American Journal of Epidemiology

DOI: 10.1093/aje/kww196

Original Contribution

Associations of Accelerometer-Measured and Self-Reported Sedentary Time With Leukocyte Telomere Length in Older Women

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Initially submitted May 17, 2016; accepted for publication August 16, 2016.

Few studies have assessed the association of sedentary time with leukocyte telomere length (LTL). In a cross-sectional study conducted in 2012–2013, we examined associations of accelerometer-measured and self-reported sedentary time with LTL in a sample of 1,481 older white and African-American women from the Women's Health Initiative and determined whether associations varied by level of moderate- to vigorous-intensity physical activity (MVPA). The association between sedentary time and LTL was evaluated using multiple linear regression models. Women were aged 79.2 (standard deviation, 6.7) years, on average. Self-reported sedentary time was not associated with LTL. In a model adjusting for demographic characteristics, lifestyle behaviors, and health-related factors, among women at or below the median level of accelerometer-measured MVPA, those in the highest quartile of accelerometer-measured sedentary time had significantly shorter LTL than those in the lowest quartile, with an average difference of 170 base pairs (95% confidence interval: 4, 340). Accelerometer-measured sedentary time was not associated with LTL in women above the median level of MVPA. Findings suggest that, on the basis of accelerometer measurements, higher sedentary time may be associated with shorter LTL among less physically active women.

accelerometry; leukocyte telomere length; moderate- to vigorous-intensity physical activity; sedentary time; telomeres

Abbreviations: LTL, leukocyte telomere length; MVPA, moderate- to vigorous-intensity physical activity; OPACH, Objective Physical Activity and Cardiovascular Health; SD, standard deviation; VM, vector magnitude; WHI, Women's Health Initiative.

Telomeres are repetitive DNA-protein structures located at the ends of chromosomes that protect and maintain chromosomal stability and integrity (1). Telomeres progressively shorten with age, leading to cellular senescence and apoptosis (2, 3). Shortened leukocyte telomere length (LTL) has been associated with cardiovascular disease, type 2 diabetes, and major cancers (3–6).

Emerging evidence has linked LTL to modifiable factors such as smoking, body mass index, and physical activity (7–12). Sedentary behavior has also been studied in relation to LTL, but with mixed findings. In the Nurses' Health Study, there was no association of total sedentary time or specific sedentary behaviors with LTL (12), but in 2 recent studies, reduced sedentary time was associated with longer LTL (13, 14). However, these studies were limited by several factors, including failure to measure sedentary time objectively (i.e., by accelerometer). Accelerometer-measured sedentary time is not highly correlated with self-reported time, the latter of which often underestimates actual time spent in sedentary behaviors (15). These studies also did not measure LTL using the Southern blot method, which has low measurement error (16, 17). Additionally, they did not determine whether associations of sedentary time with LTL varied by level of physical activity. In previous studies, associations of

sedentary time with adverse health outcomes were stronger among persons with low levels of physical activity (18–21).

In a cross-sectional study, we assessed associations of accelerometer-measured and self-reported sedentary time with LTL in older white and African-American women from the Objective Physical Activity and Cardiovascular Health (OPACH) Study, an ancillary study of the Women's Health Initiative (WHI). We also determined whether associations varied by hours of moderate- to vigorous-intensity physical activity (MVPA), race/ethnicity, or physical function. Understanding the relationship between sedentary time and LTL, a purported biomarker of cellular aging (22), is important among older adults, who spend 8.5–10.7 hours/day sedentary and are particularly vulnerable to the adverse health consequences (e.g., obesity, type 2 diabetes, and all-cause mortality) associated with prolonged sedentary time (19, 23–25).

METHODS

Study population and data collection

The WHI is a large US prospective study investigating the determinants of chronic diseases in postmenopausal women. Details on the study have been previously published (26, 27). Briefly, a racially and ethnically diverse cohort of 161,808 postmenopausal women aged 50–79 years was recruited from 40 clinical centers nationwide during 1993–1998. Women were randomized into one or more of 3 clinical trials, including one of 2 hormone therapy trials, or an observational study. In 2005, 77% of eligible women agreed to be followed through 2010 in the first WHI Extension Study. In 2010, 87% of women consented to an additional 5 years of follow-up in the second WHI Extension Study. Over 7,800 women from Extension Study 2 were enrolled in the WHI Long Life Study, which consisted of a one-time in-person visit conducted between March 2012 and May 2013. The population of the current study included women from OPACH, an ancillary study of the Long Life Study that enrolled 7,048 women.

At the 1993–1998 baseline examination, participants completed self-administered questionnaires assessing demographic characteristics, medical history, and lifestyle behaviors. The 2012–2013 visit involved collection of a blood sample and assessment of physical measurements (blood pressure, height, and weight) and physical functioning status. Study participants additionally wore an accelerometer for 1 week and completed a sleep log and physical activity questionnaire. A random sample of women from the Long Life Study was selected for participation in a case-cohort study on the relationship between LTL and coronary heart disease. The present study was exclusive to women with LTL measurements and complete information on either accelerometer-measured (n = 1,297) or self-reported (n = 1,383) sedentary time. There were 1,481 women in the final analytical sample.

All participants provided written informed consent, and institutional review board approval was received by all participating institutions.

