Brief bouts of device-measured intermittent lifestyle physical activity and its association with major adverse cardiovascular events and mortality in people who do not exercise: a prospective cohort study

Matthew N Ahmadi, Mark Hamer, Jason M R Gill, Marie Murphy, James P Sanders, Aiden Doherty, Emmanuel Stamatakis

Summary

Background Guidelines emphasise the health benefits of bouts of physical activity of any duration. However, the associations of intermittent lifestyle physical activity accumulated through non-exercise with mortality and major adverse cardiovascular events (MACE) remain unclear. We aimed to examine the associations of bouts of moderate-to-vigorous intermittent lifestyle physical activity (MV-ILPA) and the proportion of vigorous activity contributing within these bouts with mortality and MACE.

Methods In this prospective cohort study, we used data from the UK Biobank on adults who do not exercise (ie, those who did not report leisure-time exercise) who had wrist-worn accelerometry data available. Participants were followed up until Nov 30, 2022, with the outcome of interest of all-cause mortality obtained through linkage with NHS Digital of England and Wales, and the NHS Central Register and National Records of Scotland, and MACE obtained from inpatient hospitalisation data provided by the Hospital Episode Statistics for England, the Patient Episode Database for Wales, and the Scottish Morbidity Record for Scotland. MV-ILPA bouts were derived using a two-level Random Forest classifier and grouped as short (<1 min), medium (1 to <3 min; 3 to <5 min), and long (5 to <10 min). We further examined the dose–response relationship of the proportion of vigorous physical activity contributing to the MV-ILPA bout.

Findings Between June 1, 2013, and Dec 23, 2015, 103 684 Biobank participants wore an accelerometer on their wrist. 25 241 adults (mean age 61·8 years [SD 7·6]), of whom 14 178 (56·2%) were women, were included in our analysis of all-cause mortality. During a mean follow-up duration of 7·9 years (SD 0·9), 824 MACE and 1111 deaths occurred. Compared with bouts of less than 1 min, mortality risk was lower for bouts of 1 min to less than 3 min (hazard ratio [HR] 0·66 [0·53–0·81]), 3 min to less than 5 min (HR 0·56 [0·46–0·69]), and 5 to less than 10 min (HR 0·48 [0·39–0·59]). Similarly, compared with bouts of less than 1 min, risk of MACE was lower for bouts of 1 min to less than 3 min (HR 0·71 [0·54–0·93]), 3 min to less than 5 min (0·62 [0·48–0·81]), and 5 min to less than 10 min (0·59 [0·46–0·76]). Short bouts (<1 min) were associated with lower MACE risk only when bouts were comprised of at least 15% vigorous activity.

Interpretation Intermittent non-exercise physical activity was associated with lower mortality and MACE. Our results support the promotion of short intermittent bouts of non-exercise physical activity of moderate-to-vigorous intensity to improve longevity and cardiovascular health among adults who do not habitually exercise in their leisure time.

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Mackenzie Wearables Research Hub, Charles Perkins Centre and School of Health Sciences, Faculty of Medicine and Health, University of Sydney, Sydney, NSW, Australia (M N Ahmadi PhD, E Stamatakis PhD); Institute of Sport, Exercise and Health, Division of Surgery and Interventional Science, University College London, London, UK (M Hamer PhD); School of Cardiovascular and Metabolic Health, University of Glasgow, Glasgow, UK (J M R Gill PhD); Centre for Exercise Medicine, Physical Activity and Health, Sports and Exercise Sciences Research Institute, Ulster University, Newtownabbey, UK (M Murphy PhD); School of Sport, Exercise and Health Sciences, National Centre for Sport and Exercise Medicine, Loughborough University, Loughborough, UK (J P Sanders PhD); Nuffield Department of Population Health, Big Data Institute, University of Oxford, Oxford, UK (A Doherty PhD)

Correspondence to:
Dr Matthew Ahmadi, Mackenzie Wearables Research Hub, Charles Perkins Centre, Faculty of Medicine and Health, University of Sydney, Sydney, NSW 2050, Australia
matthew.ahmadi@sydney.edu.au

Introduction

Cardiovascular disease is the leading cause of death globally[1] and although there has been a recent decrease in cardiovascular disease mortality, this has been accompanied by a growing number of hospital admissions for acute manifestations of cardiovascular events such as heart failure and stroke. Physical inactivity is a leading behavioural risk factor for cardiovascular disease but remains challenging to address, especially among patients considered to be at high risk of cardiovascular disease.[2] Clinical and public health research and practice have traditionally focused on the health impact of exercise-based physical activity, accrued primarily from longer bouts done during leisure time. For most adults, incorporating moderate-to-vigorous intermittent lifestyle physical activity (MV-ILPA) into their day, defined as brief bouts (<10 min) done as part of activities of daily living, might be more feasible than sustained bouts of planned and structured exercise. Due to the incidental nature of MV-ILPA bouts, this type of activity requires no time commitment or preparation, no specialist equipment or facilities, and as such might be

Research in context

Evidence before this study

We searched PubMed, Web of Science, and Ovid MEDLINE from database inception to Jan 1, 2023, without language restrictions, for relevant articles using the search terms: "(physical activity OR bouts OR moderate to vigorous OR MVPA OR moderate intensity OR vigorous intensity) and (mortality OR death OR "cardiovascular disease" OR atheroscle*, OR myocardial OR infarction OR "heart failure" OR "coronary heart disease", OR stroke OR "major adverse cardiovascular events" OR MACE)". We included any randomised controlled trial and community-based intervention with longitudinal follow-up assessing clinical endpoints or cardiovascular disease risk factors. Most studies focused on the health and cardiovascular impact of exercise-based physical activity done during leisure time, accrued primarily from longer bouts lasting for at least 10–15 min, and most used self-reported physical activity. Few studies have assessed short bouts of activity embedded into activities of daily living. For most adults, incorporating brief moderate-to-vigorous bouts into their day, might be more accessible and feasible than longer bouts of planned and structured exercise during leisure time. Although national and WHO guidelines emphasise the importance of brief activity bouts, there is a paucity of evidence to directly support the potential benefits of short intermittent moderate-to-vigorous bouts of daily living activities.

Added value of this study

Our study found that moderate-to-vigorous intermittent lifestyle physical activity (MV-ILPA) bouts of between

1 min and 5 min were associated with reductions in all-cause mortality and major adverse cardiovascular events and that these associations were similar for MV-ILPA bouts of 5 min to less than 10 mins, for which risk of all-cause mortality and major cardiovascular events was 29–44% lower than bouts of less than 1 min. These associations were independent of total physical activity. Accumulating physical activity in MV-ILPA bouts of less than 1 min was associated with lower all-cause mortality risk. However, bouts of less than 1 min were only associated with a lower risk of major adverse cardiovascular events when bouts included some activity of vigorous intensity. A higher proportion of vigorous intensity (>12 to 15%) enhanced the associations across all MV-ILPA bout lengths in a dose–response manner.

