associated with greater mortality risk.</td></tr>
<tr><td>Location: United States</td></tr>
<tr><td>Sample: 2,918
Attrition Rate: 51.32%
Sample Power: Not Reported</td></tr>
<tr><td>Exposure Measurement
Device-Measured: Activity monitor, time (minutes/24 hours) spent sleeping, sedentary behavior (metabolic equivalent ≤ 1.50); compared across quartiles of time spent engaging in sedentary behavior.
Measures Steps: No
Measures Bouts: No</td></tr>
<tr><td>Refers to Other Materials: Yes
Examine Cardiorespiratory Fitness as Outcome: No</td><td>Outcomes Examined: Mortality: participants contacted every four months to ascertain vital status; death certificates and cause of death due to cardiovascular disease, cancer, or other cause adjudicated by central physician review.</td></tr>
<tr><td>Populations Analyzed: Adults ≥71, Male</td><td>Author-Stated Funding Source: National Institutes of Health</td></tr>
</table>

<table>
<tr><td colspan="2">Original Research
Citation: Grace MS, Lynch BM, Dillon F, Barr, EM, Owen, N, Dunstan, DW. Joint associations of smoking and television viewing time on cancer and cardiovascular disease mortality. Int J Cancer. 2017;140(7):1538-1544. doi:10.1002/ijc.30580.</td></tr>
<tr><td colspan="2">Purpose: To examine the associations of a common sedentary behavior—television viewing time—with smoking status on cancer and cardiovascular disease mortality among adults.</td></tr>
<tr><td>Study Design: Prospective cohort study</td><td rowspan="4">Abstract: Excessive sitting time and smoking are pro-inflammatory lifestyle factors that are associated with both cancer and cardiovascular disease (CVD) mortality. However, their joint associations have not been investigated. We examined the associations of television (TV) viewing time with cancer and CVD mortality, according to smoking status, among 7,498 non-smokers (34% ex-smokers) and 1,409 current-smokers in the Australian Diabetes, Obesity and Lifestyle Study. During 117,506 person-years (median 13.6 years) of follow-up, there were 346 cancer and 209 CVD-related deaths. Including an interaction between TV time and smoking status in the model significantly improved the goodness of fit for cancer (p = 0.01) but not CVD mortality (p = 0.053). In the multivariate-adjusted model, every additional hr/d of TV time was associated with increased risk of cancer-related (HR 1.23; 95% CI 1.08-1.40), but not CVD-related mortality (HR 1.16; 95% CI 0.97-1.38) in current-smokers. Elevated multivariate-adjusted cancer mortality HRs were observed for current-smokers watching 2 to <4 hr/d (HR 1.45; 95% CI 0.78-2.71) and >/=4 hr/d (HR 2.26; 95% CI 1.10-4.64), compared to those watching <2 hr/d. Current-smokers watching 2 to <4 hr/d (HR 1.07; 95% CI 0.45-2.53) and >/=4 hr/d (HR 1.92; 95% CI 0.76-4.84) did not have a significantly higher risk of CVD mortality, compared to <2 hr/d. No associations were observed for non-smokers. These findings show an association of TV, a common sedentary behavior, with cancer mortality in current-smokers. The association with CVD mortality was less clear. Further exploration in larger data sets is warranted. Limiting TV viewing time may be of benefit in reducing cancer mortality risk in current-smokers.</td></tr>
<tr><td>Location: Australia</td></tr>
<tr><td>Sample: 8,907
Attrition Rate: 20.81%
Sample Power: Not Reported</td></tr>
<tr><td>Exposure Measurement
Self-Reported: Interviewer-administered questionnaire, total time spent watching television or videos in previous 7 days (continuous), three categories of television time (<2, >2 to <4, and >4 hours/day).
Measures Steps: No
Measures Bouts: No</td></tr>
<tr><td>Refers to Other Materials: Yes
Examine Cardiorespiratory Fitness as Outcome: No</td><td>Outcomes Examined: Mortality status and underlying contributory causes of death: Australian National Death Index, deaths attributed to cancer and cardiovascular disease separated by International Classification of Diseases codes.</td></tr>
<tr><td>Populations Analyzed: Adults ≥25</td><td>Author-Stated Funding Source: Not Reported</td></tr>
</table>

<table>
<tr><td colspan="2">Original Research
Citation: Lee J, Kuk JL, Ardern CI. The relationship between changes in sitting time and mortality in post-menopausal US women. J Public Health (Oxf). 2016;38(2):270-278. doi:10.1093/pubmed/fdv055.</td></tr>
<tr><td colspan="2">Purpose: To assess the relationship between sitting time at baseline and year six of follow-up with mortality among post-menopausal women.</td></tr>
<tr><td>Study Design: Prospective cohort study</td><td rowspan="4">Abstract: BACKGROUND: Prolonged sitting is linked to various deleterious health outcomes. The alterability of the sitting time (ST)-health relationship is not fully established however and warrants study within populations susceptible to high ST. METHODS: We assessed the mortality rates of post-menopausal women from the Women's Health Initiative (WHI) observational study, a 15-year prospective study of post-menopausal women aged 50-79 years, according to their change in ST between baseline and year six. A total of 77 801 participants had information at both times on which to be cross-classified into the following: (i) high ST at baseline and follow-up; (ii) low ST at baseline and follow-up; (iii) increased ST and (iv) decreased ST. Cox regression was used to assess the relationship between all-cause, CVD and cancer mortality with change in ST. RESULTS: At the end of follow-up, there were 1855 deaths. Compared with high ST maintainers, low ST maintainers had a 51 and 48% lower risk of all-cause and cancer mortality, respectively. Reducing sitting also resulted in a protective rate of 29% for all-cause and 27% for cancer mortality. CONCLUSIONS: These results highlight not only the benefit of maintaining minimal ST, but also the utility of decreasing ST in older women, if current levels are high.</td></tr>
<tr><td>Location: United States</td></tr>
<tr><td>Sample: 77,801
Attrition Rate: 16.17%
Sample Power: Not Reported</td></tr>
<tr><td>Exposure Measurement
Self-Reported: Questionnaire ("During a usual day and night, about how many hours do you spend sitting?"), total daily sitting time assessed at baseline and at year six of follow-up. Participants were initially divided into quartiles of sitting time (<5, 6–9, 10–13, >14) to assess dose-response. The sitting time variable at baseline and follow-up was dichotomized as "low-to-moderate" (<9 hours) or "high" (>10 hours).
Measures Steps: No
Measures Bouts: No</td></tr>
<tr><td>Refers to Other Materials: Yes
Examine Cardiorespiratory Fitness as Outcome: No</td><td>Outcomes Examined: Death from all-cause, cardiovascular disease, or cancer: trained physician adjudicators established the end points from hospitalization and emergency room records, death certificates, autopsy reports, and coroner’s reports. Cause-specific mortality categorizations were based on the cause of death rather than the immediate or contributing cause of death.</td></tr>
<tr><td>Populations Analyzed: Adults 50–79; Diabetes; Other; Congestive Heart Failure; Post-menopausal; Smoking</td><td>Author-Stated Funding Source: Canadian Institute of Health Research</td></tr>
</table>

