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Original Contribution

Potential Effects on Mortality of Replacing Sedentary Time With Short Sedentary Bouts or Physical Activity: A National Cohort Study

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Little is known concerning the type of activity that should be substituted for sedentary time and its potentially most hazardous form (prolonged sedentary bouts) to impart health benefit. We used isotemporal substitution techniques to examine whether 1) replacing total sedentary time with light-intensity or moderate to vigorous physical activity (LIPA or MVPA) or 2) replacing prolonged sedentary bouts with shorter sedentary bouts is associated with reductions in all-cause mortality risk. Participants (n = 7,999) from the Reasons for Geographic and Racial Differences in Stroke (REGARDS) study, a national cohort of US adults aged ≥45 years, were studied. Sedentary time was measured by accelerometry between 2009 and 2013. There was a beneficial association with mortality risk for replacing total sedentary time with both LIPA (per 30 minutes, hazard ratio (HR) = 0.83; 95% confidence interval (CI): 0.80, 0.87) and MVPA (per 30 minutes, HR = 0.65; 95% CI: 0.50, 0.85). Similarly, there was a beneficial association for replacing prolonged sedentary-bout time with LIPA and MVPA but not for replacement with shorter sedentary bouts (per 30 minutes, HR = 1.00; 95% CI: 0.96, 1.03). These findings suggest short sedentary bouts still carry mortality risk and are not a healthful alternative to prolonged sedentary bouts. Instead, physical activity of any intensity is needed to mitigate the mortality risks incurred by sedentary time.

accelerometer; epidemiology; mortality; physical activity; sedentary

Abbreviations: CI, confidence interval; HR, hazard ratio; LIPA, light-intensity physical activity; MVPA, moderate to vigorous physical activity; NHANES, National Health and Nutrition Examination Survey; REGARDS, Reasons for Geographic and Racial Differences in Stroke; SD, standard deviation.

Technological advancements have fostered changes in transportation, communication, the workplace, and domestic entertainment that have led to an increasingly sedentary lifestyle in developed nations (1). US adults now spend, on average, 11–12 hours per day sedentary (2). Evidence indicates that time spent in sedentary behavior is associated with incident cardiovascular disease and mortality (3, 4). Experimental studies, furthermore, show that accumulation of sedentary time in prolonged, uninterrupted bouts (e.g., sitting for hours at a time) elicits greater detrimental cardiometabolic effects compared with sedentary behavior that is periodically interrupted, suggestive that prolonged sedentary bouts might be the most hazardous type of sedentary behavior (5). Importantly, the risk conferred by prolonged sedentariness is eliminated only by high levels of moderate to vigorous physical activity (MVPA) (6). As such, sedentary behavior is now believed to represent a clinically important aspect of a person's physical activity profile (7).

Studies linking sedentary behavior to health outcomes have relied almost exclusively on self-reported sedentary time, methodology subject to reporting bias and measurement error that is incapable of assessing patterns of sedentary time accumulation (8). Thus, it has been largely unknown which aspects of sedentary behavior should be targeted for intervention (e.g., target reductions in overall sedentary time or target interrupting prolonged sedentary bouts) to mitigate health risk. Recently, we analyzed objective data from a national cohort study to elucidate whether the total volume of sedentary time and its pattern of accumulation individually or jointly contributed to mortality risk (9). We reported that total sedentary time and sedentary bout duration were synergistically associated with mortality risk, suggestive that reducing and regularly breaking up sedentary time might be an important adjunct to existing physical activity guidelines. Although these data are useful to inform which sedentary behavior features to target, they do not provide information concerning what type of activity should be substituted for sedentary time to impart health benefit. For example, is substituting sedentary time with light-intensity physical activity (LIPA) sufficient to reduce mortality risk, or is MVPA needed? Furthermore, does substituting sedentary time with short episodes (or bouts) of physical activity (e.g., 1 minute) reduce mortality risk, or are long episodes (e.g., 10 minutes) needed? Finally, does substituting longer sedentary bouts with shorter sedentary bouts reduce mortality risk, or is physical activity needed? From a public health perspective, given that less than 25% of US adults meet MVPA guidelines (10), elucidating whether any movement (particularly, LIPA and short episodes of activity) confers mortality benefit might have important implications for the widespread adoption of future guidelines. Few studies, however, have explored the mortality benefits of replacing sedentary time (and prolonged sedentary bouts) with alternative activities.

