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REVIEW

Sedentary Time and Its Association With Risk for Disease Incidence, Mortality, and Hospitalization in Adults

A Systematic Review and Meta-analysis

Aviroop Biswas, BSc; Paul I. Oh, MD, MSc; Guy E. Faulkner, PhD; Ravi R. Bajaj, MD; Michael A. Silver, BSc; Marc S. Mitchell, MSc; and David A. Alter, MD, PhD

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.

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For author affiliations, see end of text.

Adults are advised to accumulate at least 150 minutes of weekly physical activity in bouts of 10 minutes or more (1). The intensity of such habitual physical activity has been found to be a key characteristic of primary and secondary health prevention, with an established preventive role in cardiovascular disease, type 2 diabetes, obesity, and some cancer types (2, 3). Despite the health-enhancing benefits of physical activity, this alone may not be enough to reduce the risk for disease and illness. Population-based studies have found that more than one half of an average person's waking day involves sedentary activities ubiquitously associated with prolonged sitting, such as watching television and using the computer (4). This lifestyle trend is particularly worrisome because studies suggest that long periods of sitting have deleterious health effects independent of adults meeting physical activity guidelines (5–7). Moreover, physical activity and sedentary behaviors may be mutually exclusive. For example, some persons who achieve their recommended physical activity targets may be highly sedentary throughout the remainder of their waking hours, whereas others who may not regularly participate in physical activity may be nonsedentary because of their leisure activities, workplace environments, or both (8). Although studies and subgroups of systematic reviews have explored the independent association between sedentary behaviors and outcomes after adjustment for physical activity, the magnitude and consistency of such associations and the manner by which they change according to the level of participation in physical activity remain unclear (9–11).

The objective of this meta-analysis was to quantitatively evaluate the association between sedentary time and health outcomes independent of physical activity participation among adult populations. We hypothesized that sedentary time would be independently associated with both cardiovascular and noncardiovascular outcomes after adjusting for participation in physical activity but that the relative hazards associated with sedentary times would be attenuated in those who participate in higher levels of physical activity compared with lower levels (10).

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METHODS

Data Sources and Searches

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines were followed in the conduct and reporting of this meta-analysis (9). Published studies on the association between sedentary behavior and various health outcomes were identified and cross-checked by 2 reviewers through a systematic search of the MEDLINE, PubMed, EMBASE, CINAHL, Cochrane Library, Web of Knowledge, and Google Scholar databases. The health outcomes included all-cause mortality, cardiovascular disease incidence (including diabetes), cardiovascular disease mortality, cancer incidence, cancer mortality, and all-cause hospitalizations. Searches were restricted to English-language primary research articles through August 2014 with no publication date limitations (**Supplement**, available at www.annals.org). The following keywords were applied to the search: (exercise OR physical activity OR habitual physical activity) AND (sedentar* OR inactivity OR television OR sitting) AND (survival OR morbidity OR mortality OR disease OR hospital* OR utilization). References from relevant publications and review articles were hand-searched to supplement the electronic searches. A broad and comprehensive search strategy was chosen to encompass the range of outcomes associated with sedentary behavior among different populations or settings and variations in the operational definition of leisure-time sedentary behavior.

Study Selection

The inclusion criteria were primary research studies that assessed sedentary behavior in adult participants as a distinct predictor variable, independent of physical activity and correlated to at least 1 health outcome. We broadly defined sedentary behavior as 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 (11). We allowed for studies that assessed the effects of varying intensities of physical activity, provided that they also correlated a measure of sedentary behavior with an outcome. We excluded studies that assessed nonadult populations (such as children and youth), those that did not adjust for physical activity in their statistical regression models or only assessed sedentary behavior as a reference category to the effects of physical activity, and those that measured sedentary behavior as the lowest category of daily or weekly physical activity.

Data Extraction and Quality Assessment

Data were extracted from all articles that met selection criteria and deemed appropriate for detailed review by 3 authors. If several articles of the same study were found, then data were extracted from the most recently published article. Details of individual studies were collected and characterized on the basis of authors or year of publication; study design; sample size or characteristics (age and sex); data collection methods; study outcomes; study limitations; and hazard ratios (HRs), odds ratios, or relative risk ratios (and their associated 95% CIs or SEs). We restricted studies reporting health outcomes to those with direct associations with death, disease incidence (that is, risk for disease in a given period), and health service use (that is, change in health service use) outcomes. This led to the exclusion of studies reporting indirect surrogate outcomes with inconsistent clinical end points and cutoffs (such as insulin sensitivity, quality of life, activities of daily living, metabolic biomarkers, the metabolic syndrome, and weight gain). Our study's primary exposure was overall sedentary or sitting time (hours per week or hours per day). Studies reporting information on total screen time (television or computer screen use), television viewing time, and metabolic equivalents (hours per week) were also abstracted when information on the primary exposure was unavailable.

We assessed articles for quality on the basis of methods used by Proper and colleagues (12). Their quality assessment tool had been previously validated (face and content) and evaluated to limit the risk of bias from study participation, study attrition, measurement of prognostic factors, measurement of and controlling for confounding variables, measurement of outcomes, and analysis approaches (13, 14). Each study was evaluated according to a standardized set of predefined criteria consisting of 15 items (**Table 1**) (15). The use of the original quality assessment tool was expanded to permit and score nonprospective studies. The items of the tool assessed study quality within the domains of study population, study attrition, data collection, and data analysis. Each quality criterion was rated as positive, negative, or unknown. As with other meta-analyses, we required positive quality criteria of 8 items or more to be included in our study (12, 16). Two reviewers independently scored each article for quality. Any scoring inconsistencies were discussed with an additional reviewer. Scores from each reviewer were averaged to attain a final quality score assessment and verified by a single reviewer. When such data were available, we also considered whether the effects of prolonged bouts of sedentary time were modified by the highest or lowest reported participation in physical activity (herein termed as "joint effects").

Data Synthesis and Analysis

All meta-analyses were done using Comprehensive Meta-analysis, version 2 (Biostat), and the metafor package of R (R Foundation for Statistical Computing) (17, 18). Odds ratios, relative risk ratios, and HRs with associated 95% CIs were collected from studies for each outcome, if available. We considered relative risk ratios to be equal to HRs, and when only odds ratios were provided, they were approximated to relative risk ratios in which we used the assumption of rare events according to methods described and demonstrated elsewhere (19, 20). When studies presented several statistical risk-adjustment models, we only considered relative risk ratios associated with the statistical models that contained the fewest number of additional covari-

Table 1. Criteria List for the Assessment of the Quality of Prospective and Nonprospective Studies*

