Patterns of sedentary behavior and mortality in U.S. middle-aged and older adults: A national cohort study

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Abstract

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Background—Excessive sedentary time is ubiquitous in Westernized societies. Previous studies have relied on self-report 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 of objectively-measured sedentary behavior (its total volume and accrual in prolonged, uninterrupted bouts) with all-cause mortality.

Design—Prospective cohort study.

Setting—Contiguous United States

Participants—7,985 black and white adults   45 years.

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 2-4 to quartile 1 for each exposure (quartile cutpoints: 689.7, 746.5, and 799.4 min/day for total sedentary time; 7.7, 9.6, and 12.4 min/bout for sedentary bout duration) in models that included moderate-vigorous physical activity.

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

Limitations—Participants may not be representative of the general US population.

Conclusions—The total volume of sedentary time as well as how one accrues sedentary time are both associated with all-cause mortality; suggestive that physical activity guidelines should target reducing *and* interrupting sedentary time to reduce mortality risk.

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INTRODUCTION

Adults spend an alarming 9-10 hours/day sedentary.(1) Accordingly, the phrase "sitting is the new smoking" has been coined by popular press to describe a current epidemic of developed nations.(2–4) Evidence indicates sedentary time is associated with incident cardiovascular disease (CVD), incidence of CVD-related risk factors, and mortality.(5, 6) Importantly, the risk conferred by prolonged sedentariness is eliminated only with high levels of moderate-vigorous intensity physical activity (MVPA, ~60-75 min/day) which exceed physical activity recommendations.(7, 8) As such, sedentary behavior is now thought to represent a clinically important aspect of an individual's physical activity profile and is no longer considered simply to be 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 – methodology subject to reporting bias and measurement error. (9) A 2015 systematic review identified only one study that examined the association of

objectively-measured sedentary time with health outcomes;(5) a study (the National Health and Nutrition Examination Survey [NHANES]) limited by a small event rate.(10) New studies utilizing NHANES data have since been published with longer follow-up and higher event rates.(11–15) However, conflicting results have been reported as objectively-measured sedentary time was associated with mortality in some studies,(11, 14, 15) but not others.(12, 13) Additional cohort studies are thus needed to rectify evidence gaps. Furthermore, studies utilizing accelerometers to objectively measure sedentary behavior conventionally operationalize sedentary time as the total number of minutes/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 two distinct patterns of sedentary time accrual. Experimental studies have demonstrated that acute periods of prolonged, uninterrupted sedentary behavior elicit greater detrimental cardio-metabolic effects compared to sedentary behavior that is periodically interrupted,(16–18) suggestive that it is not just total sedentary time that is relevant to health outcomes, but also the manner in which it is accumulated. Few longitudinal studies, however, have explored the association of prolonged uninterrupted sedentary behavior with morality to corroborate these findings.

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

METHODS

Study Population

REGARDS is a population-based study designed to examine racial and regional disparities in stroke. It is comprised of 30,239 white and black adults 45 years of age, enrolled between 2003 and 2007 from across the contiguous U.S.(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 upon enrollment. A detailed summary of baseline measures is provided in the Appendix (available at www.annals.org). Participants (or their proxies) were then followed at 6-month intervals to ascertain vital status. Objective measurements of sedentary behavior were collected from active REGARDS participants from 2009 to 2013 (mean years from study enrollment: 5.7 years [standard deviation, SD: 1.5 years]; range: 1.9-9.5 years). (22) A total of 7,985 participants provided compliant accelerometer wear (4 days with accelerometer wear 10 hours) and follow-up data and were available for the current analyses (Appendix Figure 1). Appendix Table 1 shows the characteristics of REGARDS

participants who were included vs. excluded from the current analyses. All participants provided informed consent.

Accelerometer Data Collection

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

Activity counts were summed over 1-minute epochs. Non-wear periods were defined as ≥150 consecutive minutes of 0 activity counts. This non-wear algorithm was previously validated against daily log sheets in REGARDS participants.(26) Counts of 0-49 counts per minute (cpm), 50-1064 cpm, and ≥1065 cpm distinguished sedentary behavior, light intensity physical activity (LIPA), 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 <50 cpm. A sedentary break was defined as at least 1 minute in which counts registered ≥50 cpm after a sedentary bout. Both sedentary bouts and breaks were exclusively continuous periods with no interruptions or non-wear 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 occurring through September 4, 2015 were included in the current analysis.