Implications of all the available evidence

MV-ILPA might be a feasible alternative for adults who are not willing or able to exercise in leisure time due to the high participation barrier of structured activities. The proliferation of consumer wearable devices in the population provides further opportunities to record brief bursts of non-exercise activity occurring across the day. Our findings both highlight the potential public health value of brief intermittent physical activity bouts of moderate-to-vigorous intensity performed outside the domain of structured exercise, and provide information for intervention goal setting and monitoring.

more practical and accessible than prolonged exercise done during leisure time, particularly among groups at risk, such as physically inactive and middle-aged to older adults (≥40 years) who are unfit and unaccustomed to exercise.[3] From a behavioural perspective, MV-ILPA might be a more feasible alternative for adults who are not willing or able to be physically active in leisure time.

The large majority of studies have measured physical activity using questionnaires, which do not capture short bouts (eg <10 min) of incidental physical activity, particularly when it is done during daily living and for short bursts.[4] Data obtained from wearable devices show that as few as four short bouts of vigorous physical activity totalling approximately 2–3 min per day are associated with a substantially lower risk of all-cause cardiovascular disease and cancer mortality.[5,6] Public health guidelines[7] emphasise the health value of short bouts of intermittent physical activity, including non-exercise activities, to lower mortality and cardiovascular disease risk. Such guidance is based on absence of evidence to support a minimum bout duration (previously set to 10 min), rather than direct evidence for the health benefits of shorter intermittent bouts. At present, guidance is framed around moderate-to-vigorous

physical activity (MVPA); higher contributions of vigorous physical activity are associated with better health outcomes[8] due to the pronounced cardioprotective adaptations promoted by higher physical exertion.[9,10] Although vigorous physical activity is a time-efficient way to achieve health targets, vigorous exercise programmes (eg, high intensity interval training) have low participation rates among middle-aged and older adults[11–13] and might not be appealing to physically inactive adults who are at the highest risk of cardiovascular events.

We aimed to assess the dose–response associations of device-measured MV-ILPA with total mortality and major adverse cardiovascular events (MACE) in a large UK population cohort of adults who do not exercise (ie, those who did not report leisure-time exercise). To better understand the role of bout length, we examined whether associations differed for short (<1 min), medium (1 to <3 min; ≥3 to <5 min), and long MV-ILPA (5 to <10 min) bouts. We also examined if the proportion of vigorous physical activity within these bouts was associated with the outcomes beyond total MV-ILPA duration. We hypothesised that non-exercise physical activity accrued through short bouts is associated with lower risk of all-cause mortality and MACE.

Methods

Study design and participants

This was a prospective, population-based cohort study of participants enrolled in the UK Biobank. Participants were recruited via postal invitation, and all participants were enrolled in the UK Biobank between March, 2006 and July, 2010. Participants had physical examinations done by trained staff and completed touchscreen questionnaires. Between June 1, 2013, and Dec 23, 2015, 103 684 UK Biobank participants agreed to wear an Axivity AX3 accelerometer (Axivity, Newcastle, UK) on their dominant wrist for 24 h per day for 7 days.[14] Devices were calibrated and non-wear periods were detected using standard procedures.[15,16] All participants provided informed written consent for data collection, analysis, and linkage and ethical approval was obtained from the UK National Health Service (NHS) National Research Ethics Service (11/NW/0382).

We included participants with at least 3 valid wear days (≥16 h of wear-time), including at least 1 weekend day. As described previously,[5] non-exerciser status was determined by excluding participants who reported participation in exercise or sport during leisure time or walked for recreation more than once a week (appendix pp 38–39). We excluded participants with missing covariate data or an event within the first 24 months of follow-up. In the analyses with MACE as an outcome, we excluded participants with prevalent cardiovascular disease (ascertained through self-report and hospital admission records).

Procedures

Physical activity intensity was classified with a validated accelerometer-based two-level Random Forest machine learning activity scheme that first classifies activity type and then intensity.[5,6,17] A complete description of the activity classifier is provided in the appendix (pp 40–45).

We categorised MV-ILPA bouts by length: short (<1 min), medium (1 to <3 min; ≥3 to <5 min), and long (5 to <10 min). Volume for each of the four MV-ILPA bouts was obtained by summing the duration spent in each bout category. Exposure groupings were based on physical activity bouts of low-to-moderate duration that is achievable through intermittent lifestyle physical activity.[18] Participants were categorised on the basis of their longest MV-ILPA bout; this ensured there was no cross-bout overlap that would have occurred if mean bout duration was used. This also allowed adjustment for MV-ILPA volume that occurred outside of the specified bout length category. A standard day interspersed with MV-ILPA bouts comprising a variety of everyday activities is shown in the appendix (pp 11–12). The two-level physical activity classification scheme minimised the possibility of false-positive MV-ILPA from stationary activities with high wrist movement, such as ironing and cleaning dishes because activities have to be classified first by level 1 as ambulatory activities and level 2 as

moderate or vigorous. We calculated the proportion of vigorous physical activity in all four bout length exposures, total MV-ILPA volume, and MVPA bouts of at least 10 min.

Participants were followed up until Nov 30, 2022, with deaths obtained through linkage with the NHS Digital of England and Wales or the NHS Central Register and National Records of Scotland. Inpatient hospitalisation data were provided by either the Hospital Episode Statistics for England, the Patient Episode Database for Wales, or the Scottish Morbidity Record for Scotland. MACE was defined[2] as incidence of ST-elevated or non-ST-elevated myocardial infarction, stroke, heart failure, surgeries for valve replacement and coronary artery bypass grafting, and fatal cardiovascular events (appendix p 1).

Covariates

Covariates were age, sex, smoking status, alcohol consumption, fruit and vegetable consumption, sedentary time, sleep duration, highest attained education level, frailty index score,[19] self-reported parental history of cardiovascular disease and cancer, and cholesterol, anti-hypertensive, or diabetes medication use, which were measured during clinic visits at baseline (appendix p 13). MV-ILPA volume not accrued from the categorised bout group exposure (eg, volume from <5 min bouts for the 5 to <10 min exposure group), and volume accrued from 10 min bouts or longer were included as covariates. MV-ILPA exposure volume was strongly correlated with total (non-exposure) MVPA (r=0·52–0·86). We therefore used the residual method in which total MVPA was regressed on the bout exposure volume. The resulting residuals were independent variables in the analyses consistent with previous research assessing activity volume over a fixed time interval.[20,21] For the analysis of the percentage contribution of vigorous physical activity, we adjusted for MV-ILPA volume to minimise the possibility that any observed effects are attributed to the higher amounts of activity achieved through vigorous physical activity. In sensitivity analyses, we adjusted for clinical factors that might be mediators (baseline waist circumference, glycated haemoglobin, HDL, LDL, diastolic and systolic blood pressure, and triglycerides). Complete covariate definitions are in the appendix (p 2).

