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The Relationship of Sedentary Behavior and Physical Activity to Incident Cardiovascular Disease: Results from the Women's Health Initiative

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Abstract

Objectives—The aim was to examine the independent and joint associations of sitting time and physical activity with risk of incident cardiovascular disease (CVD).

Background—Sedentary behavior is recognized as a distinct construct beyond lack of leisure-time physical activity, but limited data exists on the interrelationship between these two components of energy balance.

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Methods—Participants in the prospective Women's Health Initiative Observational Study (N = 71,018), aged 50–79 and free of CVD at baseline (1993–1998), provided information on sedentary behavior, defined as hours of sitting per day, and usual physical activity at baseline and during follow-up through September 2010. First CVD (coronary heart disease or stroke) events were centrally adjudicated.

Results—Sitting ≥ 10 hours/day compared to ≤ 5 hours/day was associated with increased CVD risk (HR=1.18, 95% CI 1.09, 1.29) in multivariable models including physical activity. Low physical activity was also associated with higher CVD risk (P, trend <0.001). When women were cross-classified by sitting time and physical activity (P, interaction = 0.94), CVD risk was highest in inactive women (≤1.7 MET-hrs/week) who also reported ≥10 hrs/day of sitting. Results were similar for CHD and stroke when examined separately. Associations between prolonged sitting and risk of CVD were stronger in overweight versus normal weight women and women aged 70 years and older compared to younger women.

Conclusions—Prolonged sitting time was associated with increased CVD risk, independent of leisure-time physical activity, in postmenopausal women without a history of CVD. A combination of low physical activity and prolonged sitting augments CVD risk.

Keywords

cardiovascular disease; women; physical activity; sedentary behavior

INTRODUCTION

Lack of leisure-time physical activity is a major risk factor for coronary heart disease (CHD), stroke, and increased cardiovascular mortality (1 – 4). Humans are spending increasingly more time in sedentary behaviors and this global trend is likely to continue, given the increasing availability and popularity of personal computers and television, automation of chores at home, increase in sedentary occupations, and transportation trends (5 – 6). Time spent in sedentary behavior displaces time spent in higher-intensity activities, for example activities of daily living, contributing to an overall reduction in total energy expenditure (7).

Emerging evidence suggests that sedentary behavior has independent effects on human metabolism, physical function, and potentially on health outcomes from low leisure-time physical activity. Sedentary behavior defined in various ways (e.g. sitting, T.V. watching, energy expenditure of 1.0–1.5 METs) has been associated with increased risk of obesity, metabolic syndrome, type 2 diabetes and cardiovascular disease (CVD) mortality, suggesting that it be treated as a construct distinct from physical activity (8 – 9). Thus, even among individuals who meet current physical activity guidelines, excessive sedentary behavior may have adverse metabolic and prognostic implications, particularly in older adults (10).

Sitting, a unique aspect of human behavior, may not simply represent the extreme low end of the physical activity continuum (7). We previously reported that both low levels of recreational physical activity and higher sitting time were associated with elevated CVD risk in the Women's Health Initiative Observational Study (WHI-OS) (4). However, the independent and joint associations of sedentary time and physical activity with CVD events were not reported. We now extend follow-up of the cohort for an additional 10 years, update sitting and activity variables during follow-up, and examine the interrelationship of sitting time and physical activity in detail. Thus, the purpose of this study was to examine the independent and joint associations of sedentary time and physical activity with risk of incident CVD in older women. Given the limited data available on this subject, the WHI-OS affords an excellent opportunity to elucidate the complex interplay of these two separate components of energy balance.

METHODS

Study Population

The multiethnic Women's Health Initiative Observational Study (WHI-OS) cohort of 93,676 postmenopausal women, aged 50 – 79 years at study entry, was enrolled between 1994 and 1998 across 40 U.S. clinical centers. Details of the scientific rationale, study design, eligibility requirements, and baseline characteristics of the cohort have been previously published (11). Exclusion criteria included the presence of any medical condition associated with predicted survival of less than three years (e.g., class IV congestive heart failure, obstructive lung disease requiring supplemental oxygen, or severe chronic liver or kidney disease), alcoholism, mental illness, or dementia. Additional exclusions for the current analysis included history of CVD or cancer at baseline; reporting an inability to walk at least one block; or missing sedentary time or physical activity data, leaving 71,018 women for these analyses.

