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ORIGINAL RESEARCH

Patterns of Sedentary Behavior and Mortality in U.S. Middle-Aged and Older Adults

A National Cohort Study

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Background: Excessive sedentary time is ubiquitous in Western societies. Previous studies have relied on self-reporting to evaluate the total volume of sedentary time as a prognostic risk factor for mortality and have not examined whether the manner in which sedentary time is accrued (in short or long bouts) carries prognostic relevance.

Objective: To examine the association between objectively measured sedentary behavior (its total volume and accrual in prolonged, uninterrupted bouts) and all-cause mortality.

Design: Prospective cohort study.

Setting: Contiguous United States.

Participants: 7985 black and white adults aged 45 years or older.

Measurements: Sedentary time was measured using a hip-mounted accelerometer. Prolonged, uninterrupted sedentariness was expressed as mean sedentary bout length. Hazard ratios (HRs) were calculated comparing quartiles 2 through 4 to quartile 1 for each exposure (quartile cut points: 689.7, 746.5, and 799.4 min/d for total sedentary time; 7.7, 9.6, and 12.4 min/bout for sedentary bout duration) in models that included moderate to vigorous physical activity.

Results: Over a median follow-up of 4.0 years, 340 participants died. In multivariable-adjusted models, greater total sedentary time (HR, 1.22 [95% CI, 0.74 to 2.02]; HR, 1.61 [CI, 0.99 to 2.63]; and HR, 2.63 [CI, 1.60 to 4.30]; *P* for trend < 0.001) and longer sedentary bout duration (HR, 1.03 [CI, 0.67 to 1.60]; HR, 1.22 [CI, 0.80 to 1.85]; and HR, 1.96 [CI, 1.31 to 2.93]; *P* for trend < 0.001) were both associated with a higher risk for all-cause mortality. Evaluation of their joint association showed that participants classified as high for both sedentary characteristics (high sedentary time [≥12.5 h/d] and high bout duration [≥10 min/bout]) had the greatest risk for death.

Limitation: Participants may not be representative of the general U.S. population.

Conclusion: Both the total volume of sedentary time and its accrual in prolonged, uninterrupted bouts are associated with all-cause mortality, suggesting that physical activity guidelines should target reducing and interrupting sedentary time to reduce risk for death.

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Adults are sedentary for an alarming 9 to 10 hours per day (1). Accordingly, the popular press has coined the phrase "sitting is the new smoking" to describe a current epidemic of developed nations (2–4). Evidence indicates that sedentary time is associated with incident cardiovascular disease, incidence of cardiovascular disease–related risk factors, and mortality (5, 6). Of note, the risk conferred by prolonged sedentariness is eliminated only by high levels of moderate- to vigorous-intensity physical activity (MVPA) (about 60 to 75 min/d), which exceed physical activity recommendations (7, 8). As such, sedentary behavior is now believed to represent a clinically important aspect of a person's physical activity profile and is no longer considered simply the extreme low end of the physical activity continuum (5).

Studies linking sedentary behavior to health outcomes have relied almost exclusively on self-reported sedentary time, which is subject to reporting bias and measurement error (9). A 2015 systematic review (5) identified only 1 study (NHANES [National Health and Nutrition Examination Survey]) that examined the association between objectively measured sedentary time and health outcomes, a study limited by a small event rate (10). New studies using NHANES data have since been published, with longer follow-up and higher event rates (11–15). However, some of these studies have reported an association between objectively measured sedentary time and mortality (11, 14, 15), but others have not (12, 13). Additional cohort studies are thus needed to rectify evidence gaps. Furthermore, studies using accelerometers to objectively measure sedentary behavior conventionally operationalize sedentary time as the total number of sedentary minutes per day. This approach ignores patterns of accumulated sedentary behavior over time. For example, accumulation of sedentary time in a few long bouts or many short bouts represents 2 distinct patterns of sedentary time accrual. Experimental studies have shown that acute periods of prolonged, uninterrupted sedentary behavior cause greater detrimental cardiometabolic effects than sedentary behavior that is periodically interrupted (16–18), suggestive that it is not just total sedentary time that is

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relevant to health outcomes, but also the manner in which it is accumulated. Few longitudinal studies, however, have explored the association between prolonged, uninterrupted sedentary behavior and mortality to corroborate these findings.

To inform guidelines on reducing sedentary behavior (target reductions in overall sedentary time or target interruption of prolonged sedentary bouts), evidence from prospective studies is needed to 1) confirm the association between total sedentary time and mortality using objective measures, 2) determine whether prolonged sedentary bouts confer risk for death, and 3) elucidate whether the total volume of sedentary time and its pattern of accumulation individually or jointly contribute to risk for death. The purpose of this study, therefore, was to examine the association between objectively measured sedentary time (both total volume and accrual in prolonged bouts) and all-cause mortality in a national cohort of U.S. middle-aged and older adults enrolled in the REGARDS (Reasons for Geographic and Racial Differences in Stroke) study.

METHODS

Study Population

REGARDS is a population-based study designed to examine racial and regional disparities in stroke. It comprises 30 239 white and black adults aged 45 years or older enrolled between 2003 and 2007 from across the contiguous United States (19, 20). Detailed design and methods for REGARDS are described elsewhere (21). Briefly, demographic and cardiovascular risk factor data were collected by telephone interview and an in-home physical assessment on enrollment. A detailed summary of baseline measures is provided in the **Supplement** (available at Annals.org). Participants (or their proxies) were then followed for 6-month intervals to ascertain vital status. Objective measurements of sedentary behavior were collected from active REGARDS participants from 2009 to 2013 (mean time from study enrollment, 5.7 years [SD, 1.5]; range, 1.9 to 9.5 years) (22). A total of 7985 participants adhered to accelerometer wear requirements (≥4 days with accelerometer wear ≥10 hours), provided follow-up data, and were available for the current analyses (**Supplement Figure 1**, available at Annals.org). **Supplement Table 1** (available at Annals.org) shows the characteristics of included versus excluded REGARDS participants. The REGARDS study protocol was approved by the institutional review boards of participating institutions. All participants provided informed consent.