Statistical analysis

We used Cox proportional hazards regression models to estimate hazard ratios (HRs) with 95% CIs for all-cause mortality. Fine-Gray subdistribution method was used for MACE analyses with non-cardiovascular deaths treated as a competing risk. We examined the association of MV-ILPA bout exposures and risk of total mortality and MACE with shorter than 1 min bouts as the reference group. We further calculated the adjusted 5-year absolute risk, cumulative risk (age as the timescale), age and sex adjusted incidence rate
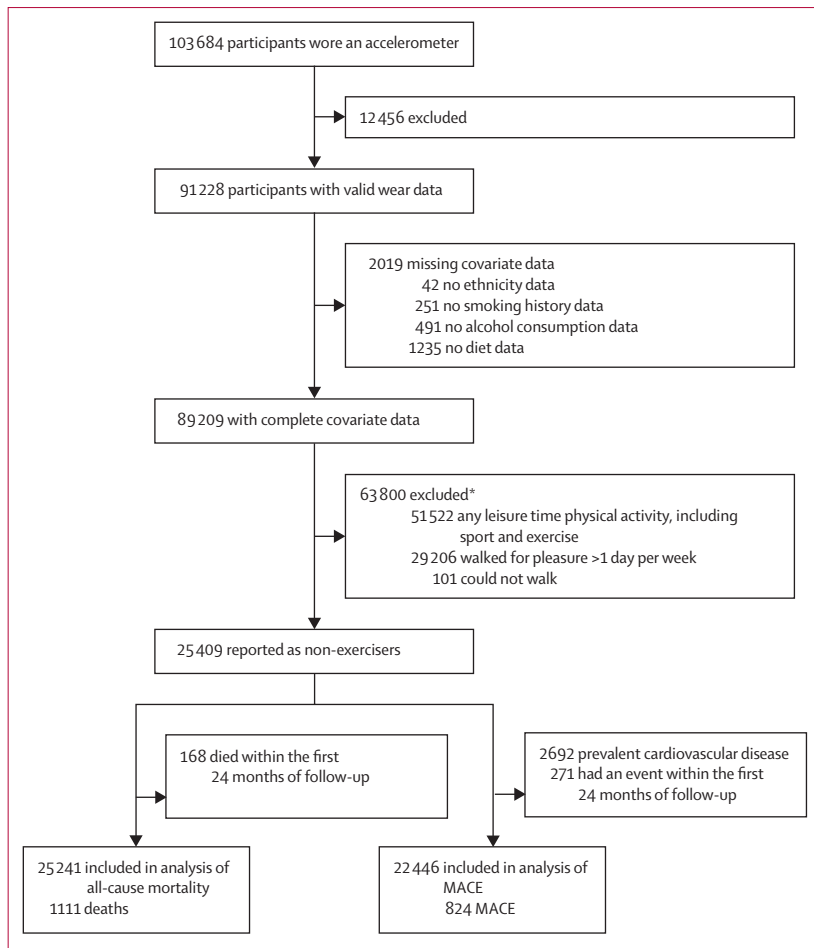
Figure 1: Study profile
MACE=major adverse cardiovascular events. *Reasons for exclusion not mutually exclusive, thus some individuals were included in both categories.

confounding than causality. We analysed MACE subtypes for cerebrovascular events, and myocardial infarction. We also did sensitivity analyses to minimise bias attributable to reverse causation by excluding underweight participants (BMI <18·5 kg/m²) and participants reporting a self-perceived rating of poor health. We did a sensitivity analysis for total mortality excluding participants with prevalent cardiovascular disease and cancer because adjustment for prevalent disease might not fully capture confounding. To assess the robustness of our results to an alternative analytic approach, we performed a sensitivity dose–response analysis stratified by bout length for relative and absolute risk. Such a presentation of data is aligned with generic accelerometry dose–response studies of physical activity volume that do not consider bout length. To further assess the veracity of the observed associations, we examined the categorical associations in the full accelerometry sample (adults who exercise and adults who do not exercise combined), used alternate bout groupings, used flexible semiparametric Cox frailty modelling, and excluded participants with a high frailty index score (≥3 of 5), or events within the first 5 years of follow-up. We further included analyses using at least 10 min bouts as the reference group, and analyses with a more stringent bout grouping definition, which excluded participants with three bouts or fewer in the originally allocated MV-ILPA exposure group.

All analyses were done using R statistical software (version 4.3.1). This study was reported in accordance with the STROBE guideline.

Role of the funding source
The funders had no role in the data collection, study design, analysis, interpretation, or writing of the manuscript.

Results
Of 103 684 UK Biobank participants who wore an accelerometer, 25 241 participants were included in our analysis of all-cause mortality. At baseline, the mean age of participants was 61·8 years (SD 7·6), of whom 14 178 (56·2%) were women, and 9114 (36·8%) had a college or university degree. During a mean follow-up time of 7·9 years (0·9), corresponding to 200 599 person-years, 1111 deaths occurred. The MACE analyses sample, which excluded participants with prevalent cardiovascular disease, included 22 446 participants with 824 events (figure 1).

The median MV-ILPA volume was 26·8 min per day (IQR 15·6–44·0). The majority of MV-ILPA was accrued in bouts of less than 1 min (59·7%) and 1 to less than 3 min (27·5%), followed by 3 to less than 5 min (5·7%) and 5 to less than 10 min (4·4%). 11 974 (47·4%) of 25 241 participants had no MV-ILPA bouts lasting 5 min or longer. Participant characteristics by their longest MV-ILPA bout are shown in the table.

ratios (IRRs), crude risk, and event rate per 1000 person-years for MV-ILPA bouts. We assessed the joint dose–response association of total daily MVPA volume (of any bout duration) and the four MV-ILPA exposures with the two study outcomes using restricted cubic splines (knots at the 10th, 50th, and 90th percentiles). The reference was the 10th percentile of the volume distribution (5 min per day) and MV-ILPA bouts of less than 1 min group. The joint dose–response association of the proportion of vigorous physical activity (knots at the 10th, 50th, and 90th percentiles) and the four MV-ILPA exposures were assessed with the same reference criteria.