The purpose of this study was to employ isotemporal substitution techniques, a statistical approach that permits evaluation of the health benefit incurred when replacing time spent in one activity type with time in another activity (11), to examine whether replacing sedentary time with LIPA or MVPA is associated with reductions in all-cause mortality risk in a sample of US middle-aged and older adults. We also evaluated the mortality benefit that would be incurred with replacing prolonged, uninterrupted sedentary bouts, potentially the most hazardous form of sedentary behavior, with shorter bouts, LIPA, or MVPA. The 2018 Physical Activity Guidelines Advisory Committee has suggested that there might be health benefit to short episodes of physical activity (12) (contrary to previous guidelines, which endorsed activity bouts of ≥10 minutes (13)); thus, we also evaluated whether the mortality benefits of replacing sedentary behavior with physical activity varies according to the length of activity episodes. Finally, given that evidence suggests the mortality benefit associated with replacing sedentary time with physical activity is dependent on one's total activity levels (14), we examined whether the replacement of sedentary time/sedentary bouts with LIPA or MVPA provided similar mortality benefits among less- and more-active adults.

METHODS

Study population

We studied participants from the Reasons for Geographic and Racial Differences in Stroke (REGARDS) study, a population-based study designed to examine racial/regional disparities in stroke. Participants comprised 30,239 white or black adults, ≥45 years of age, enrolled between 2003 and 2007 from across the United States. Design and methods for REGARDS are described elsewhere (15). Briefly, demographic and cardiovascular risk factor data were collected upon enrollment. A detailed summary of baseline measures is provided in Web Appendix 1 (available at https://academic.oup.com/aje). Participants were then followed at 6-month intervals to ascertain vital status. Objective measures of sedentary behavior were collected from active REGARDS participants from 2009 to 2013 (mean time from enrollment, 5.7 (standard deviation (SD), 1.5) years; range, 1.9–9.5 years) (16). A total of 7,999 participants provided compliant accelerometer wear (≥4 days with accelerometer wear ≥10 hours) and follow-up data. Characteristics of participants who agreed to wear the accelerometer versus those who declined, and of participants with compliant versus noncompliant wear have been reported elsewhere (2, 9, 16). Briefly, those participants who agreed to complete the accelerometer protocol had a higher socioeconomic status compared with those who did not, and those participants with noncompliant wear were more likely to be female, black, and obese compared with those with compliant wear. The REGARDS study protocol was approved by institutional review boards at participating institutions. All participants provided informed consent.

Accelerometer data collection

Methods for accelerometer data collection are described elsewhere (16). Briefly, participants were fitted with an Actical (Philips Respironics, Inc., Murrysville, Pennsylvania) secured to their right hip and were instructed to wear the device during waking hours for 7 consecutive days. The Actical has been validated for measurement of physical activity and sedentary behavior and shown to have acceptable reliability (17–19).

Activity counts were summed over 1-minute epochs. Nonwear periods were defined as >150 consecutive minutes of 0 activity counts. This nonwear algorithm was previously validated (sensitivity: 94%; specificity: 73%) against daily log sheets among REGARDS participants (20). Activity counts of 0–49, 50–1,064, and >1,065 per minute distinguished sedentary behavior, LIPA, and MVPA, respectively, as determined in a laboratory-based calibration study (21). A sedentary bout was defined as consecutive minutes in which the accelerometer registered <50 counts/minute. A physical activity bout was defined as consecutive minutes in which the accelerometer registered ≥50 counts/minute. Sedentary and physical activity variables were summed across each compliant day (≥10 hours of wear) and then averaged across all of a participant's compliant days to derive per-day values.

Outcome ascertainment

All-cause mortality was defined as any death after completion of the accelerometer protocol. Dates of death were confirmed through review of death certificates, medical records, and administrative databases. Deaths occurring through April 1, 2017, were included in the current analysis.

