Circulation

ORIGINAL RESEARCH ARTICLE

Dose Response of Incidental Physical Activity Against Cardiovascular Events and Mortality

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BACKGROUND: Few middle-aged and older adults engage in regular leisure-time exercise. Incidental physical activity (IPA) encompasses activities of daily living outside the leisure-time domain. No dose-response study is available to guide IPA-focused interventions and guidelines. We examined the associations of device-assessed IPA intensities (vigorous [VIPA], moderate [MIPA], light [LIPA]) with major adverse cardiovascular events (MACE) and mortality, and we estimated the "health equivalence" of LIPA and MIPA against 1 minute of VIPA.

METHODS: A total of 24 139 nonexercisers from the 2013 to 2015 UK Biobank accelerometry substudy (56.2% women) with a mean±SD age of 61.9±7.6 years were analyzed using a prospective cohort design. IPA energy expenditure and daily durations of VIPA, MIPA, and LIPA were calculated with a validated machine learning-based intensity classifier. MACE included incident stroke, myocardial infarction, and heart failure; CVD death; CVD mortality; and all-cause mortality.

RESULTS: Analyses included 22 107 (MACE), 22 174 (CVD mortality), and 24 139 (all-cause mortality) participants, corresponding to 908/223/1071 events over 7.9 years of follow-up. IPA volume exhibited an L-shaped association with a nadir at ≈35 to 38 $kJ \cdot kg^{-1} \cdot d^{-1}$, corresponding to hazard ratios of 0.49 (95% CI, 0.39–0.61) for MACE, 0.33 (95% CI, 0.22–0.52) for CVD mortality, and 0.31 (95% CI, 0.25–0.38) for all-cause mortality. Any amounts of VIPA or MIPA were associated with lower risk, with a plateau of ≈14 minutes per day (VIPA) and 34 to 50 minutes per day (MIPA). The median VIPA (4.6 min/d) and MIPA (23.8 min/d) durations were associated with CVD mortality hazard ratio of 0.62 (95% CI, 0.46–0.83) and 0.50 (95% CI, 0.31–0.80), respectively. LIPA showed a subtle inverse gradient which was statistically significant only for CVD mortality at levels >130 minutes per day. One minute of VIPA was equivalent to 2.8 (MACE) to 3.4 (CVD mortality) minutes of MIPA and 34.7 (CVD mortality) to 48.5 (MACE) minutes of LIPA.

CONCLUSIONS: Any daily IPA amount of vigorous or moderate intensity was associated with lower CVD risk in a dose-response manner. LIPA had weak associations with all outcomes. One minute of vigorous or ≈3.0 to 3.5 minutes of moderate IPA was associated with a similar degree of lower CVD risk. Our findings highlight the potential cardiovascular health value of incidental physical activity, especially for people who struggle to do structured exercise.

Key Words: accelerometry ■ cardiovascular diseases ■ cohort studies ■ epidemiology ■ exercise ■ fitness trackers ■ machine learning ■ wearable electronic devices

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Supplemental Material, the podcast, and transcript are available with this article at https://www.ahajournals.org/doi/suppl/10.1161/CIRCULATIONAHA.124.072253.
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Clinical Perspective

What Is New?

- In this prospective cohort of nonexercising UK adults, the median dose of vigorous (4.6 min/d) and moderate (23.8–23.9 min/d) incidental physical activity was associated with 25% to 38% and 40% to 50% lower risk of cardiovascular events (including deaths), respectively.
- On the basis of cardiovascular disease mortality and major adverse cardiovascular events, the cardiovascular health equivalence of 1 minute of vigorous incidental physical activity was 2.8 to 3.4 minutes of moderate and 35 to 48 minutes of light incidental activity (although light intensity was associated with considerably lower theoretical risk reductions).

What Are the Clinical Implications?

- For individuals who are unwilling or unable to initiate and adhere to a structured exercise program, cardiovascular health clinicians and public health practitioners could promote incidental physical activity, particularly of moderate and vigorous intensities.
- Approximately 3 to 3.5 minutes of moderate-intensity incidental physical activity may achieve the same cardiovascular benefits as 1 minute of vigorous incidental physical activity.

Nonstandard Abbreviations and Acronyms

CVD	cardiovascular disease
HR	hazard ratio
IPA	incidental physical activity
LIPA	incidental light-intensity physical activity
MACE	major adverse cardiovascular events
MET	metabolic equivalent
MIPA	incidental moderate-intensity physical activity
PAEE	physical activity energy expenditure
VIPA	incidental vigorous-intensity physical activity
WHO	World Health Organization

Cardiovascular disease (CVD) is the leading cause of death globally.[1] Most clinical and public health guidelines have traditionally been developed with evidence on the cardioprotective properties of structured exercise. For example, the majority of the evidence in the 2020 *Physical Activity and Sedentary Behaviour Guidelines*[2] of the World Health Organization (WHO) was derived from self-reported measures that primarily captured leisure-time exercise. Regular structured (leisure time) exercise may not be appealing or is inaccessible to many adults,[3] and participation rates are typically low. In the United Kingdom, for example, just 2 in 5 middle-aged adults engage in exercise (including sports) at least once per month,[3] and dropout rates in exercise-based cardiac rehabilitation programs are often extreme (eg, 56% to 82%).[4] Incidental physical activity (IPA), defined as nonexercise activities that are done as part of daily living (eg, transportation, work, housework, or other domestic activities) may have feasibility advantages for primary and secondary CVD prevention because it overcomes several barriers to structured exercise: namely, lack of time and motivation, costs, poor access to facilities, and low confidence in exercise capacity or skills.[5] Currently, the limited IPA research available is based exclusively on self-reports of different physical activity domains,[6,7] a methodology that is particularly susceptible to imprecision because of the inherent inability of recall questionnaires to capture any unplanned activities, including IPA.

Recent wearable device-based studies have reported steep inverse associations between brief bouts (<1–3 minutes) of IPA and prospective outcomes, including all-cause and CVD and cancer mortality,[8] major adverse cardiovascular events (MACE),[9] and incident cancer.[10] Clinicians and public health practitioners seeking to support patients or populations to increase IPA would need to use very different principles compared with structured exercise interventions because of the distinctively different determinants and barriers underpinning physical activity in different contexts.[11,12]

To date, no wearable device–based study has examined the dose-response association of IPA with prospective CVD-related outcomes. Despite the acknowledgment by the 2020 WHO guidelines[2] that cardiovascular health benefits can be accrued by physical activity of any domain, intensity, and bout duration, no IPA-specific evidence exists to guide physical activity prescription and public health recommendations. Furthermore, such recommendations and research studies seeking to understand the "health value" of different physical activity intensities for CVD prevention commonly apply the assumption that 1 minute of vigorous-intensity activity is equivalent to 2 minutes of moderate-intensity activity.[13–15] This heuristic equivalence is not based on evidence against specific cardiovascular health outcomes or the specific context of IPA. Instead, it represents a convenient method inspired by questionnaire-based leisure-time physical activity literature (in which moderate intensity was typically assigned 3 metabolic equivalents [METs] and vigorous was assigned 6 METs), leading to a symmetry in the minimum activity doses recommended by physical activity guidelines (vigorous, 75 min/wk; moderate, 150 min/wk).[2] No evidence-based or heuristic equivalence per minute of vigorous (>6 METs) intensity exists specifically for IPA to guide interventions promoting lifestyle (ie, nonexercise) physical activity.