We calculated E-values to estimate the plausibility of bias from unmeasured confounding. We used a negative control outcome of deaths or hospital admission from accidents (excluding cycling, self-harm, and falls incidence), an outcome that does not have an explicit mechanistic link to physical activity, to assess residual confounding.[22] If the negative control has a similar association pattern as the primary outcomes, then it is more plausible associations are due to bias and

Characteristics of excluded participants are in the appendix (pp 3–6). Event rates, crude risk, and IRRs adjusted for sex and age and by MV-ILPA groupings are in the appendix (p 7). The 5-year risk of mortality for the reference group (MV-ILPA bout <1 min) was 4·28% (95% CI 3·23–5·32) compared with 2·83% (2·20–3·45) for bouts of 1 min to less than 3 min, 2·43% (1·93–2·93) for bouts of 3 min to less than 5 min, and 2·09% (1·67–2·50) for bouts of 5 min to less than 10 min. For MACE, corresponding results were 3·50% (2·59–4·39) for the reference group, 2·27% (1·72–2·81) for bouts of 1 min to less than 3 min, 2·07% (1·62–2·51) for bouts of

3 min to less than 5 min, and 2·06% (1·64–2·48) for bouts of 5 min to less than 10 min (figure 2). Adjusted cumulative risks are shown in the appendix (pp 14–15).

Compared with the reference group (MV-ILPA bout <1 min), mortality risk was lower for bouts of between 1 min and less than 3 min (HR 0·66 [95% CI 0·53–0·81]), 3 min and less than 5 min (0·56 [0·46–0·69]), and 5 min and less than 10 min (0·48 [0·39–0·59]; figure 3A). The joint-dose response curves showed a non-linear association for total MVPA volume and MV-ILPA bout group ($p_{non-linear} < 0.008$) and a linear association for proportion of vigorous physical activity ($p_{non-linear} = 0.38$;

	<1 min (n=1415)	1 to <3 min (n=3820)	3 to <5 min (n=6739)	≥5 to <10 min (n=13 267)	Overall (n=25 241)
Follow-up, years	7·7 (1·2)	7·9 (1·0)	8·0 (0·9)	7·9 (0·8)	7·9 (0·9)
Age, years	65·1 (7·1)	62·7 (7·4)	61·8 (7·6)	61·2 (7·7)	61·8 (7·6)
Sex					
Male	562 (39·7%)	1599 (41·9%)	2869 (42·6%)	6033 (45·5%)	11 063 (43·8%)
Female	853 (60·3%)	2221 (58·1%)	3870 (57·4%)	7234 (54·5%)	14 178 (56·2%)
Daily duration of sedentary behaviour, h	11·9 (10·6–12·9)	11·2 (10·0–12·2)	10·8 (9·7–11·8)	10·6 (9·4–11·7)	10·8 (9·6–11·9)
Physical activity, min					
Light intensity	61·4 (45·7–86·5)	95·0 (67·0–132·4)	111·2 (75·6–157·8)	97·7 (68·6–151·4)	98·0 (68·0–147·0)
Moderate intensity	4·2 (2·7–6·1)	12·8 (8·7–18·5)	23·1 (15·1–34·5)	36·7 (23·7–57·8)	25·9 (14·6–43·2)
Vigorous intensity	0·4 (0·0–1·2)	2·1 (0·7–5·0)	4·1 (1·6–9·4)	6·6 (2·3–15·7)	4·4 (1·4–9·1)
MV-ILPA	4·6 (3·0–6·2)	13·5 (9·5–19·3)	24·2 (16·5–35·4)	37·6 (24·7–57·8)	26·8 (15·6–44·0)
MV-ILPA bout length	0·40 (0·22–0·42)	1·30 (1·22–1·48)	3·36 (3·17–3·68)	6·14 (5·42–7·27)	··
Percentage of MV-ILPA of vigorous intensity*	8·2% (4·0–14·7)	8·3% (4·5–14·5)	8·1% (4·4–13·7)	7·0% (3·7–12·4)	7·6% (4·0–13·2)
Sleep, h	7·1 (6·0–8·0)	7·3 (6·3–8·1)	7·3 (6·3–8·1)	7·4 (6·5–8·1)	7·4 (6·4–8·1)
Ethnicity					
Asian	12 (0·8%)	46 (1·2%)	101 (1·5%)	167 (1·3%)	326 (1·3%)
Black	12 (0·8%)	40 (1·0%)	73 (1·1%)	136 (1·0%)	261 (1·0%)
Mixed	7 (0·5%)	19 (0·5%)	46 (0·7%)	85 (0·6%)	157 (0·6%)
Other	17 (1·2%)	31 (0·8%)	59 (0·9%)	116 (0·9%)	223 (0·9%)
White	1367 (96·6%)	3684 (96·4%)	6460 (95·9%)	12 763 (96·2%)	24 274 (96·2%)
Smoking history					
Current	189 (13·4%)	430 (11·3%)	630 (9·3%)	1076 (8·1%)	2325 (9·2%)
Never	701 (49·5%)	1941 (50·8%)	3698 (54·9%)	7631 (57·5%)	13 971 (55·4%)
Previous	525 (37·1%)	1449 (37·9%)	2411 (35·8%)	4560 (34·4%)	8945 (35·4%)
Alcohol consumption†					
Never	69 (4·9%)	175 (4·6%)	283 (4·2%)	446 (3·4%)	973 (3·9%)
Ex-drinker	75 (5·3%)	144 (3·8%)	208 (3·1%)	441 (3·3%)	868 (3·4%)
Within guidelines	861 (60·8%)	2235 (58·5%)	4080 (60·5%)	7813 (58·9%)	14 989 (59·4%)
Above guidelines	410 (29·0%)	1266 (33·1%)	2168 (32·2%)	4567 (34·4%)	8411 (33·3%)
Education qualifications					
College or university degree	468 (33·1%)	1286 (33·7%)	2287 (33·9%)	5073 (38·2%)	9114 (36·1%)
Advanced placement	185 (13·1%)	523 (13·7%)	826 (12·3%)	1665 (12·5%)	3199 (12·7%)
GCSEs	299 (21·1%)	852 (22·3%)	1623 (24·1%)	2774 (20·9%)	5548 (22·0%)
Certificate of secondary education	54 (3·8%)	179 (4·7%)	358 (5·3%)	694 (5·2%)	1285 (5·1%)
National Vocational Qualifications, Higher National Diploma, or Higher National Certificate	90 (6·4%)	227 (5·9%)	415 (6·2%)	834 (6·3%)	1566 (6·2%)
Other	319 (22·5%)	753 (19·7%)	1230 (18·3%)	2227 (16·8%)	4529 (17·9%)