Accelerometer Data Collection

Methods for accelerometer data collection are described elsewhere (22). Briefly, participants were fitted with an Actical (Philips Respironics) accelerometer secured to their right hip using a nylon belt and were instructed to wear the device during waking hours for 7 consecutive days. The Actical had been validated for measurement of physical activity and sedentary behavior and was shown to have acceptable reliability (23–25).

Activity counts were summed over 1-minute epochs. Nonwear periods were defined as at least 150 consecutive minutes of 0 activity counts. This nonwear algorithm was previously validated against daily log sheets in REGARDS participants (26). Measurements of 0 to 49, 50 to 1064, and at least 1065 counts per minute were defined as sedentary behavior, light-intensity physical activity, and MVPA, respectively, as determined in a laboratory-based calibration study (27). A sedentary bout was defined as consecutive minutes in which the accelerometer registered fewer than 50 counts per minute. A sedentary break was defined as at least 1 minute in which 50 or more counts per minute were registered after a sedentary bout. Both sedentary bouts and breaks were exclusively continuous periods, with no interruptions or nonwear intervals allowed in the definition.

Outcome Ascertainment

All-cause mortality was the primary outcome, defined as any death after completion of the accelerometer protocol regardless of cause. Dates of death were confirmed through review of death certificates, medical records, and administrative databases. Deaths through 4 September 2015 were included in the current analysis.

Statistical Analysis

Sedentary and physical activity variables were averaged across compliant days (≥10 hours of wear). Because of a high correlation between total sedentary time and wear time (**Supplement Figure 2**, available at Annals.org), we corrected for the influence of wear time by standardizing total sedentary time to 16 hours of wear time per day using the residuals obtained when regressing total sedentary time on wear time (see Methods section of the **Supplement**) (28–30).

Participants were stratified into quartiles according to total sedentary time and, separately, mean sedentary bout duration (a measure of overall prolonged, uninterrupted sedentary behavior). Cox proportional hazards regression modeling was used to calculate the hazard ratio (HR) for all-cause mortality associated with quartiles of total sedentary time (and separately, mean sedentary bout length). Crude HRs were initially calculated. Subsequent HRs were calculated after adjustment for age, race, sex, region of residence, education, and season the accelerometer was worn (model 1), with further adjustment for current smoking, alcohol use, body mass index (BMI), diabetes, hypertension, dyslipidemia, estimated glomerular filtration rate less than 60 mL/min/1.73 m^2, atrial fibrillation, history of coronary heart disease, and history of stroke (model 2). Models were additionally adjusted for MVPA expressed continuously (model 3). Tests for linear trend across quartiles were conducted by including the quartile for each participant as an ordinal variable in regression models. Proportional hazards assumptions were confirmed with a Kolmogorov-type supremum test (31). The above analyses were then repeated in a fully adjusted model, testing interactions for age (<65 and ≥65 years), sex (male and female), race (black and white), BMI category (normal weight and overweight or obese), and MVPA category (<150 min/wk and ≥150 min/wk).

As a secondary analysis, we examined the continuous dose–response relationship between each sedentary characteristic and all-cause mortality in a fully adjusted model (model 3) using restricted cubic splines (32). Cubic polynomials were fitted with the mean of each sedentary characteristic set as the reference and knots placed at the 5th, 35th, 65th, and 95th percentiles (33). Nonlinear associations were evaluated using the likelihood ratio test. For nonlinear associations, spline models were used to describe the associations and when the association was determined to be linear, a linear model was used.

Because of multicollinearity between total sedentary time and mean sedentary bout duration (r = 0.61), both variables were not included in the same model.

Table 1. Characteristics of REGARDS Accelerometer Study Participants (n = 7985), by Quartile of Total Sedentary Time

Variable	Quartile 1 (n = 1996)*	Quartile 2 (n = 1996)*	Quartile 3 (n = 1997)*	Quartile 4 (n = 1996)*	P for Trend
Baseline data†					
Mean age (SD), *y*	59.2 (7.1)	61.9 (7.6)	64.4 (7.9)	68.7 (8.4)	<0.001
Male, %	48.8	45.1	43.2	46.3	0.058
Black race, %	26.0	28.4	31.3	39.8	<0.001
Region of residence, %					<0.001
Non–belt/buckle	42.5	43.9	46.8	49.0	
Stroke buckle‡	22.6	23.0	21.0	18.9	
Stroke belt§	34.9	33.1	32.2	32.1	
Education, %					<0.001
Less than high school	4.4	4.4	6.1	9.8	
High school graduate	21.9	20.4	22.6	24.6	
Some college	26.8	26.2	26.6	27.5	
College graduate	46.9	49.0	44.7	38.1	
Current smoker, %	9.9	10.2	10.9	11.7	0.043
Alcohol consumption, %‖					<0.001
None	50.0	51.5	57.6	65.0	
Moderate	44.4	42.9	38.2	31.3	
Heavy	5.6	5.6	4.2	3.7	
Mean BMI (SD), *kg/m²*	27.3 (4.8)	28.3 (5.4)	29.1 (5.8)	29.8 (6.4)	<0.001
Diabetes, %	7.6	11.8	15.3	23.5	<0.001
Hypertension, %	38.0	48.0	54.9	65.9	<0.001
Dyslipidemia, %	52.5	55.0	60.3	63.4	<0.001
eGFR <60 mL/min/1.73 m², %	1.9	4.6	8.3	13.3	<0.001
Atrial fibrillation, %	4.7	6.1	6.5	9.2	<0.001
History of CHD, %	8.6	10.9	12.6	19.8	<0.001
History of stroke, %	1.6	2.8	3.2	6.4	<0.001
Accelerometer data					
Mean age at time of accelerometer testing (SD), *y*	65.3 (7.3)	68.0 (7.7)	70.7 (8.0)	75.2 (8.5)	<0.001
Season accelerometer worn, %¶					0.20
Summer	25.8	25.1	21.7	27.0	
Autumn	26.2	25.1	24.3	24.4	
Winter	25.1	26.3	25.0	23.9	
Spring	23.0	23.6	29.0	24.8	
Mean wear time (SD), *min/d*	875.1 (107.8)	860.5 (111.9)	852.2 (112.4)	873.7 (140.8)	<0.001
Valid wear days, %					0.73
4–5 d	1.3	1.4	1.3	1.4	
6–7 d	98.7	98.6	98.7	98.6	
Mean sedentary time (SD), *min/d***	635.3 (47.7)	719.2 (16.6)	771.8 (15.1)	841.0 (33.2)	<0.001
Mean sedentary bout duration (SD), *min/bout*††	6.9 (1.4)	8.7 (1.4)	10.8 (1.7)	19.2 (12.9)	<0.001
Mean light-intensity physical activity (SD), *min/d*‡‡	285.5 (51.7)	209.1 (27.7)	159.7 (26.0)	98.2 (38.8)	<0.001
Mean MVPA (SD), *min/d*§§	26.9 (23.7)	14.9 (15.0)	8.1 (10.4)	2.9 (6.2)	<0.001

