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Association of Sedentary Time and Incident Heart Failure Hospitalization in Postmenopausal Women

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Abstract

BACKGROUND: The 2018 U.S. Physical Activity Guidelines recommend reducing sedentary behavior (SB) for cardiovascular health. SB's role in heart failure (HF) is unclear.

METHODS: We studied 80,982 women in the Women's Health Initiative Observational Study, aged 50–79, who were without known HF and reported ability to walk ≥1 block unassisted at baseline. Mean follow-up was 9 years for physician-adjudicated incident HF hospitalization (1,402 cases). SB was assessed repeatedly by questionnaire. Time-varying total SB was categorized according to awake time spent sitting or lying down (≤6.5, 6.6–9.5, >9.5 hr/day); sitting time (≤4.5, 4.6–8.5, >8.5 hr/day) was also evaluated. Hazard ratios (HR) and 95% confidence intervals (CI) were estimated using Cox regression.

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Supplemental Materials:
List of WHI Investigators.
Supplemental Tables I, II.

RESULTS: Controlling for age, race-ethnicity, education, income, smoking, alcohol, menopausal hormone therapy, and hysterectomy status, higher HF risk was observed across incremental tertiles of time-varying total SB (HR [95% CI]: 1.00 [referent], 1.15 [1.01, 1.31], 1.42 [1.25, 1.61], trend p<.001) and sitting time (1.00 [referent], 1.14 [1.01, 1.28], 1.54 [1.34, 1.78], trend p<.001). The inverse trends remained significant after further controlling for comorbidities including time-varying myocardial infarction and coronary revascularization (HRs: SB 1.00, 1.11, 1.27; sitting 1.00, 1.09, 1.37, trend p<.001 each), and for baseline physical activity (HRs: SB 1.00, 1.10, 1.24; sitting 1.00, 1.08, 1.33, trend p<.001 each). Associations with SB exposures were not different according to categories of baseline age, race-ethnicity, BMI, physical activity, physical functioning, diabetes, hypertension or CHD.

CONCLUSIONS: SB was associated with increased risk of incident HF hospitalization in postmenopausal women. Targeted efforts to reduce SB could enhance HF prevention in later life.

INTRODUCTION

The 2018 revision of the Physical Activity Guidelines for Americans emphasized the importance of reducing time spent in sedentary behaviors (SB), in addition to participating in regular physical activity, for both general and cardiovascular health.[1] At the time the initial 2008 version of the guidelines were written, there was insufficient evidence to support a clear recommendation on the role of physical activity and SB in heart failure (HF) risk.[2] The 2018 revised guidelines now indicate there is consistent evidence of lower risks of HF development associated with greater amounts of physical activity.[3] A recent review of findings from epidemiologic cohort studies and pooled analyses published between 2000 and 2017[4] uncovered only one study on SB and HF incidence, which was in men.[5] Since that review, one additional study has been published in men and women combined.[6] No study has focused on older women. The prevalence of HF and its strain on the healthcare system are projected to increase over the next few decades with population aging.[7] Enhancing current approaches for primary HF prevention is, therefore, paramount.[8] Given the high prevalence of prolonged sedentary time among U.S. adults aged 65 and older,[9] among whom HF burden is substantial,[10] understanding the role SB has in HF development is relevant to future HF prevention strategies.

We evaluated the prospective association between SB and incident HF hospitalization in postmenopausal women enrolled in the Women's Health Initiative (WHI) Observational study. Our analysis uniquely examined time-varying SB while accounting for several relevant variables including recreational physical activity, measured blood pressure, and physical functioning status at baseline, and time-varying coronary events interim to HF hospitalization. Our primary hypothesis was that greater SB would be associated with higher HF risk, independent of the amount of physical activity participation.

METHODS

Data that support the findings of this study are available from the corresponding author upon reasonable request and with permission from the WHI.

Study Design and Participants

The WHI design, recruitment, and implementation has been described elsewhere.[11, 12] There were 161,808 postmenopausal women, aged 50 to 79 who were without conditions that would limit life expectancy to 3 years or less, enrolled into either the clinical trials (CT, n=68,132) or observational study (OS, n=93,676) at 40 U.S. centers during 1992–1998. The main WHI study ended in 2005. All 161,808 women enrolled in the WHI were followed for incident acute HF hospitalization from study enrollment through September 12, 2005.

The present analysis includes only women in the WHIOS cohort because the SB questionnaire was not administered in the CT. Women with self-reported HF at enrollment (1,356) and women reporting the inability to walk one block without assistance (8,168) were excluded from these analyses. Further exclusions were made for missing information on SB (934), follow-up after baseline (359), and covariates (1,877). The final analytic cohort herein was 80,982 women. Institutional Review Board approval and participant informed consents were obtained at all 40 centers. This study conformed to STROBE guidelines for human observational studies. Here, we build upon a previous investigation wherein we demonstrated inverse associations between self-reported physical activity levels and incident HF hospitalization.[13] Our previous study did not include analysis of SB exposures, which are the focus here.