Exposure Assessment

Each WHI-OS participant had a baseline clinic visit at which she completed self-administered questionnaires related to medical history, physical activity, smoking, diet, and other lifestyle-related factors and had her height, weight, waist and hip circumferences, and blood pressure measured. Additionally, participants completed periodic health forms and repeated baseline clinic assessments three years after enrollment. All women provided written informed consent, and the study protocol was approved by the institutional review board of each center.

Sedentary behavior was assessed by questionnaire at baseline and twice during follow-up using the following question: "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." Eight categories were provided for the response, ranging from less than 4 hours per day to 16 or more hours per day.

Leisure-time physical activity was assessed at baseline and during follow-up by a detailed questionnaire on walking, including the frequency of walks outside the home, average duration, and pace of each walk, and other types of activity (strenuous, moderate, and mild), including the frequency (days per week) and duration of each type. Examples of strenuous activities, defined as activities that result in increased heart rate and sweating, were aerobics, aerobic dancing, jogging, tennis, and swimming laps. Examples of moderate activity included biking outdoors, using an exercise machine (such as a stationary bicycle or a treadmill), calisthenics, easy swimming, and popular or folk dancing. Examples of mild exercise were slow dancing, bowling, and golf. Each type of activity was assigned a metabolic equivalent task (MET) score based on its energy cost (12) and physical activity-related energy expenditure (MET-hr/wk) was computed as the summed product of frequency, duration, and intensity.

Ascertainment of End Points

The primary endpoints for this analysis were incident coronary heart disease (CHD), including nonfatal myocardial infarction (MI) and fatal CHD, and stroke. These endpoints were also combined to examine the associations of sedentary behavior and physical activity with incident CVD. Outcomes were identified on the basis of annual mailed questionnaires (response rates > 95%), with permission to obtain and review medical records. Physicians blinded to exposure data confirmed self-reported diagnoses.

Nonfatal MI was confirmed according to standardized criteria of diagnostic ECG changes, elevated cardiac enzymes, or both (13). Stroke was confirmed by diagnosis of a typical neurological defect of sudden or rapid onset lasting ≥ 24 hours or until death attributed to a cerebrovascular event. Fatal CHD was confirmed by documentation in hospital or autopsy records or if coronary disease was listed as the cause of death on death certificates and evidence of previous coronary disease was available.

Statistical Analysis

All analyses were performed using SAS statistical software, version 9.3 (SAS Institute Inc, Cary, North Carolina). Eligible participants contributed person-time from return of baseline questionnaires to the first diagnosis of CVD, death from any cause, loss to follow-up, or September 2010.

Baseline descriptive characteristics were compared according to categories of sitting time and physical activity using linear models. For each baseline covariate, medians of sitting time or physical activity categories were modeled as a function of the covariate of interest, adjusted for age, with the P-value from the resulting type 3 test used to determine statistical significance for the covariate presented.

Cox proportional hazards models were used to estimate hazards ratios (HR) and 95% confidence intervals (CI) for outcomes. Given the strong association between age and CVD, all models were stratified on age in years using the STRATA statement for PHREG in SAS. Tests for linear trend were computed by using the medians for categories modeled as an ordinal variable. Statistical significance was defined as $p < 0.05$. The possibility of non-linear relations between sitting time, physical activity, and CVD were examined non-parametrically with restricted cubic splines (14). Tests for non-linearity used the likelihood ratio test, comparing the model with only the linear term to the model with linear and cubic spline terms.

To assess independent associations of sitting time and physical activity with CVD risk, both exposures were included simultaneously in the model. Simple updated levels of sitting time and physical activity, in which outcomes were predicted from the most recent questionnaire, were used. For example, events that occurred between baseline and year 3 of follow-up were examined in relation to exposures reported on the baseline questionnaire, events occurring between year 3 and year 6 of follow-up were examined in relation to exposures reported on the year 3 questionnaire, and so forth. Sitting time and physical activity were first examined as categorical variables and then as a continuous variables to show the impact on outcomes per 1-unit increment of each exposure. Sitting was categorized as ≤ 5, 5.1–9.9, and ≥ 10 hours per day, which were approximate tertiles based on distribution of the data. For physical activity, women were classified into four categories: inactive (≤ 1.7 MET-hrs/wk), low (1.8 – 8.3 MET-hrs/wk), medium (8.4 – 20 MET-hrs/wk), and high activity (> 20 MET-hrs/wk), with accumulating 150 min/week of moderate-intensity exercise, i.e. the minimum dose of activity recommended by the federal government (15), being equivalent to at least 8.4 MET-hrs/wk of exercise. To assess the joint association of sitting time and physical activity with risk of CVD, participants were cross-classified into 12 groups according to the levels of sitting time and physical activity. The interaction was assessed by the difference in −2 log likelihood between the model containing the cross-classified sitting time-physical activity variables and the main effects model.