BMI = body mass index; CHD = coronary heart disease; eGFR = estimated glomerular filtration rate; MVPA = moderate- to vigorous-intensity physical activity; REGARDS = Reasons for Geographic and Racial Differences in Stroke.
* The cut points were <689.7, ≥689.7–<746.5, ≥746.5–<799.4, and ≥799.4 min/d.
† Demographic data, cardiovascular risk factors, and chronic disease status/medical history data were collected at the original baseline (see Methods section of the **Supplement**).
‡ Coastal plain region of North Carolina, South Carolina, and Georgia.
§ Remainder of North Carolina, South Carolina, and Georgia plus Alabama, Mississippi, Tennessee, Arkansas, and Louisiana.
‖ None: 0 drinks/wk; moderate: >0–14 drinks/wk for men and >0–7 drinks/wk for women; heavy: >14 drinks/wk for men and >7 drinks/wk for women.
¶ Summer: 21 June–20 September; autumn: 21 September–20 December; winter: 21 December–20 March; spring: 21 March–20 June.
** Minutes in which the accelerometer registered <50 counts/min. Corrected for wear time and expressed as the estimated minutes of sedentary time per day given a standardized 16 h of accelerometer wear (see Methods).
†† Consecutive minutes in which the accelerometer registered <50 counts/min.
‡‡ Minutes in which the accelerometer registered 50–1064 counts/min.
§§ Minutes in which the accelerometer registered ≥1065 counts/min.

Table 2. Characteristics of REGARDS Accelerometer Study Participants (*n* = 7985), by Quartile of Mean Sedentary Bout Duration

Variable	Quartile 1 (*n* = 1996)*	Quartile 2 (*n* = 1996)*	Quartile 3 (*n* = 1997)*	Quartile 4 (*n* = 1996)*	*P* for Trend
Baseline data†					
Mean age (SD), *y*	59.9 (7.4)	62.4 (7.8)	64.0 (8.0)	67.8 (8.8)	<0.001
Male, %	38.2	45.2	48.4	51.7	<0.001
Black race, %	31.1	27.9	30.9	35.6	<0.001
Region of residence, %					<0.001
Non-belt/buckle	41.3	44.9	46.1	49.9	
Stroke buckle‡	22.6	22.3	22.2	18.4	
Stroke belt§	36.1	32.8	26.0	31.7	
Education, %					0.35
Less than high school	5.4	5.6	5.1	8.8	
High school graduate	24.7	20.4	21.9	22.3	
Some college	29.1	25.5	26.7	25.8	
College graduate	40.8	48.5	46.3	43.1	
Current smoker, %	12.7	9.5	9.7	10.7	0.062
Alcohol consumption, %‖					<0.001
None	55.8	52.9	54.4	61.0	
Moderate	38.0	42.4	41.6	35.0	
Heavy	6.2	4.7	4.0	4.0	
Mean BMI (SD), *kg/m²*	27.2 (4.9)	28.2 (5.3)	29.1 (5.7)	30.0 (6.4)	<0.001
Diabetes, %	8.6	12.6	14.1	22.9	<0.001
Hypertension, %	42.1	47.3	54.0	63.3	<0.001
Dyslipidemia, %	51.3	56.1	60.1	63.6	<0.001
eGFR <60 mL/min/1.73 m², %	2.1	6.2	6.8	13.0	<0.001
Atrial fibrillation, %	5.4	5.6	7.1	8.3	<0.001
History of CHD, %	9.8	10.9	12.3	19.0	<0.001
History of stroke, %	2.1	2.5	3.3	6.2	<0.001
Accelerometer data					
Mean age at time of accelerometer testing (SD), *y*	66.0 (7.6)	68.6 (7.9)	70.2 (8.1)	74.3 (8.9)	<0.001
Season accelerometer worn, %¶					0.55
Summer	24.8	25.7	22.8	26.4	
Autumn	26.1	25.1	24.8	24.0	
Winter	25.2	24.6	24.2	25.3	
Spring	23.9	24.0	28.2	24.3	
Mean wear time (SD), *min/d*	855.9 (105.6)	871.6 (109.5)	871.2 (117.8)	862.8 (140.7)	<0.001
Valid wear days, %					0.34
4–5 d	1.2	1.1	1.4	1.5	
6–7 d	98.8	98.9	98.6	98.5	
Mean sedentary time (SD), *min/d***	649.3 (58.3)	717.6 (40.7)	766.0 (36.6)	834.5 (42.0)	<0.001
Mean sedentary bout duration (SD), *min/bout*††	6.5 (0.9)	8.7 (0.5)	10.9 (0.8)	19.6 (12.7)	<0.001
Mean light-intensity physical activity (SD), *min/d*‡‡	274.7 (58.2)	211.0 (42.1)	165.7 (36.7)	101.0 (42.7)	<0.001
Mean MVPA (SD), *min/d*§§	20.0 (21.1)	16.1 (18.1)	11.9 (16.0)	4.9 (10.1)	<0.001