Using a novel methodology involving a validated 2-stage machine learning–based intensity classification schema,[8] we examined the dose-response associations of total IPA volume and intensity-specific daily durations (light IPA [LIPA], moderate IPA [MIPA], and vigorous IPA [VIPA]) with MACE and CVD and all-cause mortality. Using these dose-response curves, we also estimated the cardiovascular and general health equivalence of MIPA and LIPA against each minute of VIPA.

METHODS

Sample and Design

The UK Biobank is a prospective cohort study of adults between 40 and 69 years of age at baseline (2006–2010). Participants provided informed consent, and ethics approval was provided by the national research ethics service of the UK National Health Service (Ref80 11/NW/0382).

Between 2013 and 2015, 103 684 UK Biobank participants wore a wrist-worn accelerometer for 7 days.[16,17] As described in detail previously,[8,10] we examined the effects of specific aspects of IPA (eg, vigorous intermittent physical activity lasting <1–2 minutes[8]) by separating accelerometry substudy participants who reported no structured exercise participation and no more than one recreational walk per week.[8,10] As in our previous work,[8–10] we used information on structured exercise and recreational walking participation available in the baseline of the UK Biobank study. Among the 6095 UK Biobank accelerometry sample, participants who reported no exercise at baseline and had a re-examination on average 1.5 years (SD, 1.4 years) before the accelerometry measurements, 88% maintained their nonexercise status over time.[8] We defined a valid monitoring day as wear time >16 hours. To be included in the analysis, participants were required to have at least 3 valid monitoring days, including at least 1 weekend day.[8,10,18,19] We excluded participants with insufficient valid wear days, those who had missing covariate data, and participants who reported an inability to walk. Figure S1 shows the derivation of the core analytic samples of nonexercisers.

Data Availability Statement

The data that support the findings of this study are available from the UK Biobank, but restrictions apply to the availability of these data, which were used under license for the current study and thus are not publicly available. However, data are available from the authors on reasonable request and with permission of the UK Biobank.

Physical Activity Assessment and Exposure Variables

We have described the physical activity intensity classification schema in detail previously,[8–10] and we have also appended it in the Supplemental Methods. In brief, physical activity intensity was classified into light, moderate, and vigorous with a validated[8,9] 2-stage machine learning–based Random Forest activity classifier. For the 88 nonexercisers from the Australian validation sample, the most relevant subset of participants to our study, the correct classification of predicted VIPA, MIPA, and LIPA against ground truth (direct observation through video recordings) was 97.3%, 88.1%, and 80.8%, respectively (Table S1 and S2; Figure S1 and S2).

Physical Activity Energy Expenditure

We calculated physical activity energy expenditure (PAEE)–based volume for total IPA and for each intensity band (≥6 METs for vigorous, 3–6 METs for moderate, and 2–3 METs for light activities)[20] from the accelerometer data using an established method.[21,22] This method, which has been validated against doubly labeled water,[21] estimates instantaneous PAEE from wrist movement intensity, and the time integral constitutes total PAEE.

MACE Ascertainment

Participants were followed up through November 30, 2022, with deaths obtained by linkage with the National Health Service Digital of England and Wales or the National Health Service Central Register and National Records of Scotland. Inpatient hospitalization data were provided by the Hospital Episode Statistics for England, the Patient Episode Database for Wales, or the Scottish Morbidity Record for Scotland. As done previously,[9] MACE[23] were defined as any major CVD death[9] or nonfatal incidence of ST-segment–elevated or non–ST-segment–elevated myocardial infarction, stroke, and heart failure.

Methods for the assessment of MACE, including *International Classification of Diseases, 10th Revision*, codes are provided in Table S3.

Statistical Analyses: Dose Response

To reduce the risk of reverse causation through prodromal/undiagnosed disease, we excluded those with an event within the first year of follow-up from all analyses[10,18] and those with prevalent CVD at the accelerometry baseline from the MACE and CVD mortality analyses. As previously described,[8,10,18] the lower and upper ranges of all VIPA, MIPA, and LIPA values were truncated at the 2.5th and 97.5th percentile, respectively, to minimize the effect of sparse data or outliers.

Using Fine-Gray subdistribution hazards to account for competing risks from non-CVD deaths,[24] we examined the dose response of total PAEE volume and PAEE-derived average daily duration of VIPA, MIPA, and LIPA. As in previous IPA-related work,[8] knots were placed at the 10th, 50th, and 90th percentiles of the exposures. Departure from linearity was assessed with a Wald test. Proportional hazards assumptions were tested with Schoenfeld residuals in every model with the 3 outcomes (MACE, CVD mortality, all-cause mortality); we observed no apparent violations (all $P>0.05$). Core analyses were adjusted for age, sex, education, ethnicity, fruit and vegetable consumption, smoking history, alcohol consumption, accelerometer-estimated sleep duration, discretionary screen time, prevalent cancer, CVD-related medication use (insulin, blood pressure, cholesterol), and family history of cancer and CVD (Table S4). Whenever relevant, PAEE of nonexposure intensities (eg, the analyses with LIPA as exposure) was adjusted for PAEE-based volume from incidental MIPA and VIPA. For all-cause mortality, we adjusted for prevalent CVD and cancer. The reference data point for all main models was the minimum data point of total PAEE (7.73 $kJ \cdot kg^{-1} \cdot d^{-1}$) or each intensity band (VIPA, 0 min/d; MIPA, 0 min/d; and LIPA, 33.2 min/d).

We also present point estimates (hazard ratios [HRs] and 95% CIs) associated with the median volume of each intensity band. We further examined the dose response for the optimal volume of each intensity band (ie, the nadir of the curve). We calculated E values to estimate the plausibility of bias from unmeasured confounding.[25] We conducted the following sensitivity analyses to evaluate the impact of different analytic assumptions and decisions on our:

- Total PAEE volume and each intensity band with additional adjustment for potential mediators, that is, glycated hemoglobin, low-density lipoprotein, high-density lipoprotein, triglycerides, systolic blood pressure, diastolic blood pressure, and body mass index.
- To further reduce the possibility of reverse causation bias, we also excluded participants who had poor self-rated health or a body mass index <18.5 kg/m^2 or who were current smokers[8] or a had a frailty index ≥3 (on a 0–5 scale).[26]
- To assess the influence of variations of the reference data point on intensity-specific estimates, we repeated the main analyses of each intensity band using the 10th percentile of the PAEE-derived duration distribution as referent (0.3 min/d of VIPA, 7.6 min/d for MIPA, and 45.1 min/d of LIPA).
- We tested an alternative placed knots placement on the higher-density data areas at equally distributed frequencies (10th, 33rd, and 67th percentiles)[10] to examine whether the skewness of the distribution of some exposures materially influenced the dose-response curves.
- To provide a more comprehensive exploration of the dose-response relationships with cardiovascular outcomes, we repeated the main analyses restricted to nonfatal MACE events (ie, we excluded CVD deaths not preceded by a nonfatal MACE event).

Acknowledging that active commuting (transportation domain) contains elements of planned and structured activity, we examined an alternative definition of IPA that excludes those reporting active commuting.[27]

Statistical Analyses: Intensity Equivalence

For estimating equivalence across the 3 intensity bands of IPA, we extracted the HRs from the Fine-Gray subdistribution models. We compared the intensity values by evaluating the uniformity in risk reduction. For example, for any given percentage risk reduction, the hazards of VIPA were compared with the same percentage reduction of MIPA and LIPA. Subsequently, these values were standardized to reflect the equivalence of MIPA and LIPA compared with 1 minute of VIPA.

We performed all analysis using R statistical software (version 4.3.1) with the RMS (version 6.3.0) and survival (version 3.5.5) packages. We reported this study according to Strengthening the Reporting of Observational Studies in Epidemiology guidelines (Table S5).