Statistical analyses

Isotemporal substitution models were used to estimate the theoretical effect of substituting total sedentary time with another type of activity (LIPA, MVPA) for the same amount of time while holding accelerometer wear time constant (11). In this model, LIPA, MVPA, and wear time were included in a single Cox regression model (each expressed in 30-minute units) that included adjustment for age, race, sex, region of residence, education, current smoking, alcohol use, body mass index, diabetes, hypertension, dyslipidemia, estimated glomerular filtration rate of <60 mL/minute/1.73 m^2, atrial fibrillation, history of coronary heart disease, and history of stroke. Sedentary time is not included in this model (i.e., it is "dropped"), and resulting hazard ratios estimate the associations for replacing 30 minutes of sedentary time with an equal amount of time in a given type of activity (LIPA or MVPA). To better understand results from the isotemporal analyses, we also fitted Cox regression models (i.e., partition models) that represented the association of each intensity category (sedentary time, LIPA, MVPA) with mortality 1) without mutual adjustment for other activity categories (single-factor models), 2) with adjustment for selected activity categories (2-factor models), and 3) with mutual adjustment for all activity categories simultaneously (3-factor models).

To estimate the theoretical effect of substituting prolonged, uninterrupted sedentary bout time with another type of activity (shorter bouts, LIPA, or MVPA) on mortality risk, shorter sedentary bout time, LIPA, MVPA, and wear time were included in a single Cox regression model (each expressed in 30-minute units) that included adjustment for the above covariates. Resulting hazard ratios estimate the associations for replacing 30 minutes of prolonged sedentary bout time with an equal amount in a given type of activity (short sedentary bouts, LIPA, or MVPA). Three different thresholds to define prolonged sedentary bouts were examined (≥30, ≥60, and ≥90 minutes) based on our previous REGARDS analyses, which showed an association between the selected thresholds and mortality risk (9). In exploratory analyses we tested additional thresholds (5, 10, 20, 40, and 50 minutes) to define prolonged sedentary bouts. We furthermore tested short and moderate bout thresholds versus prolonged bouts (short = 1–29 minutes, moderate = 30–59 minutes, and prolonged = ≥60 minutes) to allow for the possibility that pooling moderate and prolonged bout lengths could obscure associations. All possible combinations of short/moderate/prolonged-bout length thresholds were tested. The above analyses were also repeated examining the theoretical effect of substituting short sedentary bouts (<30-, <60-, and <90-minute thresholds) with another type of activity (longer bouts, LIPA, or MVPA) on mortality risk.

To evaluate whether the mortality benefits of replacing sedentary behavior with physical activity varies according to the length of activity episodes, we estimated the theoretical effect of substituting total sedentary time with physical activity accrued in short (≥1 to <5 minutes), moderate (≥5 to <10 minutes), and long (≥10 minutes) bouts on mortality risk. Short, moderate, and long physical activity bouts and wear time were included in a single Cox regression model (each expressed in 30-minute units) that included adjustment for the above covariates. Because participants accrued only small amounts of MVPA in the respective short, moderate, and long bouts (Web Table 1), physical activity bouts of any intensity were examined. Sedentary bout time could not be examined because of multicollinearity between shorter sedentary bouts and the physical activity bouts.

To evaluate whether the mortality benefit associated with replacing sedentary time with physical activity is dependent on one's total activity levels, the above analyses were repeated, testing for effect modification across high- and low-activity participants (at or above vs. below the median (21.9%) for the percent of wear time spent in physical activity; equivalent to approximately 3.5 hours/day of activity per 16-hour waking day) by including multiplicative interaction terms in the isotemporal model. Interactions for age (<65 and ≥65 years), sex (male and female), race (black and white), and body mass index category (normal weight and overweight/obese) were also examined. To evaluate the potential for reverse causality, we conducted a sensitivity analysis excluding participants who died in the first year of follow-up. Analyses were performed using SAS, version 9.4 (SAS Institute, Inc., Cary, North Carolina). All isotemporal models showed no evidence for multicollinearity (variance inflation factor < 4) and met proportional hazards assumptions.

RESULTS

Participant characteristics

Participant characteristics are presented in Table 1. Participants wore the accelerometer for a mean of 895.2 (SD, 103.1) minutes/day. On average, participants spent 188.0 (SD, 78.2) minutes/day and 13.2 (SD, 17.6) minutes/day in LIPA and MVPA, respectively. Sedentary behavior accounted for 77.6% (SD, 9.4%) of wear time, equivalent to a mean of 694.0 (SD, 116.2) minutes/day. The amount of sedentary time accrued from bouts of ≥30, ≥60, and ≥90 minutes was, on average, 346.6 (SD, 152.5) minutes/day, 193.1 (SD, 135.0) minutes/day, and 108.8 (SD, 109.8) minutes/day, respectively.