Sedentary time and physical activity measures

Accelerometer-measured variables. Participants were asked to wear a triaxial accelerometer (ActiGraph GT3X+; ActiGraph LLC, Pensacola, Florida) on their right hip for 7 consecutive days during waking and sleeping hours, except during bathing or swimming. Movement was captured along 3 axes (vertical, anteroposterior, and mediolateral) in 15-second epochs, and activity counts were provided as composite vector magnitudes (VM) of these 3 axes. Accelerometer wear time was identified using sleep logs and a computer-automated algorithm developed specifically for this study (28). Nonwear time was defined as an interval of ≥90 minutes of consecutive zero VM counts/minute, with allowance of up to 2 minutes of nonzero VM counts if no counts were detected 30 minutes upstream or downstream from that interval; any other nonzero VM counts were considered wear time (29, 30). Only participants with 4–7 valid days of accelerometer data were included in the analysis, with a valid day being defined as having ≥10 hours of wear time (31).

A calibration study was performed in 200 study participants to determine relevant cutpoints along the distribution of VM counts to define sedentary behavior and physical activity intensity in older women (32). Based on this study, sedentary behavior was defined as 0–18 VM counts per 15 seconds and MVPA as ≥519 VM counts per 15 seconds. Data are presented as the average number of hours spent per day in these behaviors. For example, hours/day of sedentary time was calculated as the sum of total sedentary time during all valid days divided by the number of valid days.

Self-reported variables. In the physical activity questionnaire, participants were asked to estimate time spent sitting in response to the 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 in a car or bus, and sitting up watching TV or talking." Participants also estimated the time spent lying down: "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." A third question asked participants to estimate the number of hours they had typically spent sleeping per night during the past 4 weeks. Total daily sedentary time was calculated as the sum of sitting time and lying time minus sleeping time. This questionnaire previously showed moderate-to-high test-retest reliability (33).

Participants also completed the Community Healthy Activities Model Program for Seniors (CHAMPS) Physical Activity Questionnaire, which was developed for older adults and measures time spent in domestic and leisure-time activities in a typical week during the past 4 weeks (34). Data are presented as average number of hours per day spent in activities of moderate-to-vigorous intensity, calculated by summing the total number of hours spent in these activities during a typical week and dividing by 7.

Covariates

Variables assessed at the WHI baseline visit, at the 2012–2013 visit, and during WHI follow-up were used as covariates. Baseline covariates included race/ethnicity, education, marital status, smoking status, and alcohol consumption. At the 2012–2013 visit, trained clinic staff measured height and weight and systolic and diastolic blood pressures. Body mass index was calculated as weight in kilograms divided by squared height in meters and was categorized according to standard cutpoints (35). Current physical functioning status was measured objectively at the 2012–2013 visit using the Established Populations for Epidemiologic Studies of the Elderly (EPESE) Short Physical Performance Battery, which provides a summary score (range, 0–12) calculated as the sum of balance, chair-stand, and gait-speed scores, with a higher score indicating better physical performance (36, 37).

Variables assessed during WHI follow-up included self-rated health and history of hormone therapy, hypertension, and chronic diseases. Self-rated health was measured by means of a single item (38); the most recent value collected within 2 years of the 2012–2013 visit was used. History of hormone therapy was defined according to self-reported use of hormones or participation in one of the WHI hormone therapy trials. History of hypertension was defined as self-reported physician diagnosis of hypertension, use of antihypertensive medication, systolic blood pressure ≥140 mm Hg, or diastolic blood pressure ≥90 mm Hg (measured at baseline, during follow-up, or at the 2012–2013 visit). History of chronic diseases was defined as occurrence of 1 or more of the following diseases, each of which has been associated with both sedentary time and LTL in previous studies (4–6, 21, 39, 40): coronary heart disease, stroke, diabetes, and cancer (excluding nonmelanoma skin cancer). Disease status was self-reported at baseline. Incident diseases were identified through the date of the 2012–2013 visit via periodic clinic visits and via mailed questionnaires sent biannually to participants in the WHI Clinical Trial and annually to Observational Study and Extension Study participants. Diagnoses of incident diseases, except for diabetes, were adjudicated by physician medical record review (41). Diabetes was defined as self-reported physician's diagnosis of diabetes treated with either oral medication or insulin (42).

Measurement of LTL

DNA samples were extracted using the 5-prime method (5 PRIME, Inc., Gaithersburg, Maryland) and were sent in batches over a 1-year period to the Center of Human Development and Aging Laboratory at Rutgers University (New Brunswick, New Jersey) for LTL measurement. Each batch consisted of randomly selected samples. The laboratory performing the LTL measurements was blinded to all participant characteristics. Quality control procedures included assessment of DNA integrity prior to LTL measurement (16). DNA integrity was assessed visually after ethidium bromide-stained 1% agarose gel electrophoresis (200 V for 2 hours) and required that DNA appear as a single compact crown-shaped band migrating in parallel with the other samples on the gel. Telomere length (in kilobases) was determined by the mean length of the terminal restriction fragments using the Southern blot method, as previously described (16). Analysis of each sample was run in duplicate on different gels, and mean LTL was used in the analyses. The average interassay coefficient of variation for blinded pair sets was 2.0%.

Statistical analysis

Data on accelerometer-measured and self-reported sedentary time variables were divided into quartiles for the analysis. Categorical variables were compared across quartiles of sedentary time using χ^2 tests. Analysis of variance and Kruskal-Wallis tests were used for comparisons of normally distributed and non-normally distributed continuous variables across quartiles of sedentary time, respectively. Because LTL was normally distributed, general linear models were used to determine age- and race/ethnicity-adjusted mean LTL values across quartiles of sedentary time. Correlations were measured using the Pearson correlation coefficient.