<table>
<tr><td colspan="2">Original Research
Citation: Matthews CE, Moore SC, Sampson J, et al. Mortality benefits for replacing sitting time with different physical activities. Med Sci Sports Exerc. 2015;47(9):1833-1840. doi:10.1249/MSS.0000000000000621.</td></tr>
<tr><td colspan="2">Purpose: To determine the marginal effects of hours of sedentary behavior, exercise, and non-exercise activity on overall mortality.</td></tr>
<tr><td>Study Design: Prospective cohort study</td><td rowspan="4">Abstract: PURPOSE: Prolonged sitting has emerged as a risk factor for early mortality, but the extent of benefit realized by replacing sitting time with exercise or activities of everyday living (i.e., nonexercise activities) is not known. METHODS: We prospectively followed 154,614 older adults (59-82 yr) in the National Institutes of Health-AARP Diet and Health Study who reported no major chronic diseases at baseline and reported detailed information about sitting time, exercise, and nonexercise activities. Proportional hazard models were used to estimate adjusted hazard ratios and 95% confidence intervals (HR (95% confidence interval)) for mortality. An isotemporal modeling approach was used to estimate associations for replacing sitting time with specific types of physical activity, with separate models fit for less active and more active participants to account for nonlinear associations. RESULTS: During 6.8 yr (SD, 1.0) of follow-up, 12,201 deaths occurred. Greater sitting time (>/=12 vs < 5 h.d(-1)) was associated with increased risk for all-cause and cardiovascular mortality. In less active adults (<2 h.d(-1) total activity), replacing 1 h.d(-1) of sitting with an equal amount of activity was associated with lower all-cause mortality for both exercise (HR, 0.58 (0.54-0.63)) and nonexercise activities (HR, 0.70 (0.66-0.74)), including household chores, lawn and garden work, and daily walking. Among more active participants (2+ h.d(-1) total activity), replacement of sitting time with purposeful exercise was associated with lower mortality (HR, 0.91 (0.88-0.94)) but not with nonexercise activity (HR, 1.00 (0.98-1.02)). Similar results were noted for cardiovascular mortality. CONCLUSIONS: Physical activity intervention strategies for older adults often focus on aerobic exercise, but our findings suggest that reducing sitting time and engaging in a variety of activities is also important, particularly for inactive adults.</td></tr>
<tr><td>Location: United States</td></tr>
<tr><td>Sample: 154,614
Attrition Rate: 0
Sample Power: Not Reported</td></tr>
<tr><td>Exposure Measurement
Self-Reported: Three sitting questions were asked about the number of hours spent in a typical 24-hour period during the last 12 months.
Measures Steps: No
Measures Bouts: No</td></tr>
<tr><td>Refers to Other Materials: Yes
Examine Cardiorespiratory Fitness as Outcome: No</td><td>Outcomes Examined: All-cause mortality, mortality from cardiovascular disease, and mortality from cancer determined through linkage with the Social Security Administration Death Master File and the National Death Index.</td></tr>
<tr><td>Populations Analyzed: Adults 59–82, Male</td><td>Author-Stated Funding Source: National Institutes of Health, National Cancer Institute</td></tr>
</table>

<table>
<tr><td colspan="2">Original Research
Citation: Schmid D, Ricci C, Baumeister SE, Leitzmann MF. Replacing sedentary time with physical activity in relation to mortality. Med Sci Sports Exerc. 2016;48(7):1312-1319. doi:0.1249/MSS.0000000000000913.</td></tr>
<tr><td colspan="2">Purpose: To explore whether reallocating 30 minutes per day from one activity behavior to an equal amount of time spent in another activity behavior is associated with mortality from any cause, cardiovascular disease (CVD), or cancer among adults.</td></tr>
<tr><td>Study Design:
Prospective cohort study
Location: United States
Sample: 3,702
Attrition Rate: 0.19%
Sample Power: Not Reported
Exposure Measurement Device-Measured:
Accelerometer, sedentary time defined as <100 counts per minute.
Measures Steps: No
Measures Bouts: No</td><td>Abstract: INTRODUCTION: Data evaluating mortality benefit from replacing sedentary time with physical activity are sparse. We explored reallocating time spent in sedentary behavior to physical activity of different intensities in relation to mortality risk. METHODS: Women and men age 50-85 yr from the National Health and Nutrition Examination Survey 2003-2004 and 2005-2006 cycles with follow-up through December 31, 2011, were included. Sedentary time and physical activity were assessed using an ActiGraph accelerometer. Isotemporal substitution models were used to estimate the effect of replacing one activity behavior with another activity behavior for the same amount of time while holding total accelerometer wear time constant. RESULTS: During a mean follow-up of 6.35 yr, 697 deaths from any cause occurred. Replacing 30 min of sedentary time with an equal amount of light activity was associated with 14% reduced risk of mortality (multivariable-adjusted hazard ratio (HR), 0.86; 95% confidence interval (CI), 0.83-0.90). Replacement of sedentary time with moderate to vigorous activity was related to 50% mortality risk reduction (HR, 0.50; 95% CI, 0.31-0.80). We also noted a 42% reduced risk of mortality when light physical activity was replaced by moderate to vigorous activity (HR, 0.58; 95% CI, 0.36-0.93). CONCLUSION: Replacing sedentary time with an equal amount of physical activity may protect against preterm mortality. Replacement of light physical activity with moderate to vigorous activity is also associated with protection from premature mortality.</td></tr>
<tr><td>Refers to Other Materials: Yes
Examine Cardiorespiratory Fitness as Outcome: No</td><td>Outcomes Examined: Mortality from any cause, CVD, or cancer: based on probabilistic match between the National Health and Nutrition Examination Survey (NHANES) and death certificate records of the National Death Index.</td></tr>
<tr><td>Populations Analyzed:
Adults 50–85, Male</td><td>Author-Stated Funding Source: No funding source used</td></tr>
</table>

Table 5. Original Research Bias Assessment Chart

Nutrition Evidence Library (NEL) Bias Assessment Tool (BAT): Original Research					
	Ensrud, 2014	Grace, 2017	Lee, 2016	Matthews, 2015	Schmid, 2016
(???) = Can't Determine					
Inclusion/exclusion criteria similar across study groups.	Yes	Yes	Yes	Yes	Yes
Strategy for recruiting or allocating participants similar across study groups.	Yes	Yes	Yes	Yes	Yes
Allocation sequence randomly generated.	N/A	N/A	N/A	N/A	N/A
Group allocation concealed (i.e., assignments could not be predicted).	N/A	N/A	N/A	N/A	N/A
Distribution of critical confounding factors similar across study groups at baseline, or analysis controlled for differences between groups.	Yes	Yes	Yes	Yes	Yes
Accounted for variations in execution of study from proposed protocol or research plan.	N/A	N/A	N/A	N/A	Yes
Adherence to study protocols similar across study groups.	Yes	Yes	Yes	Yes	Yes
Investigators accounted for unintended concurrent exposures that were differentially experienced by study groups and might bias results.	Yes	Yes	Yes	Yes	Yes
Participants blinded to their intervention or exposure status.	N/A	N/A	N/A	N/A	N/A
Investigators blinded to participants' intervention or exposure status.	N/A	N/A	N/A	N/A	N/A
Outcome assessors blinded to participants' intervention or exposure status.	N/A	N/A	N/A	N/A	N/A
Valid and reliable measures used consistently across study groups to assess inclusion/exclusion criteria, exposures, outcomes, and confounders.	Yes	Yes	No	No	Yes
Length of follow-up similar across study groups.	Yes	Yes	Yes	Yes	Yes
In cases of high or differential loss to follow-up, impact assessed through sensitivity analysis or other adjustment.	Yes	Yes	Yes	N/A	Yes
Other sources of bias taken into account in design and/or analysis of study through matching or other statistical adjustment.	Yes	Yes	Yes	Yes	Yes
Adequate statistical methods used to assess primary outcomes.	Yes	Yes	Yes	Yes	Yes

Appendices

Appendix A: Analytical Framework

Analytical Framework

Topic Area
Sedentary Behavior

Systematic Review Questions

What is the relationship between sedentary behavior and cancer mortality?

