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Continuous physical activity patterns confer greater cardiovascular benefits than sporadic patterns independent of total physical activity

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Abstract

Despite the physiological plausibility that continuous physical activity patterns are cardioprotective beyond total physical activity volume, evidence based on objectively measured activity is lacking. Here, among 58,356 UK Biobank participants with wrist-worn accelerometer data, low activity fragmentation, daily moderate-to-vigorous physical activity (MVPA) bouts lasting ≥ 10 minutes, and daily non-sedentary bouts lasting ≥ 20 minutes were associated with a higher probability of survival free of Major Adverse Cardiovascular Events (MACE) until ages 60, 65, 70, 75, 80, and 85 after adjusting for total physical activity. Dose-response modeling using Cox proportional hazard models revealed that high activity fragmentation, < 10-minute MVPA bouts, and < 20-minute non-sedentary bouts were associated with MACE hazard ratios (HR) of up to 1.38 (95% CI: 1.21, 1.58), 1.65 (1.40, 1.94), and 1.32 (1.16, 1.50) after adjusting for total physical activity. This study provides empirical evidence that, at a given volume of physical activity, more continuous physical activity patterns are associated with greater cardioprotective benefits than sporadic patterns.

Introduction

Physical activity guidance for mitigating cardiovascular risk is centered on physical activity volume[1–3]. The American Heart Association (AHA) recommends accumulating 150 to 300 minutes of aerobic moderate-to-vigorous physical activity (MVPA) per week[2], a recommendation echoed by the World Health Organization (WHO), which further promotes “every move counts towards better health,”[1] encouraging physical activity of any intensity and duration. While replacing any amount of sedentary behavior with physical activity is likely beneficial[4–7], the physiological effects of physical activity depend on the patterns of accumulation. For example, cardiac output and endothelial stress increase with the duration of physical activity bouts, with sustained bouts producing prolonged stimuli that brief bouts are unlikely to replicate at an equivalent intensity[8,9]. The primary longevity-promoting benefit of aerobic physical activity is improved cardiorespiratory fitness[10,11], often measured by peak VO_2 output[12], which is observed to be the highest among endurance athletes whose physical activity regimens primarily consist of sustained physical activity bouts[13]. Bout-duration-dependent physiological adaptations imply that physical activity continuity may shape cardiovascular risk independent of total activity volume in the general population. Nevertheless, the role of physical activity continuity in shaping cardiovascular risk remains unclear.

Recent studies have begun to examine whether physical activity patterns influence cardiovascular risk[14–17]. One study of 33,560 sub-optimally active adults in the United Kingdom categorized participants based on the bout duration in which they accumulated the highest percentage of their daily steps and found a 13.03% cumulative incidence of cardiovascular disease (CVD) in the < 5 minutes category versus only 4.39% in the ≥ 15 minutes category[16]. Another study of 25,241 non-exercisers found that moderate-to-vigorous intermittent lifestyle physical activity (MV-ILPA) performed in bouts lasting less than 1 minute was associated with a MACE hazard ratio (HR) of 1.79 (95% Confidence Interval, 95% CI: 1.40,

2.29) relative to bouts lasting 10 minutes or longer[14]. However, neither study examined associations adjusted for total physical activity, meaning it remains unclear whether physical activity continuity is a volume-independent marker of cardiovascular risk that could supplement guidance based on “every move counts” to provide more optimized recommendations. Additionally, there is a lack of evidence surrounding physical activity continuity based on exposures that directly map to commonly prescribed physical activity regimens based on frequency, timing, intensity, and type (FITT)[8]. Such evidence gaps leave considerable uncertainty regarding the true importance of physical activity continuity and a lack of translatable targets that could be integrated into public health guidance.

Examining the associations of physical activity fragmentation and the longest daily intensity-specific bout duration with MACE could fill these evidence gaps. The fragmentation of an individual’s entire pattern of physical activity accumulation can be quantified using the active-to-sedentary transition probability[18,19] (ASTP). The ASTP measures the probability of transitioning from an active to sedentary state at any given minute, with higher ASTP values being representative of less continuous physical activity patterns comprised of short, sporadic bouts[19]. By contrast, the longest daily intensity-specific bout duration captures the continuity of an individual’s peak daily sustained effort at a given intensity[20], such as MVPA. Operationalizing bout duration using the longest daily intensity-specific bout directly maps to common physical activity patterns, such as daily brisk walks, and can be easily measured without fitness-tracking equipment, making it an accessible physical activity target for the general population. Examining associations of activity fragmentation with incident MACE after adjusting for total physical activity would uncover the importance of continuous overall activity accumulation, whereas examining associations of the longest daily intensity-specific bout duration would provide actionable targets to inform future revisions of public health guidance.

Here, we examined whether physical activity fragmentation, the longest daily bout of MVPA, and the longest daily bout of non-sedentary physical activity are associated with incident MACE independent of total physical activity among 58,356 UK Biobank participants with wrist-worn accelerometer data. We examined probabilities for surviving MACE-free to ages 60, 65, 70, 75, 80, and 85 across clinically reasonable thresholds for activity fragmentation and bout duration, and we used dose-response modeling to characterize potentially non-linear relationships with MACE and individual MACE events: cardiovascular mortality, myocardial infarction, heart failure, and stroke. Our study aimed to provide empirical evidence of whether physical activity continuity may be a viable target for mitigating cardiovascular risk in addition to total physical activity.

Results

An overview of the study methods is presented in Fig. 1. The analytical sample included 58,356 middle-aged and older adults (mean age 62.7, SD 7.7 years; 59.1% female) with at least 5 days of accelerometer data. Across an average follow-up of 7.3 years (SD 1.3), a total of 3,305 MACE events, defined by the earliest occurrence of cardiovascular mortality, myocardial infarction, heart failure, and stroke for each

participant, were recorded. The average longest daily MVPA bout was 13.1 minutes (SD 7.0), the average longest daily non-sedentary bout was 38.9 (SD 15.0) minutes, and the average activity fragmentation, as measured by the active-to-sedentary transition probability[19] (ASTP), was 0.22 (SD 0.1). Complete cohort characteristics are presented in Table 1. Initial modeling using multivariable Cox proportional-hazards models, adjusted for sociodemographic factors, lifestyle factors, and total physical activity, revealed global violations of the proportional-hazards assumption, driven by a lack of proportional-hazards across men and women. Thus, all adjusted models reported hereafter were stratified on sex.

Overview of the study. Data from N = 58,356 UK Biobank participants with at least 5 days of wrist-worn accelerometer data were used in this study, and follow-up health outcomes were derived from ICD-10 codes present in linked medical record data (a). Three measures of physical activity continuity were considered: activity fragmentation (active-to-sedentary transition probability), MVPA bout duration (longest daily bout), and non-sedentary bout duration (longest daily bout) (b). MACE was defined as the earliest occurrence of stroke, myocardial infarction, heart failure, and cardiovascular mortality occurring 2 + years from baseline (c). All Cox models used in the statistical analyses were adjusted for age as the timescale, stratified on sex, and further adjusted for education, BMI, smoking, drinking, total sleep window, systolic and diastolic blood pressure, glycated hemoglobin, HDL and LDL cholesterol, and total time spent active each day (d). Unadjusted MACE-free survival probabilities were examined, as well as standardized adjusted MACE-free survival differences to landmark ages derived from multivariable Cox models, and dose-response curves derived from multivariable Cox models (e). Each MACE outcome was also considered individually in supplementary analyses (not shown). Created in BioRender. Sakal, C. (2026) https://BioRender.com/8i1cd5j.