(Table continues on next page)

	<1 min (n=1415)	1 to <3 min (n=3820)	3 to <5 min (n=6739)	≥5 to <10 min (n=13 267)	Overall (n=25 241)
(Continued from previous page)					
Fruit and vegetables, servings per day	7·4 (4·2)	7·3 (4·2)	7·4 (4·3)	7·5 (4·3)	7·4 (4·3)
Prevalent cardiovascular disease	280 (19·8%)	498 (13·0%)	722 (10·7%)	1118 (8·4%)	2618 (10·4%)
Prevalent cancer	158 (11·1%)	331 (8·7%)	521 (7·7%)	904 (6·8%)	1914 (7·6%)
Family history of cardiovascular disease	838 (59·2%)	2127 (55·7%)	3729 (55·3%)	7245 (54·6%)	13 939 (55·2%)
Family history of cancer	377 (26·6%)	976 (25·5%)	1792 (26·6%)	3299 (24·9%)	6444 (25·5%)
Medication					
Cholesterol lowering	417 (29·5%)	799 (20·9%)	1163 (17·3%)	1971 (14·9%)	4350 (17·2%)
Blood pressure lowering	480 (33·9%)	977 (25·6%)	1430 (21·2%)	2242 (16·9%)	5129 (20·3%)
Insulin	33 (2·3%)	50 (1·3%)	60 (0·9%)	91 (0·7%)	234 (0·9%)
Biomarkers					
HbA$_{1c}$, mmol/mol	38·4 (9·0)	36·9 (7·5)	36·0 (6·3)	35·6 (5·8)	36·1 (6·5)
HDL, mmol/L	1·4 (0·4)	1·4 (0·4)	1·4 (0·4)	1·5 (0·4)	1·4 (0·4)
LDL, mmol/L	3·5 (0·9)	3·6 (0·9)	3·6 (0·9)	3·6 (0·9)	3·6 (0·9)
Triglycerides, mmol/L	2·0 (1·0)	1·9 (1·1)	1·8 (1·0)	1·7 (1·0)	1·8 (1·0)
Systolic blood pressure, mm Hg	142·4 (19·8)	140·7 (18·7)	140·1 (19·1)	138·5 (19·0)	139·5 (19·1)
Diastolic blood pressure, mm Hg	83·3 (10·7)	83·1 (10·7)	82·7 (10·7)	82·0 (10·5)	82·4 (10·6)
Waist circumference, cm					
Male	104·9 (13·7)	101·7 (12·6)	98·9 (11·5)	96·4 (10·8)	98·2 (11·7)
Female	92·7 (14·8)	89·3 (13·7)	85·9 (12·8)	83·1 (11·9)	85·4 (13·0)
Self-rated health‡					
Excellent	112 (7·9%)	422 (11·0%)	836 (12·4%)	2080 (15·7%)	3450 (13·7%)
Good	677 (47·8%)	2123 (55·6%%)	3908 (58·0%)	8077 (60·9%)	14 785 (58·6%)
Fair	456 (32·2%)	1009 (26·4%)	1606 (23·8%)	2641 (19·9%)	5712 (22·6%)
Poor	164 (11·6%)	259 (6·8%)	371 (5·5%)	429 (3·2%)	1223 (4·8%)
High frailty§	163 (11·5%)	315 (8·2%)	438 (6·5%)	752 (5·7%)	1668 (6·6%)
BMI, kg/m²	30·2 (6·0)	29·1 (5·6)	27·8 (5·1)	26·8 (4·6)	27·6 (5·1)

Data are mean (SD), n (%), or median (IQR). Groupings represent a participant's longest bout of activity. MV-ILPA=moderate-to-vigorous intermittent lifestyle physical activity. GCSE=General Certificate of Secondary Education. HbA$_{1c}$=glycated haemoglobin. *Percentage of vigorous intensity per MV-ILPA bout. †UK guidelines of ≤14 units of alcohol per week; 1 unit is equivalent to 8 g of pure ethanol. ‡Due to missing data, the sum of participants in each category might not equal the total participants in each group. §Indicative of a score ≥3 on a scale (1–5) for self-reported physical activity, walking speed, weight loss, exhaustion, and grip strength.

Table: Participant baseline characteristics by MV-ILPA bout length (n=25 241)
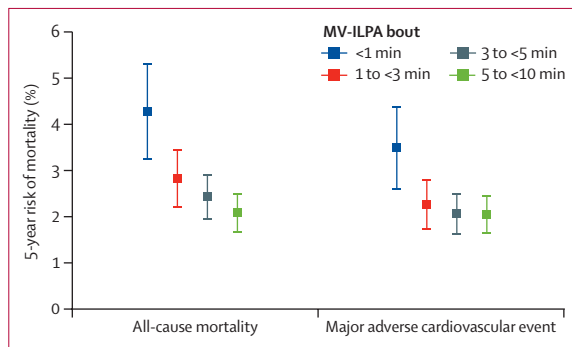

Figure 2: 5-year risk for all-cause mortality and major adverse cardiovascular events by MV-ILPA groups

Adjusted for age, sex, smoking status, alcohol consumption, sedentary behaviour, sleep duration, diet, non-MV-ILPA group volume, MVPA volume (from ≥10 min bouts), prevalent cancer and cardiovascular disease (all-cause mortality analysis), family history of cancer and cardiovascular disease, education, medication use, and frailty index. MV-ILPA=moderate-to-vigorous intermittent lifestyle physical activity. MVPA=moderate-to-vigorous physical activity.