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

Population
Adults, 18 years and older

Exposure

Sedentary behavior

- Total sitting time
- Screen time
- Leisure-time sitting
- Occupational sitting time
- Objective measures of sedentary time

Comparison
Adults who participate in varying levels and types of sedentary behavior

Endpoint Health Outcomes

Incidence of:

- Cancer mortality

Key Definition:
Sedentary Behavior: In general, it is any waking behavior characterized by an energy expenditure ≤1.5 METs while in a sitting or reclining posture (Sedentary Behaviour Research Network. Standardized use of the terms "sedentary" and "sedentary behaviours." *Appl Physiol Nutr Metab.* 2012;37:540-542).

Appendix B: Final Search Strategy[1]

Research Questions

Q1. What is the relationship between sedentary behavior and all-cause mortality?
Q2. What is the relationship between sedentary behavior and mortality from cardiovascular disease?
Q3. What is the relationship between sedentary behavior and mortality from cancer?

Search Strategy: PubMed Q1-3 (Systematic Reviews, Meta-Analyses, and Pooled Analyses)

Database: PubMed; Date of Search: 12/5/2016; 164 results

Set	Search Terms
Limit: Language	(English[lang])
Limit: Exclude animal only	NOT ("Animals"[Mesh] NOT ("Animals"[Mesh] AND "Humans"[Mesh]))
Limit: Exclude child only	NOT (("infant"[Mesh] OR "child"[mesh] OR "adolescent"[mh]) NOT (("infant"[Mesh] OR "child"[mesh] OR "adolescent"[mh]) AND "adult"[Mesh]))
Limit: Publication Date Systematic Reviews/Meta-Analyses	AND ("2000/01/01"[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])
Sedentary	AND (("Sedentary lifestyle"[mh] OR "Computer time"[tiab] OR "Computer use"[tiab] OR "Screen time"[tiab] OR "Sitting"[tiab] OR "Television"[tiab] OR "TV viewing"[tiab] OR "TV watching"[tiab] OR "Video game"[tiab] OR "Video gaming"[tiab]) OR (("Sedentary"[tiab] OR "Inactivity"[tiab] OR "Physically inactive"[tiab] OR "Sedentarism"[tiab]) NOT medline[sb]))
Mortality OR Cardiovascular Disease OR Cancer	AND (("Death"[mh] OR "Death"[tiab] OR "Dying"[tiab] OR Fatal*[tiab] OR Mortalit*[tiab] OR "Postmortem"[tiab] OR "Mortality"[mh] OR "Arteriosclerosis"[mh] OR "Death, sudden, cardiac"[mh] OR "Heart failure"[mh] OR "Myocardial ischemia"[mh] OR "myocardial infarction"[mh] OR "Stroke"[mh] OR "Subarachnoid hemorrhage"[mh] OR "Aortic Aneurysm, Thoracic"[mh] OR "Intracranial hemorrhages"[mh] OR myocardial ischemia[mh]OR "neoplasms"[mh]) OR ((Arteriosclero*[tiab] OR Atherosclero*[tiab] OR "Cerebral infarction"[tiab] OR "Cerebrovascular diseases"[tiab] OR "Cerebrovascular disease"[tiab] OR "Coronary heart disease"[tiab] OR

[1] One search was conducted to answer Q1, Q2, and Q3.

Set	Search Terms
	"Intracerebral Hemorrhage"[tiab] OR "Intracerebral Hemorrhages"[tiab] OR "Intracranial hemorrhage"[tiab] OR "Intracranial hemorrhages"[tiab] OR "ischemic"[tiab] OR "myocardial infarction"[tiab] OR "Stroke"[tiab] OR "Subarachnoid hemorrhages"[tiab] OR "Subarachnoid hemorrhage"[tiab] OR "Cancer"[tiab] OR "Neoplasm"[tiab] OR "Tumor"[tiab] OR "Carcinogenesis"[tiab] OR "Leukemia"[tiab] OR "Lymphoma"[tiab] OR "Malignan*"[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 "Rhabdomyosarcoma"[tiab] OR "Osteosarcoma"[tiab]) NOT medline[sb]))

Search Strategy: CINAHL Q1-3 (Systematic Reviews, Meta-Analyses, and Pooled Analyses)

Database: CINAHL; Date of Search: 12/1/2016; 4 results
Terms searched in title or abstract

Set	Search Terms
Sedentary	Title OR Abstract: ("Sedentary" OR "Sedentary lifestyle" OR "Inactivity" OR "Physically inactive" OR "Sedentarism" OR "Computer time" OR "Computer use" OR "Screen time" OR "Sitting" OR "Television" OR "TV viewing" OR "TV watching" OR "Video game" OR "Video gaming")
Mortality OR Cardiovascular Disease OR Cancer	AND Title OR Abstract: ("Death" OR "Dying" OR Fatal* OR Mortalit* OR "Postmortem" OR Arteriosclero* OR Atherosclero* OR "Cerebral infarction" OR "Cerebrovascular diseases" OR "Cerebrovascular disease" OR "Coronary heart disease" OR "Heart failure" OR "Intracerebral Hemorrhage" OR "Intracerebral Hemorrhages" OR "Intracranial hemorrhage" OR "Intracranial hemorrhages" OR "ischemic" OR "myocardial infarction" OR "Stroke" OR "Subarachnoid hemorrhages" OR "Subarachnoid hemorrhage" OR "Cancer" OR "Neoplasm" OR "Tumor" OR "Carcinogenesis" OR "Leukemia" OR "Lymphoma" OR "Malignan*" 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")
Systematic Reviews and Meta-Analyses	AND (“systematic review” OR “systematic literature review” OR metaanalysis OR "meta analysis" OR metanalyses OR "meta analyses"" OR "pooled analysis"[tiab] OR “pooled analyses”[tiab] OR "pooled data"[tiab])
Limits	2000-present English language Peer reviewed Exclude Medline records Human

Search Strategy: Cochrane Q1-3 (Systematic Reviews, Meta-Analyses, and Pooled Analyses)

Database: Cochrane; Date of Search: 12/5/16; 37 results
Terms searched in title, abstract, or keywords

Set	Search Terms
Sedentary	Title, Abstract, Keywords: ("Sedentary" OR "Sedentary lifestyle" OR "Inactivity" OR "Physically inactive" OR "Sedentarism" OR "Computer time" OR "Computer use" OR "Screen time" OR "Sitting" OR "Television" OR "TV viewing" OR "TV watching" OR "Video game" OR "Video gaming")
Mortality OR Cardiovascular Disease OR Cancer	AND ("Death" OR "Dying" OR Fatal* OR Mortalit* OR "Postmortem" OR Arteriosclero* OR Atherosclero* OR "Cerebral infarction" OR "Cerebrovascular diseases" OR "Cerebrovascular disease" OR "Coronary heart disease" OR "Heart failure" OR "Intracerebral Hemorrhage" OR "Intracerebral Hemorrhages" OR "Intracranial hemorrhage" OR "Intracranial hemorrhages" OR "ischemic" OR "myocardial infarction" OR "Stroke" OR "Subarachnoid hemorrhages" OR "Subarachnoid hemorrhage" OR "Cancer" OR "Neoplasm" OR "Tumor" OR "Carcinogenesis" OR "Leukemia" OR "Lymphoma" OR "Malignan*" 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")
Limits	2000-present Cochrane Reviews and Other Reviews Word variations not searched