Theoretical effects of replacing total sedentary time and sedentary bouts on all-cause mortality risk

Over a median follow-up of 5.5 years (range, 0.1–7.6 years), 647 participants died. In isotemporal substitution models, replacing 30 minutes of total sedentary time with 30 minutes of LIPA was significantly associated with a 17% lower mortality risk and replacement with 30 minutes of MVPA was significantly associated with a 35% lower mortality risk (Table 2). Similarly, there was a beneficial association of replacing short sedentary bout time and prolonged, uninterrupted sedentary bout time with both LIPA (16% lower mortality risk) and MVPA (35% lower mortality risk). Replacing prolonged, uninterrupted sedentary bout time with shorter sedentary bouts (and vice versa) was not associated with a reduction in mortality risk using 30-, 60-, or 90-minute thresholds to define prolonged bouts. All results were similar using alternative thresholds (short/long and short/moderate/long thresholds) to define sedentary bouts (data not shown).

The results from partition models are shown in Web Table 2. Total sedentary time and prolonged, uninterrupted sedentary bout time were both associated with a greater risk for mortality in single-factor models and in 2-factor models that included adjustment for MVPA. These associations, however, were no longer statistically significant in 2-factor models that included adjustment for LIPA or in the 3-factor model that mutually adjusted for all activity categories simultaneously.

Theoretical effects of replacing sedentary behavior according to physical activity bout length

Replacing 30 minutes of total sedentary time with 30 minutes of physical activity (pooling LIPA and MVPA) was significantly associated with a lower mortality risk, regardless

Table 1. Characteristics of Accelerometer Study Participants (n = 7,999), Reasons for Geographic and Racial Differences in Stroke Study, United States, 2003–2013

Variable	Mean (SD)	%
Baseline data[a]		
Age	63.5 (8.5)	
Male sex		45.9
Black race		31.3
Region of residence[b]		
Outside the Stroke Belt or Buckle		45.5
Stroke Buckle		21.4
Stroke Belt		33.1
Education		
Less than high school		6.2
High school graduate		22.4
Some college		26.8
College graduate		44.6
Current smoker		10.6
Alcohol drinking[c]		
None		56.1
Moderate		39.2
Heavy		4.7
Body mass index[d]	28.7 (5.7)	
Diabetes		14.5
Hypertension		51.6
Dyslipidemia		57.8
eGFR < 60 mL/minute/1.73 m^2		7.0
Atrial fibrillation		6.6
History of CHD		13.0
History of stroke		3.5
Accelerometer data		
Wear time, minutes/day	895.2 (103.1)	
Valid wear days		
4–5		10.7
6–7		89.3
Sedentary time, minutes/day	694.0 (116.2)	
Sedentary time from bouts ≥30 minutes, minutes/day	346.6 (152.5)	
Sedentary time from bouts ≥60 minutes, minutes/day	193.1 (135.0)	
Sedentary time from bouts ≥90 minutes, minutes/day	108.8 (109.8)	
LIPA, minutes/day	188.0 (78.2)	
MVPA, minutes/day	13.2 (17.6)	

Abbreviations: CHD, coronary heart disease; eGFR, estimated glomerular filtration rate; LIPA, light-intensity physical activity; MVPA, moderate to vigorous physical activity; SD, standard deviation.

[a] Demographic data, cardiovascular risk factors, and chronic disease status/medical history data were collected at the original baseline evaluation.

[b] Stroke Buckle: coastal plain region of North Carolina, South Carolina, and Georgia; Stroke Belt: remainder of North Carolina, South Carolina, and Georgia, plus Alabama, Mississippi, Tennessee, Arkansas, and Louisiana.

[c] None: 0 drinks/week; moderate: >0 up to 14 drinks/week for men and >0 up to 7 drinks/week for women; heavy: >14 drinks/week for men and >7 drinks/week for women.

[d] Body mass index was calculated as weight (kg)/height $(m)^2$.

of the length of physical activity bouts. There were beneficial associations of replacing total sedentary time with short (≥1 to <5 minutes; per 30 minutes, hazard ratio (HR) = 0.86; 95% confidence interval (CI): 0.76, 0.96), moderate (≥5 to <10 minutes; per 30 minutes, HR = 0.77; 95% CI: 0.63, 0.94) and long (≥10 minutes; per 30 minutes, HR = 0.82; 95% CI: 0.72, 0.92) physical activity bouts on mortality risk.

