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Nat Med. Author manuscript; available in PMC 2021 March 01.

Published in final edited form as:
Nat Med. 2020 September 01; 26(9): 1385–1391. doi:10.1038/s41591-020-1012-3.

Wearable device measured physical activity and future health risk

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Abstract

Use of wearable devices that monitor physical activity is projected to increase more than five-fold per half-decade [1]. We investigated how device-based physical activity energy expenditure (PAEE) and different intensity profiles were associated with all-cause mortality. We used a network harmonisation approach to map dominant wrist acceleration to PAEE in 96,476 UK Biobank participants (mean age 62 years, 56% female). We also calculated the fraction of PAEE accumulated from moderate-to-vigorous physical activity (MVPA). Over the median 3.1 year follow-up period (302,526 person-years), 732 deaths were recorded. Higher PAEE was associated with a lower hazard of all-cause mortality for a constant fraction of MVPA, e.g. 21% (95% CI 4-35%) lower hazard for 20 versus 15 kJ/kg/d PAEE with 10% from MVPA. Similarly, higher MVPA fraction was associated with a lower hazard when PAEE remained constant, e.g. 30% (8-47%) lower hazard when 20% versus 10% of a fixed 15 kJ/kg/d PAEE volume was from MVPA. Our results show that higher volumes of PAEE are associated with reduced mortality rates, and achieving the same volume through higher intensity activity is associated with greater reductions than through lower intensity activity. The linkage of device-measured activity to energy expenditure creates a framework for using wearables for personalised prevention.

Use of wearable devices that monitor physical activity is projected to increase more than five-fold over five years from 2016 [1]. These devices can provide insights into physical

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Author Contributions

SB, TS, KW and PCD designed the study with input from TL, JJ, MP and NW. TS undertook the analyses with assistance from SJS. TS drafted the manuscript. All authors contributed to the critical revision and approved the final version. TS had full access to all the data in the study and takes responsibility for the integrity of the data and accuracy of the data analysis.

Competing Interests

The authors declare no competing interests.

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activity energy expenditure (PAEE) and activity intensity. Whilst their validity and reliability properties are less well documented and may not match research-grade devices [2], consumer wearables offer an opportunity for individuals to self-monitor their activity levels.

National and international physical activity guidelines recommend adults undertake activity of at least moderate intensity [3–6]. This is equivalent to a steady-paced walk for most, commonly defined as activity above 3 Metabolic Equivalents of Task (METs) [7]. Updates to the US and UK guidelines in 2018/19 acknowledged the growing evidence around the benefits of light intensity activity [8–10], stating that "adults should move more and sit less throughout the day. Some activity is better than none". However, despite light activity being the main contributor to total PAEE [11], both guidelines still emphasise the benefits of moderate intensity activity, which leaves ambiguity about how inactive individuals should change their activity to maximise health benefits.

Numerous studies have shown that an equivalent amount of time spent in moderate-to-vigorous intensity physical activity (MVPA) confers greater health benefits than light intensity activity [12–14] but this does not elucidate whether it is the volume of physical activity (intensity*time; often expressed as PAEE) or the intensity alone that is important. Previous attempts to disentangle the roles of volume and intensity were unable to make strong inferences about the additional role of intensity, as they made comparisons at a group level where there was insufficient variation in the mean contribution of MVPA amongst groups with similar total volumes [15].

As physical activity volume is the product of intensity and time, volume and intensity will always be highly correlated. Potential issues of collinearity might be reduced in large cohorts where the number of individuals with atypical combinations of the two exposures is sufficient to enable estimation of the association of each exposure with the outcome [16]. We investigated whether the fraction of PAEE derived from MVPA conferred any additional mortality benefits, beyond increasing PAEE in the UK Biobank, which is the largest study of accelerometer-measured physical activity to date.

In a subsample of 96,476 UK Biobank participants (mean age 62 years, 56% female) who provided valid accelerometer data, 732 died during the median 3.1 (range 0.9-4.6) years of follow-up (302,526 person-years). Using a network harmonisation approach, dominant wrist acceleration was mapped to PAEE (median 40 kJ/kg/day) and the fraction of that PAEE derived from MVPA was calculated (median 34%; Figure 1, Table 1, Supplementary Table 1, Extended Data 1). The correlation coefficient between PAEE and fraction of PAEE from MVPA was 0.688, and 0.597 in the sensitivity analysis sub-sample (Supplementary Table 2).