Search Strategy: PubMed Q1-3 (Original Research)

Database: PubMed; Date of Search: 1/30/17; 953 results

Set	Search Terms
Limit: Language	(English[lang])
Limit: Exclude animal only	NOT ("Animals"[Mesh] NOT ("Animals"[Mesh] AND "Humans"[Mesh]))
Limit: Exclude child only	NOT (("infant"[Mesh] OR "child"[mesh] OR "adolescent"[mh]) NOT (("infant"[Mesh] OR "child"[mesh] OR "adolescent"[mh]) AND "adult"[Mesh]))
Limit: Exclude subheadings	NOT (ad[sh] OR aa[sh] OR ai[sh] OR ci[sh] OR cn[sh] OR dh[sh] OR de[sh] OR dt[sh] OR em[sh] OR en[sh] OR es[sh] OR eh[sh] OR ge[sh] OR hi[sh] OR is[sh] OR ip[sh] OR lj[sh] OR ma[sh] OR mi[sh] OR og[sh] OR ps[sh] OR py[sh] OR pk[sh] OR pd[sh] OR po[sh] OR re[sh] OR rt[sh] OR rh[sh] OR st[sh] OR sd[sh] OR tu[sh] OR th[sh] OR tm[sh] OR tr[sh] OR ut[sh] OR ve[sh] OR vi[sh])
Limit: Publication Date (Original)	AND ("2014/01/01"[PDAT] : "3000/12/31"[PDAT])
Limit: Publication Type Exclude (Original)	NOT (“comment”[Publication Type] OR “editorial”[Publication Type] OR “review”[Publication Type] OR systematic[sb] OR "meta-analysis"[publication type] 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])
Sedentary	AND (("Sedentary lifestyle"[mh] OR "Computer time"[tiab] OR "Computer use"[tiab] OR "Screen time"[tiab] OR "Sitting"[tiab] OR "Television"[tiab] OR "TV viewing"[tiab] OR "TV watching"[tiab] OR "Video game"[tiab] OR "Video gaming"[tiab]) OR (("Sedentary"[tiab] OR "Inactivity"[tiab] OR "Physically inactive"[tiab] OR "Sedentarism"[tiab]) NOT medline[sb]))
Mortality OR Cardiovascular Disease OR Cancer	AND (("Death"[mh] OR "Death"[tiab] OR "Dying"[tiab] OR Fatal*[tiab] OR Mortalit*[tiab] OR "Postmortem"[tiab] OR "Mortality"[mh] OR "Arteriosclerosis"[mh] OR "Death, sudden, cardiac"[mh] OR "Heart failure"[mh] OR "Myocardial ischemia"[mh] OR "myocardial infarction"[mh] OR "Stroke"[mh] OR "Subarachnoid hemorrhage"[mh] OR "Aortic Aneurysm, Thoracic"[mh] OR "Intracranial hemorrhages"[mh] OR "neoplasms"[mh]) OR ((Arteriosclero*[tiab] OR Atherosclero*[tiab] OR "Cerebral infarction"[tiab] OR "Cerebrovascular diseases"[tiab] OR "Cerebrovascular disease"[tiab] OR "Coronary heart disease"[tiab] OR "Heart failure"[tiab] OR "Intracerebral Hemorrhage"[tiab] OR "Intracerebral Hemorrhages"[tiab] OR "Intracranial hemorrhage"[tiab] OR "Intracranial hemorrhages"[tiab] OR "ischemic"[tiab] OR "myocardial infarction"[tiab] OR "Stroke"[tiab] OR "Subarachnoid hemorrhages"[tiab] OR "Subarachnoid hemorrhage"[tiab] OR "Cancer"[tiab] OR

Set	Search Terms
	"Neoplasm"[tiab] OR "Tumor"[tiab] OR "Carcinogenesis"[tiab] OR "Leukemia"[tiab] OR "Lymphoma"[tiab] OR "Malignan*"[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 "Rhabdomyosarcoma"[tiab] OR "Osteosarcoma"[tiab]) NOT medline[sb]))

Search Strategy: CINAHL Q1-3 (Original Research)

Database: CINAHL; Date of Search: 1/27/17; 49 results
Terms searched in title or abstract

Set	Search Terms
Sedentary	Title and Abstract: ("Sedentary" OR "Sedentary lifestyle" OR "Inactivity" OR "Physically inactive" OR "Sedentarism" OR "Computer time" OR "Computer use" OR "Screen time" OR "Sitting" OR "Television" OR "TV viewing" OR "TV watching" OR "Video game" OR "Video gaming")
Mortality OR Cardiovascular Disease OR Cancer	AND ("Death" OR "Dying" OR Fatal* OR Mortalit* OR "Postmortem" OR Arteriosclero* OR Atherosclero* OR "Cerebral infarction" OR "Cerebrovascular diseases" OR "Cerebrovascular disease" OR "Coronary heart disease" OR "Heart failure" OR "Intracerebral Hemorrhage" OR "Intracerebral Hemorrhages" OR "Intracranial hemorrhage" OR "Intracranial hemorrhages" OR "ischemic" OR "myocardial infarction" OR "Stroke" OR "Subarachnoid hemorrhages" OR "Subarachnoid hemorrhage" OR "Cancer" OR "Neoplasm" OR "Tumor" OR "Carcinogenesis" OR "Leukemia" OR "Lymphoma" OR "Malignan*" 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")
Original Research	NOT ("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")
Limits	Title or abstract 2014-present English language Peer reviewed Exclude Medline records Human