BMI = body mass index; CHD = coronary heart disease; eGFR = estimated glomerular filtration rate; MVPA = moderate- to vigorous-intensity physical activity; REGARDS = Reasons for Geographic and Racial Differences in Stroke.
* The cut points were <7.7, ≥7.7–<9.6, ≥9.6–<12.4, and ≥12.4 min/bout.
† Demographic data, cardiovascular risk factors, and chronic disease status/medical history data were collected at the original baseline (see Methods section of the **Supplement**).
‡ Coastal plain region of North Carolina, South Carolina, and Georgia.
§ Remainder of North Carolina, South Carolina, and Georgia plus Alabama, Mississippi, Tennessee, Arkansas, and Louisiana.
‖ None: 0 drinks/wk; moderate: >0–14 drinks/wk for men and >0–7 drinks/wk for women; heavy: >14 drinks/wk for men and >7 drinks/wk for women.
¶ Summer: 21 June–20 September; autumn: 21 September–20 December; winter: 21 December–20 March; spring: 21 March–20 June.
** Minutes in which the accelerometer registered <50 counts/min. Corrected for wear time and expressed as the estimated minutes of sedentary time per day given a standardized 16 h of accelerometer wear (see Methods).
†† Consecutive minutes in which the accelerometer registered <50 counts/min.
‡‡ Minutes in which the accelerometer registered 50–1064 counts/min.
§§ Minutes in which the accelerometer registered ≥1065 counts/min.

Alternatively, to examine the individual and joint associations of total sedentary time and prolonged, uninterrupted sedentary behavior with mortality, participants were classified into 4 categories: low total sedentary time (<750 min/d) and low prolonged sedentary bout time (<10 min/bout), low total sedentary time and high prolonged sedentary bout time (≥10 min/bout), high total sedentary time (≥750 min/d) and low prolonged sedentary bout time, and high total sedentary time and high prolonged sedentary bout time. Hazard ratios for all-cause mortality were calculated for each joint category in comparison with the low–low group in a fully adjusted model (model 3). Thresholds for total sedentary time (750 min/d) and mean sedentary bout duration (10 min/bout) were selected on the basis of the restricted cubic splines and were confirmed using a method described by Contal and O'Quigley (see Methods section of the **Supplement**) (34).

To allow for the possibility that sedentary bouts of a certain length may have greater or lesser association with mortality, we quantified the percentage of total sedentary time accumulated in bouts of 1 to 29, 30 to 59, 60 to 89, and 90 or more minutes. Participants were subsequently stratified into quartiles for each bout length. Analyses were then repeated to test the association between each quartile of sedentary bout threshold with risk for all-cause mortality. To determine the bout length associated with the greatest risk for death (as well as to elucidate the risk associated with each bout length after accounting for one's entire pattern of sedentary time accrual), models were mutually adjusted (that is, all bout thresholds included in a single model) in a fourth model (model 4).

Because breaks in sedentary time have received interest as a potentially important adjunct to physical activity guidelines, as a tertiary analysis we also examined the association between sedentary break characteristics (total number, breaks per sedentary hour, break duration, and break intensity) and risk for all-cause mortality. To evaluate the potential for reverse causality, we conducted a sensitivity analysis excluding participants who died in the first year of follow-up. We also conducted a sensitivity analysis to assess how substantial any unmeasured confounding would need to be to explain the observed associations (35). Analyses were conducted using SAS, version 9.4 (SAS Institute), with the PROC PHREG procedure used to compute Cox regression models and the LGTPHCURV9 macro used to compute cubic splines (36).

Role of the Funding Source

The National Institutes of Health and The Coca-Cola Company had no role in the design, conduct, or analysis of the study or in the decision to submit the manuscript for publication.

RESULTS

Participant Characteristics

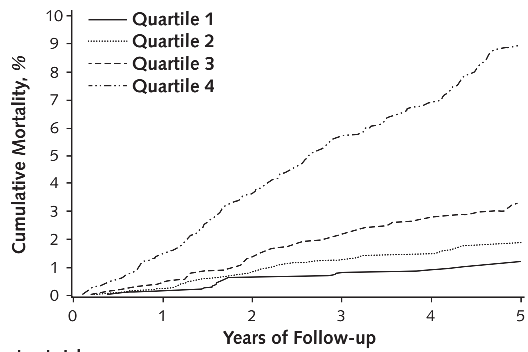
Sedentary behavior accounted for 77.4% (SD, 9.4%) of wear time, equivalent to 12.3 hours (SD, 1.4) per day over a 16-hour waking day. Mean sedentary bout length was 11.4 minutes (SD, 8.1). The percentage of total sedentary time accumulated in bouts of 0 to 29, 30 to 59, 60 to 89, and 90 or more minutes was, on average, 52.0% (SD, 15.5%), 22.1% (SD, 6.2%), 11.8% (SD, 5.7%), and 14.1% (SD, 12.8%), respectively.

Participant characteristics stratified by quartile of total sedentary time are presented in Table 1. On average, participants with greater total sedentary time were older and were more likely to be black; to smoke; to not live in a stroke belt or buckle region; and to have diabetes, hypertension, dyslipidemia, estimated glomerular filtration rate less than 60 mL/min/1.73 m^2, atrial fibrillation, history of coronary heart disease, and history of stroke. They were also less likely to be moderate or heavy drinkers, had greater BMI, and had lower levels of light-intensity physical activity and MVPA. Participant characteristics stratified by quartiles of mean sedentary bout length are presented in Table 2.

Total Sedentary Time, Sedentary Bout Length, and All-Cause Mortality

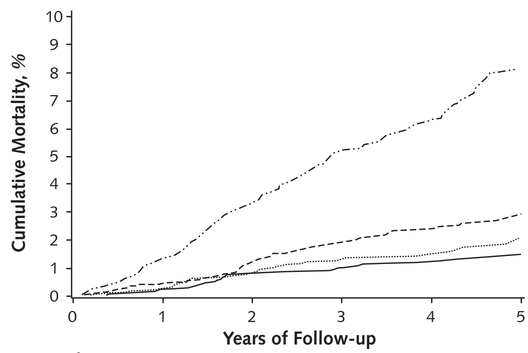
Over a median follow-up of 4.0 years (range, 0.1 to 6.1 years), 340 participants died. When expressed as quartiles, greater total sedentary time and longer mean sedentary bout duration were each dose-dependently associated with a higher risk for all-cause mortality (Figure 1 and Supplement Table 2, available at Annals.org). Adjustment for MVPA attenuated these associations, but all results remained statistically significant. The associations of total sedentary time and sedentary bout duration quartiles with all-cause mortality did not vary by age, sex, race, BMI, or MVPA category (interaction *P*

Figure 1. Adjusted cumulative mortality, by quartiles of total sedentary time (*top*) and mean sedentary bout duration (*bottom*).



