

The relationship between changes in sitting time and mortality in post-menopausal US women

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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.

Keywords chronic disease, cohort study, life expectancy, lifestyle, sedentary

Background

Currently, over 40% of US women aged 65 and older fail to meet even a minimum of 10 min of light/moderate or vigorous levels of physical activity per day.¹ More troubling, the average person will spend 7.7 h per day in sedentary pursuits, with women aged 70–85 years spending almost two-thirds of their day being sedentary.²

In the past, physical inactivity was used interchangeably with the term 'sedentary' and conceptualized to represent the very low end of the physical activity continuum.^{3–8} However, it is now understood that sedentary behaviour is distinct from physical inactivity, in that a person can accumulate the daily recommended physical activity levels, despite leading a sedentary lifestyle. Indeed, the active-sedentary individual might perform one bout of structured physical activity, but then be completely sedentary for the rest of their waking hours.^{9–11}

Sedentary behaviour, defined as activities with an energy expenditure equal to or under the resting level of 1.5

metabolic equivalent of task (MET), can include prolonged sitting at work, home, travel and/or performing other tasks that require very little energy expenditure.^{10,12} Therefore, where physical activity will encompass a more modest portion of an individual's waking hours, sedentary behaviour can be collected in several bouts and account for a large proportion of the day.

It follows that a growing body of literature now links sedentary behaviour to several negative health outcomes such as type 2 diabetes mellitus (T2DM),¹³ metabolic syndrome¹⁴ and cancer¹⁵. For example, in a study of women aged 50–79 years of age, sitting ≥ 10 h/day (versus ≤ 5 h/day), was associated with an increased risk of cardiovascular disease (CVD)

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(hazard ratio, HR = 1.18, 95% confidence interval, CI = 1.09–1.29).¹⁶ In the first epidemiological study of its kind, Katzmarzyk *et al.*¹⁷ reported progressively higher risk of all-cause and CVD mortality with higher levels of sitting time in Canadian adults. Further, in a cohort of US women, those who reported sitting for > 6 h had an ~40% higher risk of all-cause death than those sitting <3 h per day.¹⁸ All of these relationships were independent of leisure-time physical activity.

Only one study¹⁹ to date has examined actual changes in sitting time with health outcomes, despite the well-known association between changes in physical activity and health.^{2,20–22} Thus, as one of Hill's key causal criteria,²³ understanding the 'alterability' of the sitting time–mortality relationship will provide valuable insight into current health promotion efforts.^{24–26}

The purpose of the current study was to therefore assess the relationship between sitting time at baseline and year six of follow-up with mortality, in the Women's Health Initiative (WHI) observational study.

Methods

Ethics statement and data access

All participants in the WHI provided written informed consent. The protocol for this secondary data analysis was reviewed and approved by the Human Participants Review Committee of York University (Toronto, Canada). Data for this analysis were obtained through a limited data access request to the US National Heart, Lung, and Blood Institute (NHLBI).

Study sample

Sociodemographics, health behaviours and medical and family history were collected by interview or use of self-administered questionnaires from the WHI, a longitudinal health study of the risk factors and treatment of cancer, CVD and osteoporotic injury, among a sample of post-menopausal US women. Of the original sample consisting of 161 808 participants, we obtained data from the Observational Study (OS) cohort. The WHI-OS has over 15 years of follow-up (1993–2008) data from 93 676 participants (ages 50–79 years) who were recruited between 1 October 1993 and 31 December 1998. All medical and physiological exposure variables in this analysis were taken by certified personnel at the baseline and the year three clinic visit. Additional data were collected through annual self-administered questionnaires from year three to the end of the study in 2005. For our study, all participants with sitting time data were included for analysis. After excluding participants with missing sitting time

values at baseline ($N = 867$) and at year six ($n = 15\,875$), a final analytical sample of ($N = 92\,809$) and ($n = 77\,801$) was available for the baseline and change analyses, respectively. Greater details regarding the methods and design of the WHI are provided elsewhere.^{27,28}

Women's Health Initiative questionnaire

Total daily sitting time was assessed at baseline and again at year six of follow-up by self-reported 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 TV or talking.' Response options to this question were <4, 4–5, 6–7, 8–9, 10–11, 12–13, 14–15 and 16+ h/day. To facilitate comparison with similar studies,^{17,22,29,30} participants were initially divided into quartiles of sitting time (Q1: ≤5; Q2: 6–9; Q3: 10–13; Q4: 14+ h/day) to assess the dose–response relationship with mortality.