When considering the associations of PAEE alone (adjusting for all covariates but not the fraction of PAEE from MVPA) undertaking an additional 5 or 15 kJ/kg/day from a low baseline of 15 kJ/kg/day was associated with a 37% (95% CI 27-46%) or 71% (62-79%) lower hazard of all-cause mortality, respectively (Figure 2A; Supplementary Table 3). The association was non-linear, being steeper between 15-30 kJ/kg/day, then stabilising around 80% lower hazard. Accumulating 20% of PAEE from MVPA compared to 5% was associated with a 56% (24-75%) lower hazard, after adjustment for covariates and PAEE

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(Figure 2B; Supplementary Table 4). A 60% fraction was associated with a 91% (45-99%) lower hazard.

In the interaction analyses of PAEE and the fraction of PAEE from MVPA, higher levels of both exposures were associated with decreases in the hazard (Figure 3; Table 2). All comparisons were made relative to 15 kJ/kg/day PAEE, with 10% from MVPA. For a PAEE of 20 kJ/kg/day with MVPA fixed at 10%, we observed a 21% (4-35%) lower hazard. When MVPA fraction was higher at 20% but PAEE was fixed at 15 kJ/kg/day, we observed a 30% (8-47%) lower hazard. A PAEE of 30 kJ/kg/day with a 30% MVPA fraction was associated with a 72% (44-86%) lower hazard. There was evidence of a non-linear response for both exposures; the greatest hazard differences were observed at the lower end of the exposure scales. There was considerable uncertainty around whether levels of PAEE beyond 40 kJ/kg/day with a >20% fraction of MVPA conferred additional benefits. Figure 4 presents the hazard ratios for further combinations of PAEE and fraction of MVPA, grouping those with similar MVPA time (minutes).

In all analyses, additional covariate adjustment slightly attenuated the associations, but excluding those with prevalent disease slightly strengthened the associations. Results did not materially differ in the restricted sub-sample nor in the complete-case analyses (Supplementary Tables 3, 4, 5), nor by choice of intensity threshold although the low prevalence of activity intensity over 4 METs resulted in wider confidence intervals (Supplementary Tables 4, 5).

Using data from the largest study including accelerometer-measured physical activity to date, we found that both higher total volume of PAEE, as well as a higher fraction of PAEE accumulated in MVPA, were associated with lower mortality rate. A moderately higher PAEE of 20 kJ/kg/day compared to 15 kJ/kg/day was associated with 21% lower premature mortality rate, when the fraction of MVPA was fixed at 10%. The difference between these scenarios is roughly equivalent to a 35-minute stroll, with an extra 2 minutes at a brisker pace. A fixed PAEE of 15 kJ/kg/day but accumulating 20% rather than 10% from MVPA was associated with a 30% lower mortality rate - the equivalent of converting a 12-minute stroll into a brisk 7-minute walk. A combination of higher PAEE and fraction of MVPA to 20 kJ/kg/day and 20% conferred a 46% lower mortality rate. Although these results support the core message of the latest physical activity guidelines, this is the first study to show that intensity plays a role in the prospective association between physical activity and all-cause mortality, over and above total volume of activity. This is important as different strategies of behaviour change may be more appealing or practical to different individuals.

A recent meta-analysis (n=36,383, 2149 deaths, 5.8 years follow-up) concluded that a higher volume of accelerometer-measured physical activity at any intensity was associated with a reduced mortality risk [17]. We build upon this research by considering volume and intensity together, showing that activity of at least moderate intensity is associated with lower mortality, over and above its contribution to total volume.

Our findings are different to a previous accelerometer-based study which was unable to detect an association of the fraction from MVPA independent of total volume [15]. This is

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likely because we used both volume and fraction from MVPA in their naturally continuous distributed form (rather than comparisons of accumulation pattern groups) in a much larger sample providing the statistical power to detect greater individual-level variations between the two exposures.

There have been two studies investigating the associations of activity intensity beyond volume with coronary heart disease risk, although neither fully captured activity volume as they were based on self-reported data almost entirely in the MVPA range. Habitual walking pace was an independent predictor of mortality above total walking time in a large sample of female nurses in the US [18], while a 1 MET higher average self-reported leisure activity intensity was associated with a 4% lower coronary heart disease risk after adjustment for volume [19]. Potentially, our improved measurement of total volume, and light intensity activity in particular, accounts for the non-linear association we found between the fraction of MVPA and mortality risk.