Participants at risk, *n*

Quartile 1	1996	1994	1878	1649	1107	421
Quartile 2	1996	1954	1869	1624	1158	447
Quartile 3	1997	1964	1863	1606	1157	436
Quartile 4	1996	1921	1799	1493	1002	393

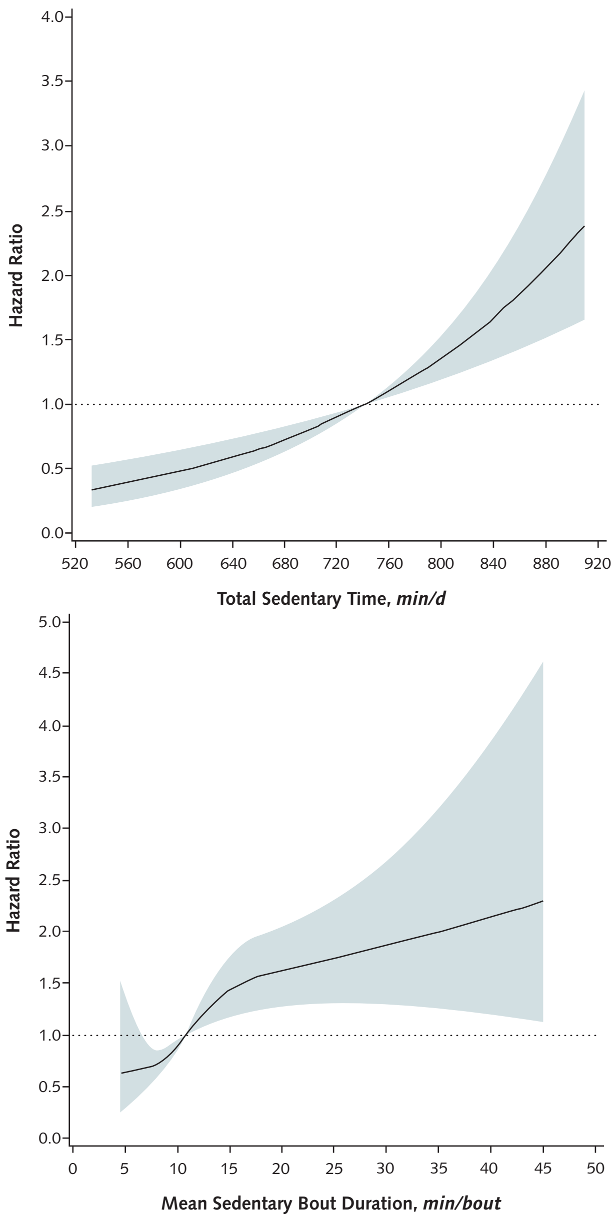


Participants at risk, *n*

Quartile 1	1996	1942	1866	1649	1119	428
Quartile 2	1996	1946	1866	1611	1119	451
Quartile 3	1997	1957	1873	1617	1204	443
Quartile 4	1996	1928	1804	1495	982	375

Models adjusted for age, sex, race, region of residence, education, season, current smoking, alcohol use, body mass index, diabetes, hypertension, dyslipidemia, estimated glomerular filtration rate <60 mL/min/1.73 m^2, atrial fibrillation, history of coronary heart disease, history of stroke, and moderate to vigorous physical activity. The quartile cut points were <689.7, ≥689.7 to <746.5, ≥746.5 to <799.4, and ≥799.4 min/d for total sedentary time and <7.7, ≥7.7 to <9.6, ≥9.6 to <12.4, and ≥12.4 min/bout for sedentary bout duration.

Figure 2. Hazard ratio of all-cause mortality as a function of total sedentary time (*top*) and mean sedentary bout duration (*bottom*) expressed continuously.



Data were fitted using restricted cubic splines with the mean of each sedentary characteristic set as the reference and 4 knots placed at the 5th, 35th, 65th, and 95th percentiles. Results are trimmed at the 1st and 99th percentiles and reported as hazard ratios (*black line*) and 95% CIs (*shaded area*). Total sedentary time is a linear model (*P* for overall effect < 0.001; *P* for nonlinear relationship = 0.70), and mean sedentary bout duration is a nonlinear model (*P* for overall effect < 0.001; *P* for nonlinear relationship < 0.001). Models were adjusted for age, sex, race, region of residence, education, season, current smoking, alcohol use, body mass index, diabetes, hypertension, dyslipidemia, estimated glomerular filtration rate <60 mL/min/1.73 m^2, atrial fibrillation, history of coronary heart disease, history of stroke, and moderate to vigorous physical activity.

values > 0.10) (Supplement Figure 3 and Figure 4, available at Annals.org).

Figure 2 shows the cubic splines for risk for all-cause mortality when total sedentary time and mean sedentary bout duration were expressed continuously. Total sedentary time was significantly associated with all-cause mortality in a linear, dose-dependent fashion (*P* for overall effect < 0.001; *P* for nonlinear relationship = 0.70). In contrast, mean sedentary bout duration was significantly associated with all-cause mortality in a nonlinear manner (*P* for overall effect < 0.001; *P* for nonlinear relationship < 0.001). A marked increase in risk for mortality was observed at approximately 10 minutes per bout, suggesting a threshold effect.

Joint Associations of Total Sedentary Time and Prolonged Sedentary Bouts With All-Cause Mortality

Figure 3 shows the joint associations of total sedentary time and sedentary bout length. Participants classified as high for both sedentary characteristics had the highest risk for all-cause mortality (HR, 2.00 [95% CI, 1.45 to 2.75]; *P* < 0.001). Participants classified into the high total sedentary time and low sedentary bout duration group (HR, 1.68 [CI, 1.07 to 2.65]; *P* = 0.026), but not those classified into the low total sedentary time and high sedentary bout duration group (HR, 1.19 [CI, 0.59 to 2.42]; *P* = 0.62), also had a statistically significant increased risk for all-cause mortality relative to the low total sedentary time and low sedentary bout duration group.