Statistical Analyses

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 (Appendix Figure 2), we corrected for the influence of wear time by standardizing total sedentary time to 16 hours of wear time/day using the residuals obtained when regressing total sedentary time on wear time (see Appendix Methods).(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 modelling was used to calculate the hazard ratio (HR) for all-cause mortality associated with total sedentary time (and separately mean sedentary bout length) quartiles. Crude HRs were initially calculated. Subsequently, HRs were calculated with 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 (eGFR) <60 ml/min/1.73 m^2, atrial fibrillation, history of coronary heart disease (CHD), 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/obese), and MVPA category (<150 min/week and 150 min/week).

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) Non-linear associations were evaluated using the likelihood ratio test. For non-linear 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. Alternatively, to examine the individual and joint associations of total sedentary time and prolonged, uninterrupted sedentary behavior with mortality, participants were classified into four categories: low total sedentary time (<750 min/day) 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/day) and low prolonged sedentary bout time, and high total sedentary time and high prolonged sedentary bout time. HRs for all-cause mortality were calculated for each joint category in comparison to the low/low group in a fully adjusted model (Model 3). Thresholds for total sedentary time (750 min/day) and mean sedentary bout duration (10 min) were selected on the basis of the restricted cubic splines and were confirmed using a method described by Contal and O'Quigley (see Appendix Methods).(34)

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

As 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 of sedentary break characteristics (total number, breaks/sedentary hour, break duration, and break intensity) with risk of 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, Cary, NC), with the PROC

PHREG procedure used to conduct Cox regression models and the LGTPHCURV9 macro used to conduct cubic splines.(36)

Institutional Review Board Approval

The REGARDS study protocol was approved by Institutional Review Boards at participating institutions.

Role of the Funding Source

The National Institutes of Health and 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 (SD: 1.4) hours/day over a 16-hour waking day. Mean sedentary bout length was 11.4 (SD: 8.1) min/bout. The percent of total sedentary time accumulated in bouts 0-29, 30-59, 60-89, and   90 min 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 total sedentary time quartile are presented in Table 1. On average, participants with greater total sedentary time were older, more likely to be black, smoke, live in a non-stroke belt/buckle region, and have diabetes, hypertension, dyslipidemia, eGFR <60 ml/min/1.73 m^2, atrial fibrillation, history of CHD, and history of stroke. They were also less likely to be moderate or heavy drinkers, had greater BMI, and had lower levels of LIPA and MVPA. Participant characteristics stratified by mean sedentary bout length quartiles are presented in Table 2.

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

There were 340 deaths over a median follow-up of 4.0 years (range 0.1 to 6.1 years). When expressed as quartiles, greater total sedentary time and longer mean sedentary bout duration were each dose-dependently associated with a higher risk of all-cause mortality (Figure 1 and Appendix Table 2). 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-values >0.10; Appendix Figures 3 and 4).

Figure 2 shows the cubic splines for risk of 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-value for overall effect <0.001, p-value for non-linear relationship=0.70). In contrast, mean sedentary bout duration was significantly associated with all-cause mortality in a non-linear manner (p-value for overall effect <0.001, p-value for non-linear relationship <0.001). A marked increase in mortality risk was observed at ~10 min/bout; suggestive of 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: 1.45-2.75]; p<0.001). Participants classified into the high total sedentary time/ low sedentary bout duration group (HR: 1.68 [95% CI: 1.07-2.65]; p=0.026), but not those classified into the low total sedentary time/high sedentary bout duration group (HR: 1.19 [95% CI: 0.59-2.42]; p=0.62), also had a statistically significant increased risk for all-cause mortality.

Sedentary Bout Length Thresholds and All-Cause Mortality

Accumulating a greater percent of sedentary time in bouts of 1-29 min was associated with less of an increased risk for all-cause mortality (Figure 4 and Appendix Table 3) when expressed as quartiles. Conversely, accumulating a greater percent of sedentary time in bouts of 60-89 min and 90 min were associated with a higher risk of all-cause mortality. To distinguish the sedentary bout duration that confers the greatest risk, models were mutually adjusted by including each sedentary bout threshold in a single model. After mutual adjustment, accumulating a greater percent of sedentary time in bouts of 1-29 min remained significantly associated with less of an increased risk of all-cause mortality. Accumulating a greater percent of sedentary time in bouts of 30-59, 60-89, and 90 min were not significantly associated with a greater risk of 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 (Appendix Figure 5).