Associations of accelerometer-measured and self-reported sedentary time with LTL were evaluated using multiple linear regression models. The first model adjusted for age and race/ethnicity, and successive models adjusted for other potential confounders, including demographic characteristics (education and marital status), lifestyle behaviors (smoking, alcohol use, body mass index, and MVPA), and health-related variables (history of chronic diseases and hormone therapy). All models for accelerometer-measured sedentary time were also adjusted for wear time. Models for accelerometer-measured sedentary time adjusted for accelerometer-measured MPVA, and those for self-reported sedentary time adjusted for self-reported MVPA.

Multicollinearity between variables was evaluated using tolerance values, with a value less than 0.10 indicating multicollinearity. However, multicollinearity was not observed in any of the models. Tests for linear trend were performed by including sedentary time variables as continuous variables in the models. Interactions between sedentary time and race/ethnicity, physical performance score, and MVPA were tested by including interaction terms for the products of these variables with sedentary time in the models. Results were stratified according to the median MVPA level, based on an a priori assumption that associations of sedentary time with LTL may vary by MVPA (18–21). Cutpoints of 0.5 hours/day of MVPA, based on current recommendations of ≥30 minutes/day of MVPA for adults (43), and 0.36 hours/day (which equates to 2.5 hours/week based on current guidelines), were also used. *P* values were 2-tailed and were considered nominally statistically significant at $P < 0.05$. All analyses were performed using SAS, version 9.3 (SAS Institute, Inc., Cary, North Carolina).

RESULTS

In the overall sample, there were 863 (58.3%) white and 618 (41.7%) African-American women. Women were aged 79.2 (standard deviation (SD), 6.7) years, on average,

ranging in age from 64 years to 95 years. Women wore the accelerometer for an average of 14.7 (SD, 1.3) hours/day over an average of 6.3 (SD, 0.8) days. The mean amounts of accelerometer-measured and self-reported sedentary time were 9.2 (SD, 1.5) hours/day and 8.6 (SD, 4.3) hours/day, respectively. The mean amounts of accelerometer-measured and self-reported MVPA were 0.8 (SD, 0.5) hours/day and 0.5 (SD, 0.6) hours/day, respectively. Accelerometer-measured and self-reported sedentary time were weakly correlated ($r = 0.27$; $P < 0.001$); accelerometer-measured and self-reported MVPA were similarly weakly correlated ($r = 0.28$; $P < 0.001$). Mean LTL was 6.6 (SD, 0.6) kilobases and ranged from 4.9 kilobases to 8.9 kilobases. LTL was inversely associated with age ($r = -0.38$; $P < 0.001$), and telomeres were longer in African-American women than in white women (age-adjusted mean lengths were 6.75 (standard error, 0.02) kilobases and 6.52 (standard error, 0.02) kilobases, respectively; $P < 0.001$).

Women with greater amounts of accelerometer-measured sedentary time were more likely to be older, white, and obese (Table 1). They were also more likely to have high blood pressure, a history of chronic diseases, a lower physical performance score, and fewer hours/day of MVPA and to have experienced a fall in the past 12 months. Women with higher self-reported sedentary time were more likely to be older, white, and obese and to have a history of chronic diseases (Table 2). They also had a lower physical performance score and lower levels of self-reported MVPA, and they were less likely to be in excellent or very good health.

In a model adjusting only for wear time, accelerometer-measured sedentary time was significantly associated with LTL (Table 3). After further adjustment for age and race/ethnicity, findings were no longer significant; in additional models, no significant findings were observed. After stratifying by the median accelerometer-measured MVPA value (0.69 hours/day), significant associations between accelerometer-measured sedentary time and LTL were not observed among women with MVPA levels above the median (Table 4). Among women at or below the median MVPA level, only women in the highest quartile of sedentary time had significantly shorter LTL in the full-adjustment model. LTL was on average 170 (95% confidence interval: 4, 340) base pairs shorter in the most sedentary women than in the least sedentary women. Although the stratum-specific signal for sedentary time and LTL was stronger among women at or below the median MVPA level, there was no significant interaction between sedentary time and MVPA ($P_{\text{interaction}} = 0.80$).

After stratification on a cutpoint of 0.5 hours/day of MVPA, all P values for trend were significant among women with less than 0.5 hours/day of MVPA. At a cutpoint of 0.36 hours/day of MVPA, associations of accelerometer-measured sedentary time with LTL were stronger among women with less than 0.36 hours/day of MVPA; LTL was 369 (95% confidence interval: 60, 679) base pairs shorter among the most sedentary women than among the least sedentary women in the full-adjustment model. Sedentary time was not significantly associated with LTL among women with ≥0.36 or ≥0.5 hours/day of MVPA (data not shown).

In the model with no adjustment for covariates, self-reported sedentary time was significantly associated with LTL (Table 5). In subsequent models adjusting for age, race/ethnicity, and other factors, findings were no longer significant. Results did not vary by level of self-reported MVPA (data not shown).

Results did not vary by race/ethnicity, by physical performance score, or after exclusion of participants with a history of cancer (data not shown).

DISCUSSION

Among older women who were less physically active as measured by accelerometry, a greater amount of accelerometer-measured sedentary time was significantly associated with shorter LTL. Findings persisted after adjustment for demographic characteristics, lifestyle behaviors, and body mass index but were attenuated after adjustment for a history of chronic diseases and use of hormone therapy. In the full-adjustment model, LTL was on average 170 base pairs shorter in the most sedentary women compared with the least sedentary women. Since women may lose on average 21 base pairs/year (8), this suggests that the most sedentary women were biologically older by 8 years. Our findings have important implications for an aging population, in which greater time spent sedentary and less physical activity tends to be the norm (23).