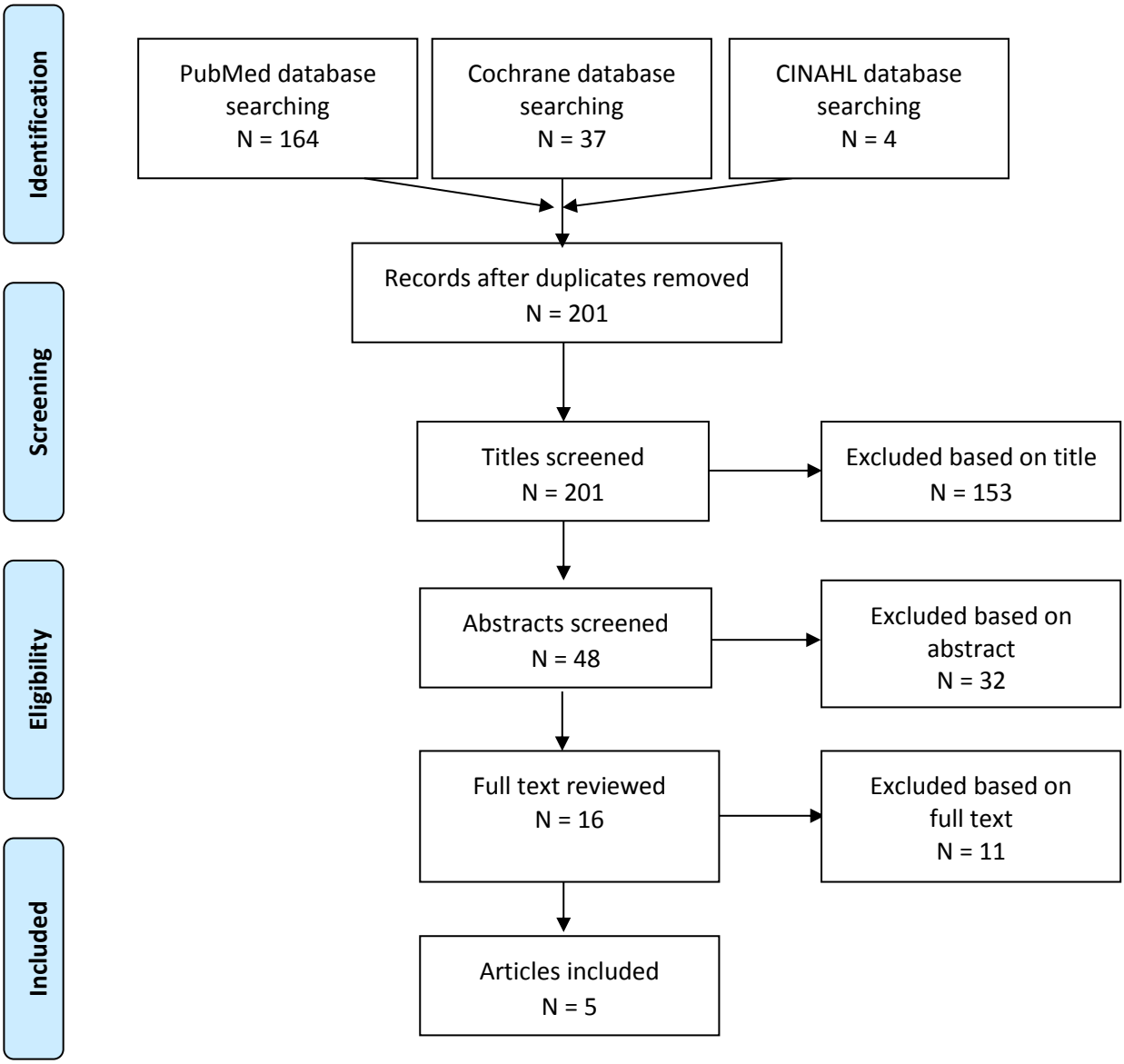
Search Strategy: Cochrane Q1-3 (Original Research)

Database: Cochrane; Date of Search: 1/27/17; 325 results
Terms searched in title, abstract, or keywords

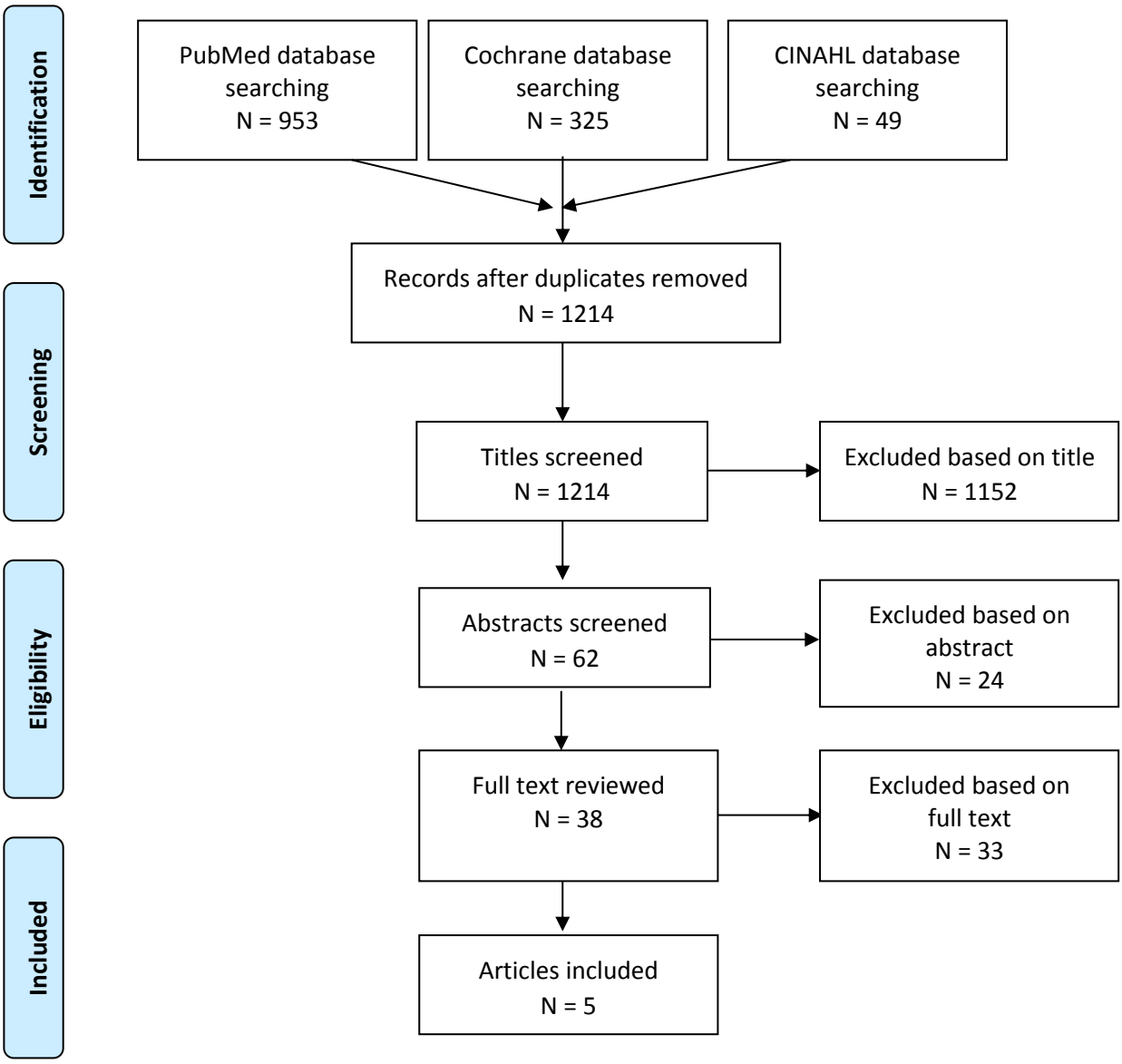
Set	Search Terms
Sedentary	Title, Abstract, Keywords: ("Sedentary" OR "Sedentary lifestyle" OR "Inactivity" OR "Physically inactive" OR "Sedentarism" OR "Computer time" OR "Computer use" OR "Screen time" OR "Sitting" OR "Television" OR "TV viewing" OR "TV watching" OR "Video game" OR "Video gaming")
Mortality OR Cardiovascular Disease OR Cancer	AND ("Death" OR "Dying" OR Fatal* OR Mortalit* OR "Postmortem" OR Arteriosclero* OR Atherosclero* OR "Cerebral infarction" OR "Cerebrovascular diseases" OR "Cerebrovascular disease" OR "Coronary heart disease" OR "Heart failure" OR "Intracerebral Hemorrhage" OR "Intracerebral Hemorrhages" OR "Intracranial hemorrhage" OR "Intracranial hemorrhages" OR "ischemic" OR "myocardial infarction" OR "Stroke" OR "Subarachnoid hemorrhages" OR "Subarachnoid hemorrhage" OR "Cancer" OR "Neoplasm" OR "Tumor" OR "Carcinogenesis" OR "Leukemia" OR "Lymphoma" OR "Malignan*" 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")
Limits	2014-present Word variations not searched Trials

Appendix C: Literature Tree

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



Original Research Literature Tree



Appendix D: Inclusion/Exclusion Criteria

Sedentary Subcommittee

Q3. What is the relationship between sedentary behavior and cancer mortality?