Table 1
Cohort characteristics

Characteristic*	Mean (SD) or No. (%)		
	Overall (N = 58,356)	Male (N = 23,856)	Female (N = 34,500)
Age (years)	62.72 (7.7)	63.42 (7.8)	62.24 (7.7)
Sex			
Female	34,500 (59.1)	0 (0.0)	34,500 (100.0)
Male	23,856 (40.9)	23,856 (100.0)	0 (0.0)
Education			
A levels	7,698 (13.2)	2,815 (11.8)	4,883 (14.2)
CSEs	2,148 (3.7)	796 (3.3)	1,352 (3.9)
NVQ NHD HNC	2,930 (5.0)	1,875 (7.9)	1,055 (3.1)
O levels	11,923 (20.4)	4,082 (17.1)	7,841 (22.7)
Other not listed	4,774 (8.2)	1,970 (8.3)	2,804 (8.1)
Other professional	2,845 (4.9)	997 (4.2)	1,848 (5.4)
University	26,038 (44.6)	11,321 (47.5)	14,717 (42.7)
Smoker			
Never	33,820 (58.0)	12,680 (53.2)	21,140 (61.3)
Former	20,826 (35.7)	9,331 (39.1)	11,495 (33.3)
Current	3,710 (6.4)	1,845 (7.7)	1,865 (5.4)
BMI	26.61 (4.5)	27.17 (4.0)	26.22 (4.8)
Drinker			
Drinker	55,149 (94.5)	22,814 (95.6)	32,335 (93.7)
Non-drinker	3,207 (5.5)	1,042 (4.4)	2,165 (6.3)
Systolic blood pressure (mmHg)	139.06 (19.3)	142.72 (18.0)	136.52 (19.8)
Diastolic blood pressure (mmHg)	81.73 (10.5)	83.85 (10.3)	80.26 (10.4)
Glycated hemoglobin (HbA1c, mmol/mol)	35.35 (5.4)	35.59 (6.1)	35.18 (4.8)
HDL cholesterol (mmol/L)	1.51 (0.4)	1.32 (0.3)	1.64 (0.4)
LDL cholesterol (mmol/L)	3.61 (0.8)	3.56 (0.8)	3.65 (0.8)

Characteristic*	Mean (SD) or No. (%)		
	Overall (N = 58,356)	Male (N = 23,856)	Female (N = 34,500)
Family history of CVD	31,960 (54.8)	12,572 (52.7)	19,388 (56.2)
Total sleep window (hours)	9.57 (2.1)	9.91 (2.3)	9.33 (1.9)
Time spent active per day (hours)	5.21 (1.6)	4.85 (1.6)	5.46 (1.5)
Physical activity fragmentation	0.22 (0.1)	0.23 (0.1)	0.21 (0.1)
Longest daily non-sedentary bout (mins)	38.87 (15.0)	38.04 (15.6)	39.45 (14.6)
Longest daily MVPA bout (mins)	13.07 (7.0)	13.54 (7.3)	12.75 (6.8)
MACE	3,305 (5.7)	1,896 (7.9)	1,409 (4.1)
MACE follow-up (years)	7.25 (1.3)	7.12 (1.5)	7.35 (1.2)
Cardiovascular mortality	564 (1.0)	357 (1.5)	207 (0.6)
Cardiovascular mortality follow-up (years)	7.46 (0.9)	7.42 (1.0)	7.48 (0.9)
Heart failure	758 (1.3)	454 (1.9)	304 (0.9)
Heart failure follow-up (years)	7.42 (1.0)	7.37 (1.1)	7.46 (0.9)
Myocardial infarction	1,741 (3.0)	1,074 (4.5)	667 (1.9)
Myocardial infarction follow-up (years)	7.32 (1.2)	7.20 (1.4)	7.40 (1.1)
Stroke	1,088 (1.9)	542 (2.3)	546 (1.6)
Stroke follow-up (years)	7.40 (1.0)	7.35 (1.1)	7.44 (1.0)

**CSE = Certificate of Secondary Education, NVQ = National Vocational Qualification, NHD = Higher National Diploma, HNC = Higher National Certificate, BMI = Body Mass Index, HDL = High Density Lipoprotein, LDL = Low Density Lipoprotein, CVD = Cardiovascular Disease, MVPA = Moderate to Vigorous Activity, MACE = Major Adverse Cardiovascular Events.*

MACE-free survival probabilities to landmark ages across categorizations of activity fragmentation and bout duration

Unadjusted Kaplan-Meier curves with age as the timescale showed divergent MACE-free survival trajectories across categorizations of high (above-average) versus low (average or below) activity fragmentation, longest daily MVPA bouts lasting ≥ 10 minutes versus < 10 minutes, and longest daily non-sedentary bouts lasting ≥ 20 minutes versus < 20 minutes (Fig. 2a-c). Low fragmentation, ≥ 10

minute longest daily MVPA bouts, and ≥ 20 minute longest daily non-sedentary bouts corresponded to higher MACE-free survival probabilities, particularly after the age of 65.

Adjusted survival estimates and standardized survival differences, obtained by applying the g-formula to adjusted Cox models, showed that low fragmentation, ≥ 10 minute MVPA bouts, and ≥ 20 minute non-sedentary bouts were associated with a significantly higher likelihood of MACE-free survival to ages 60, 65, 70, 75, 80, and 85 (Fig. 2d-f). Compared to high fragmentation, low fragmentation was associated with a 2.2 percentage point (95% CI: 0.6, 3.7) higher likelihood of becoming an octogenarian without experiencing a MACE event. Longest daily MVPA bouts lasting ≥ 10 minutes were associated with a 3.4 percentage point (95% CI: 1.9, 4.8) higher likelihood than shorter bouts, and longest daily non-sedentary bouts were associated with a 3.0 percentage point (95% CI: 0.8, 5.3) higher likelihood, after adjusting for total physical activity and other confounding factors. Across all primary exposures, differences in the adjusted probability of reaching landmark ages MACE-free were smallest for age 60 and increased with age, with the largest difference for surviving to age 85 MACE-free.

MACE-free survival probabilities across categories of activity fragmentation, MVPA bout duration, and non-sedentary bout duration among N = 58,356 UK Biobank participants. Unadjusted survival probabilities are presented as Kaplan-Meier curves using age as the timescale (a,b,c). Covariate-adjusted absolute MACE-free survival probabilities and MACE-free survival differences (d,e,f) in percentage points (pp) for reaching landmark ages 60, 65, 70, 75, 80, and 85 were computed by applying the g-formula to Cox models adjusted for age as the timescale, stratified on sex, and further adjusted for education, BMI, smoking, drinking, total sleep window, systolic and diastolic blood pressure, glycated hemoglobin, HDL and LDL cholesterol, and total physical activity volume (minutes spent active per day). Error bars for all covariate-adjusted estimates were obtained from 1000 non-parametric bootstrap resamples.