We observed that self-reported sedentary time was not associated with LTL, similar to a previous study of 7,813 Nurses' Health Study participants who were aged 59 years on average (12). Although results were not stratified by physical activity in the Nurses' Health Study, joint classification of sedentary time and physical activity through a combined variable showed that women who were less active and more sedentary had shorter LTL than those who were more active and less sedentary. In a study of 2,401 primarily female white twins aged 49 years, on average, Cherkas et al. (8) observed that the LTL of inactive participants was 200 base pairs shorter than that of the most active participants; however, total sedentary time was not specifically evaluated. It is difficult to directly compare our results with those of other studies due to differences in sample size, methods used to assess sedentary time, the age ranges of the study populations, and low correlation between accelerometer-measured and self-reported sedentary time. Unlike previous studies, our study focused on older women and used accelerometer-measured sedentary time—an important consideration given that time spent sedentary may be underestimated in self-reported data (15). An absence of association between self-reported sedentary time and LTL may, to a large extent, reflect measurement imprecision in questionnaire assessments of sedentary time, particularly among older adults.

Although we did not observe a significant statistical interaction between sedentary time and MVPA, several studies examining joint associations of sedentary time and physical activity with adverse health outcomes have observed that disease and mortality incidence risks associated with higher sedentary time were either attenuated or

Table 1. Characteristics of Older Women in the Women's Health Initiative OPACH Study, by Accelerometer-Measured Sedentary Time (n = 1,297), 2012–2013[a]

Characteristic	Quartile of Accelerometer-Measured Sedentary Time, hours/day												*P* Value		
	<8.18 (n = 322)			8.18–9.23 (n = 326)			9.24–10.21 (n = 324)			≥10.22 (n = 325)					
	No. of Women	%	Mean (SD/SE)	No. of Women	%	Mean (SD/SE)	No. of Women	%	Mean (SD/SE)	No. of Women	%	Mean (SD/SE)	ANOVA[b]	χ^2 Test[c]	GLM[d]
Age, years[e]			77.8 (6.6)			78.9 (6.8)			79.6 (6.7)			80.4 (6.5)	<0.01		
Age group, years														<0.01	
64–69	36	11.2		32	9.8		26	8.0		19	5.9				
70–74	71	22.1		66	20.3		62	19.1		46	14.2				
75–79	83	25.8		67	20.6		56	17.3		61	18.8				
80–84	84	26.1		78	23.9		93	28.7		110	33.9				
≥85	48	14.9		83	25.5		87	26.9		89	27.4				
Race/ethnicity[f]														<0.01	
White	155	48.1		181	55.5		196	60.5		224	68.9				
African-American	167	51.9		145	44.5		128	39.5		101	31.1				
Education[f]														0.79	
Less than high school	14	4.4		9	2.8		9	2.8		12	3.7				
High school diploma	50	15.5		50	15.4		53	16.5		50	15.4				
Some college	107	33.2		126	38.9		124	38.5		129	39.8				
College graduate	151	46.9		139	42.9		136	42.2		133	41.1				
Baseline marital status[f]														0.48	
Married/living as married	190	59.2		194	59.9		183	56.5		177	54.6				
Widowed	46	14.3		55	17.0		56	17.3		68	21.0				
Divorced/separated	73	22.7		60	18.5		75	23.2		65	20.1				
Never married	12	3.7		15	4.6		10	3.1		14	4.3				
Baseline smoking history[f]														0.12	
Never smoked	170	53.1		183	56.3		172	54.1		169	52.8				
Past smoker	133	41.6		127	39.1		115	36.2		133	41.6				
Current smoker	17	5.3		15	4.6		31	9.8		18	5.6				
Baseline alcohol consumption[f]														0.81	
Nondrinker	40	12.6		37	11.4		35	10.8		40	12.3				
Past drinker	61	19.2		68	20.9		71	22.0		56	17.2				
Current drinker	217	68.2		220	67.7		217	67.2		229	70.5				
Body mass index[g]														<0.01	
Underweight (<18.5)	6	1.9		3	0.9		4	1.2		3	0.9				
Normal weight (18.5–24.9)	125	38.9		106	33.0		96	29.8		65	20.4				
Overweight (≥25)	113	35.2		114	35.5		105	32.6		122	38.2				
Obese (≥30)	77	24.0		98	30.5		117	36.3		129	40.4				