RESULTS

Sample

Figure S3 shows the sample derivation process that resulted in 22 107 (MACE, 908 events), 22 174 (CVD mortality, 223 events), and 24 139 (all-cause mortality, 1072 events) participants being included in the analyses.

Table 1 presents the characteristics of the sample by levels of daily incidental PAEE. The mean±SD age of participants was 61.9±7.6 years; 56.2% were women; and the mean follow-up was 7.9±1.1 years, corresponding to 171 247 (MACE), 171 704 (CVD mortality), and 170 011 (all-cause mortality) person-years. This was a sample of predominantly White participants (96.1%) who never smoked (55.5%) and reported drinking alcohol within current guidelines (59.5%). Higher IPA volume was inversely correlated to age, male sex, current smoking, college-level education, screen time, CVD medication, cancer diagnosis, and sleep duration and positively correlated to drinking alcohol above guidelines and never smoking. Figure S4 shows the distribution of daily VIPA, MIPA, and LIPA across samples.

Dose-Response Associations of Total IPA Volume

Adjusted for potential confounders, higher PAEE volume was inversely associated with risk of MACE, CVD mortality, and all-cause mortality (Figure 1) in an L-shaped fashion with steep risk decline up to ≈35–38 kJ·kg^{-1}·d^{-1}. Compared with the reference PAEE values (eg, 7.73 kJ·kg^{-1}·d^{-1} for MACE and CVD mortality), the median incidental PAEE of 24.9 kJ·kg^{-1}·d^{-1} corresponded to an HR of 0.54 (95% CI, 0.44–0.67) for MACE, 0.38 for CVD mortality (95% CI, 0.26–0.58), and 0.37 for all-cause mortality (95% CI, 0.30–0.44; Table S6). Figure 2 presents the adjusted absolute risk dose-response curves of the different intensities with the 3 outcomes. In particular, MIPA and VIPA showed steep linear risk dose-response associations with MACE and all-cause mortality, whereas the LIPA curves showed a considerably subtler (and less statistically significant) gradient across all outcomes.

Dose-Response Associations of Intensity-Specific IPA

Figure 3 presents the mutually and multivariable-adjusted dose-response associations of VIPA, MIPA, and LIPA with the 3 outcomes. Compared with the lowest data points (VIPA and MIPA, 0 min/d; LIPA, 33.2 min/d), all 3 intensity bands showed inverse dose-response associations with all outcomes. Specifically, VIPA showed steep inverse gradients for all outcomes that were nearly linear for CVD mortality and all-cause mortality. For MACE, the VIPA curve leveled off at ≈10 minutes per day. The median daily VIPA dose (4.3–4.6 min/d) was associated with an HR of 0.75 (95% CI, 0.65–0.87) for MACE, 0.62 (95% CI, 0.46–0.83) for CVD mortality, and 0.76 for all-cause mortality (95% CI, 0.67–0.87). MIPA also showed a steep inverse gradient with all outcomes up to a nadir of 34 to 35 minutes per day for all-cause mortality and CVD mortality and 50 minutes per day for MACE. These optimal points were followed by a plateau for MACE and an inversion for CVD mortality and all-cause mortality.

Table 1. Participant Baseline Characteristics by Incidental PAEE Volume (n=24 139)

Physical activity volume quartiles, kJ·kg^{-1}·d^{-1}	5–20	20–25	25–30	≥30	Overall
Sample size (n)	679	6392	8803	8265	24 139
Follow-up, mean±SD, y	7.6±1.4	7.9±1.1	8.0±0.9	8.0±0.9	7.9±1.0
Age, mean±SD	65.7±7.1	64.0±7.2	62.2±7.5	60.7±7.7	62.3±7.6
Male, n (%)	345 (50.8)	2919 (45.7)	3753 (42.6)	3546 (42.9)	10 563 (43.8)
Race and ethnicity, n (%)					
White	661 (97.6)	6169 (96.9)	8503 (96.8)	7890 (95.6)	23 223 (96.5)
Asian or Asian British	1 (0.1)	67 (1.1)	85 (1.0)	100 (1.2)	253 (1.1)
Black or Black British	5 (0.7)	41 (0.6)	84 (1.0)	111 (1.3)	241 (1.0)
Chinese	1 (0.1)	7 (0.1)	13 (0.1)	24 (0.3)	45 (0.2)
Mixed	3 (0.4)	33 (0.5)	47 (0.5)	69 (0.8)	152 (0.6)
Others	6 (0.9)	48 (0.8)	48 (0.5)	56 (0.7)	158 (0.7)
Smoking history, n (%)					
Current	114 (16.8)	632 (9.9)	763 (8.7)	694 (8.4)	2203 (9.1)
Never	319 (47.0)	3444 (53.9)	4913 (55.8)	4723 (57.1)	13 399 (55.5)
Previous	246 (36.2)	2316 (36.2)	3127 (35.5)	2848 (34.5)	8537 (35.4)
Alcohol consumption, n (%)*					
Never	29 (4.3)	245 (3.8)	307 (3.5)	319 (3.9)	900 (3.7)
Ex-drinker	31 (4.6)	226 (3.5)	286 (3.2)	268 (3.2)	811 (3.4)
Within guidelines	413 (60.8)	3821 (59.8)	5234 (59.5)	4891 (59.2)	14 359 (59.5)
Above guidelines	206 (30.3)	2100 (32.9)	2976 (33.8)	2787 (33.7)	8069 (33.4)
Education, n (%)					
College	267 (39.3)	2365 (37.0)	3335 (37.9)	2831 (34.3)	8798 (36.4)
A/AS level	70 (10.3)	849 (13.3)	1098 (12.5)	1045 (12.6)	3062 (12.7)
O level	122 (18.0)	1398 (21.9)	1926 (21.9)	1882 (22.8)	5328 (22.1)
CSE	19 (2.8)	236 (3.7)	423 (4.8)	557 (6.7)	1235 (5.1)
NVQ/HND/HNC	51 (7.5)	393 (6.1)	511 (5.8)	516 (6.2)	1471 (6.1)
Other	150 (22.1)	1151 (18.0)	1510 (17.2)	1434 (17.4)	4245 (17.6)
Fruit and vegetable consumption, n (%)†	7.1 (4.2)	7.2 (4.1)	7.4 (4.3)	7.6 (4.4)	7.4 (4.3)
Discretionary screen time, mean (SD)	5.2 (2.8)	4.5 (2.4)	4.1 (2.1)	3.8 (2.1)	4.1 (2.2)
Medication, n (%)					
Cholesterol	157 (23.1)	1323 (20.7)	1394 (15.8)	1135 (13.7)	4009 (16.6)
Insulin	8 (1.2)	60 (0.9)	63 (0.7)	35 (0.4)	166 (0.7)
Blood pressure	207 (30.5)	1449 (22.7)	1443 (16.4)	990 (12.0)	4089 (16.9)
Diagnosed cancer, n (%)	85 (12.5)	684 (10.7)	771 (8.8)	592 (7.2)	2132 (8.8)
Family history of CVD, n (%)	370 (54.5)	3634 (56.9)	4888 (55.5)	4457 (53.9)	13 349 (55.3)
Sleep duration, mean±SD	437.9±77.8	438.5±66.4	435.3±64.4	430.9±63.3	434.7±65.0
VIPA, mean±SD, min/d	1.2±2.0	3.4±4.9	6.4±7.2	11.6±10.5	7.3±8.7
MIPA, mean±SD, min/d	5.9±4.6	14.5±9.6	25.3±12.9	45.0±21.6	28.6±20.2
LIPA, mean±SD, min/d	49.8±21.2	78.2± 37.7	104.9±48.7	123.9±55.6	102.8±52.0
MACE incidence, n (%)	75 (11.2)	357 (5.9)	322 (3.9)	221 (3.0)	975 (4.4)
CVD mortality, n (%)	18 (2.7)	96 (1.6)	63 (0.8)	46 (0.6)	223 (1.0)
ACM mortality, n (%)	91 (13.4)	405 (6.3)	328 (3.7)	247 (3.0)	1071 (4.4)

ACM indicates all-cause mortality; CVD, cardiovascular disease; LIPA, incidental light-intensity physical activity; MACE, major adverse cardiovascular event; MIPA, incidental moderate-intensity physical activity; PAEE, physical activity energy expenditure; and VIPA, incidental vigorous-intensity physical activity.