Sedentary Behavior Assessment

SB was assessed by questionnaire at baseline and again at Years 3, 6, 9, using two questions: (1) "*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.*", and (2) "*During a usual day and night, about how many hours do you spend sleeping or lying down with your feet up? Be sure to include the time you spend sleeping or trying to sleep at night, resting or napping, and lying down watching TV."* There were eight response categories for each question, ranging from <4 hours to 16 or more hours per day. Total awake SB time was calculated by combining the reported hours of sitting and lying time and then subtracting reported hours sleeping (asked separately from the above questions) as done in previous WHI studies.[14] We also evaluated daily sitting time (hours/day) as a separate exposure. Test-retest reliability for response to the sitting and sleep questions reported three months apart in 564 women was Kappa = 0.60.[12] This is similar to the test-retest reliability for the SB questions repeated three months apart among women in the EPIC cohort (Kappa 0.74).[15] A positive correlation (r = 0.31) has been demonstrated between responses to the WHI sitting question and accelerometer measured sedentary time.[16] Both total SB and sitting time were evaluated as time-varying exposures in the present study.

HF Ascertainment

A standardized WHI protocol for identifying incident HF hospitalizations was followed as described in our previous study on physical activity and HF.[13] Self-reported information on HF hospitalization was collected annually and adjudicated by trained physicians using medical records.[17] Adjudicated cases required a diagnosis of acute HF on the hospital admission, and at least one of the following 4 clinical observations: (a) physician diagnosis of HF with medical treatment; (b) symptoms plus documentation in the current medical record of a history of imaging procedure showing impaired systolic or diastolic left ventricular function; (c) pulmonary congestion/edema on chest radiograph during current admission; (d) dilated ventricle(s), or "poor" left or right ventricular function by echocardiography, radionuclide or other contrast ventriculography. This method has good agreement (Kappa .79) comparing central and local adjudicated HF[18]; and, demonstrates modest Kappa coefficients (0.10–0.32), high sensitivity (0.80–0.95) and moderate positive predictive values (0.62–0.68) when compared with other published HF algorithms used in epidemiological studies.[19]

Covariate Information

Self-administered questionnaires were completed by participants at baseline to provide information on demographics, history of physician-diagnosis and treatment with medication for diabetes, hypertension, and dyslipidemia, history of atrial fibrillation, stroke, coronary heart disease (CHD; myocardial infarction or coronary revascularization procedures [CABG, PCI]), hysterectomy status, medication use, and lifestyle behaviors.[11, 12] Self-reported total recreational physical activity was summarized in metabolic equivalent hours per week (MET-hr/wk).[13] Height and weight were measured in clinic, and body mass index calculated (BMI; kg/m^2). Resting blood pressure was measured using a mercury sphygmomanometer and auscultatory methods with cuff size based on measured arm circumference in accord with guidelines contemporaneous to WHI baseline.[20] The average of two measures was used in analyses. Physical functioning was assessed using the RAND-36 instrument.[11]