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 of all-cause mortality (Appendix Table 4).

In sensitivity analyses, we found no evidence of reverse causality after the exclusion of 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 uppermost total sedentary time quartile 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 uppermost mean sedentary bout duration quartile below 1.00, it would have to both increase the probability of being in the uppermost quartile and increase risk for all-cause mortality by 2.0 fold.

DISCUSSION

In this prospective study of a U.S. national cohort of middle- and older-aged 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 (e.g. high total sedentary time *and* high sedentary bout duration). 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 demonstrated that total sedentary time is associated with CVD and mortality, independent of MVPA.(5, 37) However, these findings are largely based on self-reported sedentary time, data which 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-report data. Nonetheless, only one study has reported on the association of 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) has yielded conflicting results with some studies reporting a significant association between objectively-measured sedentary time and all-cause mortality, (10, 11, 14, 15) but not others.(12, 13) Differences in inclusion/exclusion criteria, covariates, and follow-up time have been attributed to differences across analyses.(12) A relatively small sample size (n=1,096-4,840) and low minority representation (~9-14% black) have also limited previous findings from NHANES. Thus, our findings add to the literature by confirming the association of total sedentary time and mortality risk in a national, biracial cohort of ~8,000 middle- and older-aged adults, the largest study to date with objective measures of sedentary behavior and prospective health outcomes. The magnitude of the association of total sedentary time with all-cause mortality (2.6-fold greater risk for quartile 4 vs. quartile 1) is notably higher than reported in meta-analyses (HR=1.22 [95% CI: 1.09-1.41])(5), which could be attributed to use of objective measures and/or the analytic sample (e.g. middle- and older-aged adults, more blacks), and further underscores the total volume of sedentary behavior as a potent risk factor.

A key finding of this study is that it is the first to report 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/day (the reciprocal to mean sedentary bout length) and cardiometabolic biomarkers.(28, 39) These findings led to the "prolonger" vs. "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 all age groups minimize their amount of sedentary time.(41) These guidelines, however, are generalized and stop short of specific recommendations about how one should reduce sedentariness. Our finding of a joint

association between the volume and pattern of sedentary behavior 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. Importantly, 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 60-89 min and 90 min bouts were associated with a greater risk for all-cause mortality, while conversely, accumulation of sedentary time in 1-29 min bouts was associated with less of an increased mortality risk. With respect to the latter finding, it should be noted that accumulation of large volumes of sedentary time is a hazardous health behavior irrespective of how it's accumulated. Nonetheless, this finding would suggest that accruing sedentary time in shorter bouts is the least harmful pattern of accumulation.

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

Several limitations should be noted when interpreting our findings. First, the Actical™ cannot distinguish between different postures (e.g. sitting, 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, several years (~6 years) prior to wearing the accelerometer, and may have changed (e.g., diabetes status). Thus, there may be residual confounding from misclassification of participants with respect to important confounders. However, in sensitivity analysis, for an unmeasured confounder to explain the association of total sedentary time or mean sedentary bout duration with all-cause mortality it would have to both increase the likelihood of being in the uppermost quartile for either sedentary characteristic and increase the risk of all-cause mortality by 2.0-3.0 fold above and beyond the measured covariates. This would constitute a substantial confounding. Fourth, there were a number of differences among REGARDS participants included vs. excluded from the current analyses. Excluded participants were more likely to be black, smoke, and have lower education levels, diabetes, hypertension, eGFR <60 mL/min/1.73 m^2, and history of CHD and had a greater risk for all-cause mortality compared to included participants (Appendix Table 5). 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 that were high for only one of the sedentary characteristics (e.g., high total sedentary time/low sedentary bout time and low total sedentary time, high sedentary bout time). Although the association of total sedentary time alone, but not sedentary bout duration alone, with mortality is suggestive that the volume of sedentary time may be the more hazardous sedentary characteristic, the small number of events and wide confidence intervals in these groups render these findings inconclusive. Caution is thus warranted when interpreting these results. Finally, the relatively short follow-up period may have led to reverse causation.