Criteria	Quality Criteria of Informativeness or Validity/Precision	Prospective Studies Meeting Criteria, *n/N (%)*	Nonprospective Studies Meeting Criteria, *n/N (%)*
Study population and participation (baseline)			
1. Adequate (sufficient information to be able to repeat the study) description of the source population	Informativeness	32/38 (84)	7/9 (78)
2. Adequate (sufficient information to be able to repeat the study) description of the sampling frame, recruitment methods, period of recruitment, and place of recruitment (setting and geographic location)	Validity/Precision	33/38 (87)	9/9 (100)
3. Participation rate at baseline ≥80% or if the nonresponse was not selective (show that the baseline study sample does not significantly differ from the population of eligible participants)	Informativeness	17/38 (45)	6/9 (67)
4. Adequate description of the baseline study sample (i.e., persons entering the study) for key characteristics (number, age, sex, sedentary behavior, and health outcome)†	Informativeness	32/38 (84)	8/9 (89)
Study attrition			
5. Provision of the exact number at each follow-up measurement	Informativeness	19/38 (50)	0/9 (0)
6. Provision of the exact information on follow-up duration	Validity/Precision	24/38 (63)	0/9 (0)
7. Response at short-term follow-up (≤12 mo) was ≥80% of the number at baseline, and response at long-term follow-up was ≥70% of the number at baseline	Validity/Precision	20/38 (53)	0/9 (0)
8. Information on nonselective nonresponse during the follow-up measurement(s)‡	Validity/Precision	6/38 (16)	0/9 (0)
Data collection			
9. Adequate measurement of sedentary behavior: done by objective measures (i.e., accelerometry, heart rate monitoring, and observation) and not by self-report (self-report = no; no/insufficient information = unknown)	Validity/Precision	5/38 (13)	2/9 (22)
10. Sedentary behavior was assessed at a time before the measurement of the health outcome	Validity/Precision	38/38 (100)	9/9 (100)
11. Adequate measurement of the health outcome: objective measurement of the health outcome done by trained personnel by means of a standardized protocol(s) of acceptable quality and not by self-report (self-report = no; no/insufficient information = unknown)	Validity/Precision	27/38 (71)	5/9 (56)
Data analyses			
12. The statistical model was appropriate§	Validity/Precision	38/38 (100)	9/9 (100)
13. The number of cases was ≥10 times the number of independent variables	Validity/Precision	33/38 (87)	8/9 (89)
14. Presentation of point estimates and measures of variability (CI or SE)	Informativeness	38/38 (100)	9/9 (100)
15. No selective reporting of results	Validity/Precision	29/38 (76)	8/9 (89)

* Criteria were rated as follows: "Yes" refers to an informative description of the criterion at issue and met the quality criterion, "no" refers to an informative description but an inadequate execution or lack of description of the criterion, and "unknown" refers to an unclear or incomplete description of the criterion.
† "Yes" was given only if adequate information (sufficient information to be able to repeat the study) was given on all criteria.
‡ "Yes" was given only if nonselective withdrawal on key characteristics (such as age, sex, sedentary behavior, and health outcomes) was reported in the text or tables.
§ "Yes" was given only if a multivariate regression model was used.

ates beyond physical activity to enhance comparability across studies. Adjustment for physical activity (rather than moderate to vigorous physical activity) allowed for a broader range of studies, some of which may not have specified the intensity of physical activity in regression models. Knapp–Hartung small sample estimation was used to pool the analysis of the overall effect size for each outcome. Studies that separately presented results for men and women were combined using a fixed-effects model. We received a 79% response rate from authors we had contacted to provide additional statistical information for our meta-analysis (11 out of 14).

Potential modifying effects of physical activity on sedentary time were examined by comparing the statistical effect sizes of any studies that reported the longest period of sedentary time with the highest and lowest duration and intensity of physical activity. Statistical heterogeneity was assessed using the Cochran *Q* statistic and the I^2 statistic of the proportion of total variation because of heterogeneity (21). When we saw substantial heterogeneity, we considered a Knapp–Hartung modified random-effects model (22). For the summary estimate, a *P* value less than 0.05 was considered statistically significant. The potential for small study effects, such as publication bias, was explored graphically using funnel plots through the Egger test of asymmetry and quantitatively by the Egger linear regression method (23). We also did a sensitivity analysis on the effect of individual studies on the pooled meta-

analysis results of each outcome. The exclusion of each individual study and the corresponding changes on effect size allowed for the determination of whether any particular study was influencing the pooled point estimate and CI.

Role of the Funding Source

This study received no specific external funding.

RESULTS

Literature Search Results

A total of 20 980 studies were identified through database searching (7354 from PubMed, 3854 from MEDLINE, 2591 from Web of Knowledge, 2751 from EMBASE, 1119 from CINAHL, 2561 from Google Scholar, and 750 from the Cochrane Library), and 25 studies were added after hand-searching in-text citations (Appendix Figure, available at www.annals.org). Forty-one studies provided statistical effects relevant to the meta-analyses on all-cause mortality (829 917 participants) (24–36), cardiovascular disease-related incidence and mortalities (551 366 participants) (24, 27, 29, 30, 32, 36–39), cancer-related incidence and mortalities (744 706 participants) (24, 27, 29, 30, 32, 36, 40–47), and type 2 diabetes incidence (26 700 participants) (5, 6, 48–50). One study examined the association between sedentary time and potentially preventable hospitalization that met our inclusion criteria (51).

Study Characteristics

The characteristics of the studies assessed for quality in our meta-analysis are summarized in Table 1. No study was excluded solely because of low-quality scores less than 8 (<50%). No randomized, controlled trials met our selection criteria. Most studies used prospective cohort study designs, and 3 studies used cross-sectional and case–control study designs. All but 1 study used self-reported methods to measure patterns of sedentary behavior and physical activity, and these were collected either by trained staff or directly from the persons being observed. Definitions for sedentary time varied across studies, and a range of criteria was used to collect information on sedentary time from self-report questionnaires (Appendix Table, available at www.annals.org).

Publication Bias and Heterogeneity

There was statistical evidence of publication bias among studies reporting all-cause mortality (Egger regression intercept, 2.63 [$P = 0.015$]) and cancer incidence (Egger regression intercept, 1.870 [$P = 0.046$]) but no statistical evidence of publication bias for cardiovascular disease mortality (Egger regression intercept, 1.51 [$P = 0.160$]) and cancer mortality (Egger regression intercept, 0.957 [$P = 0.156$]). Publication bias was not assessed for cardiovascular disease incidence and type 2 diabetes incidence because the relatively few studies may overestimate the effects of bias.

Figures 1 and 2 summarize the degree of heterogeneity across studies. As per Higgins and colleagues' classification (52), heterogeneity within studies reporting all-cause mortality and cardiovascular disease incidence as outcomes may be high. Heterogeneity was found to be low for cardiovascular disease mortality, cancer mortality, cancer incidence, and type 2 diabetes incidence.

Independent Effects of Sedentary Time on Health Outcomes

Greater sedentary time was found to be positively associated with an increased risk for all-cause mortality, cardiovascular disease mortality, cancer mortality, cardiovascular disease incidence, cancer incidence, and type 2 diabetes incidence (Figures 1 and 2). The largest statistical effect was associated with the risk for type 2 diabetes (pooled HR, 1.910 [CI, 1.642 to 2.222]). Among studies assessing cancer mortality and incidence, significant associations were specifically found with breast, colon, colorectal, endometrial, and epithelial ovarian cancer (3, 12, 21, 45, 52). The only study that evaluated associations with all-cause hospitalization was a prospective study that examined whether sedentary behavior (among other modifiable health behaviors) was correlated with potentially modifiable hospitalization (defined as avoidable or ambulatory care–sensitive hospitalizations) (51). Conducted among a large cohort of men and women aged 45 years or older in Australia, the study found that participants self-reporting fewer than 8 hours of sitting time per day had a 14% lower risk for potentially preventable hospitalization (HR, 0.86 [CI, 0.83 to 0.89]). The multivariate regression model was adjusted for age, sex, education, marital status, income, geographic remoteness of residence, language spoken at home, health insurance, chronic disease history, previous admission for potentially preventable hospitalization, moderate to vigorous physical activity, and other health behaviors.