Effect modification by total physical activity levels

Total physical activity levels moderated the mortality benefit of replacing total sedentary time, short sedentary bouts, and prolonged, uninterrupted sedentary bouts with physical activity (P for interaction < 0.05). For low-activity participants, there was a beneficial association for replacing total sedentary time, short sedentary bout time, and prolonged, uninterrupted sedentary bout time with both LIPA and MVPA on mortality risk (Table 3, upper section). In contrast, there was no mortality benefit observed among high-activity participants (Table 3, lower section). Replacing prolonged, uninterrupted sedentary bout time with shorter sedentary bouts (and vice versa) was not associated with a reduction in mortality risk in either low-activity or high-activity participants. The associations of replacing total sedentary time and prolonged, uninterrupted sedentary bouts with physical activity or shorter bouts (and vice versa) did not vary by age, sex, race, or body mass index category (P for interaction > 0.10, Web Tables 3–6).

Sensitivity analyses

In sensitivity analyses, we found no evidence of reverse causality after excluding early deaths; the pattern of all results was similar (Web Tables 7 and 8).

DISCUSSION

In this prospective study of a US national cohort of middle-aged and older adults, isotemporal substitution modeling suggests that replacing total sedentary time and prolonged, uninterrupted sedentary bouts with either LIPA or MVPA was associated with a reduction in all-cause mortality risk, particularly among those who were less active. Replacing prolonged sedentary bouts with shorter bouts, however, was not associated with a reduction in mortality risk. In the absence of randomized controlled trials examining the benefits of reducing sedentary time (and prolonged sedentary bouts) on mortality, these prospective observational data provide important information that can be used to support the development of evidence-based recommendations for reducing sedentary behavior.

In light of evidence that sedentary behavior is associated with cardiovascular morbidity and mortality, several health agencies have disseminated guidelines that recommend minimizing time spent sedentary (22, 23). Due to insufficient evidence, however, these guidelines stop short of specific recommendations about how one should reduce their sedentariness. Based on the "prolonger" versus "breaker" hypothesis (24) and the supporting evidence that suggests that the manner in which sedentary time is accrued carries clinical relevance (25), many interventions have been designed to target promoting frequent breaks in sedentary behavior (26). However, the ideal replacement

Table 2. Hazard Ratios[a] for Risk of All-Cause Mortality With Substitution of 30 Minutes Per Day of Total Sedentary Time, Short Sedentary Bout Time, and Prolonged, Uninterrupted Sedentary Bout Time With an Equal Amount of Time Spent in Other Activities (n = 7,999), Reasons for Geographic and Racial Differences in Stroke Study, United States, 2009–2017

Sedentary Characteristic	Sedentary Time From Prolonged Bouts of >*N* minutes[b]		Sedentary Time From Short Bouts of <*N* minutes[c]		LIPA		MVPA	
	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI
Total sedentary time					0.83	0.80, 0.87	0.65	0.50, 0.85
Sedentary time from short bouts of <30 minutes	1.01	0.97, 1.04			0.84	0.77, 0.92	0.65	0.50, 0.85
Sedentary time from short bouts of <60 minutes	1.00	0.98, 1.03			0.84	0.79, 0.90	0.65	0.50, 0.85
Sedentary time from short bouts of <90 minutes	1.01	0.98, 1.03			0.84	0.79, 0.89	0.65	0.50, 0.85
Sedentary time from prolonged bouts of ≥30 minutes			1.00	0.96, 1.03	0.84	0.79, 0.89	0.65	0.50, 0.85
Sedentary time from prolonged bouts of ≥60 minutes			1.00	0.97, 1.02	0.84	0.80, 0.88	0.65	0.50, 0.85
Sedentary time from prolonged bouts of ≥90 minutes			1.00	0.97, 1.02	0.84	0.80, 0.87	0.65	0.50, 0.85

Abbreviations: CI, confidence interval; HR, hazard ratio; LIPA, light-intensity physical activity; MVPA, moderate to vigorous physical activity.

[a] Models adjusted for age, sex, race, region of residence, education, current smoking, alcohol use, body mass index, diabetes, hypertension, dyslipidemia, estimated glomerular filtration rate of <60 mL/minute/1.73 m^2, atrial fibrillation, history of coronary heart disease, and history of stroke.