All multivariable models were stratified by age in years and included the following covariates: race/ethnic group, family income, education, marital status, smoking, parental history of premature MI, depression, alcohol intake, hours of sleep, intake of total calories, saturated fat, and fiber. Covariates that were reassessed during follow-up were updated over time using the most recent value. Secondary analyses were additionally adjusted for history of hypertension, diabetes, high cholesterol levels, and body mass index (BMI).

Whether associations between sedentary time and CVD were modified by BMI (< 25 vs. ≥ 25 kg/m^2), age (< 70 vs. ≥ 70 years), or employment status (employed vs. unemployed) was also examined. Interactions were tested by examining the difference in −2 log likelihood between the model containing interactions with the potential effect modifiers and the main effects model.

As a secondary analysis, the association between change in sitting time and CVD risk was examined. Change in sitting time between baseline and year 3 was used to examine events that occurred between year 3 and year 6 of follow-up; change in sitting time between year 3 and year 6 was used to examine events that occurred from year 6 on. Change in sitting time was examined as a continuous variable and using the following categories: decreased sitting by more than 2 hours/day, no change, and increased sitting by more than 2 hours/day.

RESULTS

During a median follow-up of 12.2 years (interquartile range: 8.7 – 14.0 years), 2411 incident cases of CHD, 2050 incident strokes, and 4235 first CVD events were documented. Baseline sitting time and physical activity in relation to other potential risk factors for CVD are presented in Table 1. Women who reported ≥ 10 hours/day of sitting were more likely to be White, to have attended college, and to have a higher income compared to women who reported ≤ 5 hours/day of sitting; whereas, the opposite was true of women reporting less physical activity compared to highly active women. Additionally, greater time spent sitting and less physical activity were positively associated with current smoking, higher BMI, and self-reported depression (Table 1).

In multivariable-adjusted analyses, increased sitting time and decreased physical activity were positively associated with risk of CHD and stroke (Table 2). As the results for CHD and stroke were similar, the end points were combined to examine total CVD. In multivariable models that included physical activity, the hazard ratio (HR) for total CVD comparing ≥ 10 hours/day of sitting time to ≤ 5 hours/day was 1.18 (95% CI 1.09, 1.29) (P for trend < 0.001). With high physical activity, i.e. > 20 MET-hrs/wk, as the reference group, the CVD risks for medium (8.4 – 20 MET-hrs/wk), low (1.8 – 8.3 MET-hrs/wk) activity, and inactive (≤ 1.7 MET-hrs/wk) groups were 1.16 (1.06, 1.27), 1.30 (1.18, 1.42), and 1.47 (1.33, 1.62), respectively (P for trend <0.001). All associations were mildly attenuated after adjustment for BMI and history of comorbidities, but remained statistically significant (Table 2). When examined as continuous variables, each hour/day of sitting time was associated with 2% higher risk of CVD (HR = 1.02, 95% CI 1.01, 1.03) and each MET-hour/week of physical activity with a 1% lower risk of CVD (HR = 0.990, 95% CI 0.987, 0.992). There was no evidence of non-linearity when applying restricted cubic splines to the association between sitting time (p= 0.87) or physical activity (p = 0.60) and risk of CVD.

When participants were cross-classified based on both sitting time and leisure-time physical activity, only 18% of the high activity group reported sitting for ≥ 10 hours/day compared to 32% of physically inactive group. Except in the most active women, more time spent sitting increased CVD risk in each physical activity group (Figure 1), with CVD risk being highest in physically inactive women who also reported ≥ 10 hrs/day of sitting (HR = 1.63, 95% CI

= 1.39, 1.90); however, the interaction between sitting time and physical activity was not statistically significant (P for interaction = 0.94).

There were significant interactions of sitting time with CVD risk within subgroups defined by BMI and age, but not by employment status (Figure 2; P for interaction=0.044, 0.026, and 0.22, respectively). Time spent sitting was associated with increased CVD risk in women with BMI ≥ 25 (HR = 1.26, 95% CI 1.13, 1.40 for sitting ≥ 10 hrs/day; P for trend <0.001), but not in women with BMI < 25 (HR = 1.02, 95% CI 0.88, 1.19; P for trend = 0.85). Sitting time was also associated with a higher CVD risk among women aged 70 years and older (HR = 1.22, 95% CI 1.09, 1.36 for sitting ≥ 10 hrs/day; P for trend <0.001), but not among younger women (HR = 1.08, 95% CI 0.94, 1.25; P for trend = 0.23). Although the interaction was not statistically significant (P for interaction = 0.22), more sitting time was associated with higher CVD risk in unemployed women (HR = 1.21, 95% CI 1.10, 1.34; P for trend <0.001), but not employed women (HR = 1.07, 95% CI 0.89, 1.30; P for trend = 0.36).