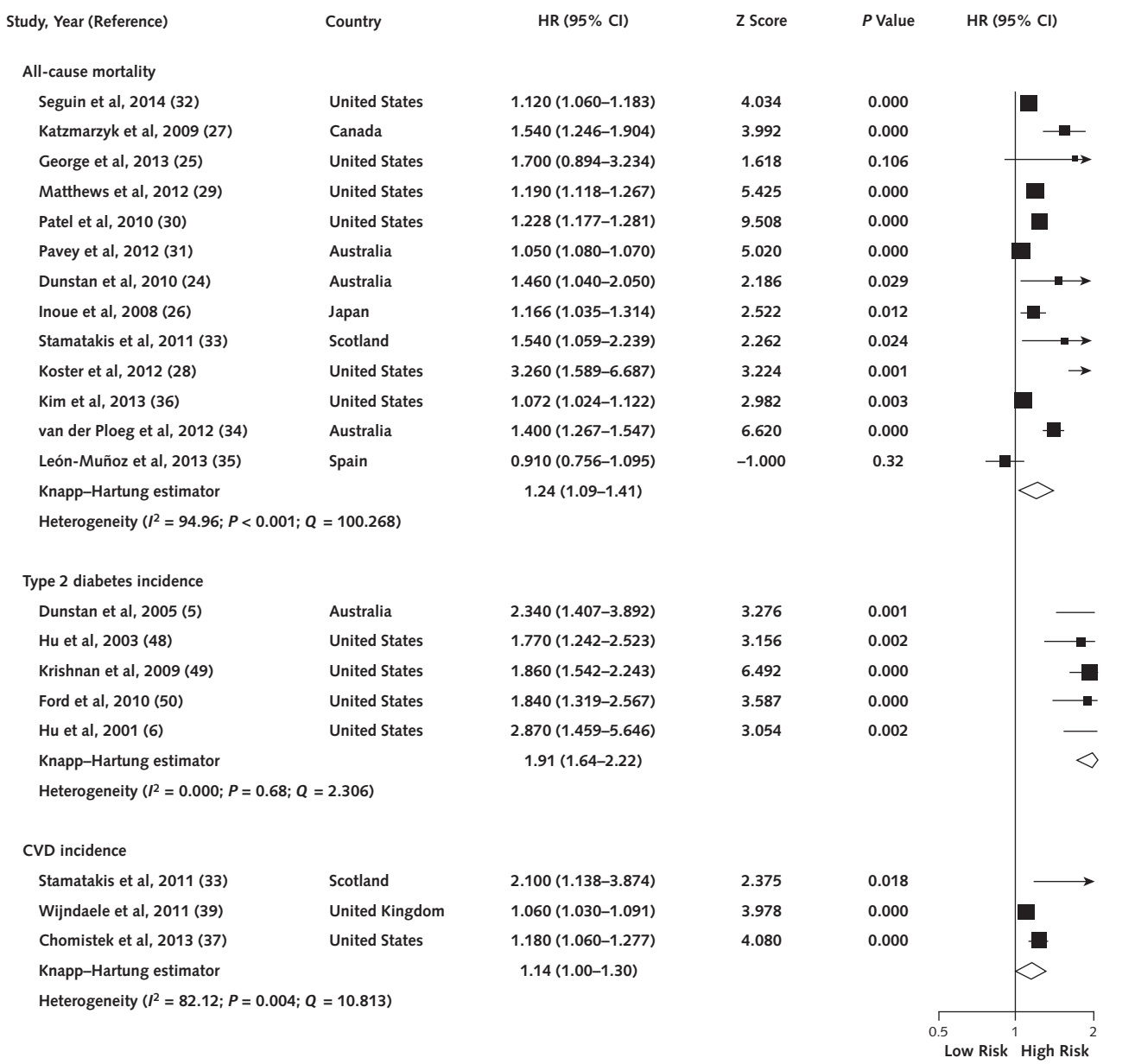
Joint Effects Among Physical Activity, Sedentary Time, and Health Outcomes

Ten studies reported joint effects among sedentary time, physical activity, and health outcomes (29–32, 34, 36, 37, 49). The relative hazards associated with sedentary time on outcomes varied according to physical activity levels and were generally more pronounced at lower levels than at higher levels (Table 2). However, given the limited number of available studies, our meta-analysis examining the joint effects between physical activity and exercise was restricted to all-cause mortality. Sedentary time was associated with a 30% lower relative risk for all-cause mortality among those with high levels of physical activity (pooled HR, 1.16 [CI, 0.84 to 1.59]) as compared with those with low levels of physical activity (pooled HR, 1.46 [CI, 1.22 to 1.75]) (Figure 3).

Sensitivity Analysis

The pooled effect estimates for the associations between sedentary time and risk for all-cause mortality, cardiovascular disease mortality, cancer mortality, cancer incidence, and diabetes did not change substantially with the exclusion of any individual study. The exclusion of nonprospective studies as well as applying

Figure 1. Association between high sedentary time and health outcomes, adjusted for physical activity.



An HR >1 suggests that high sedentary time is harmful. Diamonds indicate pooled HRs with associated 95% CIs. CVD = cardiovascular disease; HR = hazard ratio.

the DerSimonian–Laird random effects estimator did not affect the statistical significance of outcomes.

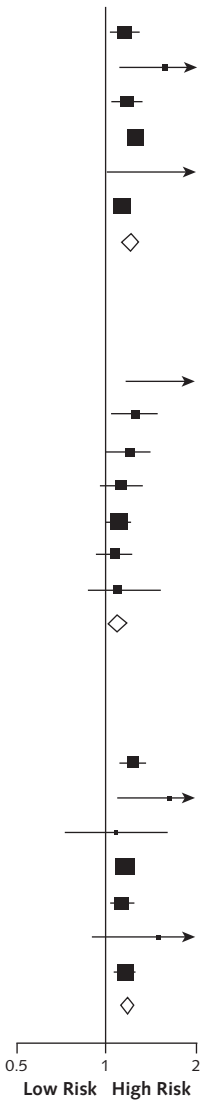
DISCUSSION

Our study demonstrated that after statistical adjustment for physical activity, sedentary time (assessed as either daily overall sedentary time, sitting time, television or screen time, or leisure time spent sitting) was independently associated with a greater risk for all-cause mortality, cardiovascular disease incidence or mortality, cancer incidence or mortality (breast, colon, colorectal, endometrial, and epithelial ovarian), and type 2 diabetes in adults. However, the deleterious outcome effects associated with sedentary time generally decreased in magnitude among persons who participated in higher levels of physical activity compared with lower levels.

Our study builds on the previous body of literature examining the associated effects of sedentary time on various health outcomes. Before this review, a MEDLINE search through August 2014 found 2 meta-analyses that positively associated increasing sedentary time with an independent risk for cardiovascular disease (including diabetes), all-cause mortality, and

Figure 2. Association between high sedentary time and health outcomes, adjusted for physical activity.

Study, Year (Reference)	Country	HR (95% CI)	Z Score	*P* Value
CVD mortality				
Seguin et al, 2014 (32)	United States	1.140 (1.018–1.277)	2.262	0.024
Katzmarzyk et al, 2009 (27)	Canada	1.540 (1.091–2.173)	2.438	0.014
Matthews et al, 2012 (29)	United States	1.160 (1.020–1.319)	2.262	0.024
Patel et al, 2010 (30)	United States	1.228 (1.139–1.324)	5.323	0.000
Dunstan et al, 2010 (24)	Australia	1.800 (0.998–3.245)	1.955	0.051
Kim et al, 2013 (36)	United States	1.115 (1.032–1.205)	2.753	0.006
Knapp–Hartung estimator		1.18 (1.11–1.24)		
Heterogeneity (I^2 = 19.22; P = 0.170; Q = 7.766)				
Cancer incidence				
Friberg et al, 2006 (41)	Sweden	1.800 (1.142–2.836)	2.534	0.011
Howard et al, 2008 (42)	United States	1.240 (1.026–1.498)	2.228	0.026
Zhang et al, 2004 (43)	China	1.190 (1.000–1.416)	1.960	0.050
George et al, 2010 (44)	United States	1.120 (0.954–1.315)	1.383	0.167
Hildebrand et al, 2013 (45)	United States	1.100 (1.010–1.198)	2.188	0.029
Teras et al, 2012 (46)	United States	1.066 (0.923–1.232)	0.867	0.386
Peplonska et al, 2008 (47)	Poland	1.100 (0.803–1.506)	0.594	0.552
Knapp–Hartung estimator		1.13 (1.05–1.21)		
Heterogeneity (I^2 = 0.00; P = 0.39; Q = 6.355)				
Cancer mortality				
Seguin et al, 2014 (32)	United States	1.220 (1.097–1.357)	3.674	0.000
Campbell et al, 2013 (40)	United States	1.620 (1.073–2.446)	2.294	0.022
Katzmarzyk et al, 2009 (27)	Canada	1.070 (0.716–1.600)	0.330	0.742
Patel et al, 2010 (30)	United States	1.146 (1.062–1.236)	3.521	0.000
Matthews et al, 2012 (29)	United States	1.120 (1.016–1.235)	2.275	0.023
Dunstan et al, 2010 (24)	Australia	1.480 (0.880–2.490)	1.478	0.140
Kim et al, 2013 (36)	United States	1.149 (1.063–1.241)	3.517	0.000
Knapp–Hartung estimator		1.16 (1.10–1.22)		
Heterogeneity (I^2 = 0.23; P = 0.54; Q = 5.039)				