Associations of activity fragmentation and bout duration with MACE

Lower activity fragmentation, longer MVPA bouts, and longer non-sedentary bouts were significantly associated with a lower risk of MACE when modeled continuously in multivariable Cox models adjusted for total physical activity and other confounding factors (Fig. 3a). Every 1-SD decrease in activity fragmentation was associated with a MACE hazard ratio (HR) and 95% confidence interval (95% CI) of 0.88 (95% CI: 0.83, 0.93, $p < 0.0001$), while every 10-minute increase in MVPA bout duration was associated with a MACE HR of 0.85 (95% CI: 0.79, 0.90, $p < 0.0001$), and every 10-minute increase in non-sedentary bout duration was associated with a MACE HR of 0.93 (95% CI: 0.90, 0.97, $p = 0.0001$).

Dose-response modeling in Cox models revealed more nuanced relationships between fragmentation and bout duration with incident MACE events (Fig. 3b-d). Compared to the average fragmentation, the lowest fragmentation was associated with a MACE HR of 0.79 (95% CI: 0.72, 0.87), while the highest fragmentation was associated with a MACE HR of 1.38 (95% CI: 1.21, 1.58). When using the WHO's previous 10-minute MVPA bout duration recommendation as a reference[21], all bout durations less than 10 minutes were associated with a higher risk of MACE, up to a MACE HR of 1.65 (95% CI: 1.40, 1.94),

while MVPA bouts lasting 20 minutes were associated with an even lower risk, corresponding to a MACE HR of 0.88 (95% CI: 0.83, 0.94). Similarly, compared to non-sedentary bouts lasting 20 minutes long, all bout durations shorter than 20 minutes were associated with a heightened MACE risk, up to a MACE HR of 1.32 (95% CI: 1.16, 1.50), whereas bouts longer than 20 minutes were associated with a lower risk. Activity fragmentation was modeled linearly in dose-response models, whereas bout duration was modeled non-linearly based on tests of non-linearity in restricted cubic splines (RCS, Supplementary Table S1). Generalized Variance Inflation Factors did not identify any concerning levels of collinearity between total physical activity and each physical activity continuity exposure in the fully adjusted dose-response models (Supplementary Table S2). Unadjusted and demographics-adjusted models for both linear and dose-response modeling are presented in Supplementary Figures S3 and S4.

Associations of activity fragmentation, MVPA bout duration, and non-sedentary bout duration with incident MACE among N = 58,356 UK Biobank participants. Subplot (a) presents associations per 1-SD decrease in activity fragmentation, per 10-minute increase in MVPA bout duration, and per 10-minute increase in non-sedentary bout duration from Cox models, where each primary exposure was modeled linearly. Subplots b,c, and d present dose-response associations using the mean as the reference for activity fragmentation, 10 minutes as the reference for MVPA bout duration, and 20 minutes as the reference for non-sedentary bout duration. Activity fragmentation was modeled linearly due to no significant evidence of non-linearity, whereas MVPA and non-sedentary bout duration were modeled using restricted cubic splines based on significant evidence of non-linearity (Supplementary Table S1). All Cox models adjusted for age as the timescale, stratified on sex, and further adjusted for education, BMI, smoking, drinking, total sleep window, systolic and diastolic blood pressure, glycated hemoglobin, HDL and LDL cholesterol, and total physical activity volume (minutes spent active per day).

Associations of activity fragmentation and bout duration with individual MACE events

Dose-response modeling using multivariable Cox models further revealed that the associations of activity fragmentation and bout duration with individual MACE events were non-uniform in their significance and effect sizes (Fig. 4). Longer MVPA bouts were significantly associated with a lower risk of all MACE components: stroke ($p = 0.0026$), myocardial infarction ($p < 0.0001$), heart failure ($p < 0.0001$), and cardiovascular mortality ($p = 0.0002$). Lower activity fragmentation was significantly associated with a lower risk of stroke ($p = 0.0002$), myocardial infarction ($p = 0.0177$), and heart failure ($p = 0.0001$), but not cardiovascular mortality ($p = 0.3595$). Lastly, longer non-sedentary bouts were associated with a lower risk of stroke ($p = 0.0182$), myocardial infarction ($p = 0.0276$), and heart failure ($p = 0.0014$), but not cardiovascular mortality ($p = 0.2643$). Effect sizes per 1-SD increase in activity fragmentation and per 10-minute increase in MVPA and non-sedentary bout duration are also presented in Fig. 4a.

Linear (a) and dose-response (b-m) associations of physical activity fragmentation, MVPA bout duration, and non-sedentary bout duration with individual MACE events among N = 58,356 UK Biobank participants. Subplot (a) presents associations per 1-SD decrease in activity fragmentation, per 10-minute increase in MVPA bout duration, and per 10-minute increase in non-sedentary bout duration from Cox models where each primary exposure was modeled linearly. Subplots b-m present dose-response associations where exposures were modeled linearly or non-linearity following tests for non-linearity based on restricted cubic splines (Supplementary Table S1). All Cox models adjusted for age as the timescale, stratified on sex, and further adjusted for education, BMI, smoking, drinking, total sleep window, systolic and diastolic blood pressure, glycated hemoglobin, HDL and LDL cholesterol, and total physical activity volume (minutes spent active per day).

Sensitivity analyses

Lower activity fragmentation and longer bouts of MVPA and non-sedentary activity remained associated with a lower MACE risk across several sensitivity analyses based on the linear and dose-response multivariable Cox models. First, further adjustment for family history of CVD did not change the significance or directionality of our findings in the linear models (all $p \leq 0.0001$) or dose-response models (all $p < 0.0001$, Supplementary Figure S4). Similarly, when we used data-driven knot selection rather than literature-informed values, as recommended by Harrell[22], the significance and shape of the dose-response curves remained consistent with those in the main analysis (Supplementary Figure S5). When modeling was undertaken using a competing risk framework based on Fine-Gray substitution models[23], all findings were consistent with those from our main analysis (Supplementary Figure S6). Finally, when adjusting for total MVPA volume instead of total physical activity volume, all main exposures remained significant in their respective dose-response models (Supplementary Figure S7).

Discussion

This large-scale accelerometer study of 58,356 middle-aged and older adults in the UK Biobank uncovered that physical activity continuity is a total physical activity and MVPA volume-independent marker of cardiovascular risk. At an equivalent volume of physical activity, lower fragmentation, longer daily MVPA bouts, and longer daily non-sedentary bouts were associated with a significantly lower risk of incident MACE. The most fragmented activity patterns were associated with a 38% higher MACE hazard, the shortest MVPA bouts a 65% higher MACE hazard, and the shortest non-sedentary bouts a 32% higher MACE hazard relative to 10-minute MVPA bouts, 20-minute non-sedentary bouts, and the mean fragmentation. Additionally, differences in the adjusted probability of MACE-free survival widened from ages 60 to 85, indicating that physical activity continuity becomes an increasingly relevant marker of cardiovascular risk with age. Our findings establish physical activity continuity as a distinct dimension of physical activity that could be targeted to reduce future risk of MACE.