figure 3B). A gradient dose–response was observed for high MV-ILPA bouts when compared with the reference group of 5 min per day (10th percentile of MVPA) accrued in bouts shorter than 1 min (figure 4A). For example, the multivariable adjusted HR was 0·92 (0·88–0·96) for the accumulation of 10 min of MVPA per day and having only MV-ILPA bouts shorter than 1 min; the HR for the same duration of MVPA activity was 0·69 (0·56–0·86) for MV-ILPA bouts of 1 min to less than 3 min and 0·64 (0·51–0·80) for MV-ILPA bouts of 5 min to less than 10 min. MV-ILPA bouts of less than 1 min were associated with lower risk of all-cause mortality when at least 12% of the MV-ILPA duration was comprised of vigorous intensity physical activity (HR 0·78 [0·60–0·99]; figure 4B). In direct comparison, when 3 to less than 5 min MV-ILPA bouts were comprised of approximately 12% vigorous intensity (22 to <40 s per bout), the HR for all-cause mortality was 0·45 (0·32–0·64).
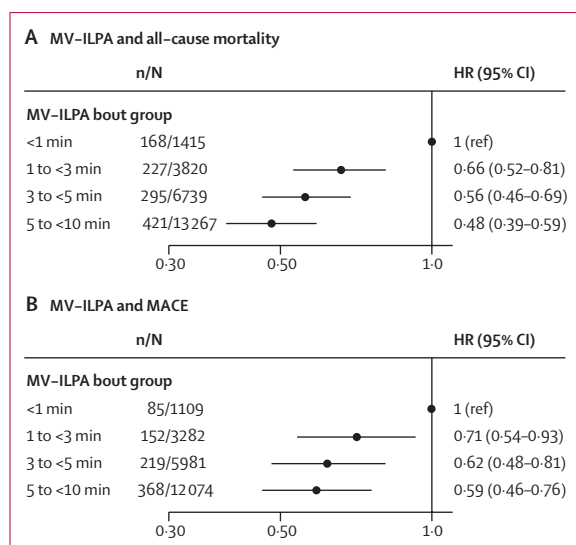
Figure 3: Association of MV-ILPA, all-cause mortality, and MACE
Forest plots of the association between MV-ILPA bout length and all-cause mortality (A) and between MV-ILPA bout length and MACE (B). Models were adjusted for age, sex, smoking status, alcohol consumption, sedentary behaviour, sleep duration, diet, non-MV-ILPA group volume, MVPA volume (from ≥10 min bouts), prevalent cancer and cardiovascular disease, family history of cancer and cardiovascular disease, education, medication use, and frailty index. n=number of events. N=number of participants. HR=hazard ratio. MV-ILPA=moderate-to-vigorous intermittent lifestyle physical activity. MACE=major adverse cardiovascular events. MVPA=moderate-to-vigorous physical activity.

Figure 4: Dose-response association of MVPA, MV-ILPA bouts, proportion of vigorous intensity activity, and all-cause mortality
Dose-response curves for MVPA volume and MV-ILPA bout group (A) and the proportion of vigorous intensity relative to IL-MVPA bout group (B). The reference groups were the 10th percentile of MVPA volume and <1 min IL-MVPA group and the 10th percentile of vigorous intensity and <1 min IL-MVPA group, respectively. The models in part A were adjusted for age, sex, smoking status, alcohol consumption, sedentary behaviour, sleep duration, diet, non-MV-ILPA group volume, MVPA volume (from ≥10 min bouts), prevalent cancer and cardiovascular disease, family history of cancer and cardiovascular disease, education, medication use, and frailty index. The model in part B was additionally adjusted for total MV-ILPA volume using the residual method. MVPA=moderate-to-vigorous physical activity. MV-ILPA=moderate-to-vigorous intermittent lifestyle physical activity. HR=hazard ratio.

Compared with the equivalent results for risk of all-cause mortality, we observed associations of smaller effect size with less evidence of a gradient for MACE events from MV-ILPA bouts of 1 to less than 3 min (HR 0·71 [95% CI 0·54–0·93]), 3 to less than 5 min (0·62 [0·48–0·81]), and 5 to less than 10 min (0·59 [0·46–0·76]) when compared with less than 1 min (figure 3B). There was a joint inverse linear association between MVPA volume and MV-ILPA bout group ($p_{non-linear}$=0·19). No association was identified for MV-ILPA bouts shorter than 1 min, regardless of the accrued volume (ie, the upper 95% CI bound did not cross 1; figure 5A). Accumulating MV-ILPA in 1 to less than 3 min and 3 to less than 5 min bouts had a similar association with MACE risk. For example, the multivariable adjusted HR for 10 min of MVPA per day and 1 to less than 3 min MV-ILPA bouts was 0·72 (0·55–0·95), and the HR for 3 to less than 5 min MV-ILPA bouts was 0·70 (0·52–0·92). The association was not markedly different for MV-ILPA bouts of 5 to less than 10 min (HR 0·69 [0·51–0·93] at a total duration of 10 MVPA min per day). Higher proportions of vigorous intensity physical activity were associated with lower MACE risk across all four MV-ILPA bout groups in an inverse linear direction ($p_{non-linear}$=0·61). We observed MV-ILPA accrued through less than 1 min bouts was associated with lower MACE risk when at least 15% of the MV-ILPA duration was comprised of vigorous intensity physical activity (figure 5B). When vigorous intensity
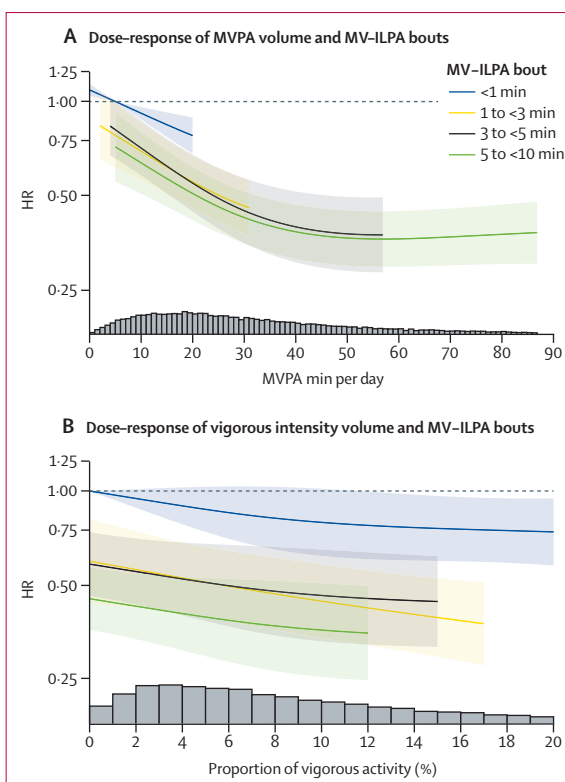
contributed 15% of 1 to less than 3 min bouts (approximately 9 to <27 s of vigorous activity per bout) MACE risk was 0·67 (0·51–0·89) and 0·56 (0·43–0·74) for bouts of 3 to less than 5 min (approximately 27 to <45 s per bout).