An HR >1 suggests that high sedentary time is harmful. Diamonds indicate overall HRs with associated 95% CIs. CVD = cardiovascular disease; HR = hazard ratio.

certain cancer types (20, 53). However, unlike our systematic review and meta-analysis, which focused exclusively on studies that adjusted for physical activity, only a few studies included in these 2 previous meta-analyses adjusted for physical activity, and did so only among a limited subgroup of available studies. Previous studies lacked precision in the estimated independent effect sizes of associations between sedentary time and outcomes. Moreover, previous meta-analyses were not designed to examine the extent to which levels of physical activity may potentially modify associations between sedentary time and outcomes. The consistency in the magnitude of effects associated with sedentary time across various cardiovascular and non-cardiovascular outcomes after adjustment for physical activity underscores the validity and strength of association and provides confidence that such associations may indeed be causally linked. Although more research is required to better understand how changes in physical activity may modify the deleterious effects of prolonged sedentary time, our study suggests that these associations may vary according to the level of physical activity and become less pronounced as participation in physical activity increases.

Our study has also provided greater insight into the various sources of heterogeneity than previously published systematic reviews. Statistical heterogeneity was highest for studies examining all-cause mortality

and cardiovascular disease incidence. Moreover, the sources of such heterogeneity were multifactorial. First, there were marked variations in methodological quality and design across studies. Second, there were several operational definitions and quantitative cutoffs during categorization of sedentary time and physical activity. Third, self-reported measures were predominantly used to assess physical activity exposure and were more vulnerable to biased estimates than those ascertained through more objective measurement techniques (such as accelerometry) (54, 55). Last, there were large variations in the comprehensiveness of the risk-adjustment method across studies, with some studies adjusting for covariates that may overlap or lie within the same causal pathways as those that are believed to mediate the adverse effects from sedentary behaviors themselves (such as adiposity). Future studies must address such sources of heterogeneity to improve the interpretability, comparability, and implications of physical activity–behavioral outcomes research.

Until recently, public health programs and policies have primarily focused on the promotion of physical activity. Health-promotion messaging advocating for a reduction in sedentary time is far less common and faces many challenges. Comprehensive clinical outpatient programs, such as cardiac rehabilitation, have demonstrated effectiveness in helping patients recover from and manage their risk for cardiovascular disease and other chronic diseases, but have done so by focusing predominantly on exercise and lifestyle modification rather than the avoidance of sedentary behavior per se (56, 57). Less is known about optimal prescribing methods for reducing sedentary time because strategies have remained highly variable (58, 59). Moreover, such strategies may necessitate different integrative approaches across populations to align with demographic and sociocultural norms (60–62).

Several limitations must be considered when interpreting these findings. Our search strategy was limited to English-only studies, which may have resulted in a language or cultural bias. Nonetheless, our expansive search across several databases has incorporated numerous studies conducted outside of the English-speaking world. We also acknowledge the presence of publication bias with the possibility that selective reporting may have further undermined the generalizability of our findings. Furthermore, the examination of joint effects among sedentary time, physical activity levels, and outcomes yielded overlapping CIs. More studies will be required to confirm and better quantify how associations between sedentary time and outcomes attenuate at higher levels of physical activity. Finally, we did not have access to individual-level data. Although we attempted to contact individual authors to confirm statistical effects and received a good response rate in so doing, we were ostensibly reliant on the quality of individual studies provided and the statistical effect sizes reported.

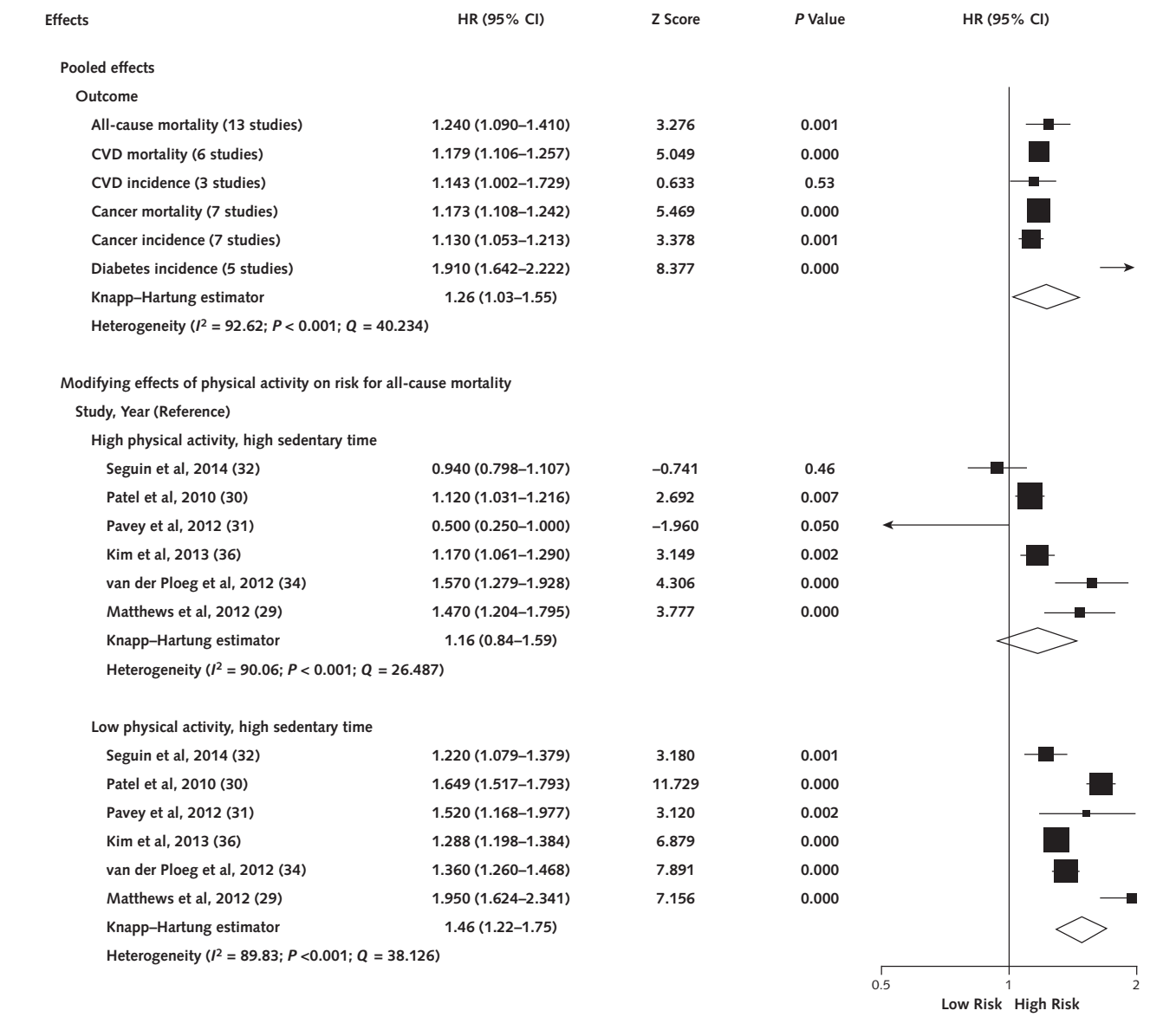
In conclusion, our findings suggest that prolonged sedentary time, independent of physical activity, is pos-