Statistical Analysis

Baseline characteristics were compared according to categories of total SB using a linear (continuous covariates) or logistic (dichotomous covariates) model with the covariate of interest as a function of linear trend across SB categories, using the median value within each. Cox proportional hazards regression was used to estimate hazard ratios (HR) and 95% confidence intervals for incident HF hospitalization in relation to time-varying SB exposures. Ties were handled using the approximate likelihood of Efron.[21] The proportional hazards assumption was examined by graphically plotting survival by SB categories, and by modeling the HF outcome as a function of the interaction between total SB and follow-up time. In both cases, no appreciable violations were noted. Time-to-event was accrued from date of enrollment in the WHIOS to the date of first hospitalization for acute HF, death, loss to follow-up, or September 12, 2005, whichever came first. Cox regression models were estimated with increasing control for potential confounding, beginning with a model including baseline sociodemographic factors, smoking, alcohol use, menopausal hormone therapy, and hysterectomy status, then adding comorbidities and factors that potentially mediate the association between SB and HF. The primary exposure variable was time-varying total SB time defined categorically as ≤6.5, 6.6–9.5 and >9.5 hr/d for consistency with previous WHI studies.[22] Time-varying sitting time (≤4.5, 4.6–8.5 and >8.5 hr/d) was also evaluated. SB information was updated at years 3, 6, and 9. These updates were incorporated in the time-varying SB models, with the SB variable being updated over the course of follow-up within the model. Tests for linear trend were conducted across median values of categorical SB exposures. Stratification by baseline age, race-ethnicity, BMI, diabetes, hypertension, CHD, and physical function was used to explore consistency of associations between SB and HF between these specified cohort subgroups. We also stratified on baseline self-reported total recreational physical activity levels to understand whether an association between SB and HF was limited to women who reported a certain amount of physical activity. Tests for interaction were based on the interaction term from a proportional hazards model with HF as a function of SB categories, the subgroup of interest, and their interaction. All baseline covariates remained fixed during follow-up, except CHD, which was a time-varying covariate based on CHD history at enrollment and adjudicated myocardial infarction or coronary revascularization during follow-up interim to HF diagnosis. Sensitivity analyses were conducted to evaluate the potential impact of baseline subclinical morbidity by discarding the first two years of follow-up, by excluding women with any difficulty in ADLs and those with a self-report of no recreational physical activity, and by stratifying the primary results on baseline physical functioning and CHD history. Population-attributable risk (PAR) percentages were calculated to evaluate the potential impact of risk factor reduction from a public health perspective: PAR% = $P_c(1–1/HR_{adj}) \times 100\%$, where P_c is the risk factor prevalence among HF cases and HR_{adj} is the multivariable adjusted HR for HF associated with the risk factor.[23] P-values are for two-sided hypothesis tests at alpha .05, which were conducted using SAS (Windows v.9.4; SAS Institute, Carey, NC).

RESULTS

The cohort at baseline (Table 1) was, on average, 63 years of age and educated beyond high school, with a racial-ethnic distribution of 84.9% white, 7.1% black, 3.4% Hispanic, 2.9% Asian, 0.4% Native American. About 6% and 42% reported current or past smoking, respectively, and 45% reported current menopausal hormone therapy use. Baseline prevalence of diabetes, CHD and atrial fibrillation was relatively low, whereas more than one third of women reported treated hypertension. On average, participants reported 7 hours/day of total awake SB time and reported high physical functioning. About 11% of the cohort reported no recreational physical activity. All baseline characteristics in Table 1, except for diastolic BP and history of diabetes, CHD, stroke and atrial fibrillation were significantly (P<.05) associated with total SB, although some of the differences between SB groups were relatively small. Additionally, each baseline characteristic differed significantly according to incident HF hospitalization status (Supplemental Table I).

We identified 1,402 (1.7%) cases of incident acute HF hospitalization during 728,838 person-years follow-up. Rates of HF hospitalization (per 1,000 person-years) were 1.9, 2.2, and 2.4 over time-varying total SB categories of ≤6.5, 6.6–9.5 and >9.5 hr/d, and were 1.9, 2.3, and 2.4 over time-varying sitting categories of ≤4.5, 4.6–8.5 and >8.5 hr/d (Table 2). After controlling for demographic factors, smoking, alcohol, menopausal hormone therapy, and hysterectomy, a positive association with incident HF hospitalization was observed with total SB and sitting time (trend, P<.001 each). Women had a 42% (95% CI: 25–61%) and 54% (95% CI: 34–78%) greater HF risk when comparing the highest with lowest category of total SB and sitting time, respectively. The significant associations persisted and were of similar magnitude after controlling further for several comorbid potential mediating factors, including time-varying CHD (Model 3; trend, P<.001 each), and for baseline recreational physical activity (Model 4; trend, P<.001 each).

Stratified associations with incident HF hospitalization are given for total SB in Table 3 and for sitting time in Supplemental Table II. Crude rates of HF hospitalization were positively associated with baseline age, BMI, treated diabetes and hypertension, and history of CHD, and were inversely associated with physical functioning and recreational physical activity. Rates were similar between white and black women. The multivariable associations with incident HF hospitalization for total SB and sitting time were not significantly different between any of the subgroups evaluated (interaction P >.05 all).

Sensitivity analyses excluding cases of HF hospitalization occurring in the first two years of follow-up and excluding women with functional limitations and those reporting no recreational physical activity were conducted to understand potential reverse causation biases. Multivariable relative risks and their positive trends (P<.01 all) across categories of SB exposures were consistent with the primary results (Table 4).

For public health context, PAR was estimated to quantify the theoretical proportion of HF hospitalization in the source population that might be averted, assuming a causal association, if women's baseline total SB was less than the highest exposure category (9.5 hr/d). PAR was also estimated for other modifiable HF risk factors obesity, diabetes, hypertension at baseline and for CHD based on combined information at baseline and interim to HF hospitalization. PARs were 24.1% for hypertension, 15.0% for CHD, 9.6% for obesity, 8.9% for diabetes, and 7.3% for SB (Table 5).