In the subset of participants with sitting time at baseline and year six, a further set of analyses were conducted. Here, the sitting time variable at baseline and follow-up was dichotomized as 'low-to-moderate' (≤9 h of daily sitting) or 'high' (≥10 h of daily sitting). These cut-offs were based on a preliminary analysis, wherein stronger relationships between sitting time and mortality were seen for participants who sat in excess of 9 h. To test for changes in sitting time and corresponding mortality risk, we compared four groups: (i) women who reported a high sitting duration at both baseline and follow-up ('stayed high/maintained high sitting'; RR = 1.00, referent); (ii) women who were low to moderate at baseline but high at follow-up ('increased sitting'); (iii) women who were high at baseline but low to moderate at follow-up ('decreased sitting') and (iv) women who reported low to moderate sitting time at both baseline and follow-up ('stayed low/maintained low sitting').

Ascertainment of mortality

Death from all-cause, CVD or cancer was the end point for this study. Trained physician adjudicators established the end points from hospitalization and emergency room records, death certificates, autopsy and coroner's reports. Cause-specific mortality categorizations were based on the cause of death, rather than the immediate or contributing cause of death, as follows: CVD mortality (ICD-9 codes 390–449) included death from coronary heart disease, cerebrovascular disease, pulmonary embolism, congestive heart failure and other cardiovascular causes, and cancer mortality (ICD-9 codes 140–239) included all carcinomas, lymphomas, sarcomas (including metastatic cancer from unknown primaries)

and haematological malignancies (including blood, bone marrow and lymph nodes).³¹

Confounding variables

The following variables were treated as potential confounders for the baseline analyses: age (years), weight (lbs), education, current employment status (no or full-/part-time), ethnicity, leisure-time physical activity (calculated in MET-minutes per week), current smoking status, alcohol consumption, general health (based on a quality-of-life subscale ranging from 0 to 100, with a higher score indicating a more favourable health state), physical functioning score (based on quality-of-life subscale on physical functioning ranging from 0 to 100, with a higher score indicating a more favourable health state, measured from the Rand 36-Item Health Survey), treatment ever for diabetes and history of CVD (yes/no) and any cancer (yes/no) or stroke (yes/no).

For the change analysis, models included both baseline and year six measures as potential confounders. When a variable adjusted for in the baseline analysis was not collected at year six, we used other year six covariates that would allow the best comparison between the two analyses. Specifically, the baseline dose–response analyses measured lifetime alcohol consumption (never, past, present), while the change analyses adjusted for alcohol consumption within the last 3 months (yes, no). Moreover, weight, instead of body mass index (BMI), was assessed at both baseline and year six, as information on BMI was not available at this follow-up.

Statistical analysis

Characteristics of the sample are presented as mean and standard deviation (SD) for continuous variables, and frequencies and percentages for categorical variables. Differences in sociodemographic and clinical measures were subsequently assessed by ANOVA and χ^2 analysis, respectively. Kaplan–Meier curves were used to examine survival probabilities, stratified by baseline sitting time and changes in sitting time. Differences in survival probability were determined by the log-rank statistic. Censored observations included those who were either lost to follow-up, dropped out or were alive at the end of the follow-up. To account for potential bias due to underlying disease, a sensitivity analysis was completed; women with pre-existing, sub-clinical disease and those who died within the first 2 years of follow-up were excluded, and compared with the analysis within the full sample.

Cox proportional hazards regression was used to estimate the relationship between baseline sitting time and changes in sitting time with all-cause, CVD and cancer mortality, after adjusting for confounders. Covariates included age, weight,

education, current employment status, ethnicity, leisure-time physical activity, current smoking status, alcohol consumption and a variety of health indicators at baseline and year six. Baseline covariates included: general perception of own health, physical functioning score, ever treated for diabetes, and history of CVD, cancer or stroke. Year six covariates included: new treatment for diabetes, new onset of congestive heart failure and/or angina and occurrence of at least one fracture of the hip, foot, pelvis, knee, upper leg, lower leg or tailbone. All covariates were selected to ensure ease of comparison with earlier studies.^{17,30,32} To examine the proportional hazards assumption, time-dependent covariates were included in the model, and visual inspection of the negative log-by-log plots was performed.

To explore the potential for effect modification, two-way interactions of covariates were probed, and the relationship between change in sitting time and all-cause mortality was subsequently stratified by age, leisure-time physical activity, smoking status, treatment for diabetes, incidence of lower body injuries and onset of congestive heart failure (Table 4). All analyses were performed using SAS v9.3 (SAS, Inc, Cary, NC, USA), with statistical significance set at $\alpha < 0.05$.