Table 2. Joint Effects Among Physical Activity, Sedentary Time, and Health Outcomes Reported in Studies

Study, Year (Reference)	Sedentary Time	Highest PA	HR (95% CI)	Lowest PA	HR (95% CI)
All-cause mortality					
Seguin et al, 2014 (32)	≥11 h/d total sedentary time	≥19.75 MET h/wk	0.94 (0.80–1.11)	0–3 MET h/wk	1.22 (1.08–1.38)
Patel et al, 2010 (30)	≥6 h/d sitting time	≥52.5 MET h/wk	Men: 1.07 (0.97–1.18) Women: 1.25 (1.07–1.45)	<24.5 MET h/wk	Men: 1.48 (1.33–1.65) Women: 1.94 (1.70–2.20)
Pavey et al, 2012 (31)	≥11 h/d sitting time	Meeting PA guidelines	0.50 (0.25–1.00)	Not meeting PA guidelines	1.52 (1.17–1.98)
Kim et al, 2013 (36)	≥5 h/d watching television	>33.4 MET h/wk ≥20 MET h/wk	Men: 1.12 (0.98–1.28) Women: 1.23 (1.06–1.41)	<33.4 MET h/wk <20 MET h/wk	Men: 1.22 (1.11–1.36) Women: 1.39 (1.24–1.55)
van der Ploeg et al, 2012 (34)	≥1 h/d sitting time	≥300 min/wk PA	1.57 (1.28–1.93)	0 min/wk PA	1.36 (1.26–1.92)
Matthews et al, 2012 (29)	≥7 h/d watching television	>7 h/wk MVPA	1.47 (1.20–1.79)	1–3 h/wk MVPA	1.95 (1.63–2.35)
CVD incidence and mortality					
Seguin et al, 2014 (32)	≥11 h/d total sedentary time	≥19.75 MET h/wk	0.89 (0.66–1.22)	0–3 MET h/wk	1.20 (0.95–1.51)
Matthews et al, 2012 (29)	≥7 h/d watching television	>7 h/wk MVPA	2.00 (1.33–3.00)	1–3 h/wk MVPA	2.63 (1.81–3.84)
Chomistek et al, 2013 (37)	≥10 h/d sitting time	>20 MET h/wk	1.05 (0.83–1.32)	≤1.8 MET h/wk	1.63 (1.39–1.90)
Cancer mortality					
Seguin et al, 2014 (32)	≥11 h/d total sedentary time	≥19.75 MET h/wk	1.30 (1.00–1.68)	0–3 MET h/wk	1.21 (0.97–1.50)
Diabetes incidence					
Krishnan et al, 2009 (49)	≥5 h/d watching television	>3 h/wk MVPA	2.03 (no CI provided)	<1 h/wk MVPA	3.64 (no CI provided)

CVD = cardiovascular disease; HR = hazard ratio; MET = metabolic equivalent; MVPA = moderate to vigorous physical activity; PA = physical activity.

Figure 3. Pooled associations between high sedentary time and health outcomes and modifying effects of physical activity.



An HR >1 suggests that high sedentary time is harmful. Diamonds indicate overall HRs with associated 95% CIs. CVD = cardiovascular disease; HR = hazard ratio.

itively associated with various deleterious health outcomes. These results and others reaffirm the need for greater public awareness about the hazards associated with sedentary behaviors and justify further research to explore the effectiveness of interventions designed to target sedentary time independently from, and in addition to, physical activity.

From the Institute of Health Policy, Management and Evaluation, and the Faculty of Kinesiology and Physical Education, University of Toronto; University Health Network–Toronto Rehabilitation Institute, Cardiovascular Prevention and Rehabilitation Program; Sunnybrook Health Sciences Centre; York University; and Institute for Clinical Evaluative Sciences, Toronto, Ontario, Canada.

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Requests for Single Reprints: David A. Alter, MD, PhD, Institute for Clinical Evaluative Sciences, 2075 Bayview Avenue,

G1-06, Toronto, Ontario M4N 3M5, Canada; e-mail, dalter@ices.on.ca.

Current author addresses and author contributions are available at www.annals.org.

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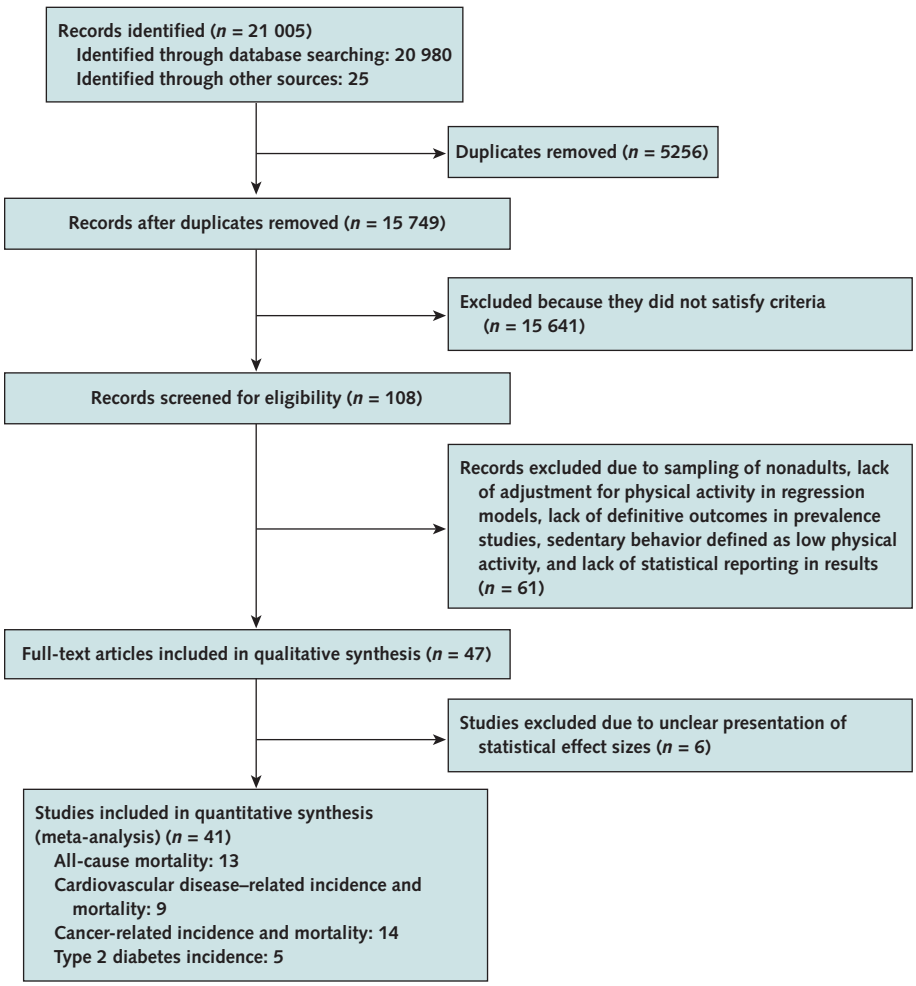
Current Author Addresses: Mr. Biswas: Institute of Health Policy, Management and Evaluation, University of Toronto, 4th Floor, 155 College Street, Toronto, Ontario M5T 3M6, Canada.
Dr. Oh: University Health Network–Toronto Rehabilitation Institute, 347 Rumsey Road, Toronto, Ontario M4G 1R7, Canada.
Dr. Faulkner and Mr. Mitchell: Faculty of Kinesiology and Physical Education, University of Toronto, 55 Harbord Street, Toronto, Ontario M5S 2W6, Canada.
Dr. Bajaj: Department of Cardiology, Sunnybrook Health Sciences Centre, 2075 Bayview Avenue, Toronto, Ontario M4N 3A5, Canada.
Mr. Silver: Osgoode Hall Law School, York University, 4700 Keele Street, Toronto, Ontario M3J 1P3, Canada.
Dr. Alter: Institute for Clinical Evaluative Sciences, 2075 Bayview Avenue, G1-06, Toronto, Ontario M4N 3M5, Canada.