In conclusion, in a geographically diverse, biracial population-based sample of middle- and older aged 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 mortality risk and that breaking up sedentary time every 30 min may be protective 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.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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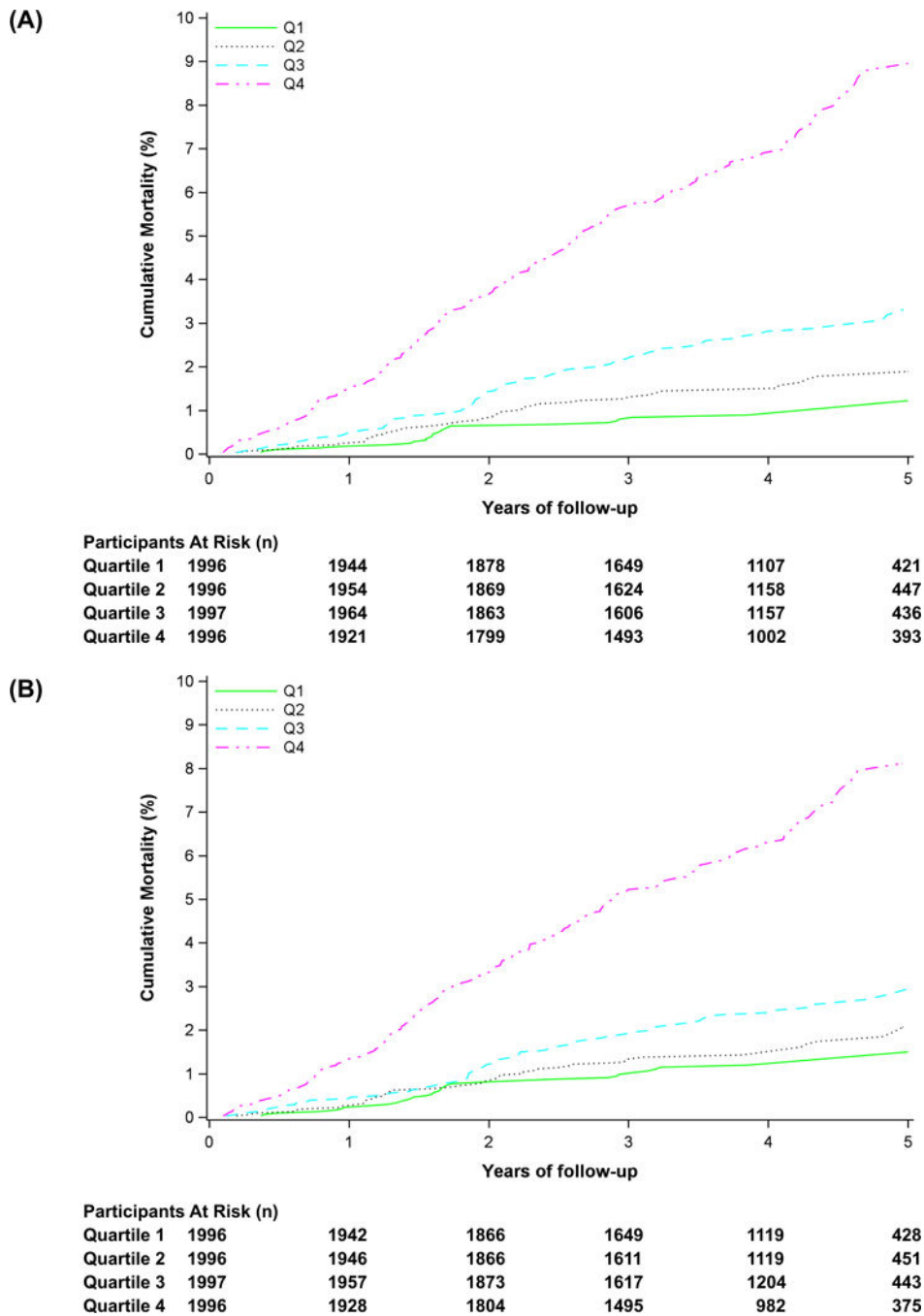
Figure 1. Adjusted cumulative mortality by total sedentary time (Panel A) and mean sedentary bout duration (Panel B) quartiles