Results

Baseline characteristics

Table 1 outlines the descriptive profile of the study participants according to their change in daily sitting time category between baseline and year six. On average, women who sustained low sitting times were roughly 3 years older (69.1 ± 7.0 versus 65.6 ± 7.5 , $P < 0.0001$), weighed less (lbs) (151.6 ± 30.4 versus 166.2 ± 41.1) and were more likely to meet leisure-time physical activity guidelines (55 versus 41%) than those who sustained high levels. Meanwhile, women who maintained high sitting time or increased sitting by the follow-up were more likely to be white, a current smoker and be employed, compared with the other change groups.

Baseline sitting time

After a follow-up time of up to 10.8 years from baseline, and a mean age of 63.61 ± 7.4 years, there were a total of 6188 (6.7%) deaths [cancer: $N = 2629$; CVD: $N = 1782$, and other: $N = 1777$]. Inspection of Fig. 1 reveals differences in all-cause survival probability across quartiles of sitting time (log-rank $\chi^2 = 22.59$, $df = 3$, P -value < 0.0001), whereas Table 2 shows the all-cause, CVD and cancer mortality risk associated with baseline sitting time. In fully adjusted models, those in Q3 and Q4 were at higher risk for all-cause (Q3: HR = 1.20, 95% CI = 1.10–1.32; Q4: 1.25, 1.07–1.46) and

Table 1 Characteristics of study population by change in sitting time between baseline and follow-up

	<i>Change in sitting time from baseline to follow-up</i>			
	<i>Maintained high sitting</i>	<i>Increased sitting</i>	<i>Decreased sitting</i>	<i>Maintained low sitting</i>
<i>n</i>	8208 (10.6)	6699 (8.6)	10 969 (14.1)	51 925 (66.7)
Age, mean (SD), years	65.6 (7.5)	68.6 (7.8)	66.8 (7.0)	69.1 (7.0)
Age				
50–59	2099 (25.6)	1030 (15.4)	1852 (16.9)	5509 (10.6)
60–69	3618 (44.1)	2490 (37.2)	5310 (48.4)	20 787 (40.03)
70–79	2069 (25.2)	2590 (38.6)	3294 (30.0)	22 004 (42.4)
80–89	422 (5.14)	589 (8.8)	513 (4.7)	3625 (7.0)
Leisure-time physical activity ^a				
Meets guidelines	3371 (41.1)	2816 (42.0)	5732 (52.3)	28 581 (55.0)
Ethnicity				
White	7169 (87.5)	5771 (86.3)	9344 (85.3)	44 389 (85.7)
Black	509 (6.3)	476 (7.1)	817 (7.5)	3457 (6.7)
Hispanic	142 (1.7)	146 (2.2)	306 (2.8)	1807 (3.5)
Other ^b	371 (4.5)	288 (4.3)	481 (4.4)	2126 (4.1)
Current weight, mean (SD), lbs	166.2 (41.1)	160.7 (37.7)	157.2 (33.6)	151.1 (30.4)
Smoking now				
Yes	390 (4.8)	327 (4.9)	480 (4.4)	1822 (3.5)
Alcohol in past 3 months				
Yes	5286 (66.7)	3918 (60.7)	7023 (66.6)	32 093 (64.3)
Currently employed				
Yes	3980 (48.7)	1991 (29.9)	3030 (27.7)	9903 (19.2)

Data are presented as number (percentage) unless otherwise indicated and are based on the information collected at follow-up. $P < 0.0001$ in test for heterogeneity across change groups for all variables.

^aMeeting leisure-time physical activity guidelines equates to a minimum of 500 MET minutes per week to reap health benefits. MET, metabolic equivalent of task.

^bOther defined as being American Indian/Alaska Native or Asian/Pacific Islander or unknown race.

cancer mortality, (Q3: 1.30, 1.14–1.49; Q4: 1.35, 1.08–1.70) compared with Q1 (referent).

Changes in sitting time at year six

The 77 801 women included in the change analysis were followed for an average of 5.1 years from year six, to the end of the study in 2005. In total, there were 1855 (2.4%) deaths [cancer: $n = 736$; CVD: $n = 493$, and other: $n = 626$]. The mean age of this sample was 68.4 ± 7.2 , with greater deaths in the youngest and oldest age groups [50–59 y: $n = 95$ (5.1%); 60–69 y: $n = 452$ (1.4%); 70–79 y: $n = 942$ (3.1%); 80+ y: $n = 366$ (7.1%)].