A major strength of this study, apart from its large sample size, is our method for anchoring the accelerometer-derived metrics of movement to the more easily interpretable scale of energy expenditure, using equations derived from combined heart rate and trunk acceleration sensors, validated in UK age-matched samples against the gold-standard criterion of doubly-labelled water [20,21]. Although this inference has some limitations, the approach is generic and uses a simple acceleration metric easily derivable from wearables, most of which are also wrist-worn. This fully transparent framework is therefore a first step towards personalised risk prediction from wearables. It could be implemented by any device manufacturer enabling users to receive immediate feedback on daily activity levels in terms of health outcome predictions.

The present findings represent the first comprehensively adjusted prospective results using these data; previous analyses had a median of 1 year of follow-up and did not adjust for prevalent disease [22] meaning the risk of reverse causality was severe [23]. Our recent work informed our decision to analyse at the median follow-up 3.1 years (range 0.9-4.6). We showed stronger associations between physical activity and mortality at follow-up times <7 years, but little difference between 4 and 7 years when stringent analytical approaches to account for reverse causality were employed [23]. Furthermore, this study's main findings are robust to the exclusion of those with prevalent disease. It is plausible, if not expected, that the present results would be attenuated if we were to repeat the analyses when more follow-up data become available as longer follow-up time increases the risk of regression dilution bias.

Limitations include our inability to make firm causal conclusions as our study is observational with physical activity measured at a single time point. Also, the intrinsic correlation between PAEE and the fraction of PAEE from MVPA means joint results cannot be interpreted in its two constituent parts. Our analytical approach ensured that our results are not biased by statistical collinearity but we have purposely avoided using the phrase 'independent effects' because of the inherent inter-dependence between the two exposures.

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Another limitation is the unrepresentativeness of the sample which may impact external validity. The main UK Biobank sample had a 5.5% response rate and has been shown to be healthier and more affluent than the general population [24]. The accelerometer sub-study was subject to further selection pressures (e.g. survival five years after baseline, contacted by email) that likely exacerbated some of these differences. However, our median value of PAEE of 40 kJ/kg/day is comparable with nationally representative age-specific estimates [25].

We considered intensity relative to overall absolute activity volume, although intensity relative to maximal capacity may be more critical to driving adaptations [26]. However, we did adjust for mobility limitations that are associated with low physical capacity, and performed sensitivity analyses around the MVPA threshold and found similar results.

An intrinsic limitation to these data is that covariate measurement was not undertaken at the present study baseline (accelerometer mail-out) but at the physical visits to the UK Biobank assessment centres, a median of 5.7 years prior. Extended Data 2 and 3 show the change in covariates over this time period for the subsamples that undertook more than one assessment centre visit. The responses are generally stable over time with the exception of medication use (for hypertension and high cholesterol) and employment status – indicators of health status and retirement, respectively. Our use of hospital episode statistics to identify prevalent disease status up until the present study baseline should identify the most serious cases of ill-health and mitigate some measurement error. The use of age as the underlying timescale may also reduce the residual confounding for inadequate measurement of both health and retirement status.

Future research should confirm these findings in other populations, with longer follow-up time, repeat exposure measures and with different disease endpoints or biomarkers to shed light on potential mechanisms. Limited activity above 4 METs prevented us from exploring associations at higher intensities, but other cohorts may be able to contribute to the existing literature that suggests beneficial associations of vigorous activity independent of MVPA [27,28].

In conclusion, our results show that higher volumes of activity energy expenditure are associated with lower mortality rates, and achieving the same energy expenditure through higher intensity activity is associated with even greater benefits than through lower intensity activity. Our approach for converting device-measured activity signals to energy expenditure and relating this to health risk creates a framework for future personalised prevention from wearables.

Methods

Study population

The UK Biobank is a large prospective cohort study of over 500,000 middle-aged adults living in Great Britain, whose methods have been described elsewhere [29]. A sub-sample of 103,695 participants responded to an email invitation to wear a wrist-worn accelerometer, a median 5.3 years after their recruitment into the main study. Ethical approval for the UK Biobank studies was given by the NHS National Research Ethics Service (Ref 11/NW/0382)

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and informed consent was obtained. See Life Sciences Reporting Checklist for consistency and transparency information.