Table continues

Table 1. Continued

Characteristic	Quartile of Accelerometer-Measured Sedentary Time, hours/day												*P* Value		
	<8.18 (*n* = 322)			8.18–9.23 (*n* = 326)			9.24–10.21 (*n* = 324)			≥10.22 (*n* = 325)					
	No. of Women	%	Mean (SD/SE)	No. of Women	%	Mean (SD/SE)	No. of Women	%	Mean (SD/SE)	No. of Women	%	Mean (SD/SE)	ANOVA[b]	χ^2 Test[c]	GLM[d]
Self-rated health														0.07	
Excellent	42	13.6		22	7.0		25	8.2		25	8.0				
Very good	131	42.3		143	45.3		126	41.3		119	38.1				
Good	112	36.1		120	38.0		116	38.0		134	43.0				
Fair/poor	25	8.1		31	9.8		38	12.5		34	10.9				
Current high blood pressure[h]	52	16.5		44	13.6		68	21.2		68	21.4			0.03	
History of hypertension	252	78.3		263	80.7		268	82.7		261	80.3			0.56	
History of use of hormone therapy	224	71.1		210	65.6		228	71.0		231	72.2			0.26	
History of chronic diseases															
CHD	14	4.4		16	4.9		19	5.9		30	9.2			0.04	
Stroke	10	3.1		4	1.2		16	4.9		11	3.4			0.06	
Diabetes	49	15.2		71	21.8		71	21.9		76	23.4			0.05	
Cancer	43	13.4		67	20.6		68	21.0		63	19.4			0.05	
Any of the above	104	32.3		135	41.4		141	43.5		140	43.1			0.01	
Experienced a fall in the past 12 months	74	23.9		106	34.2		102	32.3		99	31.3			0.03	
Physical performance score[e]			8.5 (2.2)			8.2 (2.4)			7.9 (2.7)			7.4 (2.6)	<0.01		
Accelerometer-measured MVPA, hours/day[i,j]			1.24 [0.02]			0.86 [0.02]			0.68 [0.02]			0.39 [0.02]			<0.01
Self-reported sedentary time, hours/day[e]			7.2 (3.6)			8.3 (4.1)			9.2 (4.4)			10.0 (4.2)	<0.01		
LTL, kilobases[e]			6.70 (0.59)			6.68 (0.60)			6.56 (0.60)			6.54 (0.60)	<0.01		
Age- and race-adjusted LTL, kilobases[j]			6.66 [0.03]			6.68 [0.03]			6.60 [0.03]			6.62 [0.03]			0.20

Abbreviations: ANOVA, analysis of variance; CHD, coronary heart disease; GLM, general linear model; MVPA, moderate- to vigorous-intensity physical activity; OPACH, Objective Physical Activity and Cardiovascular Health; LTL, leukocyte telomere length; SD, standard deviation; SE, standard error.

[a] All characteristics represent current status, unless otherwise noted. Sample sizes for variables in each column do not sum to totals because of missing data.

[b] *P* value was calculated using ANOVA.

[c] *P* value was calculated using a χ^2 test.

[d] *P* value was calculated using a GLM.

[e] Values are expressed as mean (standard deviation).

[f] Determined at the 1993–1998 baseline visit.

[g] Weight (kg)/height $(m)^2$.

[h] Systolic blood pressure ≥140 mm Hg or diastolic blood pressure ≥90 mm Hg.

[i] Adjusted for hours of wear time.

[j] Values are expressed as mean [standard error].

Table 2. Characteristics of Older Women in the Women's Health Initiative OPACH Study, by Self-Reported Sedentary Time (n = 1,383), 2012–2013[a]

Characteristic	Quartile of Self-Reported Sedentary Time, hours/day												*P* Value		
	<6 (n = 329)			6–7.5 (n = 279)			8–10.5 (n = 382)			≥11 (n = 393)					
	No. of Women	%	Mean (SD/SE)	No. of Women	%	Mean (SD/SE)	No. of Women	%	Mean (SD/SE)	No. of Women	%	Mean (SD/SE)	ANOVA[b]	χ^2 Test[c]	GLM[d]
Age, years[e]			77.7 (6.1)			79.3 (6.6)			79.7 (6.7)			79.4 (7.1)	<0.01		
Age group, years														<0.01	
64–69	39	11.9		19	6.8		31	8.1		37	9.4				
70–74	69	21.0		51	18.3		66	17.3		78	19.9				
75–79	78	23.7		71	25.5		72	18.9		58	14.8				
80–84	101	30.7		74	26.5		110	28.8		115	29.3				
≥85	42	12.8		64	22.9		103	27.0		105	26.7				
Race/ethnicity[f]														<0.01	
White	144	43.8		160	57.4		243	63.6		257	65.4				
African-American	185	56.2		119	42.7		139	36.4		136	34.6				
Education[f]														0.70	
Less than high school	9	2.7		11	3.9		14	3.7		9	2.3				
High school diploma	57	17.4		38	13.6		59	15.5		58	14.9				
Some college	129	39.3		98	35.1		137	36.0		153	39.2				
College graduate	133	40.6		132	47.3		171	44.9		170	43.6				
Baseline marital status[f]														0.67	
Married/living as married	187	56.8		148	53.6		230	60.4		214	54.7				
Widowed	60	18.2		50	18.1		66	17.3		67	17.1				
Divorced/separated	71	21.6		67	24.3		71	18.6		89	22.8				
Never married	11	3.3		11	4.0		14	3.7		21	5.4				
Baseline smoking history[f]														0.74	
Never smoked	179	55.6		150	54.0		210	55.4		203	52.1				
Past smoker	122	37.9		113	40.7		149	39.3		156	40.0				
Current smoker	21	6.5		15	5.4		20	5.3		31	8.0				
Baseline alcohol consumption[f]														0.06	
Nondrinker	47	14.4		35	12.7		41	10.7		41	10.5				
Past drinker	78	23.9		44	15.9		66	17.3		79	20.2				
Current drinker	202	61.8		197	71.4		275	72.0		272	69.4				
Body mass index[g]														<0.01	
Underweight (<18.5)	4	1.2		3	1.1		5	1.3		4	1.0				
Normal weight (18.5–24.9)	106	32.6		98	35.3		120	31.8		95	24.6				
Overweight (≥25)	111	34.2		106	38.1		141	37.3		118	30.5				
Obese (≥30)	104	32.0		71	25.5		112	29.6		170	43.9				