Sedentary Bout Length Thresholds and All-Cause Mortality

Accumulating a higher percentage of sedentary time in bouts of 1 to 29 minutes was associated with less of an increased risk for all-cause mortality (Figure 4 and Supplement Table 3, available at Annals.org) when expressed as quartiles. Conversely, accumulating a higher percentage of sedentary time in bouts of 60 to 89 and 90 or more minutes was associated with a higher risk for all-cause mortality. To distinguish the sedentary bout duration that conferred the greatest risk, models were mutually adjusted by including each sedentary bout threshold in a single model. After mutual adjustment, accumulating a higher percentage of sedentary time in bouts of 1 to 29 minutes remained significantly associated with less of an increased risk for all-cause mortality. Accumulating a higher percentage of sedentary time in bouts of 30 to 59, 60 to 89, and 90 or more minutes was not significantly associated with a greater risk for all-cause mortality after mutual adjustment. The associations of each sedentary bout threshold quartile with all-cause mortality did not vary by age, sex, race, BMI, or MVPA category (interaction *P* values > 0.10). All results were similar when sedentary bout thresholds were expressed continuously in restricted cubic splines, with linear relationships observed for all bout thresholds (Supplement Figure 5, available at Annals.org).

Tertiary and Sensitivity Analyses

In unadjusted and multivariable-adjusted models, a higher number, longer duration, and greater intensity of sedentary breaks were each associated with a lower risk for all-cause mortality (**Supplement Table 4**, available at Annals.org).

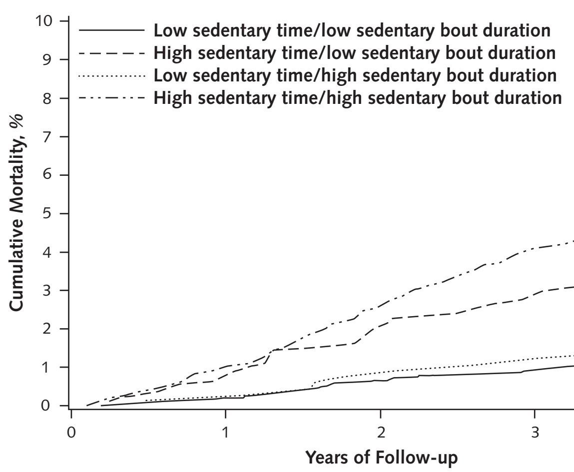
In sensitivity analyses, we found no evidence of reverse causality after excluding early deaths as the pattern of all results was similar (data not shown). We also investigated the effect of a simulated unmeasured confounder on risk for all-cause mortality. For an unmeasured confounder to bring the upper confidence limit of the HR of the uppermost quartile of total sedentary time below 1.00, it would have to be associated with a 2.5-fold increased probability of being in the uppermost quartile and a 3.0-fold increase in risk for all-cause mortality. For an unmeasured confounder to bring the upper confidence limit of the HR of the uppermost quartile of mean duration of sedentary bout below 1.00, it would have to increase both the probability of being in the uppermost quartile and the risk for all-cause mortality by 2.0-fold.

Discussion

In this prospective study of a U.S. national cohort of middle-aged and older adults, both total sedentary time and prolonged, uninterrupted sedentary bouts were associated with an increased risk for all-cause mortality. These associations were independent of MVPA and cardiovascular risk factors (albeit with some attenuation in risk estimates). When the joint associations of both sedentary characteristics were evaluated, high total sedentary time and high sedentary bout duration together were associated with the highest risk for all-cause mortality. These findings highlight the importance of the total volume of sedentary time and its accumulation in prolonged bouts as important health risk behaviors.

Meta-analyses have shown that total sedentary time is associated with cardiovascular disease and mortality, independent of MVPA (5, 37). However, these findings are largely based on self-reported sedentary time, data that may underestimate the magnitude of the relationship between sedentariness and health risk (38). Use of accelerometers reduces potential biases and measurement error inherent in self-reported data. Nonetheless, only 1 study has reported on the association between objectively measured sedentary time and mortality. This previous study, which comprised adults enrolled in NHANES and has been reported in several separate analyses (10–14), have yielded conflicting results: Some analyses reported a statistically significant association between objectively measured sedentary time and all-cause mortality (10, 11, 14, 15), but others did not (12, 13). Differences in inclusion and exclusion criteria, covariates, and follow-up time have been attributed to differences across analyses (12). Relatively small sample sizes (n = 1096 to 4840) and low minority representation (9% to 14% black) have also limited previous findings from NHANES. Thus, our findings add to the literature by confirming the association between total sedentary time and mortality in a national, biracial co-