DISCUSSION

The prospective findings from the present study support the hypothesis that greater self-reported SB is associated with significantly higher risk of incident acute HF hospitalization in older postmenopausal women, independent of self-reported physical activity levels. The significant positive associations for time-varying total SB and sitting time with risk of HF hospitalization were evident when controlling for several sociodemographic factors and potential mediating factors measured at baseline, and for time-varying CHD events interim to HF hospitalization. When associations were stratified on baseline subgroups, including race-ethnicity, history of treated diabetes, hypertension, and CHD, recreational physical activity, and physical function status, associations were consistent across strata and tests for interaction were not statistically significant. Despite lack of statistical evidence of an interaction between SB and physical activity, among women in the highest category of physical activity (≥7.5 MET-hr/wk), which is consistent with guideline recommendations that we previously showed was associated with lower HF risk,[19] those whose total SB exceeded 9.5 hr/d had a significant 24% higher multivariable-adjusted risk of incident HF hospitalization. Even greater HF hospitalization risk (42% higher risk) in this physical activity subgroup was evident in women whose sitting time exceeded 8.5 hr/d. This suggests that prolonged exposure to SB may substantially elevate risk of developing HF even in older women who report being physically active. The present findings build on and expand those of our previous investigation that demonstrated an inverse association between self-reported physical activity levels and incident HF hospitalization.[13] As such, efforts to reduce sedentary time and increase activity-related energy expenditure, even through habitual walking,[13] may be needed for effective HF prevention in later life. Because national prevalence of SB[9] and physical inactivity[24] is high in older women, and because numbers of adults 60 and older are expected to increase from 33 to 79 million between 2010 and 2050,[25] improved strategies to reduce SB and increase physical activity in these individuals should enhance public health efforts for HF prevention.

We used PAR, which takes into account both the amount (prevalence) of a risk factor and its relative strength of association (HR) with disease in a defined population, as a theoretical indicator of the potential impact that reducing SB time might have on HF prevention. If women were not exposed to prolonged SB (>9.5 hr/d), 7.3% of incident HF hospitalizations might have been avoided. By comparison, PARs for other modifiable HF risk factors were 24.1%, 15.0%, 9.6%, and 8.9% for hypertension, CHD (time-varying), obesity, and diabetes, respectively. Our PAR computation is based on the multivariable-adjusted HR (Model 4, Table 2), thus the above PARs control for differences in demographic, clinical, and lifestyle factors, in addition to each of the risk factors for which PAR was computed. The PARs for hospitalized HF estimated in our study on postmenopausal women are consistent with those for hypertension (28%), CHD (16%), obesity (12%), and diabetes (10%) in women in the Olmsted County Study.[26] Prolonged SB has relevance to the burden of HF in postmenopausal women enrolled in the WHI similar to that of well-recognized HF risk factors obesity and diabetes. Development of effective approaches for reducing population levels of SB could have considerable impact on HF in later life because SB is also a risk factor for each of the above modifiable HF risk factors.[3]

We are aware of only two published studies focused on the association between SB and HF risk. Young and coworkers[5] studied over 82,000 men who at enrollment in the California Men's Health Study were 45 years and older and without known HF. These men self-reported daily time spent watching television, sitting at a computer or reading at baseline, and were then followed a mean of 8 years during which 3,472 HF cases were identified. After controlling for several of the same covariates as in our present study, relative risks were 1.09 and 1.27 for the middle (3–4 hr/d) and highest (≥5 hr/d) compared with the lowest (≤2 hr/d; referent) tertile of baseline sitting time (Trend, P<.001). These associations were of similar magnitude as seen for time-varying total SB and sitting time in the present study (Table 2, model 4). Unlike in our study, where SB was associated with significantly higher HF risk among women reporting the highest amount of recreational physical activity, prolonged sitting was not associated with HF risk among men with high physical activity levels in the California Men's Health Study. In the Multiethnic Study of Atherosclerosis (MESA), spending more than 1890 minutes/week (4.5 hr/d) in SB was not significantly associated with HF risk when compared to ≤1890 minutes/week in cohort of 6,814 U.S. women and men, who were aged 45–84 at baseline and followed 11 years for HF.[6] This study likely had limited statistical power due to the small numbers of HF (178 cases). Our findings from the WHI and those from the California Men's Health Study[5] provide consistent evidence for an adverse association between prolonged SB and HF risk in women and in men.