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 m2, atrial fibrillation, history of coronary heart disease, history of stroke, and moderate-vigorous physical activity. The quartile cutoff points were <689.7, 689.7 to <746.5, 746.5 to <799.4, and 799.4 min/day 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.
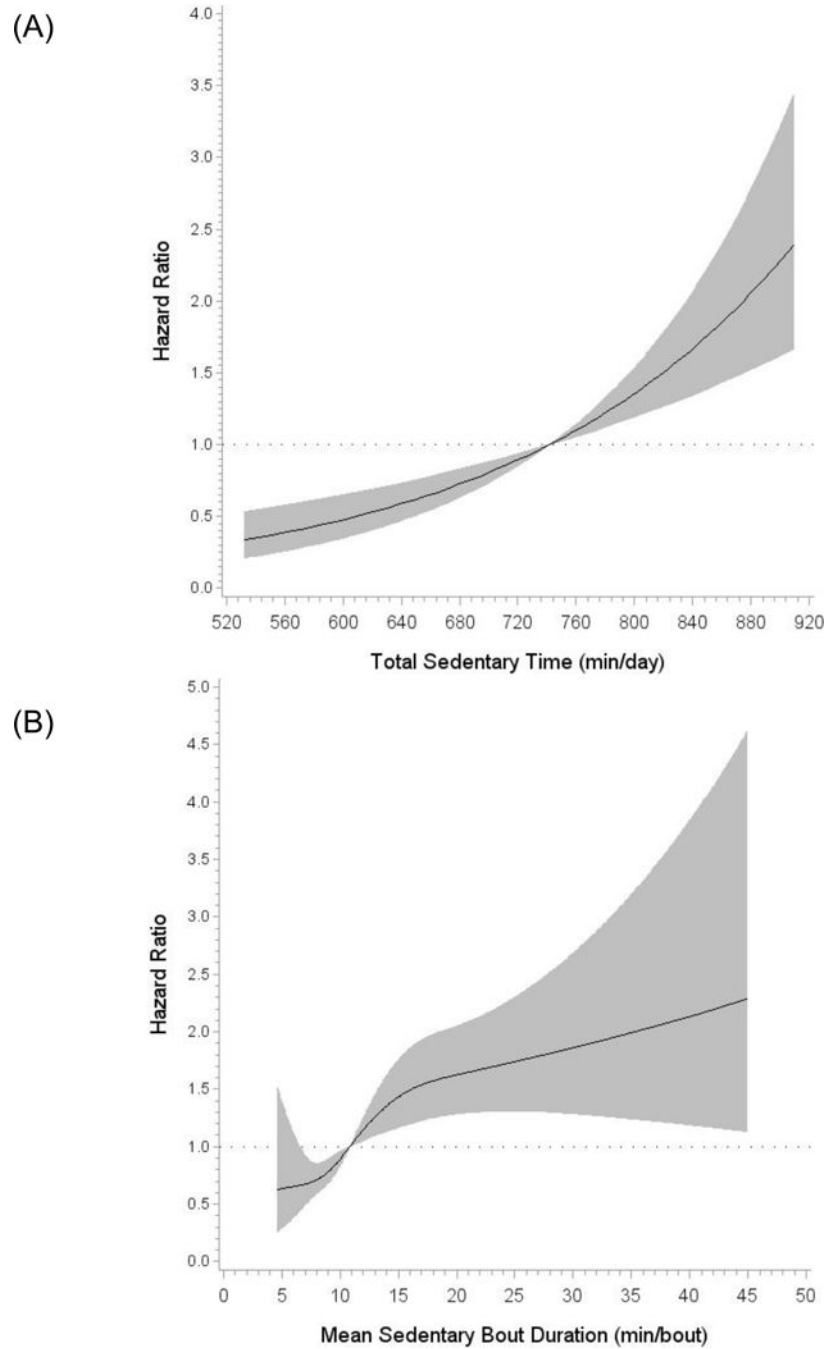
Figure 2. Hazard ratio of all-cause mortality as a function of total sedentary time (Panel A) and mean sedentary bout duration (Panel B) expressed continuously