Finally, an increase in sitting time over a three year period was associated with an increased risk of CVD. Compared to participants who reported no change in sitting time, the HR for participants who increased sitting time by more than 2 hours/day was 1.18 (95% CI 1.07, 1.31) after adjusting for covariates, while the HR for participants who decreased sitting time by more than 2 hours/day was 1.01 (95% CI 0.91, 1.13). When examined continuously, a 1 hour/day increase in sitting time over a three-year period was associated with a 1.4% increase in CVD risk (HR = 1.014, 95% CI, 1.001, 1.027, p = 0.03) in the multivariable-adjusted model.

DISCUSSION

In this large, prospective study of postmenopausal U.S. women, prolonged sitting time was associated with increased risk of incident CHD, stroke, and total CVD, independent of leisure-time physical activity; however, low levels of leisure-time physical activity were also strongly associated with increased CVD risk, after adjusting for sitting time. Women who were physically inactive and reported ≥ 10 hours per day of sitting time, comprising 6% of our study population, were at 63% greater CVD risk than highly active women who reported sitting ≤ 5 hours per day, after adjusting for several cardiovascular risk factors. Associations between prolonged sitting and risk of CVD were stronger in overweight and obese versus normal weight women and women aged 70 years and older compared to younger women.

Few studies have examined the association between sitting time and risk of incident cardiovascular disease; to date, the outcome of interest has been largely limited to CVD mortality (4, 10, 16 – 18). Thus, the current analysis, which includes incident CHD and stroke separately in relationship to sitting time and physical activity habits within a large well-characterized cohort of older postmenopausal women, as well as combined CVD events, is an important contribution to the literature. Our results are also consistent with prior studies which have reported an increased risk of CVD mortality as time spent sitting increases, independent of usual leisure-time physical activity.

The association between physical activity, hours spent sitting, and CVD has been previously reported among WHI-OS participants (4). Manson and colleagues reported that high levels of recreational physical activity were associated with 30–40% reductions in CVD risk over a mean 3.2 years of follow-up; and, using baseline measures of sitting time, women who spent at least 16 hours per day sitting had an increased CVD risk (HR=1.68, 95% CI 1.07, 2.64), compared to those who spent less than 4 hours per day sitting. The joint effects of sitting time and physical activity were not reported in this previous study.

Although the interaction between sitting time and physical activity was not statistically significant in the present analysis, clinically significant attenuation of CVD risk was found in all women, except for those in the high activity group, who reported sitting less than 5 hours per day. As the least active women were also the most likely to report prolonged time spent sitting, reducing sitting time could potentially reduce CVD risk substantially among less active women. The finding that the association between prolonged sitting and CVD is attenuated among the most active women is similar to studies of mortality (16, 18) and shows that it may be beneficial to participate in regular exercise despite engaging in other potentially detrimental behaviors, like prolonged sitting. The most active group in our study reported > 20 MET-hrs/week of physical activity, which exceeds the physical activity guidelines substantially. However, women engaging in 8.4 – 20 MET-hrs/wk of physical activity, which meets the physical activity guidelines, were still at increased CVD risk if they reported prolonged sitting.

The association between prolonged sitting time and increased CVD risk was significant only in overweight women and women 70 years and older. Previous studies (16, 18) have reported similar results where the positive association between time spent sitting and mortality was stronger in overweight and obese versus normal weight individuals. These findings emphasize the importance of limiting time spent sitting, particularly in overweight and obese individuals. The fact that the association between sitting time and CVD was stronger in older compared to younger women may be due to sitting time including both occupational and leisure sitting in this study. Thus, in older women, sitting may comprise more television watching as they are more likely to be retired compared to younger women. Television watching has previously been found to be more detrimental than overall sitting time (10).

Additionally, increasing sitting time over a three-year period was associated with a higher risk of CVD. Reducing time spent sitting, however, was not associated with CVD risk in this study. This finding may indicate that change in sitting time needs to be assessed over a longer period of time. Alternatively, a better measurement of sitting time, like accelerometers, or a randomized controlled trial may be necessary to truly examine the effect of changing sedentary behaviors.