Evidence suggests that SB is not merely the lower end of the physical activity energy expenditure continuum, but that SB has distinct physiological influences on cardiovascular health.[27] The adverse cardiometabolic,[28] hemostatic, and inflammatory[29] biomarker profiles associated with prolonged SB promote atherosclerosis onset and progression, thus, increasing risk for ischemic HF.[30] Mechanisms may also involve pathways influencing myocardial contractility, relaxation, or both. In the landmark 1968 Dallas Bedrest Study, marked reductions in cardiac function were documented in healthy college-aged men following 20 days of voluntary bedrest.[31] Although bedrest is not completely comparable to habitual SB because of periodic interruption in SB and different gravitational forces, the bedrest study did stimulate interest in the adverse structural and functional cardiac responses to prolonged inactivity. More recently, self-reported SB has been associated with wall stiffening in large conductance arteries,[32] reduced arterial distensibility,[33] greater left ventricular mass and mass-to-volume ratio,[34] reduced left ventricular compliance,[35] and impaired systolic[36] and diastolic[37] functions. A major contributing factor for vascular dysfunction associated with prolonged SB is reduced arterial wall shear stress secondary to reduced blood flow that results from infrequent skeletal muscle contraction.[38] Low skeletal muscle metabolic demand during prolonged SB is accompanied by reduced vasodilatory metabolites, leading to further reductions in blood flow. Reduced arterial blood flow and shear stress lead to uncoupling of endogenous nitric oxide synthase from nitric oxide production and a resulting increase in endothelial cell secretion of endothelin-1, which promotes vasoconstriction. Over time, this can lead to increases in total peripheral resistance, elevated systemic blood pressure, and increased left ventricular afterload. SB is also associated with increased sympathetic nervous system activity.[39] Higher sympathetic tone exacerbates vasoconstriction and can lead to reduced renal blood flow and glomerular filtration rate as well as increased renin and aldosterone activity, which increases cardiac afterload and left ventricular myocardial workload. Pericardial ectopic fat deposition is positively associated with time spent sitting,[40] and adversely effects cardiac function.[41]

Strengths of the current study include the large cohort size of older postmenopausal women, use of time-varying SB exposures, physician-adjudicated cases of incident acute HF hospitalization, and extensive control for potential confounding factors including time-varying CHD events interim to HF hospitalization. A positive association between time-varying SB and risk of incident HF hospitalization in older women not only builds upon our previous finding of inverse associations between HF risk and physical activity levels,[13] but adds needed evidence on SB and HF to a sparse existing literature. Limitations include assessment of SB using a questionnaire, which inevitably can result in some degree of exposure misclassification. Because of the prospective study design, wherein SB assessment preceded disease occurrence, any misclassification would most likely be non-differential resulting in associations biased toward the null.[23] Baseline prevalence of diabetes, CHD, and atrial fibrillation were lower than what might be expected for women in the age range studied. Women who chose to enroll in the WHIOS might have been somewhat healthier than the general population of women of similar age, which could have resulted in a lower rate of incident HF hospitalization, and possibly weaker associations with SB. Recent studies using accelerometer measures of SB, including within WHI,[42] suggest that the pattern of SB accrual (e.g., bout frequency and duration) as opposed to only total SB time is important to cardiovascular health. Questionnaires are not able to discern SB patterns, and therefore we could not evaluate their relevance to HF risk in the present study. Reverse causation bias is a reasonable concern when prospectively assessing HF risk in relation to SB, which might be influenced by reductions in energy levels and aerobic capacity during the pre-clinical phases of HF.[43] We cannot completely rule this out as an alternative explanation for the positive associations we observed, though associations persisted after excluding HF cases that occurred during the first two years of follow-up and did not differ significantly across physical functioning categories. Our previous study showed recreational physical activity was inversely associated with HF with reduced and preserved ejection fraction[13] in a subcohort of WHI women for whom records on echocardiographic and other imaging information was available to allow HF subtype determination.[30] Unfortunately, we did not have sufficient information to evaluate SB and HF subtypes here.

In conclusion, prolonged SB is associated with a significantly increased risk of incident HF hospitalization in older postmenopausal women. These findings provide evidence for an additional adverse cardiovascular outcome of prolonged SB that could help refine future physical activity guidelines. Results of this study underscore the need for effective strategies to reduce daily SB time, in addition to increasing recreational physical activity, as part of population efforts for HF prevention.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Non-standard Abbreviations and Acronyms:

ADL	activities of daily living
HF	heart failure
CI	confidence interval
CT	clinical trial
HR	hazard ratio
MET	metabolic equivalent
MET-hrs/wk	metabolic equivalent hours per week
PAR	population attributable risk
SB	sedentary behavior

WHI	Women's Health Initiative
WHIOS	Women's Health Initiative Observational Study

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Commentary:

What is new?

- Sedentary behavior (an understudied exposure) was prospectively evaluated with heart failure hospitalization risk
- Postmenopausal women (an understudied population) were studied exclusively

What are the clinical implications?