The column breakdown corresponds to total volume of physical activity. Values represent mean±SD unless specified otherwise.

*Alcohol consumption measured in units per week (1 unit=8 g ethanol).

†Fruits and vegetable consumption measured in servings per day.

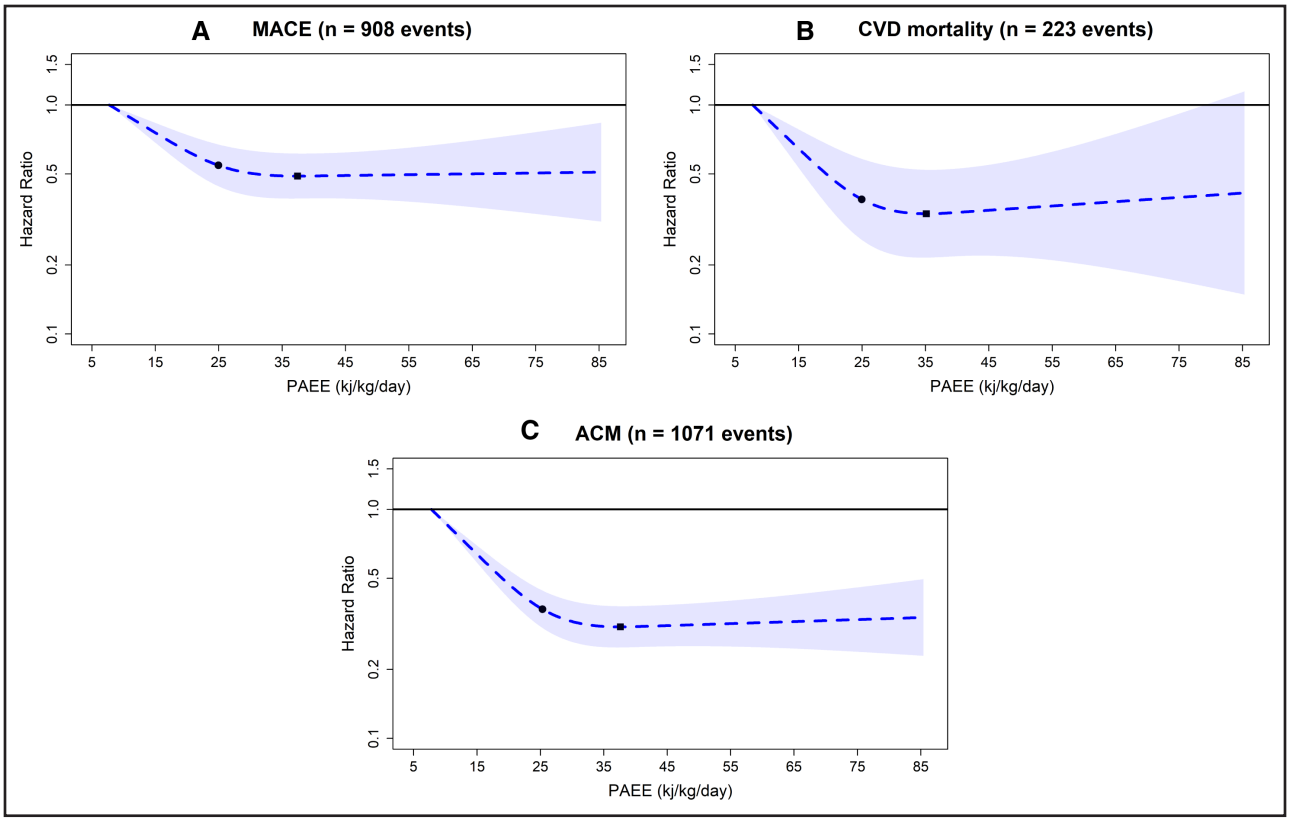

Figure 1. Adjusted dose-response associations of total daily volume of IPA with overall MACE, CVD mortality, and all-cause mortality.

A, Total major adverse cardiovascular events (MACE; n=22 107; events=908). **B**, Cardiovascular disease (CVD) mortality (n=22 174; events=223). **C**, All-cause mortality (ACM; n=24 139; events=1071). Dashed lines represent hazard ratios (HRs) and shaded areas represent their 95% CIs. Analyses were adjusted for sex, age, education, ethnicity, fruit and vegetable consumption, smoking history, alcohol consumption, sleep duration, discretionary screen time, previous cancer incidence, CVD-related medication use (insulin, blood pressure, and cholesterol), and family history of cancer and CVD. The reference point was the minimum value of the energy expenditure of physical activity (7.73 $kJ \cdot kg^{-1} \cdot d^{-1}$ PAEE). ACM analysis was additionally adjusted for previous incidence of CVD. All analyses excluded participants who had an event in the first year of follow-up and prevalent major CVD diagnosis at or before the accelerometry baseline. The circle shows the HR associated with the median PAEE value; the square shows the nadir of the dose-response curve. PAEE indicates physical activity energy expenditure.

The median daily MIPA dose (23.4–23.9 min/d) was associated with an HR of 0.60 (95% CI, 0.47–0.76) for MACE, 0.50 (95% CI, 0.31–0.80) for CVD mortality, and 0.53 (95% CI, 0.43–0.65) for all-cause mortality. LIPA showed a subtle inverse gradient with all outcomes with a statistical significance that was more visible for CVD mortality only at values above ≈130 minutes per day. Excluding frail individuals (≥3 on a 0–5 scale)[26] produced clearer dose-response associations across all outcomes (Figure 4). This was particularly true for CVD and all-cause mortality where the dose response for VIPA became significantly steeper, and the inversion of MIPA was attenuated. The dose-response associations of total incidental PAEE with all MACE and CVD and all-cause mortality were also clearer when frail individuals were excluded (Figure S5).