[b] Separate isotemporal models were fitted defining short sedentary bout time as <30 minutes (vs. ≥30 minutes), <60 minutes (vs. ≥60 minutes), and <90 minutes (vs. ≥90 minutes). That is, 3 separate isotemporal models were fitted wherein shorter sedentary bout time (using <30-, <60-, or <90-minute thresholds), LIPA, MVPA, and wear time were included in a single Cox regression model. Prolonged sedentary bout time is omitted from the model; thus resulting HRs estimate associations for replacing 30 minutes of prolonged sedentary bout time with an equal amount in a given type of activity (short sedentary bouts, LIPA, or MVPA).

[c] Separate isotemporal models were fitted defining prolonged, uninterrupted sedentary bout time as ≥30 minutes (vs. <30 minutes), ≥60 minutes (vs. <60 minutes), and ≥90 minutes (vs. <90 minutes). That is, 3 separate isotemporal models were fitted wherein prolonged sedentary bout time (using ≥30-, ≥60-, or ≥90-minute thresholds), LIPA, MVPA, and wear time were included in a single Cox regression model. Short sedentary bout time is omitted from the model; thus resulting HRs estimate associations for replacing 30 minutes of short sedentary bout time with an equal amount in a given type of activity (prolonged sedentary bouts, LIPA, or MVPA).

activities for such prolonged bouts is unclear. To our knowledge, the present study is the first to elucidate the specific activities that are healthful alternatives to prolonged, uninterrupted sedentary bouts with respect to all-cause mortality risk. Although we and others have proposed keeping sedentary bouts shorter in duration (e.g., <30 or <60 minutes) (7, 9), our finding that replacing prolonged sedentary bouts with shorter bouts was not associated with a reduction in mortality risk underscores the fact that sedentary behavior is hazardous, regardless of how it is accumulated, and that simply keeping sedentary bouts short in duration does not alone incur mortality benefit. Instead, physical activity of any intensity is needed.

In the REGARDS cohort, we previously reported that participants who accrued higher amounts of sedentary time in short bouts (e.g., <30 minutes) had a lower mortality risk (9), which could be inferred to suggest that sedentary time is not harmful as long as it is accrued in shorter bouts. While seemingly contradictory, the isotemporal substitution models presented here provide important context for our prior work by highlighting that sedentary behavior incurs risk irrespective of how it is accrued. We postulate that the lower mortality risk among REGARDS participants who accrued their sedentary time largely in short bouts is driven by the fact that such individuals have more opportunity to engage in physical activity, particularly LIPA, which, in our prior work, was not included as a covariate. Results from our partition models corroborate this hypothesis, given that short sedentary bout time was no longer associated with lower mortality risk after adjustment for LIPA. As such, the benefits of interrupting sedentary time more frequently might be that it provides more opportunity to be physically active (and accrue LIPA/MVPA over the course of the day rather than in one occurrence) and accordingly might still be an important public health strategy, because accruing physical activity in long bouts (for example, 2 hours) to offset the risks of sedentary time is likely to be difficult for many to achieve.

Our finding that any physical activity provided mortality risk reduction underscores an important public health message that movement in itself (doing “something”), irrespective of intensity, is beneficial. This might be particularly pertinent for largely sedentary individuals (who comprise much of the US population) and older adults for whom LIPA might be a more practical and achievable preventive strategy. Nonetheless, it should be acknowledged that MVPA provided the most mortality benefit and, thus, should ultimately be the primary target for individuals seeking to mitigate health risk. Previous data from the National Health and Nutrition Examination Survey (NHANES) have similarly demonstrated that replacing total sedentary time with either LIPA or MVPA is associated with a reduction in all-cause mortality risk, with the greatest reduction in mortality risk incurred by MVPA (14, 27, 28). Our study confirms these findings in a larger sample (n = 7,994 vs. n = 3,029–4,840 in NHANES) with greater minority representation (31% black vs. 9%–14% black in NHANES) and extends them to confirm that the mortality benefits of physical activity also pertain to the

Table 3. Hazard Ratios[a] for Risk of All-Cause Mortality With Substitution of 30 Minutes Per Day of Total Sedentary Time, Short Sedentary Bout Time, and Prolonged, Uninterrupted Sedentary Bout Time With an Equal Amount of Time Spent in Other Activities Among High- and Low-Activity Participants (n = 7,999), Reasons for Geographic and Racial Differences in Stroke Study, United States, 2009–2017