Our findings provide nuance to a growing body of evidence regarding the importance of physical activity continuity. Studies have linked bout duration, fragmentation, and other measures of continuity to all-cause mortality risk[15,17,18,24,25], but evidence regarding cardiovascular outcomes is more limited in scope[14,16,17]. Daily steps primarily accumulated in longer bouts[16], longer bouts of MV-ILPA[14], and MVPA accumulated in sessions lasting 30 minutes or longer[17] are all associated with lower cardiovascular risks than each exposure's less continuous counterparts. However, prior to the present study, it remained unclear whether physical activity is simply a proxy for greater total activity. Our study directly addressed this gap by showing that physical activity continuity is independently associated with MACE risk beyond total physical activity.

Several possible mechanisms may explain the associative cardioprotective benefits of physical activity continuity observed in the present study. Absent physical activity performed at near-peak aerobic capacity, such as high-intensity interval training[26] (HIIT), which is uncommon in the general population[27,28], prolonged physical activity may be required to elicit positive adaptations in cardiorespiratory fitness, endothelial function, and lipid profiles[8,9,29]. However, a deeper mechanistic investigation is needed, as the associations of physical activity continuity with individual MACE outcomes were heterogeneous in the present study. Longer MVPA bouts were associated with a lower risk of our catch-all MACE outcome and all individual MACE events: stroke, myocardial infarction, heart failure, and cardiovascular mortality. In comparison, activity fragmentation and longest daily non-sedentary bout duration were not associated with cardiovascular mortality. Activity intensity may explain the differences. Activity intensity has previously been found to modify the relationships between physical activity continuity and mortality[24]. Activity fragmentation and non-sedentary bout duration capture physical activity continuity with a lower intensity threshold, which has inherent benefits among older adult populations where significant MVPA accumulation is not as prevalent. However, MVPA bout duration quantifies physical activity continuity with a higher intensity threshold. The combination of continuity and intensity captured by MVPA bout duration likely explains the stronger associations with MACE events relative to the other exposures.

Our findings have direct implications for physical activity guidance. Current guidance from the American Heart Association[2], European Society of Cardiology[3], and World Health Organization[1] recommends 150 to 300 minutes of MVPA per week. The WHO's decision to remove its 2010 recommendation for 10-minute MVPA bouts in favor of the principle that "every move counts towards better health" has shifted its guidelines to be more inclusive of shorter, less intense physical activity. Herein, at a given total physical activity volume, MVPA bouts shorter than 10 minutes and non-sedentary bouts shorter than 20 minutes were associated with substantially higher MACE risk than longer bouts. While "every move counts" remains a valid and inclusive message, our study provides hypothesis-generating evidence that a tiered approach to physical activity guidelines catering to individuals with varying motivations and intrinsic capacities may be warranted. For example, Tier 1 promotes "every move counts," Tier 2 promotes 150 to 300 minutes of MVPA per week accumulated in any pattern, and Tier 3 promotes 150 to 300 minutes of MVPA per week with daily MVPA bouts exceeding 10 minutes and/or non-sedentary

bouts exceeding 20 minutes. It should be noted that tiered, multidimensional frameworks for promoting health behaviors are emerging in other domains, such as sleep, where guidance has shifted from being centered on sleep duration to further include regularity, efficiency, timing, and satisfaction[30–34]. Policymakers and experts involved in drafting future physical activity guidelines could draw such frameworks to balance adherence with health benefits across multiple dimensions of physical activity.

Our large-scale accelerometer study has several strengths. First, total physical activity volume, quantified by the total number of minutes spent active each day, was included as a confounder in our models, allowing our conclusions to directly inform discussions about the importance of physical activity continuity beyond “every move counts.” Second, by using the longest daily intensity-specific bout, our exposures map onto actionable activity patterns such as daily walks and jogs. Bout duration exposures were derived from physical activity recorded during full sleep-wake-sleep cycles, without any tolerance for dips below the intensity thresholds, and therefore are more likely to reflect genuinely sustained activity. Censoring all events within the first two years also minimized the likelihood of reverse causation biasing our findings, though we acknowledge that such biases cannot be entirely excluded. Finally, our results were consistent across changes to covariate adjustments, restricted cubic splines knot selections, and model specifications in sensitivity analyses.

Nevertheless, this study is not without limitations. First, the UK Biobank is non-representative of the UK population and is known to be a healthy volunteer cohort[35]. However, this limitation suggests that our effect estimates are likely conservative. Future studies using population-representative samples are needed to validate our results and establish broader generalizability. Second, our acceleration-defined physical activity intensity thresholds may not align with criteria based on heart rate or rating of perceived exertion (RPE), which more dynamically capture intensity based on an individual’s physiological reserve. However, because the UK Biobank accelerometers did not record heart rate, this limitation was inherent to the dataset. Future studies may wish to use wearables that continuously measure heart rate. Third, the observational design of this study precludes causal inference. Experimental studies examining how physical activity continuity interventions impact cardiovascular biomarkers are needed to elucidate the mechanisms underlying our findings. In conclusion, this study found that more continuous physical activity patterns, characterized by lower fragmentation, longer daily MVPA bouts, and longer daily non-sedentary bouts, were significantly associated with a lower risk of major adverse cardiovascular events beyond total physical activity volume. While “every move counts” and weekly MVPA volume recommendations remain valid targets for health promotion, incorporating guidance that promotes sustained, continuous physical activity accumulation may confer additional health benefits.

Methods

Data source and study design

Data for this study were gathered from the accelerometer sub-study of the UK Biobank[36], a large prospective cohort in the United Kingdom. The accelerometer sub-study was conducted between 2013

and 2015, where 106,053 UK Biobank participants were asked to wear an Axivity AX3 tri-axial accelerometer on their dominant wrist continuously for one week[36]. Consenting participants further provided self-reported health information and underwent biological sampling during visits to assessment centers. Data linkage is also provided to primary care, inpatient hospital records, cancer registries, and death registries. The UK Biobank received ethical approval from the North West Multi-Centre Research Ethics Committee (11/NW/0382). This study was conducted under the UK Biobank project number 67990.

Outcomes

MACE events were ascertained through linked inpatient hospital records based on the International Classification of Diseases, 10th revision (ICD-10) codes. Four MACE events were considered: cardiovascular mortality (ICD-10 codes: I00 – I78)[37], heart failure (ICD-10 codes: I50)[37,38], myocardial infarction (ICD-10 codes: I21 – I25)[38], and stroke (ICD-10 codes: I60 – I69)[37]. A catch-all MACE outcome was derived as the primary outcome in this study, defined by the earliest occurrence of cardiovascular mortality, heart failure, myocardial infarction, or stroke. Individual MACE events were further considered as secondary outcomes. The follow-up period was defined as the time from the end of each participant's accelerometer wear period until death or May 31, 2022. To minimize the likelihood of our analytical findings being biased due to reverse causation, we censored all events within the first two years of follow-up at the time of event[39].