Data were fitted using restricted cubic splines with the mean 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 are reported as hazard ratios (black line) and 95% confidence intervals (gray shaded area). Total sedentary time is a linear model (p-value for overall effect <0.001, p-value for non-linear relationship=0.70) and mean sedentary bout duration is a non-linear model (p-value for overall effect <0.001, p-value for non-linear relationship <0.001). Models were adjusted for age, sex, race, region of residence, education, season, current smoking,
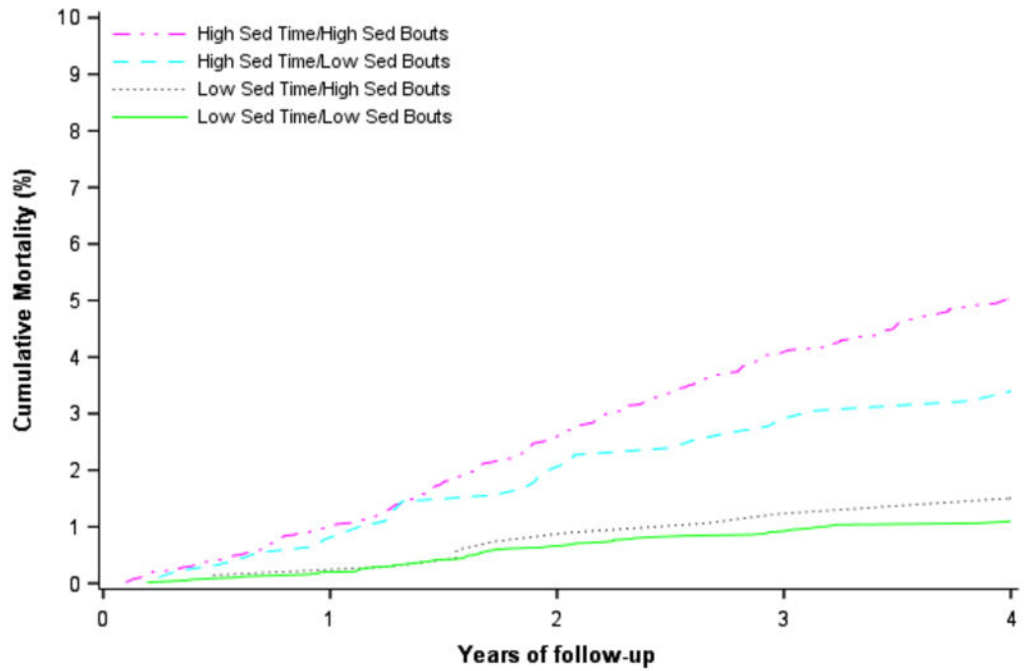
alcohol use, body mass index, diabetes, hypertension, dyslipidemia, estimated glomerular filtration rate <60 mL/min/1.73 m^2, atrial fibrillation, history of coronary heart disease, history of stroke, and moderate-vigorous physical activity.