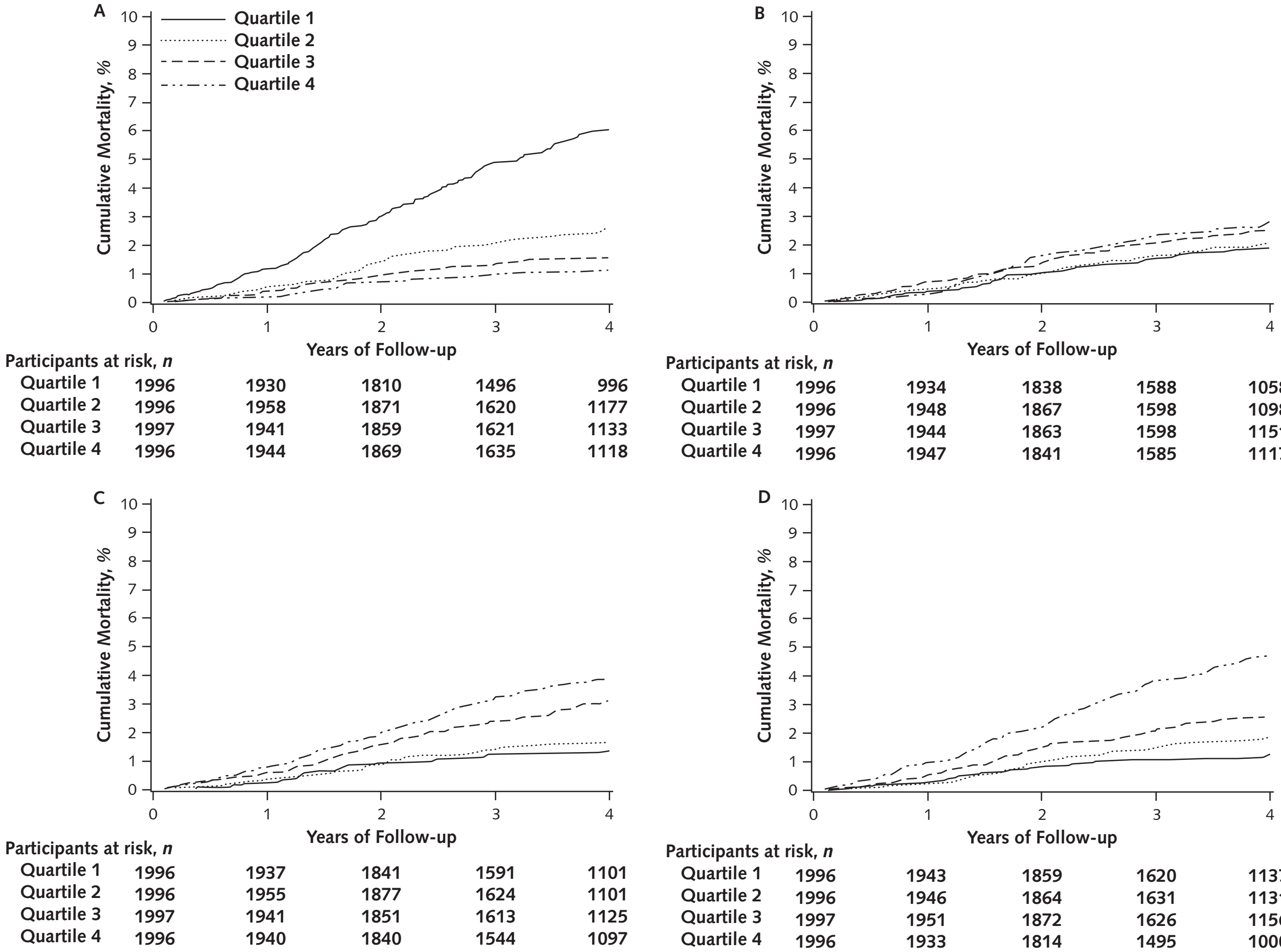
Figure 3. Adjusted cumulative mortality according to joint associations of total sedentary time and prolonged, uninterrupted sedentary bouts.



Participants at risk, *n*					
Low sedentary time/low sedentary bout duration	3689	3600	3462	3031	2077
Low sedentary time/high sedentary bout duration	446	440	420	362	269
High sedentary time/low sedentary bout duration	628	605	573	491	347
High sedentary time/high sedentary bout duration	3222	3128	2954	2488	1731

Models adjusted for age, sex, race, region of residence, education, season, current smoking, alcohol use, body mass index, diabetes, hypertension, dyslipidemia, estimated glomerular filtration rate <60 mL/min/1.73 m^2, atrial fibrillation, history of coronary heart disease, history of stroke, and moderate to vigorous physical activity. High groups were defined as ≥12.5 h/d for total sedentary time and ≥10.0 min/bout for mean sedentary bout duration; low groups were defined as <12.5 h/d and <10 min/bout, respectively. The sample size and number of deaths for each group, respectively, were 3689 and 62 for low total sedentary time and low sedentary bout time, 628 and 30 for high total sedentary time and low sedentary bout time, 446 and 9 for low total sedentary time and high sedentary bout time, and 3222 and 239 for high total sedentary time and high sedentary bout time.

Figure 4. Adjusted cumulative mortality, by quartile of sedentary bout threshold.



A Participants at risk, *n*

	0	1	2	3	4
Quartile 1	1996	1930	1810	1496	996
Quartile 2	1996	1958	1871	1620	1177
Quartile 3	1997	1941	1859	1621	1133
Quartile 4	1996	1944	1869	1635	1118

B Participants at risk, *n*

	0	1	2	3	4
Quartile 1	1996	1934	1838	1588	1058
Quartile 2	1996	1948	1867	1598	1098
Quartile 3	1997	1944	1863	1598	1151
Quartile 4	1996	1947	1841	1585	1117

C Participants at risk, *n*

	0	1	2	3	4
Quartile 1	1996	1937	1841	1591	1101
Quartile 2	1996	1955	1877	1624	1101
Quartile 3	1997	1941	1851	1613	1125
Quartile 4	1996	1940	1840	1544	1097

D Participants at risk, *n*

	0	1	2	3	4
Quartile 1	1996	1943	1859	1620	1137
Quartile 2	1996	1946	1864	1631	1131
Quartile 3	1997	1951	1872	1626	1156
Quartile 4	1996	1933	1814	1495	1000

Models adjusted for age, sex, race, region of residence, education, season, current smoking, alcohol use, body mass index, diabetes, hypertension, dyslipidemia, estimated glomerular filtration rate <60 mL/min/1.73 m^2, atrial fibrillation, history of coronary heart disease, history of stroke, and moderate to vigorous physical activity. **A.** Percentage of sedentary time from bouts of 1 to 29 min. The quartile cut points were <42.2%, ≥42.2% to <53.0%, ≥53.0% to <62.8%, and ≥62.8%. **B.** Percentage of sedentary time from bouts of 30 to 59 min. The quartile cutpoints were <18.1%, ≥18.1% to <22.1%, ≥22.1% to <26.2%, and ≥26.2%. **C.** Percentage of sedentary time from bouts of 60 to 89 min. The quartile cutpoints were <7.6%, ≥7.6% to <11.3%, ≥11.3% to <15.5%, and ≥15.5%. **D.** Percentage of sedentary time from bouts ≥90 min. The quartile cutpoints were <5.2%, ≥5.2% to <10.9%, ≥10.9% to <19.0%, and ≥19.0%.

hort of approximately 8000 middle-aged and older adults. To our knowledge, this is the largest study to date with objective measures of sedentary behavior and prospective health outcomes. The magnitude of the association between total sedentary time and all-cause mortality (2.6-fold greater risk for quartile 4 vs. quartile 1) is notably higher than that reported in meta-analyses (HR, 1.22 [CI, 1.09 to 1.41]) (5). This difference could be attributed to use of objective measures or our analytic sample (middle-aged and older adults and more blacks) and further underscores the total volume of sedentary behavior as a potent risk factor.