Exposure derivation: mapping acceleration to energy expenditure

Between 2013-2015, invitations for the accelerometer sub-study were sent to all those that had provided a valid email address (n=236,519). This did not include those in the North-West as the burden of other sub-studies was deemed to be too high. Participants were instructed to wear a triaxial accelerometer (AX3, Axivity, UK) on their dominant wrist for seven consecutive days, at all times including swimming, bathing, and sleeping. Raw acceleration was collected at 100Hz resolution, calibrated to local gravity whilst also taking into account ambient temperature [30]. This involves selecting periods of non-movement in individual data records (standard deviation <13mg in all three axes) as the vector magnitude (Euclidean Norm) at that point should be 1*g*. The nine calibration parameters that influence deviation from this were optimised using an iterative procedure. This was done for each individual; if an individual did not have sufficient non-movement periods from which to calibrate, calibrations were taken from the measurements obtained from the subsequent user of the same device.

The Euclidean Norm of calibrated acceleration in the three axes was calculated after removing machine noise using a fourth-order Butterworth low-pass filter at 20 Hz. From this, 1*g* was subtracted and any negative values were truncated to zero. As done previously, we denote this measure Euclidian Norm Minus One, or ENMO [31].

Non-wear time was considered to be time periods of ≥60 minutes where the standard deviation of acceleration in each of the three axes was <13 mg [32]. Missing data due to non-wear time was imputed based on similar time-of-day segments from that individual.

The average ENMO over 5-second epochs, i.e. the intensity time-series, was summarised into average proportions of daily time spent at different movement intensity levels (Supplementary Table 6). We excluded n=6,996 due to insufficient accelerometry wear time (<72 hours or no wear data in each one-hour period of the 24-hour cycle) and n=4 due to poor device calibration (Extended Data1).

Time spent at each intensity level was converted to PAEE in kJ/kg/day using a network harmonisation framework approach [33]. This involved mapping dominant to non-dominant wrist acceleration, before predicting instantaneous PAEE assessed by individually calibrated combined heart rate and movement sensing in a separate validation study. Average daily PAEE was calculated as the sum of energy expenditure from all intensity levels. Individual components of this framework have been validated [21,34–39] as well as the overall volume estimate from dominant wrist acceleration against the gold-standard doubly-labelled water method in 97 UK adults with a correlation of 0.644 (r^2=0.415) and no mean bias [20]. The fraction of PAEE from MVPA was the sum of energy expenditure from activity above 3 METs divided by total PAEE, expressed as a percentage (Supplementary Table 7). MVPA time (minutes/day) was calculated directly from the original time variables for the intensity categories above 3 METs. Figure 1 presents an overview of the study methods.

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Two individuals were excluded whose values of PAEE were clearly outliers (>9 standard deviations from the mean, Extended Data 5).

Covariate measurement

All participants completed a touchscreen questionnaire and anthropometric assessment at recruitment into the main study. Some participants took part in up to two further touchscreen interviews (n=8,503 and n=15,140; Extended Data 6). Covariate data from the interview undertaken closest to the accelerometry were used, the accelerometry time-point being the analytical baseline for this present analysis. Exceptions to this were sex and Townsend Index of deprivation (based on postcode) that were only obtained at baseline; ethnicity (assumed not to have changed), and family medical history where a condition was counted at any of the measurement points. Implausible changes from previous or current smoker to never smoker, or from having a qualification to no qualification were set to either previous or current smoker, or their previously reported qualification level (n=512 and n=224, respectively).

There were stable responses for most of the covariates between baseline and the additional visits (Extended Data 2 and 3). Exceptions were employment status and medication use, where there were trends towards unemployment and greater medication use at later visits.

We divided the covariates into two groups based on potentially being on the causal pathway between physical activity and mortality, or not. Those that were not on the causal pathway included the demographic and lifestyle-related characteristics of age, sex, ethnicity (white/non-white), Townsend Index of deprivation, highest educational level achieved (degree or above/any other qualification/no qualification), employment status (unemployed/in paid or self-employment), parental history of disease, season of accelerometry wear (using two orthogonal sine functions with a period of 365 days; one with maximum=1 in Winter and minimum=-1 in the Summer; the other with maximum in the Spring and minimum in the Autumn), alcohol drinking status (never/previous/current), salt added to food (never/sometimes), oily fish intake (never/sometimes), fruit and vegetable intake (a score from 0-4 from questions on cooked and raw vegetables, fresh and dried fruit consumption), processed and red meat intake (average days per week), and sleep duration (<7, 7-8, >8 hours). Covariates that were potentially on the causal pathway included the health-related variables of blood pressure and cholesterol medication, doctor diagnosed diabetes or prescribed insulin medication, mobility limitations (self-reported longstanding illness or disability or chest pain at rest), body mass index (BMI; <25, 25-30, ≥30 kg/m^2), and a cardiovascular disease or cancer diagnosis prior to baseline (self-reported history of heart attack, angina, stroke, or cancer variables, or hospital episode with ICD-10 code I20-25, I60-69, or C00-99). Table 1 and Supplementary Table 1 display the sample descriptive statistics for these covariates by quartile of PAEE and fraction of MVPA respectively. Season of accelerometer wear is described in Extended Data 4.