Sedentary Characteristic	Sedentary Time From Prolonged Bouts of $>N$ minutes[b]		Sedentary Time from Short Bouts of $<N$ minutes[c]		LIPA		MVPA	
	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI
Low Activity[d]								
Total sedentary time					0.82	0.77, 0.88	0.32	0.18, 0.56
Sedentary time from short bouts of <30 minutes	1.01	0.96, 1.06			0.84	0.73, 0.98	0.34	0.19, 0.60
Sedentary time from short bouts of <60 minutes	0.99	0.96, 1.03			0.80	0.71, 0.90	0.34	0.19, 0.59
Sedentary time from short bouts of <90 minutes	0.99	0.96, 1.02			0.80	0.72, 0.89	0.34	0.19, 0.59
Sedentary time from prolonged bouts of ≥30 minutes			0.99	0.94, 1.04	0.84	0.75, 0.93	0.32	0.18, 0.56
Sedentary time from prolonged bouts of ≥60 minutes			1.01	0.97, 1.04	0.81	0.74, 0.89	0.32	0.18, 0.57
Sedentary time from prolonged bouts of ≥90 minutes			1.01	0.98, 1.04	0.81	0.75, 0.88	0.32	0.18, 0.57
High Activity[e]								
Total sedentary time					0.89	0.79, 1.00	0.94	0.69, 1.28
Sedentary time from short bouts of <30 minutes	0.93	0.85, 1.02			0.83	0.72, 0.97	0.89	0.65, 1.21
Sedentary time from short bouts of <60 minutes	1.01	0.92, 1.12			0.90	0.79, 1.03	0.91	0.67, 1.23
Sedentary time from short bouts of <90 minutes	1.10	0.98, 1.23			0.92	0.81, 1.04	0.91	0.67, 1.24
Sedentary time from prolonged bouts of ≥30 minutes			1.07	0.98, 1.17	0.89	0.79, 1.00	0.98	0.72, 1.35
Sedentary time from prolonged bouts of ≥60 minutes			0.99	0.90, 1.08	0.88	0.78, 1.00	0.93	0.68, 1.28
Sedentary time from prolonged bouts of ≥90 minutes			0.92	0.82, 1.03	0.84	0.73, 0.97	0.88	0.63, 1.21

Abbreviations: CI, confidence interval; HR, hazard ratio; LIPA, light-intensity physical activity; MVPA, moderate to vigorous physical activity.

[a] Models adjusted for age, sex, race, region of residence, education, current smoking, alcohol use, body mass index, diabetes, hypertension, dyslipidemia, estimated glomerular filtration rate of <60 mL/minute/1.73 m^2, atrial fibrillation, history of coronary heart disease, and history of stroke.

[b] Separate isotemporal models were fitted defining short sedentary bout time as <30 minutes (vs. ≥30 minutes), <60 minutes (vs. ≥60 minutes), and <90 minutes (vs. ≥90 minutes). That is, three separate isotemporal models were fitted wherein shorter sedentary bout time (using <30-, <60-, or <90-minute thresholds), LIPA, MVPA, and wear time were included in a single Cox regression model. Prolonged sedentary bout time is omitted from the model; thus resulting HRs estimate associations for replacing 30 minutes of prolonged sedentary bout time with an equal amount in a given type of activity (short sedentary bouts, LIPA, or MVPA).

[c] Separate isotemporal models were fitted defining prolonged, uninterrupted sedentary bout time as ≥30 minutes (vs. <30 minutes), ≥60 minutes (vs. <60 minutes), and ≥90 minutes (vs. <90 minutes). That is, three separate isotemporal models were fitted wherein prolonged sedentary bout time (using ≥30-, ≥60-, or ≥90-minute thresholds), LIPA, MVPA, and wear time were included in a single Cox regression model. Short sedentary bout time is omitted from the model; thus resulting HRs estimate associations for replacing 30 minutes of short sedentary bout time with an equal amount in a given type of activity (prolonged sedentary bouts, LIPA, or MVPA).

[d] Defined as participants below the median (21.9%) for the percent of wear time spent in physical activity (n = 3,999; deaths = 507).

[e] Defined as participants at or above the median (21.9%) for the percent of wear time spent in physical activity (n = 4,000; deaths = 140).

potentially most hazardous type of sedentary behavior (prolonged bouts).