Figure 2 reveals differences in all-cause survival across change in sitting time categories (log-rank $\chi^2 = 108.77$, $df = 3$, P -value < 0.0001). In fully adjusted models, women who lowered (HR = 0.71, 95% CI = 0.54–0.95) or maintained low sitting (HR = 0.49, 95% CI = 0.39–0.66) had lower risk of all-cause mortality (Table 3). A protective effect was also

observed for cancer mortality (lowered sitting: HR = 0.73, 95% CI = 0.55–0.97; maintained low sitting: HR = 0.52, 95% CI = 0.42–0.66) compared with the group who maintained high sitting. When we excluded women who died within the first 2 years of follow-up and those who suffered from pre-existing sub-clinical disease, similar relative risks to those of the original sample were found, allowing us to include the full sample in the final analysis.

Finally, to explore potential effect modification by key confounders, analyses were stratified by age, physical activity, smoking status, diabetes treatment, injury status and congestive heart failure (Table 4). With the exception of smoking and diabetes treatment, patterns of risk were similar across strata.

Discussion

Main finding of this study

In this large prospective cohort of post-menopausal women, the maintenance of low sitting time as well as lowering sitting

time from baseline to year six was protective against all-cause and cancer mortality, an effect that persisted even after adjustments for covariates. These findings are in line with recent

reports linking sitting time and sedentary behaviour to the incidence of endometrial, colorectal, lung^{33,34} and breast³⁴ cancer. In contrast, a lack of relationship between sitting time and CVD mortality after full adjustment may have resulted due to the general characteristics of our sample. Women in the WHI-OS were likely to be taking hormone therapy, have low dietary fat intake and have a cluster of other healthy behaviours, many of which have been known to promote a favourable cardiometabolic profile. Further, our analysis of baseline sitting time was consistent with the findings of prior studies,^{17,30,35} wherein a dose–response association between sitting time and mortality was reported.

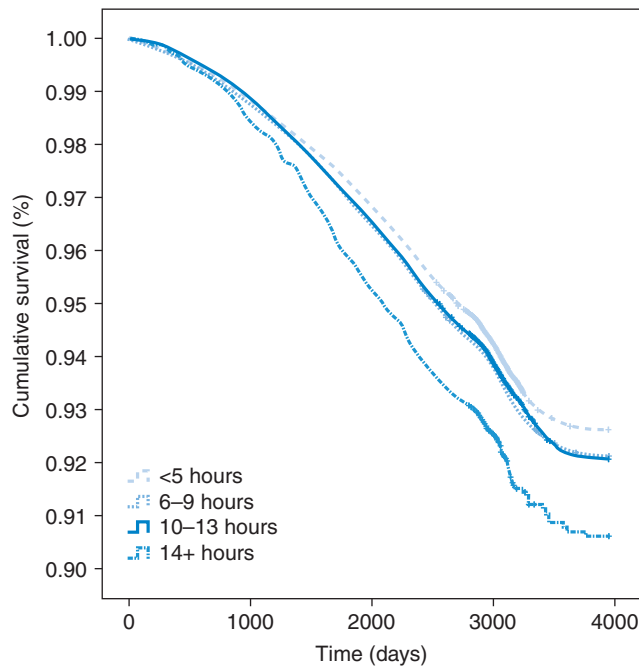


Fig. 1 Probability of survival across quartiles of sitting time.

What is already known on this topic

We are aware of only one other study to have assessed the relationship between changes in sitting time and mortality risk. Similar to the present study, León-Muñoz *et al.*¹⁹ examined a cohort of older adults in Spain ($N = 2\ 635$; ≥ 60 years) and found that those who were consistently non-sedentary had lower all-cause mortality; however, this study did not assess cause-specific mortality and explored changes to sitting time within a shorter, 2-year time span. In contrast, we also saw a significantly lower risk of all-cause mortality in women who decreased their sitting time, whereas the Spanish cohort did not.