Author Contributions: Conception and design: A. Biswas, R.R. Bajaj, M.A. Silver, D.A. Alter.
Analysis and interpretation of the data: A. Biswas, P.I. Oh, G.E. Faulkner, M.A. Silver, M.S. Mitchell, D.A. Alter.
Drafting of the article: A. Biswas, P.I. Oh, G.E. Faulkner, M.S. Mitchell, D.A. Alter.
Critical revision of the article for important intellectual content: A. Biswas, G.E. Faulkner, R.R. Bajaj, M.A. Silver, M.S. Mitchell, D.A. Alter.
Final approval of the article: A. Biswas, P.I. Oh, G.E. Faulkner, R.R. Bajaj, M.S. Mitchell, D.A. Alter.
Provision of study materials or patients: D.A. Alter.
Statistical expertise: A. Biswas, M.S. Mitchell.
Administrative, technical, or logistic support: M.A. Silver, D.A. Alter.
Collection and assembly of data: A. Biswas, M.A. Silver.

Appendix Figure. Summary of evidence search and selection.



Appendix Table. Characteristics and Potential Risk of Bias of Studies Included in Meta-analysis Reporting Associations Between Sedentary Behavior and Health Outcomes

Author, Year (Reference)	Study Design	Country; Participant Characteristics	Sedentary Behavior Definition	Method of Sedentary Behavior Assessment; Criteria	Primary Outcome; Participants, *n/N*	Follow-up Duration; Completeness	Adjusted Covariates
All-cause mortality							
Seguin et al, 2014 (32)	Prospective	United States; Women's Health Initiative Observational Study; women; 50–79 y	Overall daily hours spent sitting	Self-report questionnaire; ≤4, >4–8, >8–11, or ≥11 h/d spent sitting	All-cause mortality; 3073/20 187	12 y; 98.5%	Age, sex, physical activities, and physical function
Katzmarzyk et al, 2009 (27)	Prospective	Canada; 1981 Canada Fitness Survey; men and women; 18–90 y	"Sedentary almost all the time"	Self-report questionnaire; time spent sitting during work, school, and housework (almost none of the time, approximately 25% of the time, approximately 50% of the time, approximately 75% of the time, or almost all of the time)	All-cause mortality; both: 159/822, men: 83/370, women: 76/452	12 y; not specified	Age, sex, smoking, alcohol use, leisure time physical activity, and physical activity readiness
George et al, 2013 (25)	Prospective	United States; Healthy Eating, Activity and Lifestyle Program; women who were breast cancer survivors; 18–64 y	Television watching time	Self-report questionnaire; 0, <1, 1–2, 3–4, 5–6, 7–8, or ≥9 h/d spent sitting and watching television	All-cause mortality; 41/217	7 y; 73%	Age and moderate to vigorous physical activity
Matthews et al, 2012 (29)	Prospective	United States; NIH-AARP Diet and Health Study; men and women; 50–71 y	Overall sitting time	Self-report questionnaire; <3, 3–4, 5–6, 7–8, or ≥9 h/d spent sitting	All-cause mortality; 1492/240 819	8.5 y; 59%	Age, sex, race, education, smoking status, diet quality, and moderate to vigorous physical activity
Patel et al, 2010 (30)	Prospective	United States; CPS-II Nutrition Cohort; men and women; 50–74 y	Sitting time	Self-report questionnaire; 0, <3, 3–5, 6–8, or >8 h/d spent sitting	All-cause mortality; men: 1864/53 440, women: 1104/69 776	14 y; 67%	Age, race, marital status, education, smoking status, BMI, alcohol use, total caloric intake, comorbid conditions score, and physical activity
Pavey et al, 2012 (31)	Prospective	Australia; Australian Longitudinal Study on Women's Health; women; 76–81 y	Sitting time	Self-report questionnaire; time spent sitting while doing things, such as visiting friends, driving, reading, watching television, or working at a desk or computer on usual day (0–4, 4 to <8, 8 to <11 or ≥11 h/d)	All-cause mortality; 136/273	9 y; 83%	Age, education, marital status, area, smoking status, alcohol use, BMI, and physical activity
Dunstan et al, 2010 (24)	Prospective	Australia; Australian Diabetes, Obesity and Lifestyle Study; men and women; ≥25 y	Television viewing time	Self-report questionnaire; <2, 2–4, or >4 h/d spent watching television	All-cause mortality; 54/672	6.6 y; 43%	Age, sex, smoking status, education, total energy intake, alcohol use, diet quality, waist circumference, hypertension, total plasma cholesterol, lipid-lowering medication use, glucose tolerance status, and exercise time

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Appendix Table–Continued

Author, Year (Reference)	Study Design	Country; Participant Characteristics	Sedentary Behavior Definition	Method of Sedentary Behavior Assessment; Criteria	Primary Outcome; Participants, *n/N*	Follow-up Duration; Completeness	Adjusted Covariates
Inoue et al, 2008 (26)	Prospective	Japan; Japan Public Health Center–based Prospective Study; men and women; 45–74 y	Sedentary activities	Self-report questionnaire; <3, 3–8, or >8 h/d spent in sedentary activity	All-cause mortality; men: 322/39 183, women: 114/43 851	5 y; 97.3%	Age, area, occupation, occupation, diabetes history, smoking status, alcohol use, BMI, total energy intake, and leisure time physical exercise
Stamatakis et al, 2011 (38)	Prospective	Scotland; 2003 Scottish Health Survey; men and women; ≥35 y	Screen time	Self-report questionnaire; "How much time on an average day do you spend watching television or another type of screen, such as a computer or video game? Please do not include any time spent in front of a screen while at school, college, or work." (weekday screen time: <2, 2 to <4, ≥4 h/d)	All-cause mortality; 115/1204	4.3 y; 71%	Age, sex, BMI, smoking status, marital status, race, social class, long-standing illness, occupational physical activity, diabetes diagnosis/hypertension, and moderate to vigorous physical activity
Koster et al, 2012 (28)	Prospective	United States; National Health and Nutrition Examination Survey; men and women; ≥50 y	Sedentary time	7-d accelerometry; sedentary time defined as movements <100 counts/min	All-cause mortality; 53/476	2.8 y; 98.2%	Age, sex, race, education, smoking status, alcohol use, BMI, diabetes, CHD, CHF, cancer, stroke, mobility limitation, and moderate to vigorous physical activity
Kim et al, 2013 (36)	Prospective	United States; Multiethnic Cohort Study; men and women; 45–75 y	Total sitting time	Self-report questionnaire; total sitting time as sum of midpoints (0, <1, 1–2, 3–4, 5–6, 7–10, or ≥11 h)	All-cause mortality; men: 3116/61 395, women: 2960/73 201	13.7 y; 62.6%	Age, education, ethnicity, smoking history, history of hypertension/diabetes, alcohol use, energy intake, and physical activity
van der Ploeg et al, 2012 (34)	Prospective	Australia; 45 and Up Study; men and women; ≥45 y	Sitting time	Self-report questionnaire; "About how many hours in each 24-hour day do you usually spend sitting?" (0 to <4, 4 to <8, 8 to <11, or ≥11 h/d)	All-cause mortality; both: 649/222 497, men: 401/105 855, women: 248/116 642	4 y; 98.7%	Age, sex, education, marital status, urban or rural residence, physical activity, BMI, smoking status, self-rated health, and receiving help with daily tasks