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

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:** • Adults ages 18 and older	Sedentary behavior in youth will be addressed by youth subcommittee
Health Status of Study Subjects	**Exclude:** • Nonambulatory adults • Hospitalized patients	
Date of Publication	**Include:** • Original research, systematic reviews, and meta-analyses published from 2000 to 2016	
Study Design	**Include:** • Prospective cohort studies • Systematic reviews • Meta-analyses • Reports determined to have appropriate suitability and quality by PAGAC **Exclude:** • Randomized controlled trials • Non-randomized controlled trials	

	• Retrospective cohort studies • Case-control studies • Narrative reviews • Commentaries • Editorials • Cross-sectional studies • Before-and-after studies	
Exposure	**Include studies in which the exposure is:** • All types of sedentary behavior **Exclude:** • Studies that use sedentary behavior solely as a confounding variable	
Outcome	**Include studies in which the outcome is:** • Cancer mortality	

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	Study Design	Exposure	Not ideal fit for replacement of de novo search
Biddle SJ, Bennie JA, Bauman AE, et al. Too much sitting and all-cause mortality: is there a causal link? *BMC Public Health*. 2016;16:635. doi:10.1186/s12889-016-3307-3.	X			
Boyle T, Fritschi L,Kobayashi LC, et al. Sedentary work and the risk of breast cancer in premenopausal and postmenopausal women: a pooled analysis of two case-control studies. *Occup Environ Med*. 2016;73(11):735-741. doi:10.1136/oemed-2015-103537.	X			
Brenner DR. Cancer incidence due to excess body weight and leisure-time physical inactivity in Canada: implications for prevention. *Prev Med*. 2014;66:131-139. doi:10.1016/j.ypmed.2014.06.018.	X			
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Cong YJ, Gan Y, Sun HL, et al. Association of sedentary behaviour with colon and rectal cancer: a meta-analysis of observational studies. *Br J Cancer*. 2014;110:817-826. doi:10.1038/bjc.2013.709.	X			
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Dempsey PC, Owen N, Biddle SJ, Dunstan DW. Managing sedentary behavior to reduce the risk of diabetes and cardiovascular disease. *Curr Diab Rep*. 2014;14(9):522. doi:10.1007/s11892-014-0522-0.	X	X		

Citation	Outcome	Study Design	Exposure	Not ideal fit for replacement of de novo search
English C, Manns PJ, Tucak C, Bernhardt J. Physical activity and sedentary behaviors in people with stroke living in the community: a systematic review. *Phys Ther.* 2014;94(2):185-196. doi:10.2522/ptj.20130175.	X			
Grontved A, Hu FB. Television viewing and risk of type 2 diabetes, cardiovascular disease, and all-cause mortality: a meta-analysis. *JAMA*. 2011;305(23):2448-2455. doi:10.1001/jama.2011.812.				X
Haney EM, Huffman LH, Bougatsos C, et al. *U.S. Preventive Services Task Force Evidence Syntheses, formerly Systematic Evidence Reviews.* Screening for lipid disorders in children and adolescents. 2007;Jul(Report No. 07-0598).	X			
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Katzmarzyk PT, Lee IM. Sedentary behaviour and life expectancy in the USA: a cause-deleted life table analysis. *BMJ Open.* 2012;2e000828. doi:10.1136/bmjopen-2012-000828.	X			
Keum N, Cao Y, Oh H, et al. Sedentary behaviors and light-intensity activities in relation to colorectal cancer risk. *Int J Cancer*. 2016;138(9):2109-2117. doi:10.1002/ijc.29953.	X			
Lin JS, Eder M, Weinmann S, et al. *U.S. Preventive Services Task Force Evidence Syntheses, formerly Systematic Evidence Reviews.* Behavioral counseling to prevent skin cancer: systematic evidence review to update the 2003 U.S. Preventive Services Task Force Recommendation. 2011;82(Report No.11-05152-EF-1).	X			
Milton K, Macniven R, Bauman A. Review of the epidemiological evidence for physical activity and health from low- and middle-income countries. *Glob Public Health.* 2014;9(4):369-381. doi:10.1080/17441692.2014.894548.			X	
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Moore SC, Gierach GL, Schatzkin A, Matthews CE. Physical activity, sedentary behaviours, and the	X			

Citation	Outcome	Study Design	Exposure	Not ideal fit for replacement of de novo search
prevention of endometrial cancer. *Br J Cancer*. 2010;103(7):933-938. doi:10.1038/sj.bjc.6605902.				
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.		X		
Oczkowski W. Complexity of the relation between physical activity and stroke: a meta-analysis. *Clin J Sport Med*. 2005;15(5):399.	X			
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Park S, Kim Y, Shin HR, et al. Population-attributable causes of cancer in Korea: obesity and physical inactivity. *PLoS One*. 2014;9(7):e90871. doi:10.1371/journal.pone.0090871.	X			
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Schmid D, Leitzmann MF. Television viewing and time spent sedentary in relation to cancer risk: a meta-analysis. *J Natl Cancer Inst*. 2014;106(7). pii: dju098. doi:10.1093/jnci/dju098.	X			
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Solomon TP, Thyfault JP. Type 2 diabetes sits in a chair. *Diabetes Obes Metab.* 2013;15(11): 987-992. doi:10.1111/dom.12105.		X		
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Sun JW, Zhao LG, Yang Y, Ma X, Wang YY, Xiang YB. Association between television viewing time and all-cause mortality: a meta-analysis of cohort studies.	X			

Citation	Outcome	Study Design	Exposure	Not ideal fit for replacement of de novo search
Am J Epidemiol. 2015;182(11):908-916. doi:10.1093/aje/kwv164.				
Tarraga Lopez PJ, Albero JS, Rodriguez-Montes JA. Primary and secondary prevention of colorectal cancer. *Clin Med Insights Gastroenterol*. 2014;7:33-46. doi:10.4137/CGast.S14039.			X	
van Uffelen JG, Wong J, Chau JY, et al. Occupational sitting and health risks: a systematic review. *Am J Prev Med.* 2010;39(4):379-88. doi:10.1016/j.amepre.2010.05.024.			X	
Vancampfort D, Firth J, Schuch F, et al. Physical activity and sedentary behavior in people with bipolar disorder: a systematic review and meta-analysis. *J Affect Disord*. 2016;201:145-152. doi:10.1016/j.jad.2016.05.020.	X			
Wahid A, Manek N, Nichols M, et al. Quantifying the association between physical activity and cardiovascular disease and diabetes: a systematic review and meta-analysis. *J Am Heart Assoc*. 2016;5(9). pii: e002495. doi:10.1161/JAHA.115.002495.			X	
Wilmot EG, Edwardson CL, Achana FA, et al. Sedentary time in adults and the association with diabetes, cardiovascular disease and death: systematic review and meta-analysis. *Diabetologia*. 2012;55(11):2895-2905. doi: 10.1007/s00125-012-2677-z.	X			
Wilson LF, Page AN, Dunn NA, Pandeya N, Protani MM, Taylor RJ. Population attributable risk of modifiable risk factors associated with invasive breast cancer in women aged 45-69 years in Queensland, Australia. *Maturitas*. 2013;76(4):370-376. doi:10.1016/j.maturitas.2013.09.002.	X			
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Zhou Y, Zhao H, Peng C. Association of sedentary behavior with the risk of breast cancer in women: update meta-analysis of observational studies*. Ann Epidemiol.* 2015;25(9):687-697. doi:10.1016/j.annepidem.2015.05.007.	X			