Physiological responses associated with prolonged sitting, such as suppression of skeletal muscle lipoprotein lipase (LPL) activity, which is necessary for triglyceride uptake and high-density lipoprotein cholesterol production, and reduced glucose uptake (9, 18, 19) might explain the independent effect of sedentary behavior on CVD risk factors, and also on CVD risk. Sedentary behavior may also be related to overweight and obesity through increased energy intake and decreased energy expenditure (20).

In addition to reducing sitting time, taking breaks during prolonged periods of sitting, i.e. by standing up and taking short walks, might be beneficial in lowering CVD risk. In accelerometer studies, having a higher number of breaks in sedentary time was inversely associated with waist circumference, BMI, triglycerides, 2-h plasma glucose, and C-reactive protein independent of total time spent sitting and physical activity (21, 22). Additionally, a recent randomized trial showed that interrupting sitting time with short bouts of light- or moderate-intensity activity lowers postprandial glucose and insulin levels in overweight adults (23).

Strengths of our study include its prospective design, the large, multi-ethnic, geographically diverse cohort of postmenopausal women, detailed assessment of physical activity, and availability of several relevant covariates for analysis. Additionally, this study is the first to investigate the association with CVD using serially obtained measurements of sitting time and physical activity, thereby enabling us to update exposure status during follow-up. We were also able to assess the independent associations between sitting time and usual recreational physical activity with CVD risk.

Our study also has several limitations, including the fact that analyses were limited to postmenopausal women; therefore, findings cannot necessarily be generalized to men or younger women. Sitting time and physical activity were self-reported, although it is worth noting that physical activity measures were validated in this cohort (11, 24). Moreover, measurement error is unlikely to bias our results because sedentary time and physical activity were assessed prospectively so any reporting errors would be non-differential with respect to subsequent disease status. Nonetheless, device-based measures of sitting time and physical activity, like accelerometers, may provide more accurate assessments of these variables. Another limitation of this study is that we were unable to examine the associations with different types of sedentary behavior, like television watching or transportation, as the questionnaire only assessed total sitting time. Finally, as with most such studies, the possibility of residual confounding by other lifestyle and behavioral factors must be considered.

In conclusion, the findings from this large, multi-ethnic group of postmenopausal women indicate that prolonged sitting time significantly increases risk of CVD, independent of leisure-time physical activity. Given the projected population growth of U.S. women 65 years of age and older, and the relatively high prevalence of physical inactivity, the present findings have important public health implications. Reducing sitting time among older women who are less active could potentially reduce risk of CHD and stroke, major causes of morbidity in older women. Moreover, for individuals who are unable, or averse, to exercise, amount of time spent sitting may be more amenable to change than increasing levels of physical activity.

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ABBREVIATIONS

BMI	body mass index
CHD	coronary heart disease
CVD	cardiovascular disease
CI	confidence interval
HR	hazard ratio
MET	metabolic equivalent task
MI	myocardial infarction

OS	observational study
WHI	Women's Health Initiative

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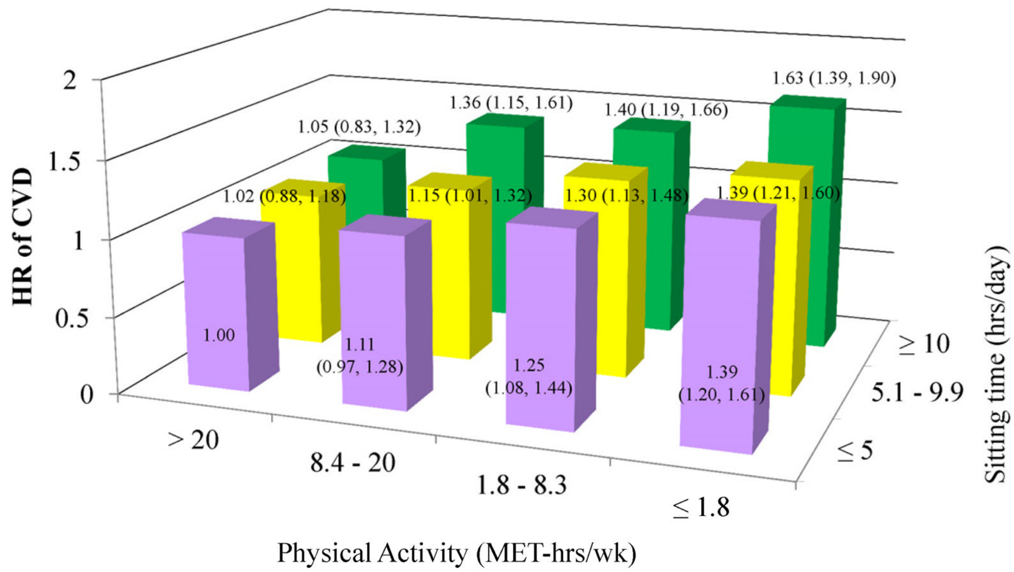