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Appendix Table–Continued

Author, Year (Reference)	Study Design	Country; Participant Characteristics	Sedentary Behavior Definition	Method of Sedentary Behavior Assessment; Criteria	Primary Outcome; Participants, *n/N*	Follow-up Duration; Completeness	Adjusted Covariates
León-Muñoz et al, 2013 (35)	Prospective	Spain; men and women; ≥60 y	Sitting time	Self-report questionnaire; "About how much time do you spend sitting down on weekdays?" (consistently sedentary, newly sedentary, formerly sedentary, consistently nonsedentary)	All-cause mortality; 203/567	2 y; 80.9%	Sex, age, education, smoking status, alcohol use, heart disease, stroke, diabetes, osteomuscular disease, cancer, physical function, physical activity, chronic lung disease, and limitations in mobility and agility
Type 2 diabetes							
Dunstan et al, 2005 (5)	Cross-sectional	Australia; Australian Diabetes, Obesity and Lifestyle Study; men and women; ≥25 y	Television watching time	Self-report questionnaire; 0–7, 7.01–14, or >14 h/wk watching television	Type 2 diabetes; 1103/20 187	1 y; 55%	Age, education, diabetes history, smoking status, diet, and physical activity
Hu et al, 2003 (48)	Prospective	United States; Nurses' Health Study; women; 35–55 y	Television watching time	Self-report questionnaire; 0–1, 2–5, 6–29, 21–40, or >40 h/wk watching television	Type 2 diabetes; 51/1464	6 y; 56.3%	Age, hormone use, alcohol use, smoking, diabetes history, and physical activity
Krishnan et al, 2009 (49)	Prospective	United States; Black Women's Health Study; black women; 21–69 y	Television watching time	Self-report questionnaire; 0, <1, 1–2, 3–4, or >5 h/d watching television	Type 2 diabetes; 712/2928	10 y; 80%	Age, time period, diabetes history, education, family income, marital status, smoking status, energy intake, coffee intake, vigorous activity, television watching, and walking
Ford et al, 2010 (50)	Prospective	Germany; European Prospective Investigation in Cancer and Nutrition–Potsdam Study; men: 35–65 y, women: 40–65 y	Television watching time	Self-report questionnaire; "On average, how many hours/day did you watch television during the last 12 months?" (<1, 1 to <2, 2 to <3, 3 to <4, or ≥4 h/d)	Type 2 diabetes; both: 131/1935	7.8 y; 90%	Age, sex, education, occupational activity, smoking status, alcohol intake, and physical activity
Hu et al, 2001 (6)	Prospective	United States; Health Professionals Follow-up Study; men; 45–75 y	Television watching time	Self-report questionnaire; 0–1, 2–5, 6–29, 21–40, or >40 h/wk watching television	Type 2 diabetes; 12/186	10 y; 73.6%	Age, smoking status, diabetes, diabetes history, alcohol intake, diet, and physical activity

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Appendix Table–Continued

Author, Year (Reference)	Study Design	Country; Participant Characteristics	Sedentary Behavior Definition	Method of Sedentary Behavior Assessment; Criteria	Primary Outcome; Participants, *n/N*	Follow-up Duration; Completeness	Adjusted Covariates
Cardiovascular disease incidence and mortality							
Seguin et al, 2014 (32)	Prospective	United States; Women's Health Initiative Observational Study; women; 50–79 y	Sedentary time	Self-report questionnaire; ≤4, >4-8, >8–11, or ≥11 h/d spent sitting	CVD mortality; 895/20 187 CHD mortality; 418/20 187	12 y; 98.5%	Age, sex, physical activities, and physical function
Katzmarzyk, 2009 (29)	Prospective	Canada; 1981 Canada Fitness Survey; both sexes, men and women; 18–90 y	"Sedentary almost all the time"	Self-report questionnaire; time spent sitting during work, school, and housework (almost none of the time, approximately 25% of the time, approximately 50% of the time, approximately 75% of the time, or almost all of the time)	CVD mortality; both: 67/822, men: 34/370, women: 33/452	12 y; not specified	Age, sex, smoking, alcohol use, leisure time physical activity, and physical activity readiness
Matthews et al, 2012 (29)	Prospective	United States; NIH-AARP Diet and Health Study; men and women; 50–71 y	Overall sitting time	Self-report questionnaire; <3, 3–4, 5–6, 7–8, or ≥9 h/d spent sitting	CVD mortality; 212/240 819	8.5 y; 59%	Age, sex, race, education, smoking status, diet quality, and moderate to vigorous physical activity
Patel et al, 2010 (30)	Prospective	United States; CPS-II Nutrition Cohort; men and women; 50–74 y	Sitting time	Self-report questionnaire; 0, <3, 3–5, 6–8, or >8 h/d spent sitting	CVD mortality; men: 685/53 440, women: 331/69 776	14 y; 67%	Age, race, marital status, education, smoking status, BMI, alcohol use, total caloric intake, comorbid conditions score, and physical activity
Dunstan et al, 2010 (24)	Prospective	Australia; Australian Diabetes, Obesity and Lifestyle Study; men and women; ≥25 y	Television viewing time	Self-report questionnaire; <2, 2–4, or >4 h/d spent television	CVD mortality; 22/672	6.6 y; 43%	Age, sex, smoking status, education, total energy intake, alcohol use, diet quality, waist circumference, medication, glucose tolerance status, and exercise time
Stamatakis et al, 2011 (33)	Prospective	Scotland; 2003 Scottish Health Survey; men and women; ≥35 y	Screen time	Self-report questionnaire; "How much time on an average day do you spend watching television or another type of screen, such as a computer or video game? Please do not include any time spent in front of a screen while at school, college, or work." (<2, 2 to <4, or ≥4 h/d)	CVD event; 65/1072	4.3 y; 71%	Age, sex, BMI, smoking status, marital status, race, social class, long-standing illness, occupational physical activity, diabetes diagnosis/ hypertension, and moderate to vigorous physical activity

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Appendix Table–Continued

Author, Year (Reference)	Study Design	Country; Participant Characteristics	Sedentary Behavior Definition	Method of Sedentary Behavior Assessment; Criteria	Primary Outcome; Participants, *n/N*	Follow-up Duration; Completeness	Adjusted Covariates
Kim et al, 2013 (36)	Prospective	United States; Multiethnic Cohort Study; men and women; 45–75 y	Total sitting time	Self-report questionnaire; total sitting time as sum of midpoints (0, <1, 1–2, 3–4 h, 5–6, 7–10, or ≥11 h/d)	CVD mortality; men: 1104/61 395, women: 1002/73 201	13.7 y; 62.6%	Age, education, ethnicity, smoking history, history of hypertension/diabetes, alcohol use, energy intake, and physical activity
Wijndaele et al, 2011 (39)	Prospective	United Kingdom; EPIC Norfolk Study; men and women; 45–79 y	Television viewing time	Self-report questionnaire. lowest: <2.5 h/d, middle: 2.5–3.6 h/d, highest: >3.6 h/d spent watching television before and after 6 p.m. on weekdays and weekends	Any CVD event; 2620/12 608	4.3 y; 61.6%	Age, sex, education, smoking status, alcohol use, medication, diabetes status, family history of CVD, sleep duration, and total physical activity energy expenditure
Chomistek et al, 2013 (37)	Prospective	United States; Women's Health Initiative Observational Study; women; 50–79 y	Sitting time	Self-report questionnaire; "During a usual day and night, about how many hours do you spend sitting? Be sure to include the time you spend sitting at work, sitting at the table eating, driving or riding a car or bus, and sitting up watching television or talking." (≤5, 5.1–9.9, or ≥10 h/d)	CHD event: 490/17 374; total CVD (nonfatal MI, fatal CHD, nonfatal and fatal stroke): 849/17 374	12.2 y; 75.8%	Age, physical activity, race, education, income, marital status, smoking, family history of MI, depression, alcohol intake, hours of sleep, calorie intake, hypertension, and diabetes/high cholesterol at baseline
Cancer-related incidence and mortality							
Seguin et al, 2014 (32)	Prospective	United States; Women's Health Initiative Observational Study; women; 50–79 y	Sedentary time	Self-report questionnaire; ≤4, >4–8, >8–11, or ≥11 h/d spent sitting	Cancer mortality; 1103/20 187	12 y; 98.5%	Age, sex, physical activities, and physical function
Campbell et al, 2013 (40)	Prospective	United States; CPS-II Nutrition Cohort; men and women	Leisure time spent sitting	Self-report questionnaire; <3, 3 to <6, or >6 h/d in the past year spent driving or sitting in a car or bus, sitting on a train, sitting and watching television, and sitting at home reading	Colorectal cancer mortality; 40/2293	16.1 y; 74%	Age, sex, smoking status, BMI, red meat intake, recreational physical activity, SEER Program summary stage, and education
Katzmarzyk et al, 2009 (27)	Prospective	Canada; 1981 Canada Fitness Survey; men and women; 18–90 y	"Sedentary almost all the time"	Self-report questionnaire; time spent sitting during work, school, and housework (almost none of the time, approximately 25% of the time, approximately 50% of the time, approximately 75% of the time, or almost all of the time)	Cancer mortality; both: 36/822; men: 21/370; women: 15/452	12 y; not specified	Age, sex, smoking, alcohol use, leisure time physical activity, and physical activity readiness