Sensitivity and Additional Analyses

Dose-response analyses with additional adjustment for potential mediators (Figures S6 and S7) produced curves that were very similar to those of the main analyses. Exclusion of those who had poor self-rated health, those with a body mass index <18.5 kg/m^2, or individuals who were current smokers[8] (Figures S8 and S9) produced clearer and slightly steeper dose-response associations for VIPA compared with the main analyses. Setting the referent data point to the 10th percentile of all exposures (0.3 min/d of VIPA, 7.6 min/d of MIPA, or 45.1 min/day of LIPA) produced clearer associations for VIPA and MIPA compared with the main analyses (Figures S10 and S11). Setting the knots to alternative placements did not materially affect the shape of the curves or magnitude of the associations (Figures S12 and S13). Compared with the main analyses, the dose-response associations for VIPA and nonfatal MACE were attenuated, whereas MIPA revealed a slightly steeper dose-response curve (Figures S14). No differences were observed for LIPA and nonfatal MACE compared with the main analyses. E values (Table S7) indicated that for our estimates to be null, the association of an unmeasured confounder with VIPA, MIPA, and LIPA

 Circulation. 2025;151:1063–1075. DOI: 10.1161/CIRCULATIONAHA.124.072253

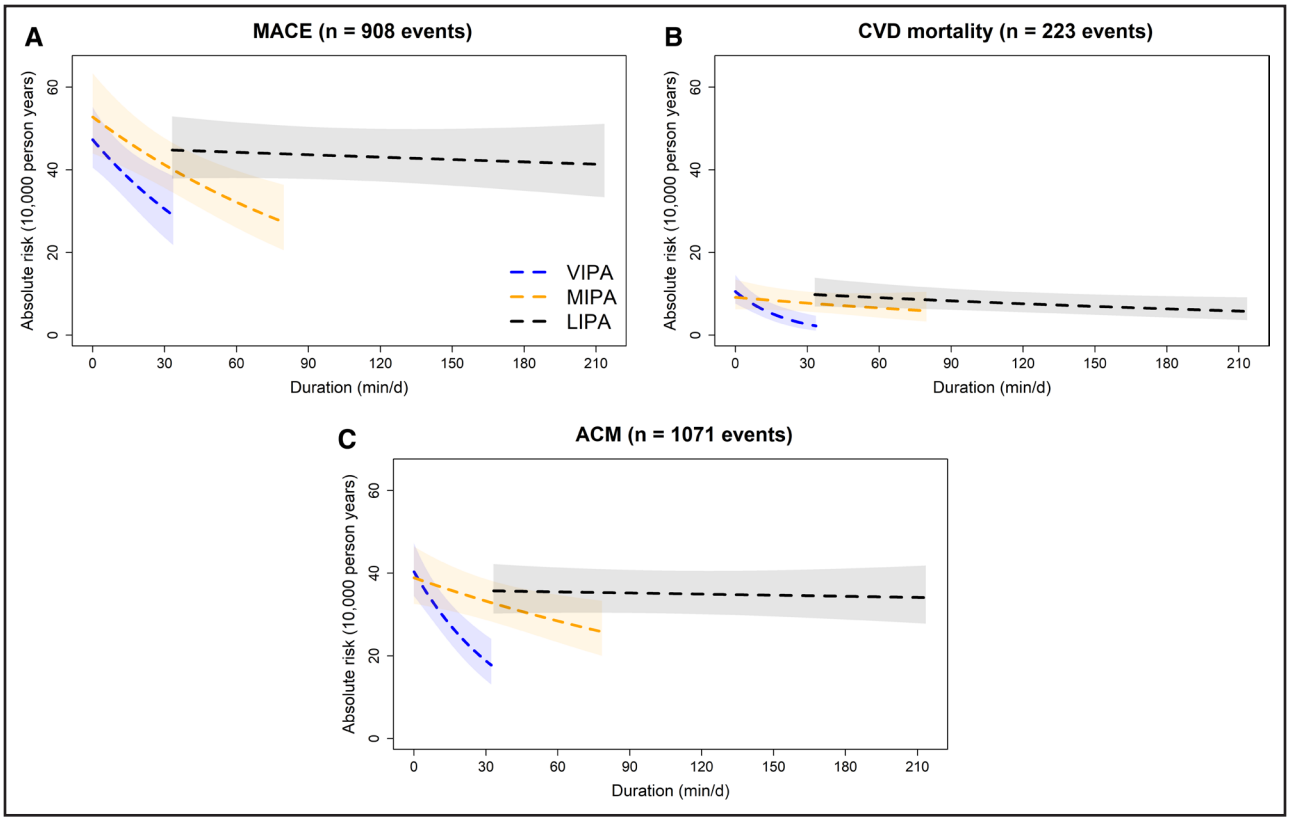

Figure 2. Adjusted absolute risk–based dose-response associations of daily incidental VIPA, MIPA, and LIPA with overall MACE, CVD mortality, and all-cause mortality.

A, Total major adverse cardiovascular events (MACE; n=22 107; events=908). **B**, Cardiovascular disease (CVD) mortality (n=22 174; events=223). **C**, All-cause mortality (ACM; n=24 139; events=1071). Dashed lines represent hazard ratios, and shaded areas represent their 95% CIs. Analyses were adjusted for sex, age, education, ethnicity, fruit and vegetable consumption, smoking history, alcohol consumption, sleep duration, discretionary screen time, previous cancer incidence, CVD-related medication use (insulin, blood pressure, cholesterol), and family history of cancer and CVD. ACM analysis was additionally adjusted for previous incidence of CVD. Each physical activity (PA) intensity-specific spline model was mutually adjusted for PA energy expenditure volume from other intensities with established methods.[21] All analyses excluded participants who had an event in the first year of follow-up and prevalent major CVD diagnosis at or before the accelerometry baseline. LIPA indicates light-intensity incidental physical activity; MIPA, moderate-intensity incidental physical activity; and VIPA, vigorous-intensity incidental physical activity.

exposures doses and MACE would need to have an HR (lower 95% CI) of 2.00 (1.56), 2.72 (1.96), and 1.60 (1.00), respectively. To explain away the associations of VIPA, MIPA, and LIPA with CVD mortality, unmeasured confounder would need to have an HR (lower 95% CI) of 2.60 (1.70), 3.41 (1.81), and 2.08 (1.00), respectively. E values for all-cause mortality were similar to those for MACE (Table S7). The alternative definition of IPA that excludes active commuting[27] (Figures S15 and S16) produced dose-response curves that were almost identical to the main set of results. Excluding events that occurred in the first 2 (Figures S17 and S18) or 3 (Figures S19 and S20) years of follow-up and replacing adjustment for self-reported screen time with device-captured sedentary time (Figures S21 and S22) did not appreciably change dose-response curves.

Equivalence of Different IPA Intensities

Table 2 and Figures S23 present the equivalence of MIPA and LIPA per 1 minute of VIPA by increments of risk reduction. At lower levels of risk reduction (≈<10% to 15%), the MIPA and LIPA equivalence per minute of VIPA was variable, stabilizing thereafter. For MACE, the overall (ie, across the entire dose-response curve) median equivalence of 1 minute of VIPA was 2.8 minutes of MIPA and 48.5 minutes of LIPA. Equivalent values for CVD mortality were relatively consistent (eg, the overall median equivalence of MIPA was 3.4 minutes and that of LIPA was 34.7 minutes). Compared with the 2 cardiovascular outcomes, all-cause mortality equivalence values were lower for MIPA and higher for LIPA (eg, the overall median all-cause mortality equivalence of 1 minute of VIPA was 2.0 MIPA minutes and 47.2 LIPA minutes; Table 2).