Physical activity guidelines have historically endorsed accumulation of physical activity in bouts of ≥10 minutes (29, 30). The 2018 Physical Activity Guidelines Advisory Committee, however, has contended that such recommendations might be at odds with public health messages (e.g., "take the stairs" or "park your car in the far end of the parking lot") that are intended to encourage lifestyle-oriented physical activity but that take less than 10 minutes (12). Recent evidence from NHANES has demonstrated that MVPA accrued in bouts of ≥5 minutes and ≥10 minutes were similarly associated with a lower risk of mortality and conferred little additional benefit beyond total MVPA (31). Similarly, a UK population-based study of older men reported that LIPA and MVPA accrued in bouts of <10 minutes and ≥10 minutes yielded similar associations with mortality risk (32). Building upon this previous work, the present study is among the first to employ isotemporal substitution techniques to simulate the mortality benefits that could be incurred by replacing sedentary time with physical activity in bouts of varying length. We report that physical activity in bouts of ≥1 to <5, ≥5 to <10, and ≥10 minutes all conferred similar mortality benefit. Such findings might be of public health importance given that they suggest that engaging in physical activity, regardless of the length of bout, confers health benefit.

A key finding of our study is that the mortality benefits of replacing sedentary time (and prolonged, uninterrupted sedentary bouts) with physical activity depend on one's total physical activity levels. Our results showed that less-active adults would incur substantial reduction in mortality by reducing sedentary time (and prolonged, uninterrupted sedentary bouts) by 30 minutes each day in favor of any intensity of physical activity (for LIPA, per 30 minutes, HR = 0.82, 95% CI: 0.77, 0.88; for MVPA, per 30 minutes, HR = 0.32, 95% CI: 0.18, 0.56). In contrast, for more-active adults, replacing sedentary time (and prolonged, uninterrupted sedentary bouts) with more physical activity did not confer additional mortality risk reduction (for LIPA, per 30 minutes, HR = 0.89, 95% CI: 0.79, 1.00; for MVPA, per 30 minutes, HR = 0.94, 95% CI: 0.69, 1.28). Secondary analyses of NHANES similarly showed that replacing total sedentary time with LIPA or MVPA reduced all-cause mortality risk in less-active individuals (at or below median of 5.8 hours/day of total activity) and had no mortality benefit among highly active adults (14). Collectively, the consistency of results across both NHANES and REGARDS—despite differences in sample characteristics, accelerometer devices (Actical vs. ActiGraph AM-7164 (ActiGraph LLC, Pensacola, Florida)), and processing methods (e.g., nonwear algorithm, sedentary threshold)—provides strong evidence that the mortality risk incurred by sedentary behavior could potentially be mitigated by physical activity and corroborates results from a meta-analysis of self-reported data showing that the mortality risk linked with sitting time is eliminated by high levels of MVPA (6). However, because both studies used different criteria to define high- and low-activity participants, future studies are needed to elucidate the optimal amount of physical activity required to mitigate the harmful consequences of sedentary behavior.

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. Therefore, sedentary time might be overestimated because some standing might also be included. Second, only 7 days of accelerometer data were collected; thus, the current study might have undersampled the exposures. Third, participant risk factors were collected at baseline, approximately 6 years before participants wore the accelerometer, and some of the risk factors (such as diabetes status) might have changed. Thus, residual confounding might exist from misclassification of participants with respect to important confounders. Fourth, the relatively short follow-up might have led to reverse causation. Fifth, because we did not have information concerning sleep duration, the isotemporal models did not take into account sleep times (which are inevitably linked to time spent sedentary or physically active). Finally, isotemporal modeling can estimate only the mortality benefits for time trade-offs between sedentary time and alternative activities using statistical models. Thus, it might not fully reflect benefits that would be incurred from actual changes in behavior. Further, it cannot delineate whether the theoretical mortality benefits are the result of reductions in sedentary time or increases in physical activity.

In conclusion, in a population-based sample of middle-aged and older US adults, replacing total sedentary time of 30 minutes/day with LIPA or MVPA (as simulated with isotemporal substitution modeling) was associated with lower all-cause mortality risk, particularly in less-active adults. Replacing prolonged, uninterrupted sedentary bouts with LIPA or MVPA, but not with shorter sedentary bouts, was also associated with lower mortality risk in less-active adults. These findings might be helpful to inform public health strategies for reducing the health risks incurred by sedentary behavior and suggest that short sedentary bouts still carry risk and are not alone a healthful alternative to prolonged sedentary bouts. Instead, physical activity of any intensity (and of any length of time) is needed to mitigate the mortality risks incurred by sedentary time, with greater benefit incurred with more intense activity.

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