Table 2 Risk of all-cause, CVD and cancer mortality based on baseline total daily sitting time

	Total daily sitting time (hours)			
	Q1	Q2	Q3	Q4
<i>N</i> (%)	32 214 (34.7)	37 859 (40.8)	18 757 (20.21)	3979 (4.29)
All-cause mortality				
Deaths	2045 (6.35)	2566 (6.78)	1253 (6.68)	324 (8.14)
Age-adjusted HR	1.00 (ref)	1.08 (1.02–1.15)	1.33 (1.24–1.43)	1.64 (1.46–1.84)
Fully adjusted HR	1.00 (ref)	1.05 (0.98–1.13)	1.20 (1.10–1.32)	1.25 (1.07–1.46)
CVD mortality				
Deaths	616 (1.9)	733 (1.9)	340 (1.8)	93 (2.3)
Age-adjusted HR	1.00 (ref)	1.02 (0.92–1.14)	1.28 (1.12–1.47)	1.66 (1.34–2.06)
Fully adjusted HR	1.00 (ref)	1.02 (0.89–1.16)	1.13 (0.96–1.34)	1.16 (0.87–1.55)
Cancer mortality				
Deaths	845 (2.6)	1087 (2.9)	555 (2.9)	142 (3.6)
Age-adjusted HR	1.00 (ref)	1.11 (1.01–1.21)	1.34 (1.21–1.50)	1.64 (1.37–1.96)
Fully adjusted HR	1.00 (ref)	1.07 (0.96–1.20)	1.30 (1.14–1.49)	1.35 (1.08–1.70)

95% confidence intervals are presented within parentheses. *N* % for deaths. *P*-values for linear trend across sitting groups were $P < 0.0001$ except for all-adjusted CVD mortality $P = 0.02$ and all-adjusted cancer mortality $P = 0.0001$. All adjusted hazard models controlled for age (continuous), current weight, education, current employment status, ethnicity, leisure-time physical activity, current smoking status, alcohol consumption, general perception of own health, physical functioning score, ever treated for diabetes, history of CVD, cancer and stroke and all at baseline. Quartiles: 1, ≤ 5 daily hours of sitting; 2, 6–9 daily hours of sitting; 3, 10–13 daily hours of sitting; 4, 14+ daily hours of sitting. CVD, cardiovascular disease; HR, hazard ratio.

What this study adds

While these findings highlight the importance of maintaining minimal sitting time, they also provide encouragement to those wishing to make positive changes to their health, who may otherwise be unable to partake in more moderate-to-vigorous activity.

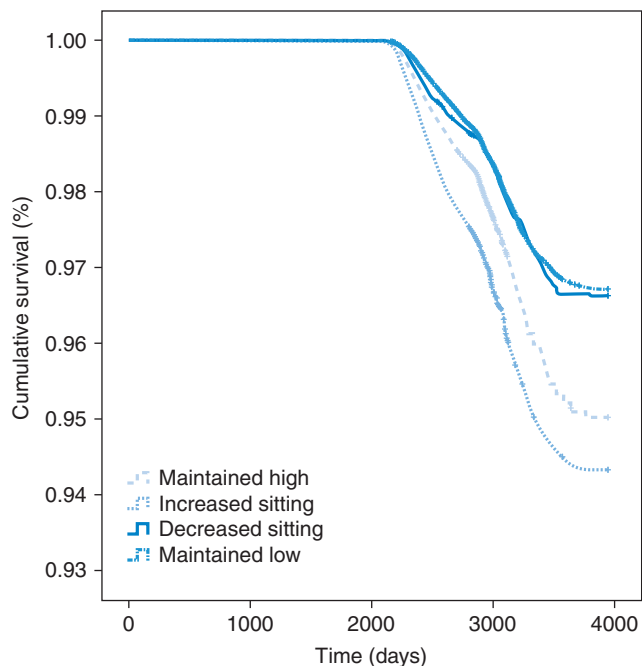


Fig. 2 Probability of survival according to changes in sitting time.

Limitations of this study

This study had several strengths and limitations that warrant discussion. First, because the baseline (but not year six) questionnaires included information on alcohol history, general health and physical functioning score, an absolute comparison between the two time points was difficult to assess. We attempted to address this by substituting the variable at year six that most closely approximated the variable used at baseline. Most notably, because BMI was collected at baseline but was not available at year six, we adjusted our analyses by weight instead of BMI. Further, sedentary behaviour is an umbrella term that has been operationalized with a wide range of activities that include 'screen time', commuting and even lying down.¹⁰ For the purposes of our study, we strictly investigated sedentary behaviour in the reclining position, meaning that 'sitting time' may not be reflective of overall sedentary behaviours. Owing to a lack of standardization, comparison of sedentary time across studies is challenging, as individual behaviour may vary (i.e. different sit-stand behaviours, twitching, dietary habits, etc.). Furthermore, as is typical of a large epidemiological cohort, physical activity was based on self-report and only captured leisure-time physical activity, potentially underestimating the true relationship between sitting time and mortality. Finally, owing to the observational nature of the data, no cause and effect can be inferred, as an individual's inclination to sit may be influenced by health- and