DISCUSSION

This study examining the associations between device-measured IPA and prospective outcome showed for the first time that physical activity volume accumulated through incidental activities (eg, during transportation

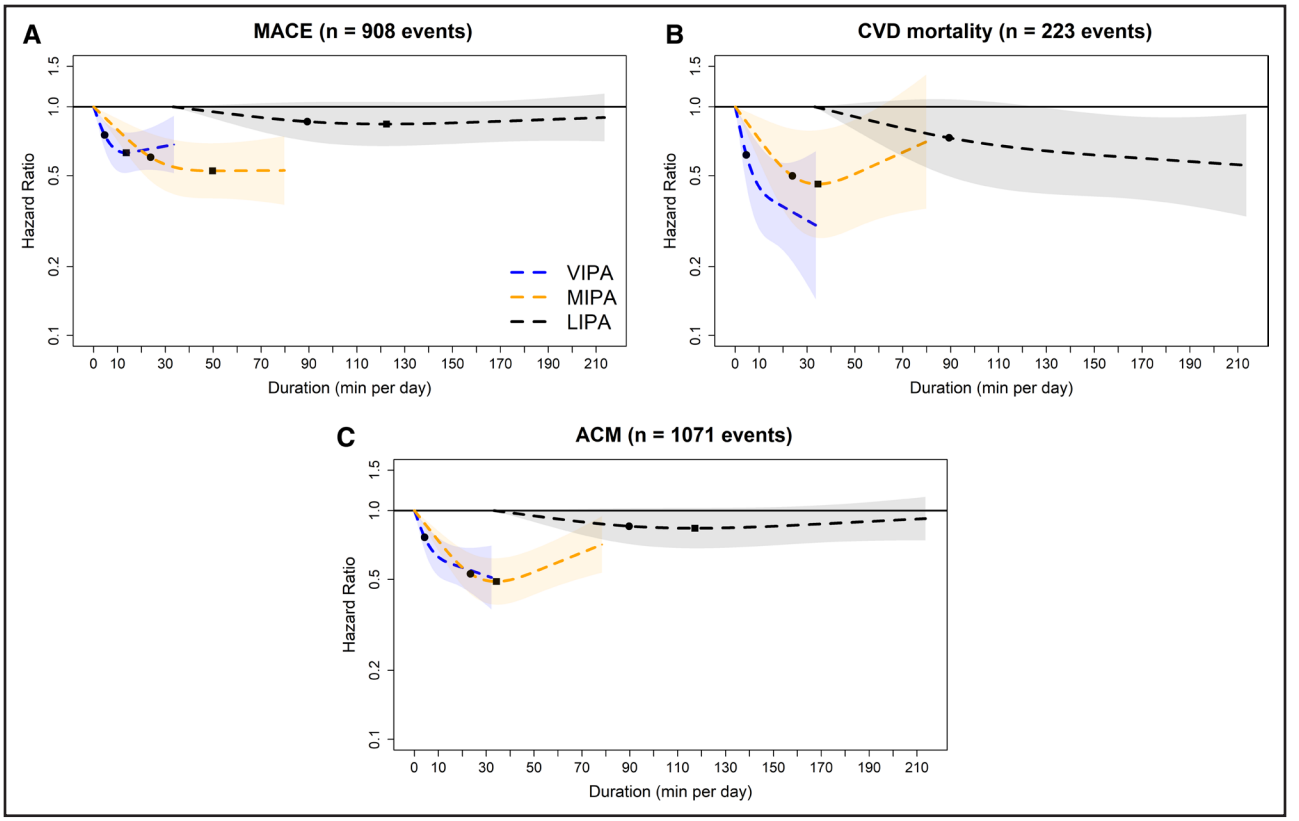

Figure 3. Adjusted dose response associations of daily incidental VIPA, MIPA, and LIPA physical activity with overall MACE, CVD mortality, and all-cause mortality.

A, Total major adverse cardiovascular events (MACE; n=22 107; events=908). **B**, Cardiovascular disease (CVD) mortality (n=22 174; events=223). **C**, All-cause mortality (ACM; n=24 139; events=1071). Dashed lines represent hazard ratios (HRs); shaded areas represent their 95% CIs. Analyses were adjusted for sex, age, education, ethnicity, fruit and vegetable consumption, smoking history, alcohol consumption, sleep duration, discretionary screen time, previous cancer incidence, CVD-related medication use (insulin, blood pressure, cholesterol), and family history of cancer and CVD. All-cause mortality analysis was additionally adjusted for previous incidence of CVD. Each physical activity (PA) intensity-specific spline model was mutually adjusted for PA energy expenditure volume from other intensities with established methods.[21] Referent data point was set to 0 for VIPA and MIPA splines and to the minimum value of LIPA (33.2 min/d) in the corresponding models. All analyses excluded participants who had an event in the first year of follow-up and prevalent major CVD diagnosis at or before the accelerometry baseline. The circle shows the HR associated with the median VLIPA value; and the square shows the nadir of the dose-response curve. LIPA indicates light-intensity incidental physical activity; MIPA, moderate-intensity incidental physical activity; and VIPA, vigorous-intensity incidental physical activity.

and in the domestic or occupational environments) was associated with MACE and mortality in an L-shaped manner. The identified optimal volume of 35 to 38 $kJ{\cdot}kg^{-1}{\cdot}d^{-1}$ corresponded to a 51% to 67% reduction in the risk of MACE and CVD mortality and 69% reduction in the risk of all-cause mortality. In addition to variations in total IPA volume, our results highlighted steep inverse dose-response curves at relatively low levels of vigorous and moderate intensities against CVD and mortality risk. For example, VIPA amounts equivalent to the median of 4.3 minutes per day (all-cause mortality) to 4.6 minutes per day (MACE and CVD mortality), less than half of the recommended lower vigorous-intensity threshold in the 2020 WHO guidelines (75 min/wk or 10.7 min/d)[2], was associated with 25%, 38%, and 24% lower risks of MACE, CVD mortality, and all-cause mortality, respectively, compared with those who did not record any VIPA. We observed analogous inverse dose-response associations for MIPA; the median daily duration of MIPA of 23.4 to 23.9 minutes (roughly 11% higher than the recommendation in the 2020 WHO guidelines of 150 minutes of moderate-intensity activity per week or 21.4 min/d[2]) was associated with 40%, 50%, and 47% lower risk of MACE, CVD mortality, and all-cause mortality risks, respectively, compared with those who did not register any MIPA.

Our health value per time unit analyses showed that the equivalence of 1 minute of VIPA varied across outcomes. Broadly, the all-cause mortality analyses confirm the generic (domain-agnostic) convention quoted in questionnaire-based cohort studies[13–15] whereby 1 minute of vigorous-intensity activity is equivalent to 2 minutes of moderate-intensity activity. In contrast, the 2 cardiovascular outcomes showed considerably higher VIPA:MIPA ratios in the region of 2.8 to 3.4 minutes per VIPA minute. Across outcomes, median amounts of LIPA in the region of 35 to 49 minutes corresponded to 1 minute of VIPA.