Figure 1. Multivariable-adjusted hazard ratios for total cardiovascular disease for the joint association between sedentary time and physical activity

The multivariable model was stratified by age and includes race, education, income, marital status, smoking, family history of myocardial infarction, depression, alcohol intake, hours of sleep, intake of total calories, saturated fat, fiber, and body mass index. The P for interaction is 0.94. HR = hazard ratio; CVD = cardiovascular disease; MET = metabolic equivalent task.

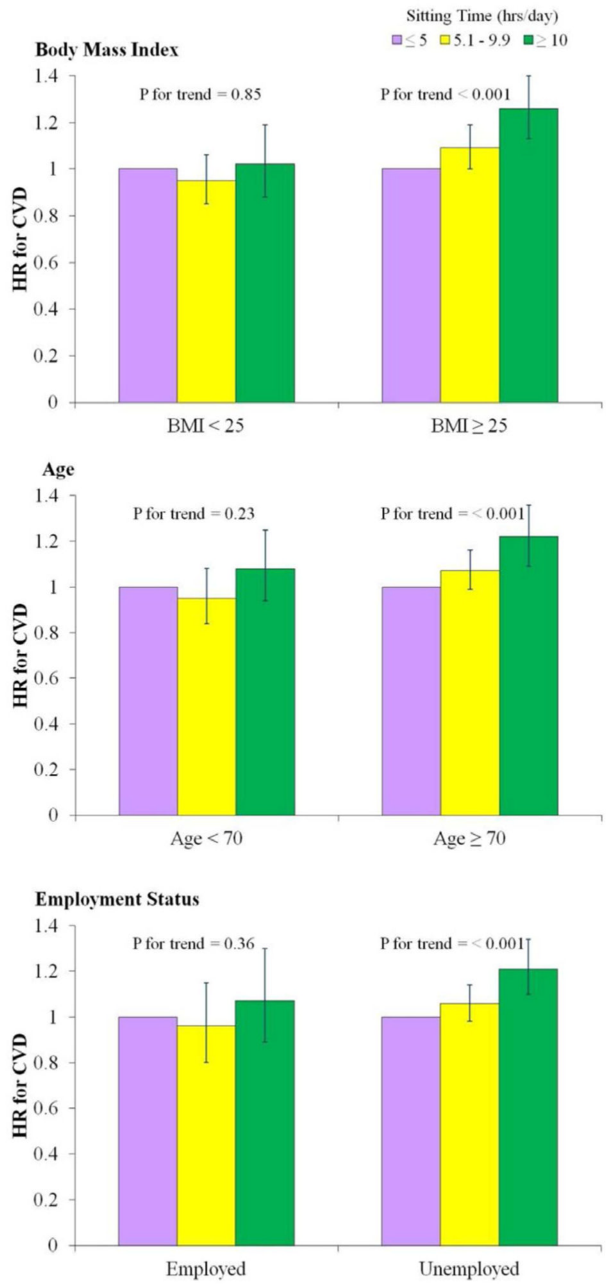

Figure 2. Multivariable-adjusted hazard ratios for total cardiovascular disease according to sedentary time in subgroups defined by body mass index (BMI), age, and employment status

The multivariable model was stratified by age and includes physical activity, race, education, income, marital status, smoking, family history of myocardial infarction, depression, alcohol intake, hours of sleep, intake of total calories, saturated fat, fiber. The P for interaction for BMI is 0.04, age is 0.03, and employment is 0.22. HR = hazard ratio; CVD = cardiovascular disease; BMI = body mass index.

Table 1

Age-standardized baseline characteristics* of participants in the Women's Health Initiative Observational Study according to categories of sitting time and physical activity.