Table continues

Table 2. Continued

Characteristic	Quartile of Self-Reported Sedentary Time, hours/day												*P* Value		
	<6 (*n* = 329)			6–7.5 (*n* = 279)			8–10.5 (*n* = 382)			≥11 (*n* = 393)					
	No. of Women	%	Mean (SD/SE)	No. of Women	%	Mean (SD/SE)	No. of Women	%	Mean (SD/SE)	No. of Women	%	Mean (SD/SE)	ANOVA[b]	χ^2 Test[c]	GLM[d]
Self-rated health														<0.01	
Excellent	38	12.2		24	8.8		33	9.0		30	8.1				
Very good	127	40.8		133	48.5		156	42.4		120	32.3				
Good	121	38.9		100	36.5		145	39.4		163	43.8				
Fair/poor	25	8.0		17	6.2		34	9.2		59	15.9				
Current high blood pressure[h]	54	16.7		48	17.7		62	16.3		74	19.5			0.67	
History of hypertension	262	79.6		211	75.6		309	80.9		329	83.7			0.07	
History of use of hormone therapy	214	66.3		190	69.6		271	71.9		283	72.6			0.26	
History of chronic diseases															
CHD	15	4.6		19	6.8		22	5.8		27	6.9			0.55	
Stroke	16	4.9		10	3.6		13	3.4		12	3.1			0.61	
Diabetes	60	18.2		64	22.9		71	18.6		107	27.2			<0.01	
Cancer	46	14.0		56	20.1		78	20.4		71	18.1			0.12	
Any of the above	111	33.7		122	43.7		152	40.0		180	45.8			<0.01	
Experienced a fall in the past 12 months	88	27.3		83	30.2		117	31.2		136	35.1			0.16	
Physical performance score[e]			8.3 (2.5)			8.4 (2.3)			8.0 (2.5)			7.5 (2.7)	<0.01		
Accelerometer-measured sedentary time, hours/day[i,j]			8.63 [0.08]			8.96 [0.09]			9.32 [0.07]			9.66 [0.07]			<0.01
Self-reported MVPA, hours/day[e]			0.7 (0.8)			0.5 (0.5)			0.5 (0.6)			0.4 (0.5)	<0.01		
LTL, kilobases[e]			6.71 (0.61)			6.63 (0.56)			6.58 (0.58)			6.61 (0.63)	0.04		
Age- and race-adjusted LTL, kilobases[j]			6.66 [0.03]			6.66 [0.03]			6.63 [0.03]			6.65 [0.03]			0.86

Abbreviations: ANOVA, analysis of variance; CHD, coronary heart disease; GLM, general linear model; MVPA, moderate- to vigorous-intensity physical activity; OPACH, Objective Physical Activity and Cardiovascular Health; LTL, leukocyte telomere length; SD, standard deviation; SE, standard error.

[a] All characteristics represent current status, unless otherwise noted. Sample sizes for variables in each column do not sum to totals because of missing data.

[b] *P* value was calculated using ANOVA.

[c] *P* value was calculated using a χ^2 test.

[d] *P* value was calculated using a GLM.

[e] Values are expressed as mean (standard deviation).

[f] Determined at the 1993–1998 baseline visit.

[g] Weight (kg)/height $(m)^2$.

[h] Systolic blood pressure ≥140 mm Hg or diastolic blood pressure ≥90 mm Hg.

[i] Adjusted for hours of wear time.

[j] Values are expressed as mean [standard error].

Table 3. Association of Accelerometer-Measured Sedentary Time With Leukocyte Telomere Length Among Older Women, Women's Health Initiative OPACH Study, 2012–2013

Model	Quartile of Accelerometer-Measured Sedentary Time, hours/day							P_{trend}[a]
	<8.18 (Referent)	8.18–9.23		9.24–10.21		≥10.22		
		β[b]	95% CI	β	95% CI	β	95% CI	
1[c]	0	−0.04	−0.13, 0.05	−0.17	−0.26, −0.07	−0.21	−0.31, −0.12	<0.01
2[d]	0	0.01	−0.07, 0.10	−0.08	−0.16, 0.01	−0.07	−0.16, 0.01	0.05
3[e]	0	0.01	−0.07, 0.10	−0.07	0.16, 0.02	−0.06	−0.16, 0.03	0.11
4[f]	0	0.02	−0.06, 0.11	−0.06	−0.15, 0.03	−0.06	−0.16, 0.04	0.15
5[g]	0	0.02	−0.07, 0.11	−0.07	−0.17, 0.03	−0.07	−0.18, 0.04	0.17
6[h]	0	0.03	−0.06, 0.12	−0.06	−0.16, 0.04	−0.06	−0.18, 0.05	0.22

Abbreviations: CI, confidence interval; OPACH, Objective Physical Activity and Cardiovascular Health.
[a] *P* values were calculated using multiple linear regression models.
[b] Beta coefficients represent the difference in leukocyte telomere length (in kilobases).
[c] Results were adjusted for hours of wear time ($n = 1,297$).
[d] Results were adjusted for model 1 variables plus age and race/ethnicity ($n = 1,297$).
[e] Results were adjusted for model 2 variables plus education and baseline marital status, smoking, and alcohol consumption ($n = 1,270$).
[f] Results were adjusted for model 3 variables plus body mass index ($n = 1,256$).
[g] Results were adjusted for model 4 variables plus hours/day of moderate- to vigorous-intensity physical activity ($n = 1,256$).
[h] Results were adjusted for model 5 variables plus history of chronic diseases and use of hormone therapy ($n = 1,235$).