Adjustment for biomarkers, waist circumference, and exclusion of participants who were underweight or reported poor health did not materially change the magnitude of the associations (appendix pp 16–17). Analyses of negative control outcomes and E-values indicated residual and unmeasured confounding had minimal impact on the findings. Specifically, with the negative control outcome, the HR point estimate pattern was inconsistent with wide 95% CIs and no significant associations were observed (appendix p 18). All-cause mortality E-values ranged from 2·40 (lower 95% CI 1·77) to 3·59 (2·78) and MACE E-values
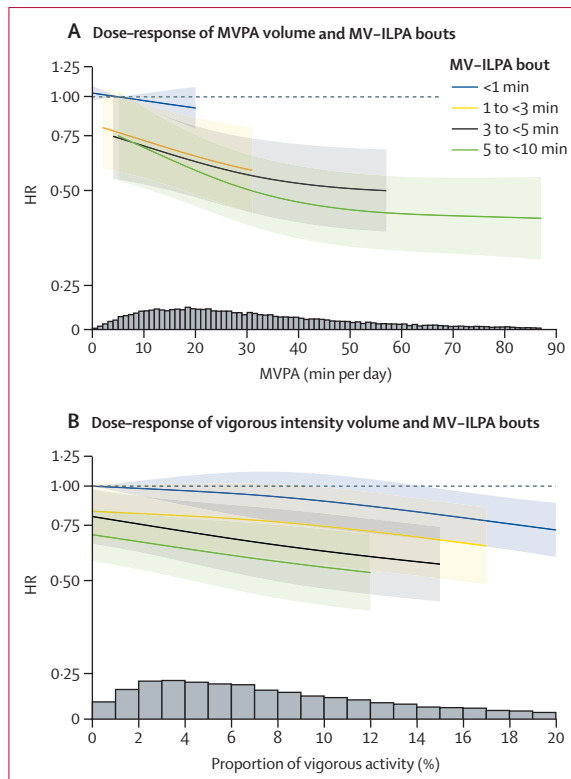
Figure 5: Dose–response association of MVPA, MV-ILPA bouts, proportion of vigorous intensity activity, and MACE

Dose–response curve for MVPA volume and MV-ILPA bout group (A) and the proportion of vigorous intensity relative to IL-MVPA bout group (B). The reference groups were the 10th percentile of MVPA volume and <1 min IL-MVPA group and the 10th percentile of vigorous intensity proportion and <1 min IL-MVPA group, respectively. The model in part A was adjusted for age, sex, smoking status, alcohol consumption, sedentary behaviour, sleep duration, diet, non-MV-ILPA group volume, MVPA volume (from ≥10 min bouts), prevalent cancer, family history of cancer and cardiovascular disease, education, medication use, and frailty index. The model in part B was additionally adjusted for total MV-ILPA volume using the residual method. MVPA=moderate-to-vigorous physical activity. MV-ILPA=moderate-to-vigorous intermittent lifestyle physical activity. MACE=major adverse cardiovascular events. HR=hazard ratio.

ranged from 2·17 (1·36) to 2·78 (1·96; appendix p 8). Exclusion of participants with prevalent cancer and cardiovascular disease for the total mortality analysis attenuated the effect sizes for each MV-ILPA bout group (HR 0·71 [0·52–0·95] for 1 to <3 min; 0·54 [0·42–0·70] for 5 to <10 min), but showed a similar pattern to the main analysis (appendix p 19). In MACE subtype analysis, the risk for myocardial infarction and heart failure was lower for bouts of at least 1 min or longer and a daily duration of at least 13 min (appendix p 20). Analysis of stroke risk showed an inverse association pattern with wide 95% CIs and no association with higher proportions of vigorous physical activity (appendix p 21). Results after stratification by bout length were broadly consistent with the main analysis (appendix pp 22–23). Additional analysis in the full accelerometry sample showed a consistent association (appendix pp 24–25) when

compared with the main analysis, and alternate bout groupings (<3 min as the reference group; appendix pp 26–27) and Cox frailty modelling (appendix pp 28–29) showed similar association patterns as the main analysis. For all-cause mortality, bouts of between 1 min and less than 10 min and for MACE, bouts of 5 to less than 10 min had a similar association as that for bouts of 10 min or longer (appendix pp 30–31). Exclusion of participants with a high frailty index score or an event in the first 5 years of follow-up did not materially change the associations (appendix pp 32–35). MV-ILPA associations remained consistent after exclusion of participants with 3 or fewer bouts in the exposure group (appendix pp 36–37).

Discussion

To our knowledge, this is the first study to examine the potential cardiovascular health benefits of short moderate-to-vigorous intensity bouts of intermittent, non-exercise physical activity done as part of daily living. We found that MV-ILPA bouts with durations between 1 min and 5 min had similar associations with mortality and MACE when compared with bouts of 5 to less than 10 min, with a 29–44% reduction in risk of mortality and MACE when compared with bouts of less than 1 min. Accumulating physical activity in bouts of less than 1 min showed beneficial associations with all-cause mortality risk. However, bouts of less than 1 min were associated with lower MACE risk only when an average of at least 15% of all recorded bouts consisted of activity that was vigorous in intensity. Higher proportions of vigorous intensity strengthened the associations across all MV-ILPA bout groups in a dose–response manner.

One of the greatest challenges to healthy ageing is that risk of a cardiovascular event increases markedly with age. When structured exercise is not a feasible, appealing, or accessible option, our findings support an important role for intermittent lifestyle (incidental) activity bouts and suggest that even bouts as short as 1 to <5 min are associated with better cardiovascular outcomes. Studies have suggested total activity volume has a stronger association with lower mortality risk than the length of activity bouts.[23,24] These studies, however, did not have granularity in their physical activity assessments to examine short bouts of activity and considered all bouts of less than 10 min or 15 min to be synonymous. The protective associations of activity bouts of less than 10 or 15 min might not be consistent across the interval, and this has hindered the translation to public health messaging. Indeed, evidence used to inform the latest US and WHO physical activity guidelines synthesised reviews of observational studies using device-based and questionnaire-based data that did not have the granularity to assess intermittent activity bouts, which has been highlighted as a limitation by policy makers.[4] Our study, which assessed short bouts of activity at a finer granularity, suggests activity bout

length might be an important characteristic of physical activity in relation to longevity and cardiovascular health. Similarly, previous studies assessing physical activity fragmentation, or the transition probability between sedentary behaviour and physical activity, have found an association between more fragmented physical activity (ie, activity done in shorter bouts) with lower functional status and higher all-cause mortality risk.[25,26]

Since fewer than one in five middle-aged adults engage in regular exercise,[12,13] the so-called micropatterns of physical activity [5,27] (short bouts of daily living activities) we investigated might be complementary to traditional exercise strategies. The potential convenience of accruing MV-ILPA through activities of daily living makes it accessible for almost everyone. We found consistent evidence of beneficial associations for incidental non-exercise MVPA with 30% lower mortality risk from approximately 10 MVPA min per day and 1 to less than 5 min MV-ILPA bouts accrued during daily living. Individuals who do not engage in structured exercise but accumulate MV-ILPA might not realise they are participating in health-enhancing physical activity.