Accelerometer exposures

Three primary exposures were considered in this study: physical activity fragmentation, MVPA bout duration, and non-sedentary bout duration. Based on prior studies[14,15,20,40], a cutoff of 100mg was used as a threshold for MVPA, whereas a cutoff of 40mg was used to differentiate between sedentary and non-sedentary ("active") activity. Physical activity fragmentation was operationalized using the active-to-sedentary transition probability (ASTP), which is defined as one divided by the number of active-to-sedentary transitions divided by the number of active epochs[19]. The ASTP theoretically ranges from 0 to 1, with low values indicating physical activity patterns composed of prolonged, continuous bouts, whereas higher values indicate patterns composed of sporadic, short bouts. MVPA bout duration and non-sedentary bout duration were operationalized using the longest daily intensity-specific bout[20]. The decision to use the longest daily bout was made to capture each individual's peak-intensity-specific sustained physical activity, to allow our findings to map to common activity patterns such as daily walks[9,27,28], and to reduce the likelihood that our bout-duration exposures were biased by unintentional movement. The process of deriving each exposure from the accelerometer data is described below.

First, we used a Hidden Markov Model-based sleep-wake algorithm that has been validated against polysomnography[41] and extensively used in prior accelerometer studies[42,43] to identify daily sleep onset

and offset times. We refer to a valid night of sleep as one in which the sleep-wake algorithm returned sleep estimates, and to a valid day of accelerometer data as all acceleration occurring between two valid nights of sleep. Only valid days of accelerometer data were used to derive activity fragmentation and bout duration, ensuring that all measures were derived from complete sleep-wake-sleep cycles and avoiding bias from incomplete days[44]. Acceleration recordings from each valid day of data were summarized in 1-minute epochs. Binary time series labeling each epoch as MVPA or not, as well as sedentary activity or not, were then created. Thereafter, the longest daily bouts of MVPA and non-sedentary activity, defined as the number of consecutive epochs spent at each intensity, were identified for all valid days, and the average was then calculated. We did not allow any tolerance for brief dips below the MVPA and non-sedentary thresholds, ensuring that each bout duration exposure represents continuous time spent at each intensity and avoiding bias that can arise from mislabeling fragmented MVPA and continuous MVPA[19]. Activity fragmentation was calculated from all valid days of accelerometer data together to represent the overall fragmentation of each participant's weekly activity patterns.

To avoid biased analytical estimates due to sparse and extreme values of fragmentation and bout duration, we winsorized the primary exposures with sparse-tailed data distributions[39]. Activity fragmentation was winsorized at the 2.5th and 97.5th quantiles, whereas MVPA bout duration and non-sedentary bout duration were winsorized at the 97.5th quantile.

Covariates

The following covariates[45] were gathered for use in statistical analyses: age, sex, education, body mass index (BMI), smoking, drinking, total sleep window (hours), systolic blood pressure, diastolic blood pressure, glycated hemoglobin, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, family history of cardiovascular disease, and total physical activity. The total sleep window was derived from accelerometer data using the sleep-wake algorithm mentioned previously[41]. Given that sleep was derived using acceleration only and in the absence of sleep diaries, the sleep window includes time in bed spent awake but still, and thus we elected to use the term sleep window instead of sleep duration. Total physical activity was defined as the average number of minutes spent active each day. Age was calculated based on the age at the start of each participant's accelerometer wear period. All other non-accelerometer-derived covariates were gathered from each participant's assessment center visit that was closest, and prior to, the accelerometer wear period.

Statistical analysis

All analyses were conducted using R version 4.5.1, and statistical significance was set at $p < 0.05$. Numeric variables were summarized based on their mean and standard deviation, whereas categorical variables were summarized based on counts and percentages.

We estimated MACE-free survival probabilities at clinically and behaviorally relevant thresholds for each primary exposure. Activity fragmentation was defined as high (above average) or low (average or below), whereas MVPA bout duration was categorized as < 10 minutes versus ≥ 10 minutes based on the WHO's prior 10-minute MVPA bout duration recommendation[1,21], and non-sedentary bout duration was categorized as < 20 minutes versus ≥ 20 minutes[20]. Unadjusted survival estimates were calculated using the Kaplan-Meier estimator with age as the timescale. Adjusted survival probabilities and standardized survival differences were obtained by applying the g-formula[46] to fully adjusted Cox proportional hazard models. The Cox models adjusted for age as the timescale, stratified on sex, and further adjusted for education, BMI, smoking, drinking, total sleep window, systolic and diastolic blood pressure, glycated hemoglobin, HDL and LDL cholesterol, and total physical activity measured by the number of minutes spent active each day. Stratification by sex was performed after finding that the proportional hazards assumption was violated across sexes, which we formally tested for using the Grambsch and Therneau approach[47]. Adjusted MACE-free survival probabilities, as well as MACE-free survival differences, were calculated for surviving MACE-free until the landmark ages of 60, 65, 70, 75, 80, and 85. The reference categories were defined by high fragmentation, MVPA bouts lasting fewer than 10 minutes, and non-sedentary bouts lasting fewer than 20 minutes.

To gain a more precise understanding of the relationships between activity fragmentation and bout duration with MACE, we further modeled each exposure linearly in fully adjusted Cox models and reported associations as hazard ratios (HRs) and 95% Confidence Intervals (95% CIs) per 1-SD decrease in activity fragmentation, per 10-minute increase in MVPA bout duration, and per 10-minute increase in non-sedentary bout duration. Covariate adjustment was identical to the models examining adjusted MACE-free survival probabilities.

Lastly, dose-response associations between activity fragmentation and bout duration with MACE were examined in fully adjusted Cox models using restricted cubic splines (RCS). For activity fragmentation, RCS knots were placed at the 10th, 50th, and 90th quantiles following Harrell's recommendations and in the absence of literature-informed values for knot selection[22]. Literature-informed knots were placed at 5, 10, and 20 minutes for MVPA bout duration and 20, 40, and 60 minutes for non-sedentary bout duration based on our prior work[20], bout duration categories in other studies[14,16], and commonly prescribed bout duration in physical activity regimens[9]. The reference points were defined by the mean fragmentation, 10 minutes for MVPA bout duration, and 20 minutes for non-sedentary bout duration, mirroring the cut-points used in the adjusted survival probability analyses. Before plotting dose-response curves, we tested for significant evidence of non-linearity using a Wald test. When no significant evidence of non-linearity was found, we refit the fully adjusted model, treating the primary exposure linearly. Dose-response curves were then plotted. MACE HRs and 95% CIs along the dose-response curve were directly reported. For activity fragmentation, we reported the HRs corresponding to the minimum, 25th quantile, 75th quantile, and maximum fragmentation values. For MVPA bout duration, we reported HRs in multiples of 5-minute bout durations. For non-sedentary bout duration, we reported HRs in multiples of 10-minute bout durations. Covariate adjustment was identical to the models examining

adjusted MACE-free survival probabilities. Generalized Variance Inflation Factors were further computed to assess whether collinearity between total physical activity and each continuously modeled bout duration exposure may be causing unstable effect estimates. Univariable and demographics-adjusted models were also fitted, where the demographics-adjusted models accounted for age as the timescale, stratified on sex, and further adjusted for education. We additionally examined associations of activity fragmentation and bout duration with individual MACE events: stroke, myocardial infarction, heart failure, and cardiovascular mortality. We followed the same procedure in the main analysis. Each exposure was initially modeled linearly in fully adjusted Cox models, and HRs were reported per 1-SD decrease and per 10-minute increase in fragmentation and bout duration, respectively. Next, dose-response figures were plotted after testing for non-linearity of RCS terms and refitting the models without RCS if necessary.