Table 4. Association of Accelerometer-Measured Sedentary Time With Leukocyte Telomere Length Among Older Women, by Hours/Day of Accelerometer-Measured Moderate- to Vigorous-Intensity Physical Activity, Women's Health Initiative OPACH Study, 2012–2013

MVPA Time and Model	Quartile of Accelerometer-Measured Sedentary Time, hours/day							P_{trend}[a]
	<8.18 (Referent)	8.18–9.23		9.24–10.21		≥10.22		
		β[b]	95% CI	β	95% CI	β	95% CI	
≤0.69 hours/day								
1[c]	0	−0.03	−0.19, 0.13	−0.16	−0.32, −0.002	−0.21	−0.38, −0.05	<0.01
2[d]	0	−0.03	−0.18, 0.12	−0.14	−0.29, 0.01	−0.16	−0.31, −0.002	0.03
3[e]	0	−0.06	−0.21, 0.09	−0.17	−0.32, −0.02	−0.19	−0.35, −0.03	0.02
4[f]	0	−0.05	−0.21, 0.10	−0.16	−0.32, −0.01	−0.19	−0.35, −0.03	0.02
5[g]	0	−0.04	−0.20, 0.11	−0.15	−0.31, 0.01	−0.17	−0.34, −0.004	0.25
>0.69 hours/day								
1	0	−0.01	−0.13, 0.11	−0.11	−0.24, 0.02	−0.11	−0.27, 0.05	0.07
2	0	0.04	−0.07, 0.14	−0.05	−0.17, 0.07	−0.02	−0.17, 0.13	0.45
3	0	0.04	−0.07, 0.15	−0.03	−0.15, 0.09	−0.01	−0.16, 0.14	0.68
4	0	0.05	−0.06, 0.16	−0.02	−0.15, 0.10	−0.01	−0.16, 0.15	0.78
5	0	0.07	−0.05, 0.18	−0.02	−0.14, 0.11	−0.02	−0.17, 0.14	0.91

Abbreviations: CI, confidence interval; MVPA, moderate- to vigorous-intensity physical activity; OPACH, Objective Physical Activity and Cardiovascular Health.
[a] *P* values were calculated using multiple linear regression models.
[b] Beta coefficients represent the difference in leukocyte telomere length (in kilobases).
[c] Results were adjusted for hours of wear time ($n = 653$ for ≤0.69 hours/day; $n = 644$ for >0.69 hours/day).
[d] Results were adjusted for model 1 variables plus age and race/ethnicity ($n = 653$ for ≤0.69 hours/day; $n = 644$ for >0.69 hours/day).
[e] Results were adjusted for model 2 variables plus education and baseline marital status, smoking, and alcohol consumption ($n = 636$ for ≤0.69 hours/day; $n = 634$ for >0.69 hours/day).
[f] Results were adjusted for model 3 variables plus body mass index ($n = 629$ for ≤0.69 hours/day; $n = 627$ for >0.69 hours/day).
[g] Results were adjusted for model 4 variables plus history of chronic diseases and use of hormone therapy ($n = 620$ for ≤0.69 hours/day; $n = 615$ for >0.69 hours/day).

Table 5. Association of Self-Reported Sedentary Time With Leukocyte Telomere Length Among Older Women, Women's Health Initiative OPACH Study, 2012–2013

Model	Quartile of Self-Reported Sedentary Time, hours/day							P_{trend}[a]
	<6 (Referent)	6–7.5		8–10.5		≥11		
		β[b]	95% CI	β	95% CI	β	95% CI	
1[c]	0	−0.07	−0.17, 0.02	−0.13	−0.22, −0.04	−0.10	−0.19, −0.01	<0.01
2[d]	0	0.00	−0.09, 0.09	−0.03	−0.11, 0.05	−0.01	−0.09, 0.08	0.43
3[e]	0	0.01	−0.08, 0.10	−0.01	−0.10, 0.07	0.01	−0.07, 0.10	0.73
4[f]	0	0.01	−0.08, 0.10	−0.01	−0.09, 0.07	0.02	−0.07, 0.10	0.86
5[g]	0	0.02	−0.07, 0.11	0.00	−0.08, 0.08	0.03	−0.06, 0.11	0.96
6[h]	0	0.03	−0.06, 0.12	0.00	−0.08, 0.09	0.04	−0.05, 0.12	0.81

Abbreviations: CI, confidence interval; OPACH, Objective Physical Activity and Cardiovascular Health.
[a] *P* values were calculated using multiple linear regression models.
[b] Beta coefficients represent the difference in leukocyte telomere length (in kilobases).
[c] Results were unadjusted (n = 1,383).
[d] Results were adjusted for model 1 variables plus age and race/ethnicity (n = 1,383).
[e] Results were adjusted for model 2 variables plus education and baseline marital status, smoking, and alcohol consumption (n = 1,354).
[f] Results were adjusted for model 3 variables plus body mass index (n = 1,339).
[g] Results were adjusted for model 4 variables plus hours/day of moderate- to vigorous-intensity physical activity (n = 1,339).
[h] Results were adjusted for model 5 variables plus history of chronic diseases and use of hormone therapy (n = 1,319).

eliminated among persons engaging in greater amounts of physical activity and were stronger in those with lower levels of physical activity (18–21). In our study, accelerometer-measured sedentary time was not associated with LTL among women who were more physically active. Additionally, sedentary time was not associated with LTL among women meeting current public health recommendations of ≥30 minutes/day of MVPA (43); in those not meeting this recommendation, higher sedentary time was associated with shorter LTL. Our findings suggest that prolonged sedentary time may be associated with shorter LTL when adequate levels of MVPA are not attained. However, our findings should be interpreted with caution given the lack of a statistical interaction, and further research is needed to determine whether there is a synergistic association of sedentary time and MVPA with LTL shortening.