Table 3 Risk of all-cause, CVD and cancer mortality based on change in total daily sitting time

	Change in sitting time from baseline to follow-up			
	Maintained high sitting	Increased sitting	Decreased sitting	Maintained low sitting
All-cause mortality				
Deaths	249 (3.0)	266 (3.9)	234 (2.1)	1106 (2.1)
Age-adjusted HR	1.00 (ref)	0.98 (0.83–1.18)	0.65 (0.54–0.77)	0.53 (0.46–0.61)
Fully adjusted HR	1.00 (ref)	0.79 (0.58–1.07)	0.71 (0.54–0.95)	0.49 (0.39–0.63)
CVD mortality				
Deaths	59 (0.7)	75 (1.1)	56 (0.5)	303 (0.6)
Age-adjusted HR	1.00 (ref)	1.09 (0.77–1.53)	0.66 (0.45–0.94)	0.57 (0.44–0.76)
Fully adjusted HR	1.00 (ref)	1.24 (0.85–1.81)	0.84 (0.56–1.26)	0.76 (0.55–1.06)
Cancer mortality				
Deaths	107 (1.3)	93 (1.4)	112 (1.0)	424 (0.8)
Age-adjusted HR	1.00 (ref)	0.88 (0.67–1.17)	0.73 (0.56–0.95)	0.51 (0.41–0.63)
Fully adjusted HR	1.00 (ref)	0.82 (0.61–1.09)	0.73 (0.55–0.97)	0.52 (0.42–0.66)

95% confidence intervals are presented within parentheses. Significant values are highlighted in bold. *N* % for deaths. *P*-values for linear trend across change in sitting groups were <0.0001 except for all-adjusted CVD mortality *P* = 0.0033. All adjusted hazard models controlled for age (continuous), current weight, education, current employment status, ethnicity, leisure-time physical activity, current smoking status, alcohol consumption in last 3 months, new treatment for diabetes, new onset of congestive heart failure and/or angina and incidence of at least one fracture, or broken bone of the hip, foot, pelvis, knee, upper leg, lower leg or tailbone and all at follow-up.

CVD, cardiovascular disease; HR, hazard ratio.

Table 4 Effect modification of the risk of all-cause mortality based on change in total daily sitting time

	Change in sitting time from baseline to follow-up				Interaction P-value ^a
	Maintained high sitting	Increased sitting	Decreased sitting	Maintained low sitting	
Age					0.488
50–59	1.00 (ref)	0.93 (0.43–2.01)	0.76 (0.40–1.49)	0.68 (0.39–1.19)	
60–69	1.00 (ref)	1.01 (0.69–1.45)	0.80 (0.57–1.12)	0.64 (0.48–0.84)	
70–79	1.00 (ref)	0.92 (0.70–1.21)	0.58 (0.43–0.78)	0.61 (0.49–0.76)	
80–89	1.00 (ref)	1.13 (0.75–1.68)	0.94 (0.60–1.46)	0.59 (0.42–0.84)	
Leisure-time physical activity ^b					0.398
Does not meet guidelines	1.00 (ref)	0.98 (0.80–1.22)	0.67 (0.54–0.85)	0.57 (0.48–0.69)	
Meets guidelines	1.00 (ref)	0.85 (0.57–1.28)	0.74 (0.51–1.07)	0.62 (0.46–0.84)	
Smoking now					0.067
No	1.00 (ref)	0.96 (0.79–1.16)	0.66 (0.54–0.81)	0.57 (0.49–0.67)	
Yes	1.00 (ref)	1.00 (0.49–2.07)	1.28 (0.65–2.53)	0.99 (0.56–1.77)	
Treated for diabetes					0.003
No	1.00 (ref)	0.96 (0.78–1.17)	0.66 (0.54–0.82)	0.55 (0.47–0.65)	
Yes	1.00 (ref)	0.93 (0.58–1.49)	0.86 (0.53–1.39)	0.92 (0.63–1.33)	
New injuries ^c					0.663
No	1.00 (ref)	0.96 (0.77–1.20)	0.65 (0.52–0.81)	0.58 (0.49–0.70)	
Yes	1.00 (ref)	0.96 (0.68–1.35)	0.84 (0.59–1.21)	0.63 (0.53–0.84)	
Congestive heart failure					0.805
No	1.00 (ref)	1.02 (0.84–1.24)	0.68 (0.56–0.84)	0.61 (0.52–0.71)	
Yes	1.00 (ref)	0.65 (0.38–1.13)	0.78 (0.44–1.37)	0.53 (0.34–0.82)	

95% confidence intervals are presented within parentheses. Significant values are highlighted in bold. Adjusted for same covariates as Table 4, except for the variable of stratification.