A key finding of our study, which we believe is the first to report, is that patterns of sedentary time accumulation are associated with mortality. Previous cross-sectional studies have reported associations between the total number of breaks in sedentary time per day (the reciprocal to mean sedentary bout length) and cardiometabolic biomarkers (28, 39). These findings led to the "prolonger" versus "breaker" hypothesis, which postulates that it is not only the amount of sedentary time that is important to cardiometabolic health, but also the manner in which it is accumulated (40). Subsequent experimental studies have corroborated this hypothesis as greater detrimental cardiometabolic effects have been observed following acute periods of prolonged, uninterrupted sedentary time relative to sedentary time that is periodically interrupted (16, 17). Our findings extend those of previous studies by providing prospective evidence that prolonged, uninterrupted sedentary behavior is associated with a greater risk for all-cause mortality.

Current physical activity guidelines recommend that all age groups minimize their sedentary time (41). These guidelines, however, are generalized and stop short of specific recommendations about how one should reduce their sedentariness. Our finding of a joint association between the volume and pattern of sedentary behavior and mortality suggests that future guidelines should consider reductions in total sedentary time as well as prolonged sedentary bouts. Future randomized controlled trials, however, are still needed. Of note, our findings also provide some of the first empirical evidence regarding how often sedentary behavior should be interrupted. We observed that accumulation of sedentary time in bouts of 60 to 89 and 90 or more minutes was associated with a greater risk for all-cause mortality; conversely, accumulation of sedentary time in 1- to 29-minute bouts was associated with less of an increased risk. With respect to the latter finding, it should be noted that accumulation of large volumes of sedentary time is a hazardous health behavior regardless of how it is accumulated. Nonetheless, this finding suggests that accruing sedentary time in shorter bouts is the least harmful pattern of accumulation.

It is unclear how often sedentary time should be interrupted to reduce the risk incurred by prolonged sedentary bouts. Sedentary breaks every 30 minutes have been proposed as a feasible recommendation (1, 42), which is supported by experimental studies showing that sedentary breaks every 30 minutes elicit beneficial cardiometabolic effects (17). Our results suggest guidelines that recommend interrupting sedentary behavior every 30 minutes could be an optimal target as it was observed that accumulation of sedentary time in bouts of 1 to 29 minutes was associated with less of an increased risk for death, even after accounting for sedentary time accrued in bouts of 60 to 89 and 90 or more minutes. From a feasibility/adoption perspective, sedentary breaks every 60 or 90 minutes may be more tenable to public health uptake. However, middle-aged and older adults average only about 2 sedentary bouts per day longer than 60 minutes and less than 1 sedentary bout per day longer than 90 minutes (43). Furthermore, in the present study, the accumulation of sedentary time in bouts of 60 to 89 and 90 or more minutes was no longer associated with mortality after accounting for the amount of sedentary time accrued in bouts of 1 to 29 minutes. However, caution is warranted when interpreting these results in light of the wide CIs surrounding the point estimates for these bout thresholds.

Our study has several limitations. First, the Actical accelerometer cannot distinguish between postures (such as sitting vs. standing); thus, we relied on an intensity-only definition of sedentary behavior (44). Second, only 7 days of accelerometer data were collected, thus the current study may have undersampled the exposure and yielded unreliable estimates of habitual sedentary time. Third, some participant risk factors were collected at baseline, about 6 years before participants wore the accelerometer, and may have changed (such as diabetes status). Thus, residual confounding may exist from misclassification of participants with respect to important confounders. However, in sensitivity analysis, for an unmeasured confounder to explain the association between total sedentary time or mean sedentary bout duration and all-cause mortality, it would have to increase both the likelihood of being in the uppermost quartile for either sedentary characteristic and the risk for all-cause mortality by 2.0- to 3.0-fold above the measured covariates. This would constitute substantial confounding. Fourth, REGARDS participants included in the current analyses differed in many ways from those excluded. Excluded participants were more likely to be black; smoke; and have lower education levels, diabetes, hypertension, estimated glomerular filtration rate less than 60 mL/min/1.73 m^2, and a history of coronary heart disease and had a greater risk for all-cause mortality than included participants (**Supplement Table 5**, available at Annals.org). Thus, our findings may not be generalizable to the entire REGARDS cohort. Furthermore, there is potential for selection bias as those who participated in REGARDS may not be representative of the general population. Fifth, in analyses examining the joint effects of total sedentary time and prolonged, uninterrupted sedentary bouts, the sample size and number of deaths were small for the groups of participants who had high levels of only 1 of the sedentary characteristics (that is, high total sedentary time and low sedentary bout time or low total sedentary time and high sedentary bout time). Although the association between total sedentary time alone (but not sedentary bout duration alone) and mortality suggests that the volume of sedentary time may be the more hazardous sedentary characteristic, the small number of events and wide CIs in these groups render these findings inconclusive. Thus, caution is warranted when interpreting these results. Finally, the relatively short follow-up may have led to reverse causation.

In conclusion, in a geographically diverse, biracial, population-based sample of middle-aged and older U.S. adults, both total sedentary time and prolonged, uninterrupted sedentary bouts were associated with an increased risk for all-cause mortality, independent of physical activity levels. Our findings suggest that total sedentary time and prolonged, uninterrupted sedentary bouts are jointly associated with increased risk for death and that interrupting sedentary time every 30 minutes may protect against the health risks incurred by prolonged sedentariness. These data may be useful to inform specific recommendations for reducing sedentary behavior and support the concept that reducing and regularly breaking up sedentary time may be an important adjunct to existing physical activity guidelines.

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Reproducible Research Statement: *Study protocol:* Available at www.regardsstudy.org. *Statistical code:* Available through written agreement with authors from Dr. Diaz (e-mail, kd2442@columbia.edu). *Data set:* Available through a data use agreement with University of Alabama at Birmingham (e-mail, regardsadmin@uab.edu).

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