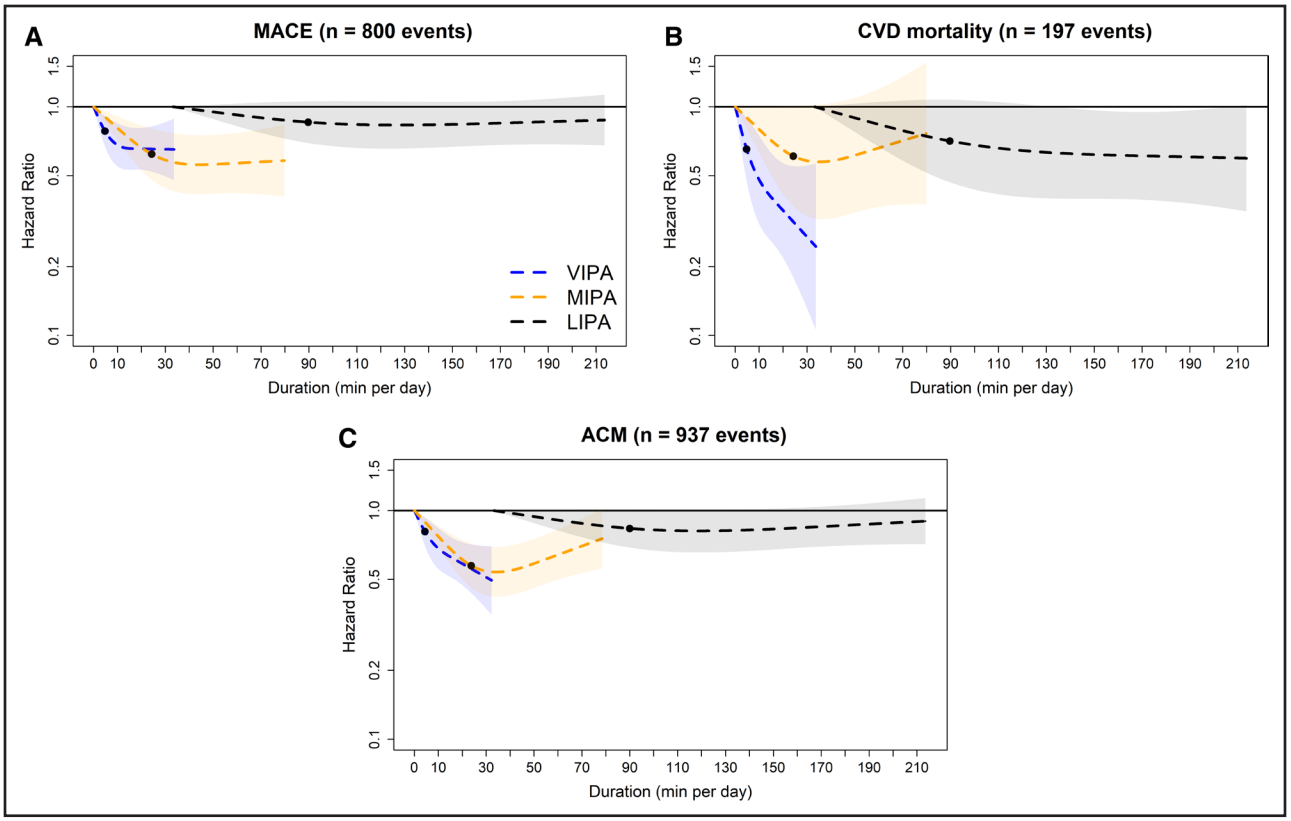

Figure 4. Adjusted dose-response associations of daily incidental VIPA, MIPA, and LIPA physical activity with overall MACE, CVD mortality, and all-cause mortality, excluding frail participants (n=1924).

A, Total major adverse cardiovascular events (MACE; n=19 932; events=800). **B**, Cardiovascular disease (CVD) mortality (n=19 989; events=197). **C**, All-cause mortality (ACM; n=21 785; events=937). Dashed lines represent hazard ratios (HRs), and shaded areas represent their 95% CIs. Analyses were adjusted for sex, age, education, ethnicity, fruit and vegetable consumption, smoking history, alcohol consumption, sleep duration, discretionary screen time, previous cancer incidence, CVD-related medication use (insulin, blood pressure, cholesterol), and family history of cancer and CVD. ACM analysis was additionally adjusted for previous incidence of CVD. Each physical activity (PA) intensity-specific spline model was mutually adjusted for PA energy expenditure volume from other intensities estimated with established methods.[21] Referent data point was set to 0 for VIPA and MIPA splines and to the minimum value of LIPA in the corresponding models. All analyses excluded participants who had an event in the first year of follow-up and prevalent major CVD diagnosis at or before the accelerometry baseline. The circle shows the HR associated with the median exposure value; the square shows the nadir of the dose-response curve. LIPA indicates light-intensityincidental physical activity; MIPA, moderate-intensity incidental physical activity; and VIPA, vigorous-intensity incidental physical activity.

Historically, public health guidelines and clinical interventions have implicitly or explicitly emphasized long bouts of moderate- to vigorous-intensity physical activity, often in the form of structured leisure-time exercise, for the prevention of chronic disease and premature mortality.[26,28] In the 1990s and 2000s, findings from the Harvard Alumni Study demonstrated that in addition to duration of physical activity, both PAEE and physical activity intensity had independent associations with health outcomes and longevity.[29–31] The 2007 update of the American College of Sports Medicine/American Heart Association guidelines recommended that 30 minutes of moderate-intensity activity 5 days per week equated to 20 minutes of vigorous-intensity activity 3 days per week.[32] However, such an equivalence was not based on direct empirical evidence. More recently, public health guidelines[2] have explicitly emphasized an equivalence of 1 minute of vigorous to 2 minutes of moderate activity done in any domain; in the latest WHO guidelines, the recommended moderate-intensity range of 150 to 300 minutes per week is exactly double the vigorous activity range of 75 to 150 minutes per week.[2] In addition to these and other analogous[33] recommendations covering distinctively different contexts (eg, sports versus housework), such an equivalence was derived from expert consensus but not backed up by evidence. The results of our study demonstrated for the first time that when it comes to cardiovascular health, each minute of incidental activity of higher intensity may be equivalent to ≈3 to 3.5 minutes of moderate-intensity and 35 to 50 minutes of light-intensity activity while acknowledging that even the largest amounts of daily LIPA could not reach the CVD risk reductions achieved by VIPA or MIPA.

Our findings add nuance to existing guidelines by informing the activity doses and contents of context-specific interventions aimed at CVD prevention and general health. Despite the excellent potential of structured exercise to prevent, treat, and manage CVD and other

Table 2. Equivalence of MIPA and LIPA per 1 minute of incidental VIPA.

MACE						
Risk reduction, %	HR	VIPA	MIPA	LIPA	MIPA equivalence per 1 min VIPA (full risk-reduction range)	LIPA equivalence per 1 min VIPA (full risk-reduction range)
5	0.95	0.70	2.00	48.40	2.9	69.1
10	0.90	1.50	4.30	67.00	2.9	44.7
15	0.85	2.40	6.80	94.10	2.8	39.2
20	0.80	3.40	9.40	…	2.8	…
25	0.75	4.60	12.20	…	2.7	…
30	0.70	6.20	15.30	…	2.5	…
35	0.65	8.90	18.90	…	2.1	…
					Average equivalence: 2.7	Average equivalence: 64.1
					Median equivalence: 2.8	Median equivalence: 48.5
CVD mortality						
5	0.95	0.40	1.40	40.90	3.5	102.3
10	0.90	0.90	3.10	49.90	3.4	55.4
15	0.85	1.40	4.80	59.60	3.4	42.6
20	0.80	2.00	6.70	70.20	3.4	35.1
25	0.75	2.50	8.60	82.50	3.4	33.0
30	0.70	3.20	10.70	98.30	3.3	30.7
35	0.65	4.00	13.10	121.30	3.3	30.3
					Average equivalence: 3.4	Average equivalence: 46.5
					Median equivalence: 3.4	Median equivalence: 34.7
ACM						
5	0.95	0.70	1.50	47.60	2.14	68.00
10	0.90	1.50	3.30	65.00	2.20	43.33
15	0.85	2.40	5.20	89.20	2.17	37.17
20	0.80	3.30	7.20	…	2.18	…
25	0.75	4.50	9.30	…	2.07	…
30	0.70	6.00	11.60	…	1.93	…
35	0.65	8.20	14.10	…	1.72	…
					Average equivalence: 1.8	Average equivalence: 62.6
					Median equivalence: 2.0	Median equivalence: 47.2

ACM indicates all-cause mortality; HR, hazard ratio; LIPA, incidental light-intensity physical activity; MACE, major adverse cardiovascular event; MIPA, incidental moderate-intensity physical activity; and VIPA, incidental vigorous-intensity physical activity.