- Time spent sedentary increases with age and is particular high in older women
- Reducing sedentary time during the day may benefit heart failure prevention additional to promotion of greater physical activity levels

Table 1.

Baseline characteristics for the overall cohort and according to categories of total SB. (Data are mean ±SD, or %).

Characteristic	All	Total Sedentary Behavior (hr/d)			P-value
		≤6.5	6.6–9.5	>9.5	
N	80,982	27,804	23,652	29,526	
Age, years	63.4 ± 7.3	64.0 ± 7.2	64.0 ± 7.2	62.2 ± 7.4	<.001
50–59	32.8	28.8	28.8	39.7	
60–69	44.2	46.1	46.1	41.1	
70–79	23.0	25.1	25.0	19.3	
Race-ethnicity					<.001 *
White	84.9	80.5	87.6	87.0	
Black	7.1	9.3	5.6	6.2	
Hispanic	3.4	5.0	2.7	2.4	
Native American	0.4	0.5	0.3	0.3	
Asian	2.9	3.2	2.9	3.0	
Unknown	1.3	1.6	1.2	1.1	
Education					<.001
High school or less	19.7	23.6	19.0	16.4	
Some college	36.1	37.2	36.1	35.1	
College graduate	43.5	38.4	44.2	47.7	
Household income					<.001
<$20,000	12.8	15.7	11.8	10.8	
$20,000 – 49,999	40.3	39.7	41.2	40.3	
$50,000 – 74,999	19.6	18.0	19.9	20.9	
≥$75,000	20.2	18.2	20.1	22.2	
Smoking status					<.001 †
Never	50.7	53.5	50.9	47.8	
Past	42.4	39.7	42.7	44.8	
Current	5.9	5.6	5.5	6.5	
Alcohol consumption					<.001
Never	10.4	13.2	9.8	8.2	
Past	17.3	18.3	16.5	17.0	
Current	71.8	67.9	73.3	74.4	
Hormone therapy use					<.001
Never	39.5	41.0	39.4	38.1	
Past	14.6	15.0	14.8	14.2	
Current	45.9	44.0	45.8	47.7	
BMI, kg/m^2	26.8 ± 5.4	26.4 ± 5.2	26.6 ± 5.3	27.3 ± 5.7	<.001
<18.5	1.2	1.4	1.2	1.0	
18.5 – 24.9	41.9	43.9	43.0	39.2	

Characteristic	All	Total Sedentary Behavior (hr/d)			P-value
		≤6.5	**6.6–9.5**	**>9.5**	
25.0 – 29.9	34.6	35.0	34.5	34.1	
≥30	22.3	19.6	21.3	25.7	
Total physical activity, MET-hr/wk	14.4 ± 14.5	16.2 ± 16.2	14.7 ± 14.2	12.5 ± 12.7	<.001
0	11.5	10.3	10.2	13.6	
>0 – 7.4	27.1	25.0	26.3	29.6	
≥7.5	61.4	64.7	63.5	56.8	
Total SB time, hr/d	7.2 ± 3.3	4.5 ± 1.6	8.0 ± 0.8	12.5 ± 2.4	<.001
Sitting time, hr/d	6.3 ± 3.0	4.6 ± 1.1	6.7 ± 1.5	10.4 ± 2.5	<.001
ADL score	4.0 ± 0.3	4.0 ± 0.3	4.0 ± 0.2	4.0 ± 0.2	<.001
Physical function score	85.5 ± 14.6	86.3 ± 14.1	85.7 ± 14.3	84.5 ± 15.2	<.001
Systolic BP, mmHg	126.3 ± 17.8	127.2 ± 18.1	126.7 ± 17.7	125.2 ± 17.6	<.001
Diastolic BP, mmHg	74.7 ± 9.3	74.6 ± 9.3	74.7 ± 9.3	74.7 ± 9.2	.20
History of:					
Hysterectomy	40.9	42.0	40.3	40.2	<.001
Diabetes[‡]	3.2	3.4	3.0	3.2	.23
Hypertension[‡]	38.9	39.7	39.4	37.8	<.001
CHD	2.6	2.6	2.6	2.5	.46
Stroke	1.1	1.2	1.1	1.1	.26
Atrial fibrillation	4.0	3.9	4.2	4.0	.67

[*]Comparing percentage of whites versus nonwhites.

[†]Comparing percentage of current versus past/never.

[‡]History of physician-diagnosis and treatment using medication.

Physical function score ranges from 0–100; higher scores reflect better functional status.

ADL, activities of daily living score ranges from 4–12; lower values reflect greater independence.

BMI, body mass index.

BP, blood pressure.