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

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-vigorous physical activity. High and low groups were defined as   12.5 and <12.5 hours/day for total sedentary time and   10.0 min/bout and <10 min/bout for mean sedentary bout duration. The sample size and number of deaths for each group were as follows: low total sedentary time/low sedentary bout time (n=3,689, deaths=62), high total sedentary time/low sedentary bout time (n=628, deaths=30), low total sedentary time, high sedentary bout time (n=446, deaths=9), high total sedentary time/high sedentary bout time (n=3,222, deaths=239).
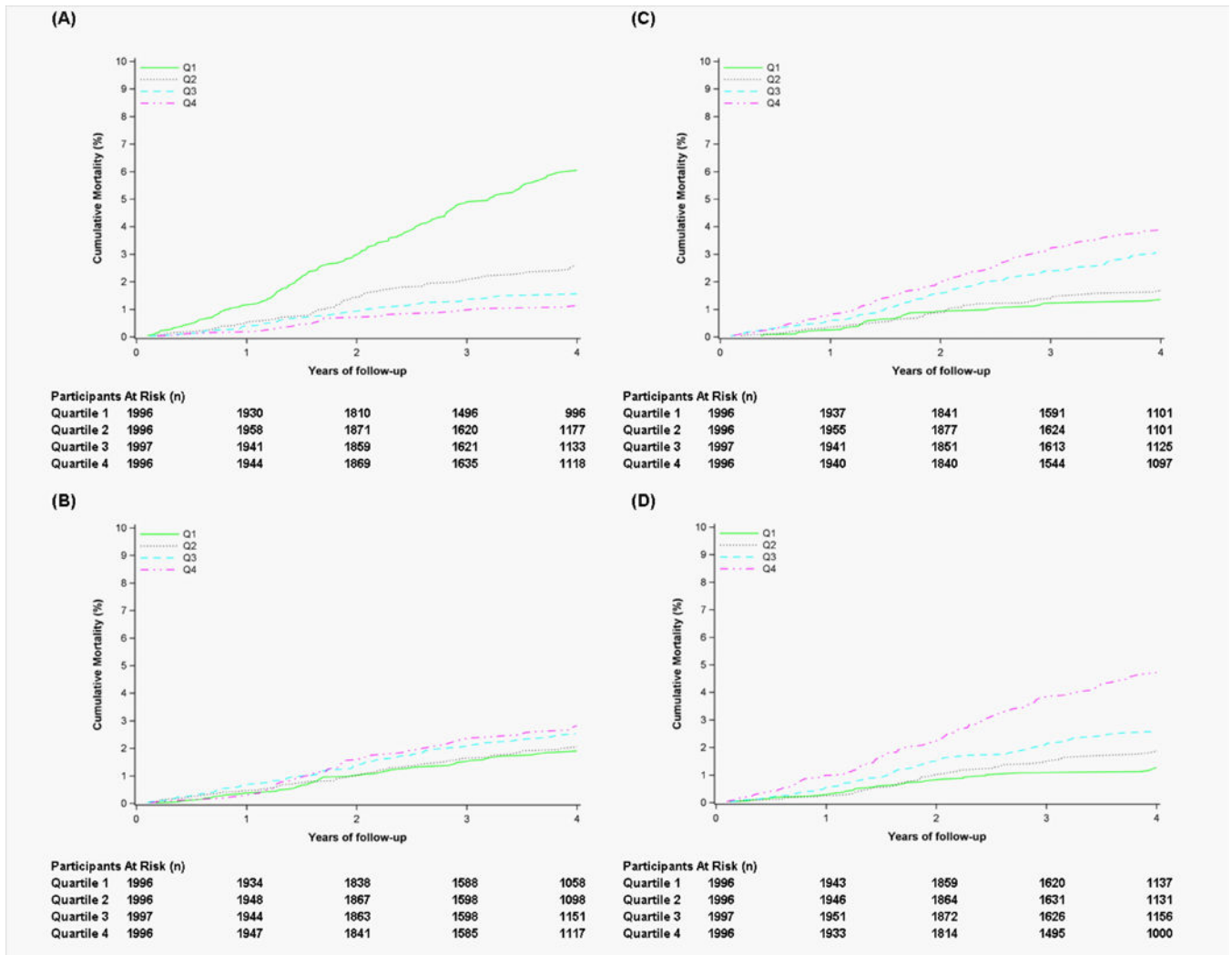
Figure 4. Adjusted cumulative mortality by quartile of sedentary bout threshold
Panel A: %Sedentary Time from Bouts 1-30 min; Panel B: %Sedentary Time from Bouts 30-60 min; Panel C: %Sedentary Time from Bouts 60-90 min; Panel D: %Sedentary Time from Bouts 90 min. Models adjusted for age, sex, race, region of residence, education, season, current smoking, alcohol use, body mass index, diabetes, hypertension, dyslipidemia, estimated glomerular filtration rate <60 mL/min/1.73 m2, atrial fibrillation, history of coronary heart disease, history of stroke, and moderate-vigorous physical activity. The quartile cutoff points were <42.2%, 42.2% to <53.0%, 53.0% to <62.8%, and 62.8% for bouts 0-30 min; <18.1%, 18.1% to <22.1%, 22.1% to <26.2%, and 26.2% for bouts 30-60 min; <7.6%, 7.6 to <11.3%, 11.3% to <15.5%, 15.5% for bouts 60-90 min; and <5.2%, 5.2% to <10.9%, 10.9% to <19.0%, and 19.0% for >90 min bouts.

Table 1

Characteristics of REGARDS accelerometer study participants (n=7,985) by total sedentary time quartile.

Variable	Quartile 1 (n=1996)	Quartile 2 (n=1996)	Quartile 3 (n=1997)	Quartile 4 (n=1996)	P-Trend
Baseline Data[*]					
Age	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 Drinking[‡] (%)					<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	
Body Mass Index (kg/m^2)	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 m^2 (%)	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					

Variable	Quartile 1 (n=1996)	Quartile 2 (n=1996)	Quartile 3 (n=1997)	Quartile 4 (n=1996)	P-Trend
Age at time of accelerometer testing	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	
Wear Time (min/day)	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 days	1.3	1.4	1.3	1.4	
6–7 days	98.7	98.6	98.7	98.6	
Sedentary Time[‖] (min/day)	635.3 (47.7)	719.2 (16.6)	771.8 (15.1)	841.0 (33.2)	<0.001
Sedentary Bout Duration (min/bout)[¶]	6.9 (1.4)	8.7 (1.4)	10.8 (1.7)	19.2 (12.9)	<0.001
LIPA[**] (min/day)	285.5 (51.7)	209.1 (27.7)	159.7 (26.0)	98.2 (38.8)	<0.001
MVPA[††] (min/day)	26.9 (23.7)	14.9 (15.0)	8.1 (10.4)	2.9 (6.2)	<0.001

Data presented as mean (standard deviation) or percent.