^aInteraction P-value calculated by including product term (change in sitting time × effect modifier of interest) into model.

^bMeeting leisure-time physical activity guidelines equates to a minimum of 500 min per week to reap health benefits. MET, metabolic equivalent of task.

^cDefined as incidence of at least one fracture or broken bone of the hip, foot, pelvis, knee, upper leg, lower leg or tailbone.

non-health-related risk factors (i.e. retirement), only some of which were accounted for here. To illustrate, it is possible that some WHI participants were retired for the duration of the study. Retirement is a critical transition period for many health behaviours, mostly favouring an increase in leisure-time physical activity but also paralleled by a greater increase in sedentary pursuits.³⁶ Nonetheless, in the absence of any randomized control evidence, our analysis provides further support for Hill's cause and effect criteria as it relates to the components of 'dose–response' (in baseline), 'consistency' (by subgroup) and 'temporality' (in change analyses).

Conclusions

The implications of our study are 2-fold. First, consistent with previous research,^{17,29,30,32} our baseline analysis revealed a dose–response relationship between sitting time and mortality. Second, our change analysis suggests that the maintenance of minimal sitting time, as well as the short-term reduction in sitting

time, is beneficial for survival among middle-aged and older women who are prone to high rates of physical inactivity and sedentary time. Future analyses in other sociodemographic groups with additional assessments of change are necessary to confirm these findings in the presence of other major lifestyle factors.

Authors' contributions

Data were acquired by J.L.K. and C.I.A., and study was conceived by J.L. and C.I.A. J.L. performed the statistical analysis and drafted the manuscript. J.L., J.L.K. and C.I.A. interpreted the results and critically reviewed and edited the manuscript. All authors read and approved the final manuscript.