The benefits of exercise are often attributed to regularly repeated sessions of sustained activity. Our study demonstrates some cardiovascular benefits might also be attainable through intermittent MVPA bouts through activities of daily living, suggesting that the two activity domains (leisure time exercise and activities of daily living) might elicit similar cardiovascular adaptations, which in turn would have similar associations for cardiac events. Moderate-intensity activities done for durations of less than 1 min might not be long enough to induce pronounced changes to the coronary vasculature when compared with longer bouts.[28,29] The absence of cardiovascular adaptations might explain why a lower risk of MACE was not observed when MV-ILPA bouts of less than 1 min were accumulated in exclusively moderate intensity or less than 15% (approximately 10 s) of vigorous intensity, regardless of total volume. These associations were generally consistent for MACE subtypes that included cerebrovascular accidents and major coronary heart disease. Variations in the dose–response curves between these two subtypes could be due to differing modifications in cardiovascular pathways affected by physical activity. One of the most recognisable risk factors for cerebrovascular events is hypertension. The antihypertensive effects of physical activity are related to improvements in lipid metabolism, improved endothelial tissue function, and decreased blood viscosity.[30] Adverse changes in cardiac structure are mitigated by physical activity, in part, through cardiomyocyte proliferation and improved sarcomeric relaxation.[31]

Our additional analyses of longer MVPA bouts showed that bouts lasting more than 10 min have some potential advantage over short bouts lasting less than 3 to 5 min for MACE risk. However, bouts lasting longer than 10 min represented only 2·7% of total MVPA, highlighting their limited feasibility at the population level. Among adults who do not exercise, it is likely that daily MV-ILPA will be accumulated during occupational physical activity. Accelerometry-based devices provide granular measures of ambulatory physical activity in contrast to stationary anaerobic activities (eg, lifting heavy external loads). On this basis, utilising the capacity of device-based measurements to isolate and measure occupational ambulatory MV-ILPA provides avenues for future studies to investigate. Our findings suggest short bouts of MV-ILPA accumulated throughout the day in the domestic, occupational, and transportation domains might lower mortality and MACE risk. The advancement and proliferation of wearables in population studies might provide new insights into the disparate findings of an umbrella review of occupational physical activity commissioned by WHO[32] and other prospective studies.[33,34]

Our findings on the dose–response of vigorous intensity contributions to total MV-ILPA support findings from smaller randomised control trials assessing high intensity exercise and cardiometabolic risk markers. We found brief bursts of vigorous intensity interspersed during MV-ILPA bouts of less than 5 min were associated with lower risk of total mortality and cardiovascular events. Meta-analyses of exercise trials have reported vigorous intensity bouts in three to four repetitions done three to five times a week enhances vascular function through cardiorespiratory fitness and autonomic adaptations, which is superior to continuous moderate intensity.[35] Such mechanistic pathways might explain the associations we observed among our sample of adults who do not exercise. Our results suggest that the effects of moderate intensity on cardiac improvements might be optimised from a few seconds of interspersed vigorous activity, which contrasts with the findings of previous questionnaire-based studies that suggested the need for sustained bouts of vigorous activity. These findings highlight comparable health benefits to high intensity exercise interventions might be achievable, through activities of daily living done in short bursts. Future trials are needed to investigate how cardiac and aerobic pathways are modulated by brief bursts of vigorous intensity interspersed with short bouts of moderate intensity.

If verified in future research, our findings could inform future public health messaging targeting the general population raising awareness of potential health benefits from short physical activity bouts in daily life, especially for adults who do not or cannot exercise. Such new guidance could complement existing public health programmes such as the Active 10 in the UK,[36] and Go4Life campaign in the USA that promote making physical activity part of daily life. The potential role of MV-ILPA could be further promoted through community connectedness and neighbourhood planning.[37,38]

Our study indicates a potential protective association of vigorous activity and cardiovascular events. There have

For more on the **Go4Life campaign** see https://www.nia.nih.gov/research/blog/2014/07/go4life-nia-health-education-campaign

been mixed findings reported in the literature, with some studies reporting an acute, albeit transient, 16–20% increase in cardiovascular events compared with the lowest activity group or no vigorous physical activity.[39,40] In our study, there was an inverse association of higher vigorous activity volume and cardiovascular risk. Vigorous activity in our study was accrued in short bouts and is therefore distinct from previous studies limited to self-report that could only assess prolonged bouts of vigorous activity, lasting a minimum of 10–15 min. The differences we observed in our study compared with studies measuring sustained vigorous bouts might be attributable to the absence of increased sympathetic stimulation, sustained haemodynamic stress, and cardiac fibrosis from short vigorous bursts. The presence of these factors has been found to accentuate exertion-related cardiovascular events.[40,41]

Strengths of our study include the sample of adults who do not exercise, which allowed us to investigate activities embedded into daily living and the use of accelerometers to objectively measure physical activity at a high resolution. The long duration of follow-up enabled us to reduce the risk of reverse causality by removing participants who had pre-existing cardiovascular disease, an event in the first 2 years of follow-up, self-rated poor health, who were underweight, or had a high frailty index score. Despite these extensive precautionary measures, the potential for reverse causation caused by prodromal disease remains. Due to the observational design, we cannot rule out the presence of unmeasured or residual confounding. However, our negative control outcomes and E-values suggest there was minimal impact on our associations. The two-level physical activity scheme minimises false-positive intensity classification; however, misclassification of MVPA may still occur. MVPA precision for lifting heavy external loads might be underestimated with accelerometry. There was a median lag of 5·5 years between the UK Biobank baseline when covariate measurements were taken and the accelerometry study, although non-exerciser status and covariates were generally stable over time, with the exception of medication. The response rate to the UK Biobank was low; however previous work has shown that poor representativeness does not materially influence the associations between physical activity and all-cause or cardiovascular mortality.[42]

In a sample of adults who do not exercise, we found that MVPA accrued through short bouts of activities of daily living was associated with a decrease in mortality and major cardiac event rates. Associations of 1 to less than 5 min bouts of moderate-to-vigorous incidental lifestyle physical activity with mortality and major cardiac events were comparable in magnitude to those of 5 to less than 10 min bouts, and more favourable than bouts of less than 1 min. Associations were stronger for higher proportions of vigorous activity. Our results support the promotion of intermittent lifestyle physical activity bouts lasting for at least 1 min to promote cardiovascular health among adults who do not exercise in their leisure time.

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