Sensitivity analyses

Several sensitivity analyses were undertaken to determine the robustness of our MACE-outcome models. First, we further adjusted for family history of CVD. Second, for MVPA and non-sedentary bout duration, we refit the models using data-driven RCS knot selection, namely by using the 10th, 50th, and 90th quantiles. Third, we refit our fully adjusted models within a competing-risks framework using Fine-Gray substitution, where non-MACE mortality was treated as a competing risk for MACE, and robust standard errors were used to calculate all confidence intervals. Fourth, we refit our full models and adjusted for total MVPA volume instead of simply active minutes per day.

Declarations

Competing interests

None.

Author Contribution

CS conceptualized the study, and all authors participated in finalizing the study design. CS preprocessed and conducted the statistical analyses with support from WX and WZ. All authors were involved in the interpretation of the study's findings. The first manuscript draft was written by CS and revised by all authors. All authors had full access to the underlying data, which was verified by CS, WX, and WZ. CS and XL provided funding for this study. The final manuscript was read and approved by all authors prior to submission.

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Data availability

Access to the UK Biobank can be obtained following an application at https://www.ukbiobank.ac.uk/use-our-data/apply-for-access/.

Code availability

All statistical analyses were undertaken using R version 4.5.1 using the following libraries: ‘rms’, ‘survival’, ‘ggsurvfit’, ‘riskRegression’, and ‘tidymodels’. Figures were created using the following libraries: ‘ggplot2’, ‘ggtext’, and ‘patchwork’.

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Figures

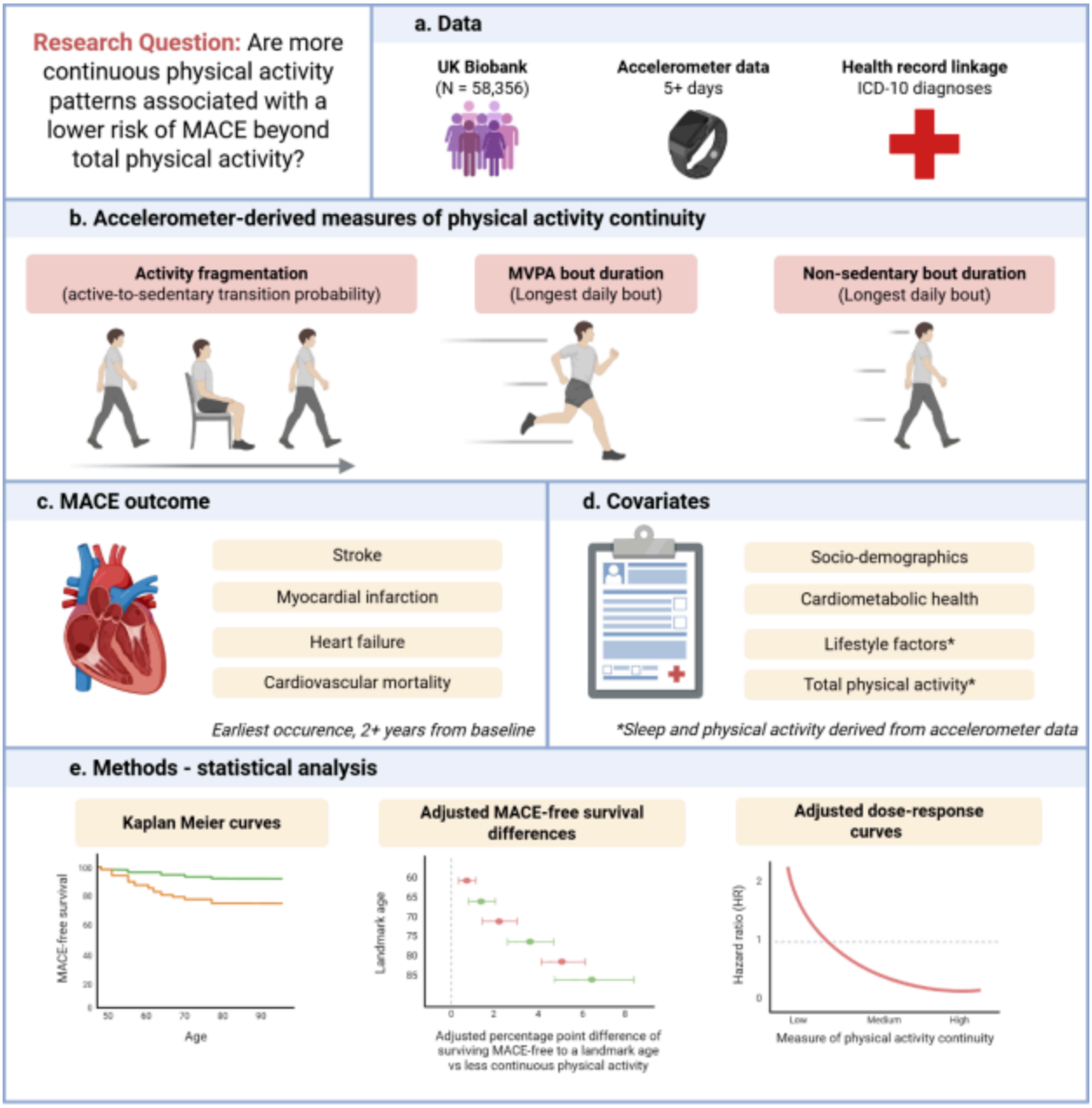


Figure 1

Study overview

Overview of the study. Data from N = 58,356 UK Biobank participants with at least 5 days of wrist-worn accelerometer data were used in this study, and follow-up health outcomes were derived from ICD-10 codes present in linked medical record data (a). Three measures of physical activity continuity were considered: activity fragmentation (active-to-sedentary transition probability), MVPA bout duration (longest daily bout), and non-sedentary bout duration (longest daily bout) (b). MACE was defined as the earliest occurrence of stroke, myocardial infarction, heart failure, and cardiovascular mortality occurring 2+ years from baseline (c). All Cox models used in the statistical analyses were adjusted for age as the

timescale, stratified on sex, and further adjusted for education, BMI, smoking, drinking, total sleep window, systolic and diastolic blood pressure, glycated hemoglobin, HDL and LDL cholesterol, and total time spent active each day (d). Unadjusted MACE-free survival probabilities were examined, as well as standardized adjusted MACE-free survival differences to landmark ages derived from multivariable Cox models, and dose-response curves derived from multivariable Cox models (e). Each MACE outcome was also considered individually in supplementary analyses (not shown). Created in BioRender. Sakal, C. (2026) https://BioRender.com/8i1cd5j.