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Appendix Table–Continued

Author, Year (Reference)	Study Design	Country; Participant Characteristics	Sedentary Behavior Definition	Method of Sedentary Behavior Assessment; Criteria	Primary Outcome; Participants, *n/N*	Follow-up Duration; Completeness	Adjusted Covariates
Patel et al, 2010 (30)	Prospective	United States; CPS-II Nutrition Cohort; men and women; 50–74 y	Sitting time	Self-report questionnaire; 0, <3, 3–5, 6–8, or >8 h/d spent sitting	Cancer mortality; men: 571/53 440; women: 411/69 776	14 y; 67%	Age, race, marital status, education, smoking status, BMI, alcohol use, total caloric intake, comorbid conditions score, and physical activity
Matthews et al, 2012 (29)	Prospective	United States; NIH-AARP Diet and Health Study; men and women; 50–71 y	Overall sitting time	Self-report questionnaire; <3, 3–4, 5–6, 7–8, or ≥9 h/d spent sitting	Cancer mortality; 632/240 819	8.5 y; 59%	Age, sex, race, education, smoking status, diet quality, and moderate to vigorous physical activity
Friberg et al, 2006 (41)	Prospective	Sweden; Swedish Mammography Cohort; 50–83 y	Leisure time inactivity (watching television/sitting)	Self-report questionnaire; <1 to >6 h/d spent watching television/sitting (inactive leisure time)	Endometrial cancer; 24/33 723	7.25 y; 70%	Age, diabetes history, fruit and vegetable intake, education, occupation, and leisure time activity
Dunstan et al, 2010 (24)	Prospective	Australia; Australian Diabetes, Obesity and Lifestyle Study; men and women; ≥25 y	Television viewing time	Self-report questionnaire; <2, 2–4, or >4 h/d spent watching television	Cancer mortality; 22/672	6.6 y; 43%	Age, sex, smoking status, education, total energy intake, alcohol use, diet quality, waist circumference, medication, glucose tolerance status, and exercise time
Howard et al, 2008 (42)	Prospective	United States; NIH-AARP Diet and Health Study; men and women; 50–71 y	Sitting time	Self-report questionnaire; <1 h, 1–2, 3–4, 5–6, 7–8, or ≥9 h/d spent watching television/videos or sitting	Colon cancer; men: 106/175 600, women: 54/125 073	6.9 y; 53%	Age, smoking status, alcohol use, education, race, family history of colon cancer, diet, and moderate to vigorous physical activity
Kim et al, 2013 (36)	Prospective	United States; Multiethnic Cohort Study; men and women; 45–75 y	Total sitting time	Self-report questionnaire; total sitting time as sum of midpoints (0, <1, 1–2, 3–4, 5–6, 7–10, or ≥11 h/d)	Cancer mortality; men: 1053/61 395, women: 1018/73 201	13.7 y; 62.6%	Age, education, ethnicity, smoking history, history of hypertension/diabetes, alcohol use, energy intake, and physical activity
George et al, 2010 (44)	Prospective	United States; NIH-AARP Diet and Health Study; women; 50–71 y	Sitting time	Self-report questionnaire; <1, 1–2, 3–4, 5–6, 7–8, or ≥9 h/d spent watching television/videos and sitting	Invasive breast cancer incidence; 224/48 594	6.9 y; 73%	Age, energy intake, recreational moderate to vigorous physical activity, parity or age of first live birth, menopausal hormone therapy use, number of breast biopsies, smoking, alcohol intake, race, and education
Hildebrand et al, 2013 (45)	Prospective	United States; CPS-II Nutrition Cohort; women; 50–74 y	Leisure time sitting	Self-report questionnaire; <3, 3–5, or ≥6 h/d spent sitting	Breast cancer incidence; 572/73 615	14.2 y; 88%	Age and MET expenditure from total recreational activities

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Appendix Table–Continued

Author, Year (Reference)	Study Design	Country; Participant Characteristics	Sedentary Behavior Definition	Method of Sedentary Behavior Assessment; Criteria	Primary Outcome; Participants, *n/N*	Follow-up Duration; Completeness	Adjusted Covariates
Teras et al, 2012 (46)	Prospective	United States; CPS-II Nutrition Cohort; men and women; 50–74 y	Sitting time	Self-report questionnaire; <3, 3–5, or ≥6 h/d spent sitting	Non-Hodgkin lymphoid neoplasm incidence; men: 151/69 849, women: 99/77 001	14.2 y; 80%	Age, family history of hematopoietic cancer, education, smoking status, alcohol intake, BMI, height, and physical activity
Peplonska et al, 2008 (47)	Case–control	Poland; women; 20–74 y	Siting time	Self-report questionnaire; hours spent sitting per day converted to MET h/wk of lifetime: <11.3, 11.3–29.7, >29.7–47.8, or >47.8 MET h/wk	Breast cancer incidence	NA; NA	Age, study site, education, BMI, age at menarche, menopausal status, age at menopause, number/age at full-term birth, breastfeeding, family history of breast cancer, previous screening mammography, and total lifetime recreational and total occupational physical activity
Zhang et al, 2004 (43)	Case–control	China; hospital-based; women; <75 y	Total sitting duration	Self-report questionnaire; 5 y ago, <4, 4–10, or >10 h/d spent sitting at work, while watching television, in car or bus, at meals, and in other activities (such as reading, playing cards, and sewing)	Epithelial ovarian cancer; 75/205	NA; NA	Age, locality, education, family income, BMI, tobacco smoking, alcohol use, tea drinking, physical activity, marital status, menopausal status, parity, oral contraceptive use, tubal ligation, hormone replacement therapy, ovarian cancer in first-degree relatives, and total energy intake

BMI = body mass index; CHD = coronary heart disease; CHF = coronary heart failure; CPS-II = Cancer Prevention Study II; CVD = cardiovascular disease; EPIC = European Prospective Investigation Into Cancer and Nutrition; MET = metabolic equivalent; MI = myocardial infarction; NA = not applicable; NIH-AARP = National Institutes of Health–American Association of Retired Persons; SEER = Surveillance, Epidemiology, and End Results.
* Rating criteria for risk of bias: low, moderate, and high.