Rationale for Exclusion at Abstract or Full-Text Triage for Original Research

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

Citation	Outcome	Study Design	Exposure
Beddhu S, Wei G, Marcus RL, Chonchol M, Greene T. Light-intensity physical activities and mortality in the United States general population and CKD subpopulation. *Clin J Am Soc Nephrol*. 2015;10(7):1145-1153. doi:10.2215/CJN.08410814.		X	
Behrend SW. Television viewing and time spent sedentary in relation to cancer risk. *Oncol Nurs Forum*. 2014;41(6):695-696. doi:10.1188/14.ONF.695-696.	X		
Bjork Petersen C, Bauman A, Gronbaek M, Wulff Helge J, Thygesen LC, Tolstrup JS. Total sitting time and risk of myocardial infarction, coronary heart disease and all-cause mortality in a prospective cohort of Danish adults. *Int J Behav Nutr Phys Act*. 2014;11:13. doi:10.1186/1479-5868-11-13.	X		
Bol O, Cebicci H, Koyuncu S, Şarlı B, Günay N. A hidden household danger: television. *Ulus Travma Acil Cerrahi Derg.* 2016;22(3):265-268. doi:10.5505/tjtes.2015.42078.			X
Borodulin K, Karki A, Laatikainen T, Peltonen M, Luoto R. Daily sedentary time and risk of cardiovascular disease: the National FINRISK 2002 Study. *J Phys Act Health*. 2015;12(7):904-908. . doi:10.1123/jpah.2013-0364.	X		
Borrell LN. The effects of smoking and physical inactivity on advancing mortality in U.S. adults. *Ann Epidemiol*. 2014;24(6):484-487. doi:10.1016/j.annepidem.2014.02.016.			X
Brown JC, Harhay MO, Harhay MN. Physical activity, diet quality, and mortality among community-dwelling prefrail and frail older adults. *J Nutr Gerontol Geriatr.* 2016;35(4):253-266.	X		
Brown JC, Harhay MO, Harhay MN. Physical activity, diet quality, and mortality among sarcopenic older adults. *Aging Clin Exp Res*. 2017;29(2):257-263. doi:10.1007/s40520-016-0559-9.	X		
Chau JY, Grunseit A, Midthjell K, et al. Sedentary behaviour and risk of mortality from all-causes and cardiometabolic diseases in adults: evidence from the HUNT3 population cohort. *Br J Sports Med*. 2015;49(11):737-742.	X		
Converse LJ. Sitting with death. *Am J Nurs*. 2016;116(12):72.		X	
Coombs N, Stamataki E, Lee IM. Physical inactivity among older adults: implications for life expectancy among non-overweight and overweight or obese individuals. *Obes Res Clin Pract*. 2015;9(2):175-179. doi:10.1016/j.orcp.2014.11.004.			X
de Rezende LF, Rabacow FM, Viscondi JY, Luiz Odo C, Matsudo VK, Lee IM. Effect of physical inactivity on major noncommunicable diseases and life expectancy in Brazil. *J Phys Act Health*. 2015;12(3):299-306. doi:10.1123/jpah.2013-0241.			X
Ding D, Rogers K, van der Ploeg H, Stamatakis E, Bauman AE. Traditional and emerging lifestyle risk behaviors and all-cause mortality in middle-aged and older adults: evidence from a large population-based Australian cohort. *PLoS Med.* 2015;12(12):e1001917. doi:10.1371/journal.pmed.1001917.	X		
Edwards MK, Loprinzi PD. All-cause mortality risk as a function of sedentary behavior, moderate-to-vigorous physical activity and cardiorespiratory fitness. *Phys Sportsmed.* 2016;44(3):223-230. doi:10.1080/00913847.2016.1221751.	X		

Citation	Outcome	Study Design	Exposure
Eijsvogels TM, George KP, Thompson PD. Cardiovascular benefits and risks across the physical activity continuum. *Curr Opin Cardiol.* 2016;31(5):566-571. doi:10.1097/HCO.0000000000000321.		X	
Evenson KR, Wen F, Herring AH. Associations of accelerometry-assessed and self-reported physical activity and sedentary behavior with all-cause and cardiovascular mortality among US adults. *Am J Epidemiol.* 2016;184(9):621-632.	X		
Evenson KR, Herring AH, Wen F. Accelerometry-assessed latent class patterns of physical activity and sedentary behavior with mortality. *Am J Prev Med.* 2017;52(2):135-143. doi:10.1016/j.amepre.2016.10.033.	X		
Everson-Hock ES, Green MA, Goyder EC, et al. Reducing the impact of physical inactivity: evidence to support the case for targeting people with chronic mental and physical conditions. *J Public Health (Oxf).* 2016;38(2):343-351. doi:10.1093/pubmed/fdv036.	X		X
Fassier P, Zelek L, Partula V, et al. Variations of physical activity and sedentary behavior between before and after cancer diagnosis: results from the prospective population-based NutriNet-Sante cohort. *Medicine (Baltimore).* 2016;95(40):e4629.	X		
Fazel-Tabar Malekshah A, Zaroudi M, Etemadi A, et al. The combined effects of healthy lifestyle behaviors on all-cause mortality: the Golestan Cohort Study. *Arch Iran Med.* 2016;19(11):752-761.			X
Fishman EI, Steeves JA, Zipunnikov V, et al. Association between objectively measured physical activity and mortality in NHANES. *Med Sci Sports Exerc.* 2016;48(7):1303-1311. doi:10.1249/MSS.0000000000000885.	X		
Fox KR, Ku PW, Hillsdon M, et al. Objectively assessed physical activity and lower limb function and prospective associations with mortality and newly diagnosed disease in UK older adults: an OPAL four-year follow-up study. *Aging*. 2015;44(2):261-268. doi:10.1093/ageing/afu168.			X
Grunseit AC, Chau JY, Rangul V, et al. Patterns of sitting and mortality in the Nord- Trøndelag health study (HUNT). *Int J Behav Nutr Phys Act.* 2017;14:8. doi:10.1186/s12966-016-0457-8.	X		
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Hayashi R, Iso H, Cui R, Tamakoshi A; JACC Study Group. Occupational physical activity in relation to risk of cardiovascular mortality: the Japan Collaborative Cohort Study for Evaluation for Cancer Risk (JACC Study). *Prev Med.* 2016;89:286-291. doi:10.1016/j.ypmed.2016.06.008.			X
Holme I, Anderssen SA. Increases in physical activity is as important as smoking cessation for reduction in total mortality in elderly men: 12 years of follow-up of the Oslo II study. *Br J Sports Med.* 2015;49(11):743-748. doi:10.1136/bjsports-2014-094522.			X
Holme I, Tonstad S. Increased predictive ability of BMI but not other risk factors with time in men: 39-year follow-up of total			X