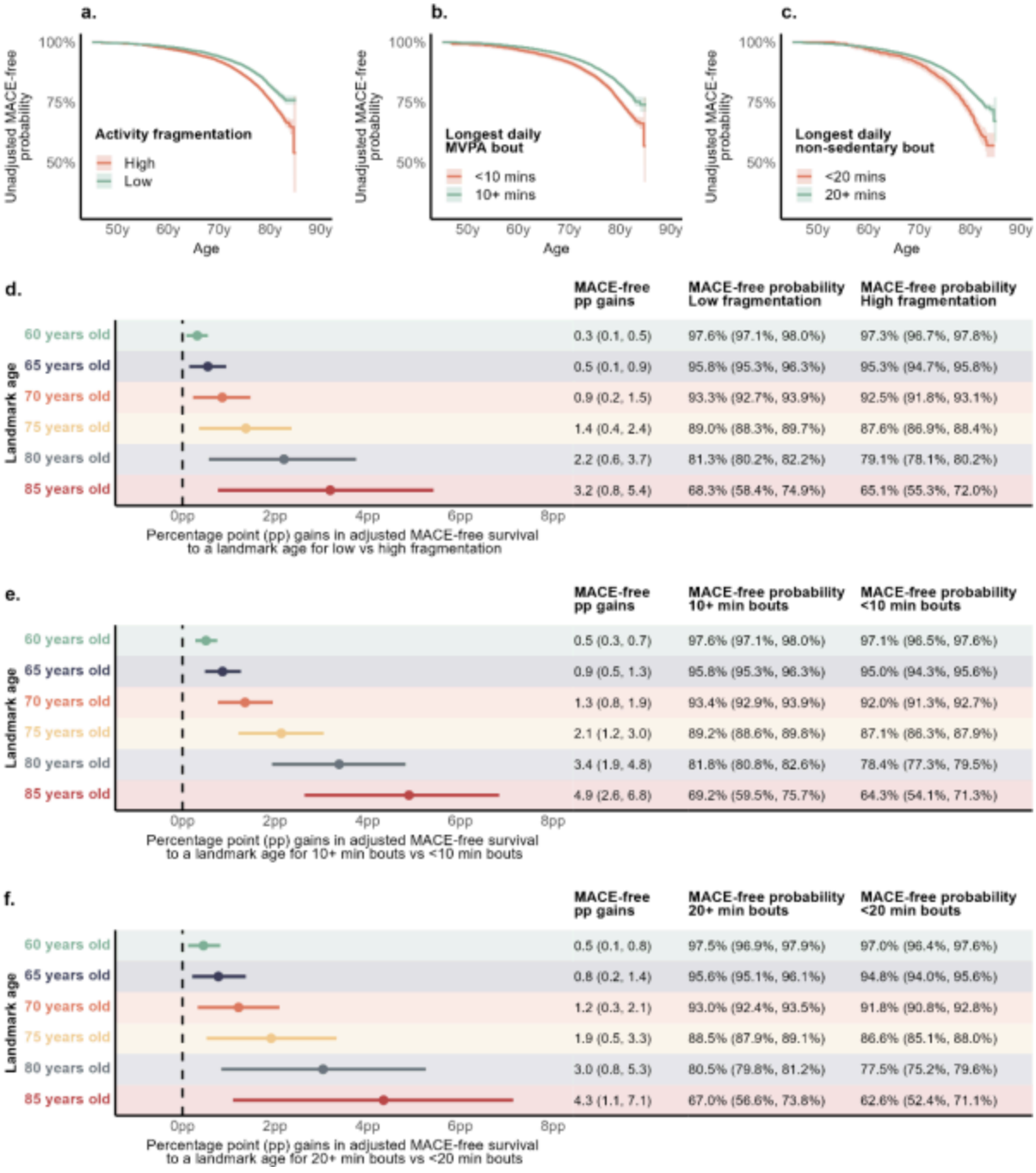


Figure 2

Probability of MACE-free survival by physical activity fragmentation and bout duration

MACE-free survival probabilities across categories of activity fragmentation, MVPA bout duration, and non-sedentary bout duration among N = 58,356 UK Biobank participants. Unadjusted survival probabilities are presented as Kaplan-Meier curves using age as the timescale (a,b,c). Covariate-adjusted absolute MACE-free survival probabilities and MACE-free survival differences (d,e,f) in percentage points (pp) for reaching landmark ages 60, 65, 70, 75, 80, and 85 were computed by applying the g-formula to Cox models adjusted for age as the timescale, stratified on sex, and further adjusted for education, BMI, smoking, drinking, total sleep window, systolic and diastolic blood pressure, glycated hemoglobin, HDL and LDL cholesterol, and total physical activity volume (minutes spent active per day). Error bars for all covariate-adjusted estimates were obtained from 1000 non-parametric bootstrap resamples.