Risk reduction based on the HRs of the dose-response curves is presented in Figure 3. Estimates are based on MACE, CVD mortality, and ACM HRs per 5% increment risk reduction.

noncommunicable conditions, there appears to be a historical ceiling of regular participation in the population at ≈15% to 25%.[15,34,35] The barriers to undertaking regular exercise in leisure time (eg, cost, time, low motivation, lifestyle priority, and poor skills or fitness)[8,12] encountered by large segments of the middle-aged and older population suggest that a shift toward feasible and sustainable physical activity patterns that can be habitually embedded into daily routines is needed. Interventions targeting incidental physical activity may be a potent yet relatively unexplored avenue to promote healthier lifestyles, especially for people who face several barriers linked to structured exercise. The availability of wearable devices able to capture high-resolution patterns continuously across the day and machine learning–based intensity classification tools[8–10,18] opens previously unavailable possibilities for understanding the health value of overall and IPA and could catalyze new interventions and guidelines. These health equivalence findings provide meaningful insight beyond the traditional "one-size-fits-all" approach by offering perspective into multiple physical activity avenues to achieve the same potential benefit. For example, light- or moderate-activity health equivalence values may help guide the duration recommendations for adults or clinical populations unable to complete vigorous physical activity.

The current findings expand on a previous analysis of overall PAEE volume (exercise and incidental combined)[22] with CVD risk, which exhibited a nearly linear

dose response. The L-shaped relationship of incidental PAEE and cardiovascular risk that we identified may reflect distinct differences in the physical activity health associations across exercising and nonexercising subpopulations.[8] For example, unlike combined exerciser and nonexerciser samples,[36] we observe unique associations of IPA whereby very high levels of nonintentional light-intensity physical activity were associated with minimal health improvements. These differences in intensity-specific health-related physical activity associations suggest that important details may be missed when context- or domain-agnostic analyses are conducted.

Our findings highlight that the associations of total IPA volume with CVD and mortality may conceal important contributions by different physical activity intensities. Previous interventional studies have demonstrated comparable improvements in various cardiometabolic outcomes among high-volume moderate-intensity exercise protocols (higher PAEE volumes) and low-volume high-intensity protocols (often lower absolute PAEE volumes).[37–39] High-intensity exercise protocols have been shown to improve cardiorespiratory fitness, a cardiovascular clinical vital sign,[40] to a greater degree than high-volume moderate-intensity training despite requiring significantly less time and using less energy.[41] The results of this study add to existing clinical trial data by showing comparable associations in cardiovascular morbidity and mortality between vigorous and moderate intensities, despite the former contributing to a significantly lower proportion of total PAEE. Together, these findings point to separate but complementary pathways by which moderate- and vigorous-intensity physical activity improves cardiovascular outcomes. Traditional studies examining the health effects of physical activity primarily used self-reported questionnaires of a variety of activities lasting >10 minutes.[42,43] Consequently, the potential benefits of IPA remain largely unresearched given that IPA typically occurs in unplanned bouts lasting far less than 10 minutes.[8–10] This study used a wearable device incorporating a 10-second epoch (time window) to provide novel insights into the unexplored health attributes of physical activity accrued through daily activities across vigorous-, moderate-, and light-intensity bands. Our findings highlight potentially more feasible avenues for reducing cardiovascular risk through activities conducted during normal daily living. For example, emphasizing the incorporation of domain-specific preventive strategies such as active transport, household activity, or work-related interventions may be more viable for behavior change for adults who are less motivated or otherwise disinclined to engage in structured exercise. The transition from light-intensity activities embedded in normal daily living to higher-intensity activities (ie, moderate or vigorous intensity) may be a more time-efficient and practical strategy for many. Our results provide support for this assertion because, for 2 of the 3 outcomes (MACE and all-cause mortality), even the nadir of LIPA (117–122 minutes) was associated with a modest and nonstatistically significant 15% lower risk (versus 2.4 VIPA and 6.8 MIPA min/d linked to the same hazard reduction). Future studies may benefit by incorporating our findings into a larger more dynamic system-level approach for implementing behavior change strategies in the broader population.[44–46] This includes comprehensive approaches that consider domain-specific and environmental and individual-level factors to effectively promote physically active lifestyles for CVD prevention, onset delay, or risk reduction.[47,48] It is important to note that our results support the role of IPA as a complementary strategy to structured exercise in both clinical and public health settings. Structured exercise is unique in that it is specifically designed to elicit cardiovascular health benefits and to promote well-being. However, because it requires conscious planning, a significant time commitment, and a high degree of motivation, only a small minority of the middle-aged and older adult population adheres to a regular exercise routine.[15] Our findings prompt for future studies examining the unique, combined, and synergistic effects of these 2 broad physical activity domains for optimal CVD prevention.

Strengths and Limitations

Strengths of this study include the implementation of a novel 2-stage physical activity intensity and posture classification system.[8–10] By examining a cohort of adults who report no leisure-time exercise, we were able to explore for the first time the associations of IPA with cardiovascular health. We used a device-measured energy expenditure estimation method[20,21] and a novel equivalence-based analytical approach that enabled us to characterize the health value of physical activity according to specific intensity bands. We incorporated a range of analyses to reduce the possibility of reverse causality, including the removal of individuals with poor health, with high frailty, or with an event in the first 1 to 3 years of follow-up that provides additional certainty to our findings.[8–10] However, limitations of this study include the 5.5-year lag time between the UK Biobank baseline measurement at which nonexercising status was determined and when accelerometry measurements were collected. Nevertheless, among the 6095 participants with repeat examination data, these questions had a high degree of stability (88%).[8–10] Despite the comprehensive list of covariates and robust E values for VIPA and MIPA, the possibility of uncaptured confounding remains. Although the UK Biobank does not reflect the characteristics of the entire UK population, previous work has shown that the low response rate (5.5%) and subsequent nonrepresentative nature of the sample do not materially influence the association of physical activity with cardiovascular or all-cause mortality.[9] Our findings and conclusions are based on observational data; future trials are needed to confirm the cardiovascular health benefits of overall IPA, VIPA, and MIPA.

Conclusions

Our novel dose-response analysis of IPA documented an L-shaped association of IPA with major cardiovascular and mortality outcomes, particularly when activity was accrued through vigorous or moderate intensities. A steep reduction in cardiovascular risk was observed for any daily duration up to ≈14 vigorous-intensity or up to 35 to 50 moderate-intensity minutes. The cardiovascular health equivalence for each 1 minute of VIPA was 2.8 to 3.4 minutes of MIPA or 35 to 48 minutes of LIPA, while acknowledging that even the largest amounts of daily LIPA were only associated with modest risk reductions. Collectively, our findings support the integration of preventive strategies aimed at encouraging particularly higher-intensity (moderate, vigorous, or both) physical activity of any duration into day-to-day activities. Our findings may expand the array of feasible and behaviorally sustainable options for cardiovascular risk reduction.

ARTICLE INFORMATION

Received September 12, 2024; accepted February 28, 2025.

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Acknowledgments

This research has been conducted using the UK Biobank Resource under application 25813. The authors thank all the participants and professionals contributing to the UK Biobank. All information and materials in the manuscript are original and have not been submitted for publication elsewhere. R.B., M.N.A., and E.S. had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Sources of Funding

This study is funded by an Australian National Health and Medical Research Council investigator grant (APP 1194510). The funder had no specific role in any of the following study aspects: the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Disclosures

Dr Stamatakis is a paid consultant and holds equity in Complement 1, a company with services related to physical activity. All other authors report no conflicts.

Supplemental Material

Supplemental Methods: wearable device-based physical activity classification
Figure S1–S23
Table S1–S7
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