Citation	Outcome	Study Design	Exposure
mortality in the Oslo Study. *Obes Facts.* 2014;7(5):311-321. doi:10.1159/000368567.			
Holtermann A, Mork PJ, Nilsen TI. Hours lying down per day and mortality from all-causes and cardiovascular disease: the HUNT Study, Norway. *Eur J Epidemiol.* 2014;29(8):559-565. doi:10.1007/s10654-014-9939-7.			X
Ikehara S, Iso H, Wada Y, et al. Television viewing time and mortality from stroke and coronary artery disease among Japanese men and women—the Japan Collaborative Cohort Study. Circ J. 2015;79(11):2389-2395. doi:10.1253/circj.CJ-14-1335.	X		
Keadle SK, Arem H, Moore SC, Sampson JN, Matthews CE. Impact of changes in television viewing time and physical activity on longevity: a prospective cohort study. *Int J Behav Nutr Phys Act*. 2015;12:156. doi:10.1186/s12966-015-0315-0.	X		
Kikuchi H, Inoue S, Odagiri Y, Inoue M, Sawada N, Tsugane S; Japan Public Health Centre (JPHC) study group. Occupational sitting time and risk of all-cause mortality among Japanese workers. *Scand J Work Environ Health.* 2015;41(6):519-528. doi:10.5271/sjweh.3526.	X		
Klenk J, Dallmeier D, Denkinger MD, Rapp K, Koenig W, Rothenbacher D; ActiFE Study Group. Objectively measured walking duration and sedentary behaviour and four-year mortality in older people. *PLoS One*. 2016;11(4):e0153779. doi:10.1371/journal.pone.0153779.	X		
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Llamas-Velasco S, Villarejo-Galende A, Contador I, Pablos DL, Hernández-Gallego J, Bermejo-Pareja F. Physical activity and long-term mortality risk in older adults: a prospective population based study (NEDICES). *Prev Med Rep*. 2016;4:546-550. doi:10.1016/j.pmedr.2016.10.002.			X
Loprinzi PD, Edwards MK, Sng E, Addoh O. Sedentary behavior and residual-specific mortality. *Health Promot Perspect*. 2016;6(4):196-201. doi:10.15171/hpp.2016.32.	X		
Loprinzi PD, Joyner C. Accelerometer-determined physical activity and mortality in a national prospective cohort study: Considerations by visual acuity. *Prev Med*. 2016;87:18-21. doi:10.1016/j.ypmed.2016.02.005.	X		
Loprinzi PD, Loenneke JP, Ahmed HM, Blaha MJ. Joint effects of objectively-measured sedentary time and physical activity on all-cause mortality. *Prev Med*. 2016;90:47-51. doi:10.1016/j.ypmed.2016.06.026.	X		

Citation	Outcome	Study Design	Exposure
Martinez-Gomez D, Guallar-Castillon P, Rodriguez-Artalejo F. Sitting time and mortality in older adults with disability: a national cohort study. *J Am Med Dir Assoc.* 2016;17(10):960.e15-e20. doi:10.1016/j.jamda.2016.07.016.	X		
Matthews CE, Keadle SK, Troiano RP, et al. Accelerometer-measured dose-response for physical activity, sedentary time, and mortality in US adults. *Am J Clin Nutr*. 2016;104(5):1424-1432.	X		
Menotti A, Puddu PE, Lanti M, Maiani G, Catasta G, Fidanza AA. Lifestyle habits and mortality from all and specific causes of death: 40-year follow-up in the Italian Rural Areas of the Seven Countries Study. *J Nutr Health Aging.* 2014;18(3):314-321. doi:10.1007/s12603-013-0392-1.			X
Nandi A, Glymour MM, Subramanian SV. Association among socioeconomic status, health behaviors, and all-cause mortality in the United States. *Epidemiology*. 2014;25(2):170-177. doi:10.1097/EDE.0000000000000038.			X
Papandreou C, Tuomilehto H. Coronary heart disease mortality in relation to dietary, lifestyle and biochemical risk factors in the countries of the Seven Countries Study: a secondary dataset analysis. *J Hum Nutr Diet*. 2014;27(2):168-175. doi:10.1111/jhn.12187.		X	
Pavey TG, Peeters GG, Brown WJ. Sitting-time and 9-year all-cause mortality in older women. *Br J Sports Med*. 2015;49(2):95-99. doi: 10.1136/bjsports-2012-091676.	X		
Pulsford RM, Stamatakis E, Britton AR, Brunner EJ, Hillsdon M. Associations of sitting behaviours with all-cause mortality over a 16-year follow-up: the Whitehall II study. *Int J Epidemiol*. 2015;44(6):1909-1916. doi:10.1093/ije/dyv191.	X		
Schmid D, Ricci C, Leitzmann MF. Associations of objectively assessed physical activity and sedentary time with all-cause mortality in US adults: the NHANES study. *PLoS One*. 2015;10(3):e0119591. doi:10.1371/journal.pone.0119591.	X		
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Shuval K, Finley CE, Barlow CE, Nguyen BT, Njike VY, Pettee Gabriel K. Independent and joint effects of sedentary time and cardiorespiratory fitness on all-cause mortality: the Cooper Center Longitudinal Study. *BMJ Open*. 2015;5(10):e008956. doi:10.1136/bmjopen-2015-008956.	X		
Stamatakis E, Rogers K, Ding D, et al. All-cause mortality effects of replacing sedentary time with physical activity and sleeping using an isotemporal substitution model: a prospective study of 201,129 mid-aged and older adults. *Int J Behav Nutr Phys Act*. 2015;12:121. doi:10.1186/s12966-015-0280-7.	X		
Stenholm S, Head J, Kivimaki M, et al. Smoking, physical inactivity and obesity as predictors of healthy and disease-free life expectancy between ages 50 and 75: a multicohort study. *Int J Epidemiol*. 2016;45(4):1260-1270.	X		X
van der Ploeg HP, Moller SV, Hannerz H, van der Beek AJ, Holtermann A. Temporal changes in occupational sitting time in the Danish workforce and associations with all-cause mortality: results from the Danish work environment cohort	X		

Citation	Outcome	Study Design	Exposure
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Warren Andersen S, Zheng W, Sonderman J, et al. Combined impact of health behaviors on mortality in low-income Americans. *Am J Prev Med*. 2016;51(3):344-355. doi:10.1016/j.amepre.2016.03.018.	X		
Wijndaele K, Sharp SJ, Wareham NJ, Brage S. Mortality risk reductions from substituting screen-time by discretionary activities. *Med Sci Sports Exerc*. 2017;49(6):1111-1119. doi:10.1249/MSS.0000000000001206.	X		
Xiao Q, Keadle SK, Hollenbeck AR, Matthews CE. Sleep duration and total and cause-specific mortality in a large US cohort: interrelationships with physical activity, sedentary behavior, and body mass index. *Am J Epidemiol*. 2014;180(10):997-1006. doi:10.1093/aje/kwu222.			X
Xu G, Sui X, Liu S, et al. Effects of insufficient physical activity on mortality and life expectancy in Jiangxi province of China, 2007-2010. *PLoS One*. 2014;9(10):e109826. doi:10.1371/journal.pone.0109826.			X

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10. Schmid D, Ricci C, Baumeister SE, Leitzmann MF. Replacing sedentary time with physical activity in relation to mortality. *Med Sci Sports Exerc*. 2016;48(7):1312-1319. doi:10.1249/MSS.0000000000000913.