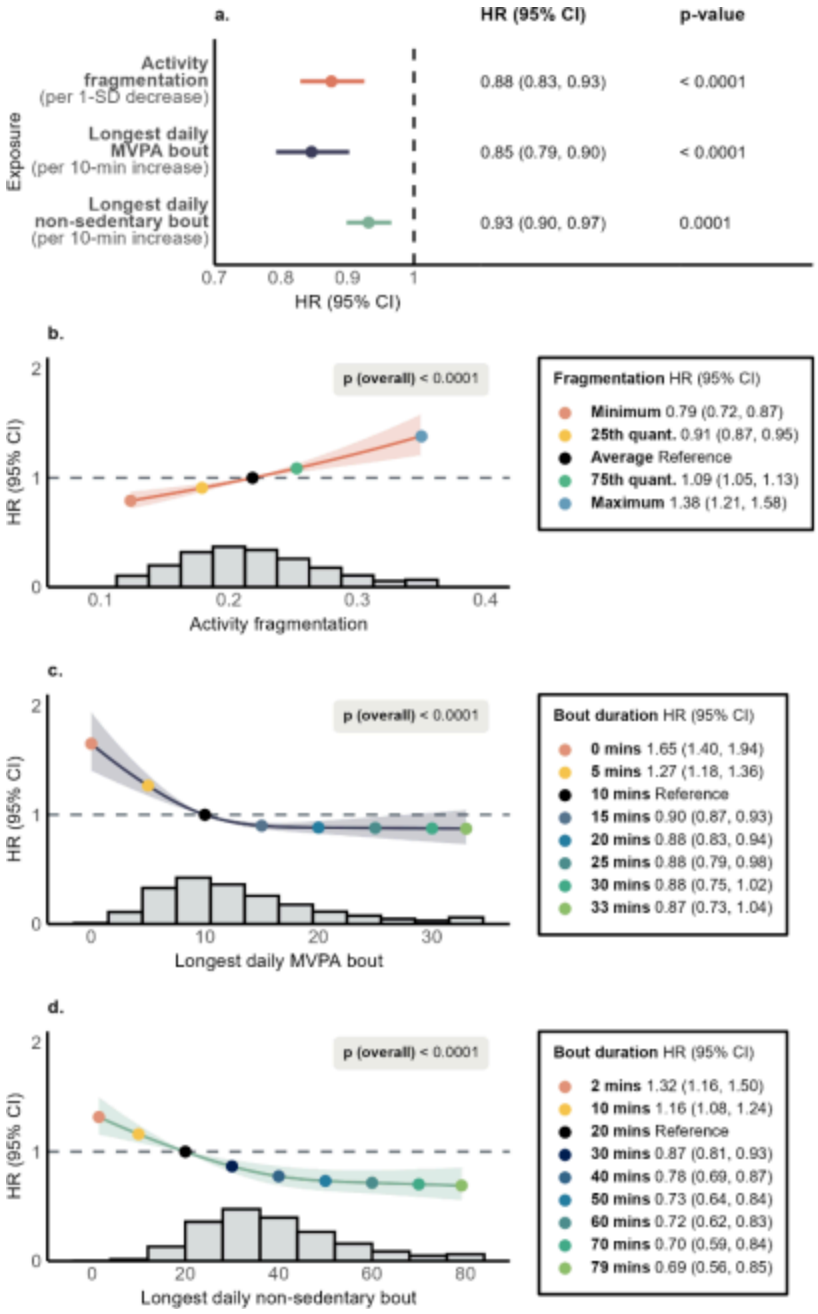


Figure 3

Linear and dose-response associations of physical activity fragmentation and bout duration with incident MACE

Associations of activity fragmentation, MVPA bout duration, and non-sedentary bout duration with incident MACE among N = 58,356 UK Biobank participants. Subplot (a) presents associations per 1-SD decrease in activity fragmentation, per 10-minute increase in MVPA bout duration, and per 10-minute increase in non-sedentary bout duration from Cox models, where each primary exposure was modeled linearly. Subplots b,c, and d present dose-response associations using the mean as the reference for activity fragmentation, 10 minutes as the reference for MVPA bout duration, and 20 minutes as the reference for non-sedentary bout duration. Activity fragmentation was modeled linearly due to no significant evidence of non-linearity, whereas MVPA and non-sedentary bout duration were modeled using restricted cubic splines based on significant evidence of non-linearity (Supplementary Table S1). All Cox models adjusted for age as the timescale, stratified on sex, and further adjusted for education, BMI, smoking, drinking, total sleep window, systolic and diastolic blood pressure, glycated hemoglobin, HDL and LDL cholesterol, and total physical activity volume (minutes spent active per day).

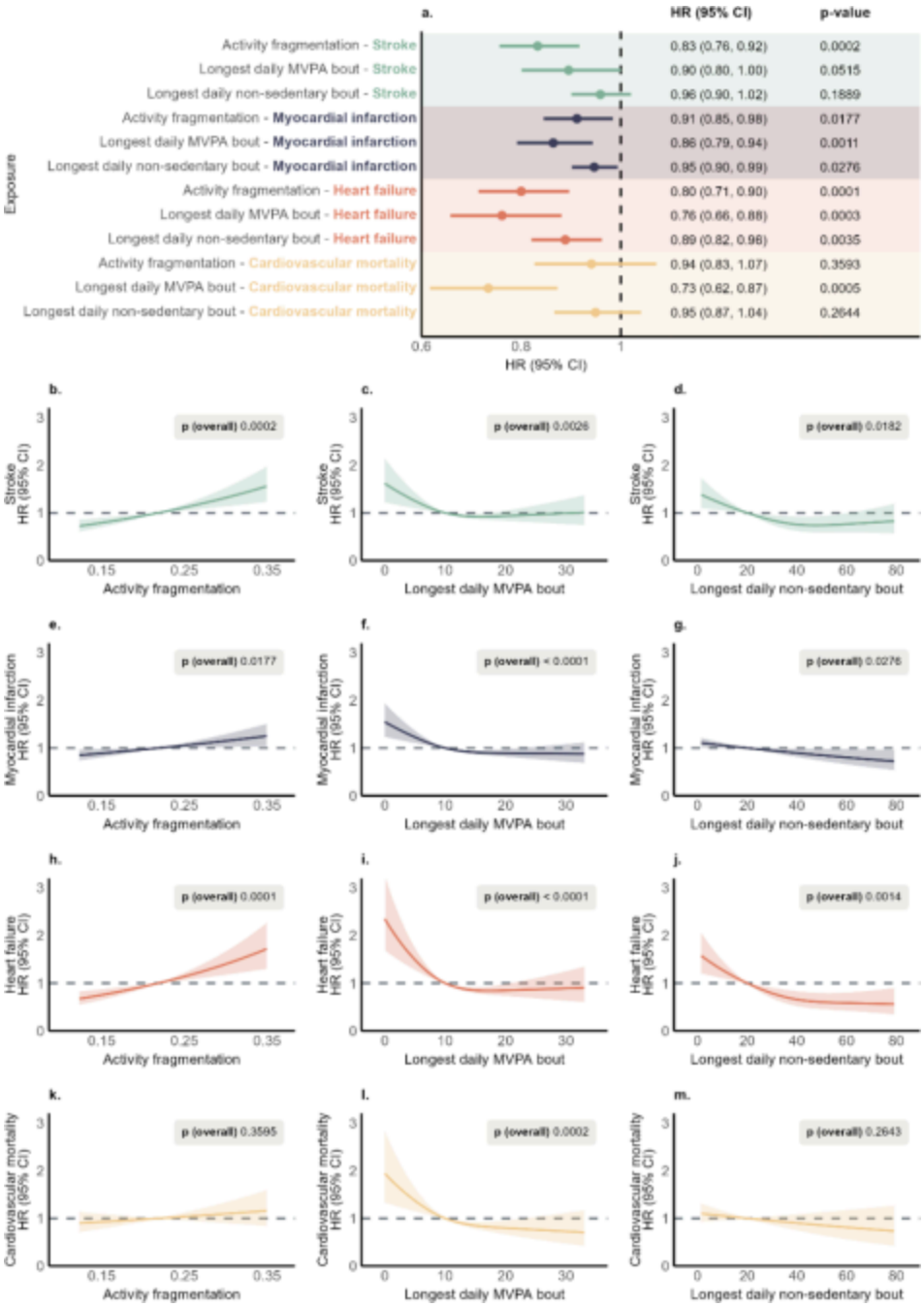


Figure 4

Linear and dose-response associations of physical activity fragmentation and bout duration with individual MACE events

Linear (a) and dose-response (b-m) associations of physical activity fragmentation, MVPA bout duration, and non-sedentary bout duration with individual MACE events among N = 58,356 UK Biobank participants. Subplot (a) presents associations per 1-SD decrease in activity fragmentation, per 10-minute increase in MVPA bout duration, and per 10-minute increase in non-sedentary bout duration from Cox models where each primary exposure was modeled linearly. Subplots b-m present dose-response associations where exposures were modeled linearly or non-linearity following tests for non-linearity based on restricted cubic splines (Supplementary Table S1). All Cox models adjusted for age as the

timescale, stratified on sex, and further adjusted for education, BMI, smoking, drinking, total sleep window, systolic and diastolic blood pressure, glycated hemoglobin, HDL and LDL cholesterol, and total physical activity volume (minutes spent active per day).

Supplementary Files

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- supplementv2.docx