We observed that women spent an average of 9.2 hours/day sedentary according to accelerometer data, in concordance with other studies carried out among older adults (44–46). In a study of 7,247 older Women's Health Study participants, Shiroma et al. (44) also observed an average of 9.2 hours/day spent in accelerometer-measured sedentary time. In our study, women reported spending an average of 8.6 hours/day sedentary. This is much higher than the total self-reported sedentary time observed in previous studies among older adults, which has ranged from 5.2 hours/day to 6.7 hours/day (23). We also observed that African-American women spent less time sedentary than white women. In a previous study carried out in a national sample of adults, Matthews et al. (47) observed that white and African-American women had similar patterns of sedentary behavior; however, older adults were not specifically evaluated.

Several mechanisms may explain the association of sedentary time with LTL. Oxidative stress and inflammation accelerate telomere attrition (2, 11, 48). It has been shown that regular engagement in physical activity increases antioxidant activity and may induce antiinflammatory responses (49, 50). Therefore, it is possible that women who spend long hours sedentary coupled with less time in MVPA may not be exposed to these antioxidant and antiinflammatory defenses. Increased time spent being sedentary and inactive may lead to insulin resistance (51), which has been previously associated with short LTL (52). The association of sedentary time with LTL may also be due to mediation by obesity. In previous studies, engaging in high amounts of sedentary behavior was associated with increased risk of obesity (25), and obesity has been associated with shorter LTL (7); however, findings persisted after adjustment for body mass index. Reverse causation due to chronic disease burden may also be possible; that is, women who have a history of chronic diseases may be more likely to have a sedentary lifestyle and shorter LTL.

Limitations of our study included its cross-sectional design, which precluded our ability to assess a temporal relationship between sedentary time and LTL. Our study was exclusive to older women, and our findings cannot be generalized to men or younger women. Our results apply to telomere length dynamics in leukocytes but not in other tissues. Women who enrolled in the WHI extension studies were more likely to be healthier at baseline; thus, those who experienced greater health-related LTL shortening may have been excluded. Strengths of our study include the diverse sample, adjustment for a large number of potential confounders, adjudication of data on chronic diseases, and accelerometer-measured sedentary time and MVPA.

In conclusion, higher accelerometer-measured sedentary time was associated with shorter LTL among less physically active women, suggesting that prolonged sedentary time and limited engagement in MVPA may act synergistically

to shorten LTL among older women. Therefore, avoidance of a highly inactive lifestyle may provide health benefits at the cellular level. Longitudinal studies assessing sedentary time and MVPA in relation to changes in LTL are currently needed. Future studies should also determine whether cardiorespiratory fitness modifies the relationship between sedentary time and LTL (53).

ACKNOWLEDGMENTS

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All authors contributed equally to this work.

This work was supported by the National Heart, Lung, and Blood Institute (contract HHSN268201300007C and grant R01 HL105065). The Women's Health Initiative is funded by the National Heart, Lung, and Blood Institute (contracts HHSN268201100046C, HHSN268201100001C, HHSN268201100002C, HHSN268201100003C, HHSN268201100004C, and HHSN271201100004C). Additional support was provided to T.M.M. by the National Heart, Lung, and Blood Institute (grant R01 HL121023) and to A.H.S. by the National Institute of Arthritis and Musculoskeletal and Skin Diseases (grant T32 AR064194).

A short list of WHI Investigators—*Program Office*: (National Heart, Lung, and Blood Institute, Bethesda, Maryland) Dr. Jacques Rossouw, Shari Ludlam, Dr. Dale Burwen, Dr. Joan McGowan, Dr. Leslie Ford, and Dr. Nancy Geller; *Clinical Coordinating Center*: (Fred Hutchinson Cancer Research Center, Seattle, WA) Dr. Garnet Anderson, Dr. Ross Prentice, Dr. Andrea LaCroix, and Dr. Charles Kooperberg; *investigators and academic centers*: (Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts) Dr. JoAnn E. Manson; (MedStar Health Research Institute/Howard University, Washington, DC) Dr. Barbara V. Howard; (Stanford Prevention Research Center, Stanford, California) Dr. Marcia L. Stefanick; (The Ohio State University, Columbus, Ohio) Dr. Rebecca Jackson; (University of Arizona, Tucson/Phoenix, Arizona) Dr. Cynthia A. Thomson; (University at Buffalo, Buffalo, New York) Dr. Jean Wactawski-Wende; (University of Florida, Gainesville/Jacksonville, Florida) Dr. Marian Limacher; (University of Iowa, Iowa City/Davenport, Iowa) Dr. Robert Wallace; (University of Pittsburgh, Pittsburgh, Pennsylvania) Dr. Lewis Kuller; (Wake Forest University School of Medicine, Winston-Salem, North Carolina) Dr. Sally Shumaker.

Conflict of interest: none declared.

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