CHD, coronary heart disease; LIPA, light intensity physical activity; MVPA, moderate or vigorous intensity physical activity.

[*] Demographic data, cardiovascular risk factors, and chronic disease status/medical history data were collected at the original baseline (see Appendix Methods).

[†] 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.

[‡] None: 0 drinks per week; Moderate: >0 to 14 drinks per week for males and >0 to 7 drinks per week for females; Heavy: >14 drinks per week for males and >7 drinks per week for females.

[§] Summer: June 21–September 20; Autumn September 21–December 20; Winter: December 21–March 20; Spring: March 21–June 20.

[‖] Minutes in which the accelerometer registered <50 counts per minute. Corrected for wear time and expressed as the estimated minutes/day of sedentary time given a standardized 16 hours of accelerometer wear (see Methods).

[¶] sedentary bout is defined as consecutive minutes in which the accelerometer registered <50 counts per min.

[**] Minutes in which the accelerometer registered 50–1064 counts per minute.

[††] Minutes in which the accelerometer registered 1065 counts per minute.

The quartile cutoff points were <689.7, 689.7 to <746.5, 746.5 to <799.4, and 799.4 min/day.

Table 2

Characteristics of REGARDS accelerometer study participants (n=7,985) by mean sedentary bout length quartile.

Variable	Quartile 1 (n=1996)	Quartile 2 (n=1996)	Quartile 3 (n=1997)	Quartile 4 (n=1996)	P-Trend
*Baseline Data**					
Age	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 Drinking [‡] (%)					<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	
Body Mass Index (kg/m^2)	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 m^2 (%)	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					

Variable	Quartile 1 (n=1996)	Quartile 2 (n=1996)	Quartile 3 (n=1997)	Quartile 4 (n=1996)	P-Trend
Age at time of accelerometer testing	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	
Wear Time (min/day)	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 days	1.2	1.1	1.4	1.5	
6–7 days	98.8	98.9	98.6	98.5	
Sedentary Time‖ (min/day)	649.3 (58.3)	717.6 (40.7)	766.0 (36.6)	834.5 (42.0)	<0.001
Sedentary Bout Duration¶ (min/bout)	6.5 (0.9)	8.7 (0.5)	10.9 (0.8)	19.6 (12.7)	<0.001
LIPA** (min/day)	274.7 (58.2)	211.0 (42.1)	165.7 (36.7)	101.0 (42.7)	<0.001
MVPA†† (min/day)	20.0 (21.1)	16.1 (18.1)	11.9 (16.0)	4.9 (10.1)	<0.001

Data presented as mean (standard deviation) or percent.

CHD, coronary heart disease; LIPA, light intensity physical activity; MVPA, moderate or vigorous intensity physical activity.

*
Demographic data, cardiovascular risk factors, and chronic disease status/medical history data were collected at the original baseline (see Appendix Methods).

†
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.

‡
None: 0 drinks per week; Moderate: >0 to 14 drinks per week for males and >0 to 7 drinks per week for females; Heavy: >14 drinks per week for males and >7 drinks per week for females.

§
Summer: June 21-September 20; Autumn September 21-December 20; Winter: December 21-March 20; Spring: March 21-June 20.

‖
Minutes in which the accelerometer registered <50 counts per minute. Corrected for wear time and expressed as the estimated minutes/day of sedentary time given a standardized 16 hours of accelerometer wear (see Methods).

¶
sedentary bout is defined as consecutive minutes in which the accelerometer registered <50 counts per min.

**
Minutes in which the accelerometer registered 50–1064 counts per minute.

††
Minutes in which the accelerometer registered 1065 counts per minute.

The quartile cutoff points were <7.7, 7.7 to <9.6, 9.6 to <12.4, and 12.4 min/bout.