	Sitting Time (hrs/day)				Physical Activity (MET-hrs/week)				
	≤ 5	5.1 – 9.9	≥10	P-value	High (> 20)	Medium (8.4 – 20)	Low (1.8 – 8.3)	Inactive (≤ 1.7)	P-value
N	24,691	28,953	17,374		18,205	21,653	18,299	12,861	
Age, years	63.8 (7.1)	63.7 (7.2)	60.9 (7.2)	<.001	62.8 (7.2)	63.2 (7.2)	63.2 (7.3)	62.7 (7.4)	0.09
Sitting time, hrs/day	3.7 (1.2)	7.4 (1.0)	11.9 (1.7)	------	6.5 (3.1)	7.2 (3.2)	7.5 (3.4)	7.8 (3.6)	<.001
Physical activity, MET-hrs/wk	16.4 (16.4)	14.1 (14.0)	11.1 (12.0)	<.001	33.9 (14.1)	13.6 (3.3)	4.9 (1.9)	0.3 (0.5)	------
Race/Ethnicity, %				<.001					<.001
White	80	86	85		87	86	82	78	
African American	9	7	7		6	6	8	11	
Hispanic/Latino	6	3	2		3	3	4	5	
Other	5	5	5		5	4	5	5	
Smoking Status, %				<.001					<.001
Current	6	6	7		4	5	7	10	
Former	40	42	45		47	43	39	38	
Never	54	52	48		49	52	54	53	
Marital Status, %				<.001					<.001
Married	68	65	55		66	65	62	61	
Single, Divorced, Widowed	32	35	45		33.4	35.0	38	39	
Education Level, %				<.001					<.001
High school or less	24	19	17		14	17	23	30	
Vocational training	11	9	8		8	9	10	11	
College	65	72	75		78	74	67	59	
Income, %				<.001					<.001
<$20,000	17	13	12		10	12	16	20	
$20,000–$74,999	62	64	65		61	64	66	65	
≥$75,000	21	22	22		29	24	18	15	
Body Mass Index (kg/m^2)	26.5 (5.3)	27.0 (5.6)	27.7 (6.2)	<.001	25.4 (4.7)	26.4 (5.2)	27.7 (5.9)	29.2 (6.6)	<.001
Waist-to-Hip Ratio	0.80 (0.08)	0.80 (0.08)	0.81 (0.08)	<.001	0.79 (0.08)	0.80 (0.08)	0.81 (0.08)	0.82 (0.08)	<.001

	Sitting Time (hrs/day)				Physical Activity (MET-hrs/week)				
	≤ 5	5.1 – 9.9	≥10	P-value	High (> 20)	Medium (8.4 – 20)	Low (1.8 – 8.3)	Inactive (≤ 1.7)	P-value
Family history of MI, %	40	42	43	<.001	41	42	42	40	0.91
Hours of sleep	6.9 (1.1)	6.9 (1.1)	6.8 (1.1)	<.001	6.9 (1.0)	6.9 (1.0)	6.8 (1.1)	6.8 (1.2)	<.001
Depression, %	9	9	10	<.001	7	8	10	13	<.001
Systolic Blood Pressure, mmHg	126.4 (17.9)	126.2(17.7)	126.0 (17.6)	0.01	124.9(17.9)	125.4 (17.7)	127.1(17.7)	128.2(17.6)	<.001
Diastolic Blood Pressure, mmHg	74.9 (9.2)	74.9 (9.2)	74.8 (9.3)	0.19	74.5 (9.2)	74.6 (9.2)	75.2 (9.3)	75.5 (9.4)	<.001
History of hypertension, %	21	22	23	0.001	17	20	25	28	<.001
History of diabetes. %	2	2	3	0.07	2	2	3	4	<.001
History of hyperlipidemia, %	7	7	8	0.04	6	8	8	7	<.001
Aspirin use, %	19	21	19	0.76	20	21	20	19	0.12
Alcohol consumption, %				<.001					<.001
None	13	10	9		8	10	12	15	
<1 /week	30	33	34		29	32	33	35	
1–7 /week	26	28	26		32	28	25	18	
>7 /week	12	13	13		16	14	11	10	
Past drinker	18	17	18		15	15	19	23	
Total energy intake, kcal/day	1499 (728)	1562 (637)	1608 (705)	<.001	1543 (643)	1539 (651)	1549 (685)	1577 (781)	<.001
% calories from saturated fat	9.7 (3.3)	10.0 (3.3)	10.2 (3.4)	<.001	8.9 (3.1)	9.7 (3.2)	10.4 (3.2)	11.2 (3.4)	<.001
Fiber, g/day	16.1 (7.7)	16.5 (7.2)	16.4 (7.4)	0.004	18.0 (7.6)	16.8 (7.3)	15.6 (7.0)	14.3 (7.0)	<.001

MET = metabolic equivalent task; MI = myocardial infarction.