CHD, coronary heart disease (myocardial infarction, coronary revascularization procedures).

MET-hr/wk, metabolic equivalent hours per week.

Table 2.

Rates and relative risks of heart failure according to categories of time-varying SB.

	Total Sedentary Behavior (hr/d)			**Trend**
	≤6.5	**6.6–9.5**	**>9.5**	**P-value**
Total SB (hr/d) median	5.0	8.0	12.0	
Cases	470	426	506	
Crude rate *	1.9	2.2	2.4	
Model 1, HR (95% CI)	1.00 (ref)	1.15 (1.01, 1.31)	1.42 (1.25, 1.61)	<.001
Model 2, HR (95% CI)	1.00 (ref)	1.11 (0.97, 1.27)	1.29 (1.14, 1.47)	<.001
Model 3, HR (95% CI)	1.00 (ref)	1.11 (0.97, 1.26)	1.27 (1.11, 1.44)	<.001
Model 4, HR (95% CI)	1.00 (ref)	1.10 (0.96, 1.25)	1.24 (1.09, 1.41)	<.001
	Sitting Time (hr/d)			
	≤4.5	**4.6–8.5**	**>8.5**	
Sitting time (hr/d) median	4.5	6.5	10.5	
Cases	488	595	319	
Crude rate *	1.9	2.3	2.4	
Model 1, HR (95% CI)	1.00 (ref)	1.14 (1.01, 1.28)	1.54 (1.34, 1.78)	<.001
Model 2, HR (95% CI)	1.00 (ref)	1.09 (0.97, 1.23)	1.39 (1.20, 1.60)	<.001
Model 3, HR (95% CI)	1.00 (ref)	1.09 (0.97, 1.23)	1.37 (1.19, 1.58)	<.001
Model 4, HR (95% CI)	1.00 (ref)	1.08 (0.95, 1.21)	1.33 (1.15, 1.54)	<.001

HR, hazard ratio; CI, confidence interval.

*Crude rate, HF cases per 1,000 person years.

Model 1 includes age (years), race-ethnicity (6 categories), education (3 categories), income (4 categories) smoking (never, past, current), alcohol consumption (never, past, current), hormone therapy use (never, past, current), history of hysterectomy.

Model 2 includes above factors and BMI (kg/m^2), systolic and diastolic BP (mmHg), physical function score (continuous), history of treated diabetes and hypertension, and history of atrial fibrillation.

Model 3 includes above factors and time-varying CHD (myocardial infarction, coronary revascularization procedures).

Model 4 includes above factors and self-reported baseline total recreational physical activity (MET-hr/wk).

Table 3.

Associations between time-varying total SB and heart failure incidence stratified on baseline subgroups.

Subgroup	N	Cases	Rate*	Total Sedentary Behavior (hr/d)			Interaction
				≤6.5	6.6–9.5	>9.5	P-value
Age, yr							
50–64	44,381	331	0.92	1.00 (ref)	1.21 (0.92, 1.61)	1.33 (1.03, 1.73)	.63
65–79	36,601	1,071	3.81	1.00 (ref)	1.08 (0.93, 1.25)	1.22 (1.06, 1.42)	
Race-ethnicity†							
White	68,787	1,250	2.27	1.00 (ref)	1.11 (0.96, 1.27)	1.26 (1.10, 1.44)	.24
Black	5,738	97	2.23	1.00 (ref)	1.39 (0.85, 2.28)	1.46 (0.91, 2.34)	
BMI, kg/m^2							
<30	62,905	940	1.87	1.00 (ref)	1.14 (0.97, 1.33)	1.28 (1.09, 1.49)	.65
≥30	18,077	462	3.29	1.00 (ref)	1.02 (0.80, 1.29)	1.19 (0.96, 1.48)	
Diabetes‡							.62
Present	2,612	195	10.29	1.00 (ref)	1.25 (0.86, 1.82)	1.36 (0.97, 1.91)	
Absent	78,285	1,202	1.93	1.00 (ref)	1.08 (0.93, 1.24)	1.22 (1.06, 1.40)	
Hypertension‡							.30
Present	22219	719	4.22	1.00 (ref)	1.21 (1.00, 1.45)	1.33 (1.11, 1.59)	
Absent	58140	670	1.43	1.00 (ref)	1.00 (0.82, 1.20)	1.14 (0.95, 1.37)	
History of CHD§							.64
Present	22,219	170	11.30	1.00 (ref)	1.30 (0.89, 1.90)	1.19 (0.82, 1.72)	
Absent	58,140	1,209	1.95	1.00 (ref)	1.09 (0.95, 1.26)	1.26 (1.10, 1.45)	
Physical Function							.84
<70 (lower)	10196	422	5.50	1.00 (ref)	1.36 (1.06, 1.76)	1.25 (0.98, 1.59)	
70–89	24329	546	2.87	1.00 (ref)	0.93 (0.75, 1.15)	1.18 (0.96, 1.44)	
≥90 (higher)	45695	417	1.13	1.00 (ref)	1.06 (0.84, 1.33)	1.21 (0.96, 1.53)	
Physical activity, MET-hr/wk							.66
0	9293	209	2.89	1.00 (ref)	1.25 (0.87, 1.80)	1.40 (1.00, 1.95)	