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References

- Go AS, Mozaffarian D, Roger VL *et al.* Heart disease and stroke statistics—2013 update: a report from the American Heart Association. *Circulation* 2013;**127**:e6–245.
- Matthews CE, Chen KY, Freedson PS *et al.* Amount of time spent in sedentary behaviors in the United States, 2003–2004. *Am J Epidemiol* 2008;**167**:875–81.
- Bijnen FC, Feskens EJ, Caspersen CJ *et al.* Baseline and previous physical activity in relation to mortality in elderly men: the Zutphen Elderly Study. *Am J Epidemiol* 1999;**150**:1289–96.
- Bulwer BE. Sedentary lifestyles, physical activity, and cardiovascular disease: from research to practice. *Crit Pathw Cardiol* 2004;**3**:184–93.
- Church TS, Martin CK, Thompson AM *et al.* Changes in weight, waist circumference and compensatory responses with different doses of exercise among sedentary, overweight postmenopausal women. *PLoS ONE* 2009;**4**:e4515.
- Lynch BM, Boyle T. Distinguishing sedentary from inactive: implications for meta-analyses. *Br J Cancer* 2014. doi:10.1038/bjc.2014.106.
- Paffenbarger RS, Hyde RT, Wing AL *et al.* Physical activity, all-cause mortality, and longevity of college alumni. *N Engl J Med* 1986;**314**:605–13.
- Sims ST, Larson JC, Lamonte MJ *et al.* Physical activity and body mass: changes in younger versus older postmenopausal women. *Med Sci Sports Exerc* 2012;**44**:89–97.
- Tremblay MS, Colley RC, Saunders TJ *et al.* Physiological and health implications of a sedentary lifestyle. *Appl Physiol Nutr Metab* 2010;**35**:725–40.
- Pate RR, O'Neill JR, Lobelo F. The evolving definition of 'sedentary'. *Exerc Sport Sci Rev* 2008;**36**:173–8.
- Owen N, Healy GN, Matthews CE *et al.* Too much sitting: the population health science of sedentary behavior. *Exerc Sport Sci Rev* 2010;**38**:105–13.
- Sedentary Behaviour Research Network. Letter to the editor: standardized use of the terms 'sedentary' and 'sedentary behaviours'. *Appl Physiol Nutr Metab* 2012;**37**:540–2.
- Hu FB, Li TY, Colditz GA *et al.* Television watching and other sedentary behaviors in relation to risk of obesity and type 2 diabetes mellitus in women. *JAMA* 2003;**289**:1785–91.
- Bankoski A, Harris TB, McClain JJ *et al.* Sedentary activity associated with metabolic syndrome independent of physical activity. *Diabetes Care* 2011;**34**:497–503.
- Cohen SS, Matthews CE, Bradshaw PT *et al.* Sedentary behavior, physical activity, and likelihood of breast cancer among Black and White women: a report from the Southern Community Cohort Study. *Cancer Prev Res (Phila)* 2013;**6**:566–76.
- Chomistek AK, Manson JE, Stefanick ML *et al.* Relationship of sedentary behavior and physical activity to incident cardiovascular disease: results from the Women's Health Initiative. *J Am Coll Cardiol* 2013;**61**:2346–54.
- Katzmarzyk PT, Church TS, Craig CL *et al.* Sitting time and mortality from all causes, cardiovascular disease, and cancer. *Med Sci Sports Exerc* 2009;**41**:998–1005.
- Patel AV, Bernstein L, Deka A *et al.* Leisure time spent sitting in relation to total mortality in a prospective cohort of US adults. *Am J Epidemiol* 2010;**172**:419–29.
- León-Muñoz LM, Martínez-Gómez D, Balboa-Castillo T *et al.* Continued sedentariness, change in sitting time, and mortality in older adults. *Med Sci Sports Exerc* 2013;**45**:1501–7.
- Gregg EW, Cauley JA, Stone K *et al.* Relationship of changes in physical activity and mortality among older women. *JAMA* 2003;**289**:2379–86.
- Steffen-Batey L, Nichaman MZ, Goff DC Jr *et al.* Change in level of physical activity and risk of all-cause mortality or reinfarction: The Corpus Christi Heart Project. *Circulation* 2000;**102**:2204–9.
- Warren TY, Barry V, Hooker SP *et al.* Sedentary behaviors increase risk of cardiovascular disease mortality in men. *Med Sci Sports Exerc* 2010;**42**:879–85.
- Hill AB. The environment and disease: association or causation? *Proc R Soc Med* 1965;**58**:295–300.
- Paffenbarger RS, Hyde RT, Wing AL *et al.* The association of changes in physical-activity level and other lifestyle characteristics with mortality among men. *N Engl J Med* 1993;**328**:538–45.
- Picavet HSJ, Wendel-vos GCW, Vreken HL *et al.* How stable are physical activity habits among adults? The Doetinchem Cohort Study. *Med Sci Sports Exerc* 2011;**43**:74–9.
- Schnohr P, Scharling H, Jensen JS. Changes in leisure-time physical activity and risk of death: an observational study of 7000 men and women. *Am J Epidemiol* 2003;**158**:639–44.
- The Women's Health Initiative Study Group. Design of the Women's Health Initiative clinical trial and observational study. *Control Clin Trials* 1998;**19**:61–109.
- Hays J, Hunt JR, Hubbell FA *et al.* The Women's Health Initiative recruitment methods and results. *Ann Epidemiol* 2003;**13**:S18–77.
- Koster A, Caserotti P, Patel KV *et al.* Association of sedentary time with mortality independent of moderate to vigorous physical activity. *PLoS ONE* 2012;**7**:e37696.
- Seguin R, Buchner DM, Liu J *et al.* Sedentary behavior and mortality in older women: the Women's Health Initiative. *Am J Prev Med* 2014;**46**:122–35.
- Curb JD, McTiernan A, Heckbert SR *et al.* Outcomes ascertainment and adjudication methods in the Women's Health Initiative. *Ann Epidemiol* 2003;**13**:S122–8.
- Pavey TG, Peeters GG, Brown WJ. Sitting-time and 9-year all-cause mortality in older women. *Br J Sports Med* 2012. doi:10.1136/bjsports-2012-091676.
- Schmid D, Leitzmann MF. Television viewing and time spent sedentary in relation to cancer risk: a meta-analysis. *J Natl Cancer Inst* 2014;**106**:dju098.
- Shen D, Mao W, Liu T *et al.* Sedentary behavior and incident cancer: a meta-analysis of prospective studies. *PLoS ONE* 2014;**9**:e105709.

- 35 Van der Ploeg HP, Chey T, Korda RJ *et al.* Sitting time and all-cause mortality risk in 222 497 Australian adults. *Arch Intern Med* 2012;**172**:494–500.
- 36 Menai M, Fezeu L, Charreire H *et al.* Changes in sedentary behaviours and associations with physical activity through retirement: a 6-year longitudinal study. *PLoS ONE* 2014;**9**:e106850.