*All values are means (SD) for continuous variables or frequencies for categorical variables, standardized to the age distribution of the study population (with the exception of age)

Table 2

Hazard ratios (95% confidence intervals) for the association between sitting time, physical activity, and risk of coronary heart disease (CHD)*, stroke†, or total cardiovascular disease (CVD)‡

	Sitting Time (hours/day)				Physical Activity (MET-hour/week)				
	≤5	**5.1–9.9**	**≥10**	**P for trend**	**High (> 20)**	**Medium (8.4 – 20)**	**Low (1.8 – 8.3)**	**Inactive (≤ 1.7)**	**P for trend**
CHD*									
Cases	902	1019	490		416	663	667	665	
Person-years	319,776	331,577	153,884		204,913	235,822	197,848	166,654	
Age-adjusted	1.00	1.03 (0.95, 1.13)	1.28 (1.15,1.43)	<.001	1.00	1.30 (1.15,1.47)	1.55 (1.37, 1.76)	1.97 (1.74, 2.22)	<.001
Multivariable-adjusted§	1.00	1.02 (0.94,1.12)	1.18 (1.05,1.32)	0.005	1.00	1.23 (1.09,1.39)	1.36 (1.20,1.54)	1.57 (1.38, 1.79)	<.001
MV§ + BMI	1.00	1.01 (0.92,1.11)	1.14 (1.02,1.28)	0.02	1.00	1.22 (1.08,1.38)	1.32 (1.16, 1.50)	1.49 (1.31, 1.70)	<.001
MV§ + BMI, comorbidities¶	1.00	1.00 (0.92, 1.10)	1.13 (1.01, 1.26)	0.04	1.00	1.20 (1.06, 1.36)	1.28 (1.13, 1.45)	1.43 (1.25, 1.63)	<.001
Stroke†									
Cases	763	876	411		399	561	563	527	
Person-years	320,330	332,260	154,220		205,519	236,427	198,065	166,798	
Age-adjusted	1.00	1.05 (0.95,1.16)	1.28 (1.14,1.45)	<.001	1.00	1.14 (1.00,1.30)	1.35 (1.19,1.54)	1.61 (1.41, 1.83)	<.001
Multivariable-adjusted§	1.00	1.05 (0.95,1.15)	1.21 (1.07,1.37)	0.003	1.00	1.10 (0.97,1.25)	1.24 (1.08,1.41)	1.39 (1.21, 1.59)	<.001
MV§ + BMI	1.00	1.04 (0.94,1.15)	1.19 (1.05,1.35)	0.006	1.00	1.09 (0.96,1.24)	1.21 (1.06,1.39)	1.35 (1.17, 1.55)	<.001
MV§ + BMI, comorbidities¶	1.00	1.03 (0.94,1.14)	1.18 (1.04,1.34)	0.008	1.00	1.08 (0.95,1.23)	1.19 (1.04,1.36)	1.30 (1.13, 1.50)	<.001
Total CVD‡									
Cases	1581	1805	849		782	1161	1172	1120	
Person-years	317,343	328,936	152,656		203,907	234,178	196,071	164,779	
Age-adjusted	1.00	1.05 (0.98,1.12)	1.27 (1.17,1.38)	<.001	1.00	1.21 (1.11,1.33)	1.45 (1.33,1.59)	1.77 (1.61, 1.94)	<.001
Multivariable-adjusted§	1.00	1.04 (0.97,1.11)	1.18 (1.09,1.29)	<.001	1.00	1.16 (1.06,1.27)	1.30 (1.18,1.42)	1.47 (1.33, 1.62)	<.001
MV§ + BMI	1.00	1.03 (0.96,1.10)	1.16 (1.06,1.26)	0.001	1.00	1.15 (1.05,1.26)	1.26 (1.15,1.39)	1.40 (1.27, 1.55)	<.001
MV§ + BMI, comorbidities¶	1.00	1.02 (0.95, 1.09)	1.15 (1.05, 1.25)	0.002	1.00	1.13 (1.04, 1.24)	1.23 (1.12, 1.35)	1.35 (1.23, 1.49)	<.001

MET = metabolic equivalent task ; MV = multivariable ; BMI = body mass index.

* CHD : Nonfatal myocardial infarction and fatal coronary heart disease

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†Stroke: Nonfatal and fatal stroke

‡CVD: Nonfatal MI, fatal CHD, nonfatal and fatal stroke

§The multivariable model was stratified by age and includes sedentary time and physical activity simultaneously as well as race, education, income, marital status, smoking, family history of myocardial infarction, depression, alcohol intake, hours of sleep, intake of total calories, saturated fat, fiber

¶History of hypertension, diabetes, or high cholesterol at baseline