Subgroup	N	Cases	Rate*	Total Sedentary Behavior (hr/d)			Interaction
				≤6.5	6.6–9.5	>9.5	P-value
>0–7.4	21916	449	2.61	1.00 (ref)	1.06 (0.84, 1.35)	1.20 (0.96, 1.51)	
≥7.5	49773	744	1.87	1.00 (ref)	1.09 (0.91, 1.30)	1.24 (1.04, 1.47)	

Data are hazard ratio (95% confidence interval). BMI, body mass index; CHD, coronary heart disease; MET-hr/wk, metabolic equivalent hours per week.

Hazard ratios from models of heart failure as a function of categorical sedentary time, the subgroup of interest, their interaction, and are adjusted for Model 4 covariates in Table 2.

*Crude rate, HF cases per 1,000 person-years.

†Insufficient data for meaningful stratification on other race-ethnic groups.

‡History of physician-diagnosis and treatment using medication.

§Not adjusted for time-varying CHD.

BMI, body mass index.

CHD, coronary heart disease (myocardial infarction, coronary revascularization procedures).

MET-hr/wk, metabolic equivalent hours per week.

Table 4.

Sensitivity analysis for associations between time-varying SB and heart failure incidence.

	Total Sedentary Behavior (hr/d)			**Trend**
	≤6.5	**6.6–9.5**	**>9.5**	**P-value**
Primary Model	1.00 (ref)	1.10 (0.96, 1.25)	1.24 (1.09, 1.41)	<.001
Excluding HF in years 1 and 2	1.00 (ref)	1.13 (0.98, 1.31)	1.31 (1.14, 1.51)	<.001
Excluding ADL ≥4 and PA = 0 MET-hr/wk*	1.00 (ref)	1.06 (0.92, 1.22)	1.21 (1.06, 1.39)	.006
	Sitting Time (hr/d)			
	≤4.5	**4.6–8.5**	**>8.5**	
Primary Model	1.00 (ref)	1.08 (0.95, 1.21)	1.33 (1.15, 1.54)	<.001
Excluding HF in years 1 and 2	1.00 (ref)	1.08 (0.95, 1.23)	1.41 (1.20, 1.65)	
Excluding ADL ≥4 and PA = 0 MET-hr/wk*	1.00 (ref)	1.06 (0.93, 1.21)	1.33 (1.13, 1.55)	<.001

Data are hazard ratio (95% confidence interval) adjusted for covariates in Model 4, Table 2.

*Excludes women who had functional limitations in activities of daily living (ADL) and reported no recreational physical activity (PA).

ADL, activities of daily living.

HF, heart failure.

MET-hr/wk, metabolic equivalent hours per week.

Table 5.

Population attributable risks for HF according to selected risk factors.

Characteristic	Prevalence (%) in HF cases	HR (95% CI)*	PAR (%) (95% CI)†
Hypertension‡	65.7	1.58 (1.40, 1.77)	24.1 (18.3, 29.5)
CHD§	21.6§	3.24 (2.84, 3.73)§	15.0 (11.8, 18.0)
Obesity (BMI ≥30)	33.0	1.41 (1.25, 1.59)	9.6 (6.0, 13.0)
Diabetes‡	13.9	2.78 (2.36, 3.28)	8.9 (6.9, 10.8)
Total SB >9.5 hr/d§	36.1§	1.25 (1.10, 1.42)§	7.3 (3.0, 11.3)

*Hazard ratio and 95% confidence interval for incident HF adjusted for Model 4 covariates in Table 2, which includes mutual adjustment for each factor shown in the table.

†PAR, population attributable risk calculated using the following formula[23]: $P_c(1–1/HR_{adj})$, where P_c is the prevalence of a risk factor among HF cases and HR_{adj} is the multivariable adjusted hazard ratio for HF incidence associated with the specified risk factor.

‡Physician-diagnosis and treatment with medication.

§Time-varying, based on combined information at baseline and during follow-up interim to HF diagnosis.

CHD, coronary heart disease (myocardial infarction, coronary revascularization procedures).

HF, heart failure.

SB, sedentary behavior.