We used multiple imputation by chained equations (five imputed datasets) for the 3,204 individuals with missing covariates. The imputation model contained all covariates, the Nelson-Aalen estimate of cumulative baseline hazard of mortality, and mortality [40]. Supplementary Table 8 displays the descriptive statistics for the imputed variables in the

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complete case and the imputed sample. There were minimal differences between these samples.

Outcome

Mortality records were linked to the UK Biobank dataset from NHS Digital (England and Wales) and from Information and Statistics Division (Scotland). The censoring dates were 31st January 2018, and 30th November 2016 respectively. Location of individuals was based on their main study baseline assessment centre. No other censoring was used.

Statistical analyses

To quantify the relationship between PAEE and the fraction of PAEE accumulated in MVPA, we calculated the Pearson's Correlation Coefficient and Variance Inflation Factor as recommended elsewhere [16].

Our main analyses excluded 217 individuals who died in the first year of follow-up to minimise the risk of reverse causality (n=96,476). Using age as the timescale in Cox proportional hazard regression models, we first investigated the associations between PAEE and mortality, where the exposure was modelled using restricted cubic splines with three evenly-spaced knots. We fit two models: Model 1 adjusted for the demographic and lifestyle covariates, and Model 2 additionally adjusted for the health-related covariates potentially on the causal pathway. Second, we investigated the association between the fraction of PAEE from MVPA, additionally adjusted for PAEE (log-transformed and centred on the mean amongst those who died) with interaction terms between activity exposures. Exposure reference values were chosen as the nearest 5 kJ/kg/day or 1% to the 1st percentile of the distribution amongst those who died. Last, we investigated the joint associations of PAEE and fraction of MVPA. We fit a spline regression for PAEE, adjusted for all covariates and the fraction of PAEE from MVPA, including interaction terms for the activity exposures. Using the coefficients, we plotted the fitted spline functions showing the association between PAEE and mortality for 10%, 20%, 30% and 40% fractions of PAEE from MVPA. We checked the proportional hazard assumptions for categorical covariates using log-log plots; those variables that failed to meet the assumptions were used to stratify the baseline hazards. The log-linear relationship between continuous covariates and hazard of mortality were checked using fractional polynomials, and variables were transformed if assumptions were not met.

We performed a number of sensitivity analyses to investigate potential sources of bias in our results. Firstly, we used the collinearity diagnostic tests to identify a sub-sample in the centre of the sample distributions of PAEE and fraction of PAEE from MVPA with a lower correlation between the exposures (n=70,609; Extended Data 4). Secondly, as collinearity can make models sensitive to over-specification, we performed the analyses without interaction terms between exposures (n=96,476). Thirdly, to further investigate potential reverse causality bias, we excluded participants with prevalent disease at baseline (n=79,205). Fourthly, we tested different wrist accelerometry thresholds corresponding to intensity between 2.5 and 4 METs (n=96,476). Fifth, we reran our main models with additional adjustment for measured hypertension (systolic blood pressure >130mmHg and/or

diastolic >80mmHg) at their initial UK Biobank assessment centre visit (n=96,476). This was to capture those most likely to be on blood pressure medication at the time of the accelerometry measurement to try to assess potential bias by not capturing medication use directly at the present study baseline. Lastly, we performed a complete-case analysis to investigate our method of dealing with missing data (n=93,272). All analyses were undertaken in Stata v15.1 (StataCorp LLC, College Station, TX), and figures were produced in RStudio (RStudio Inc., Boston, MA). Full results of these sensitivity analyses are shown in the main text and Supplementary Tables with the exception of the additional adjustment for blood pressure as results were minimally different from the main models.

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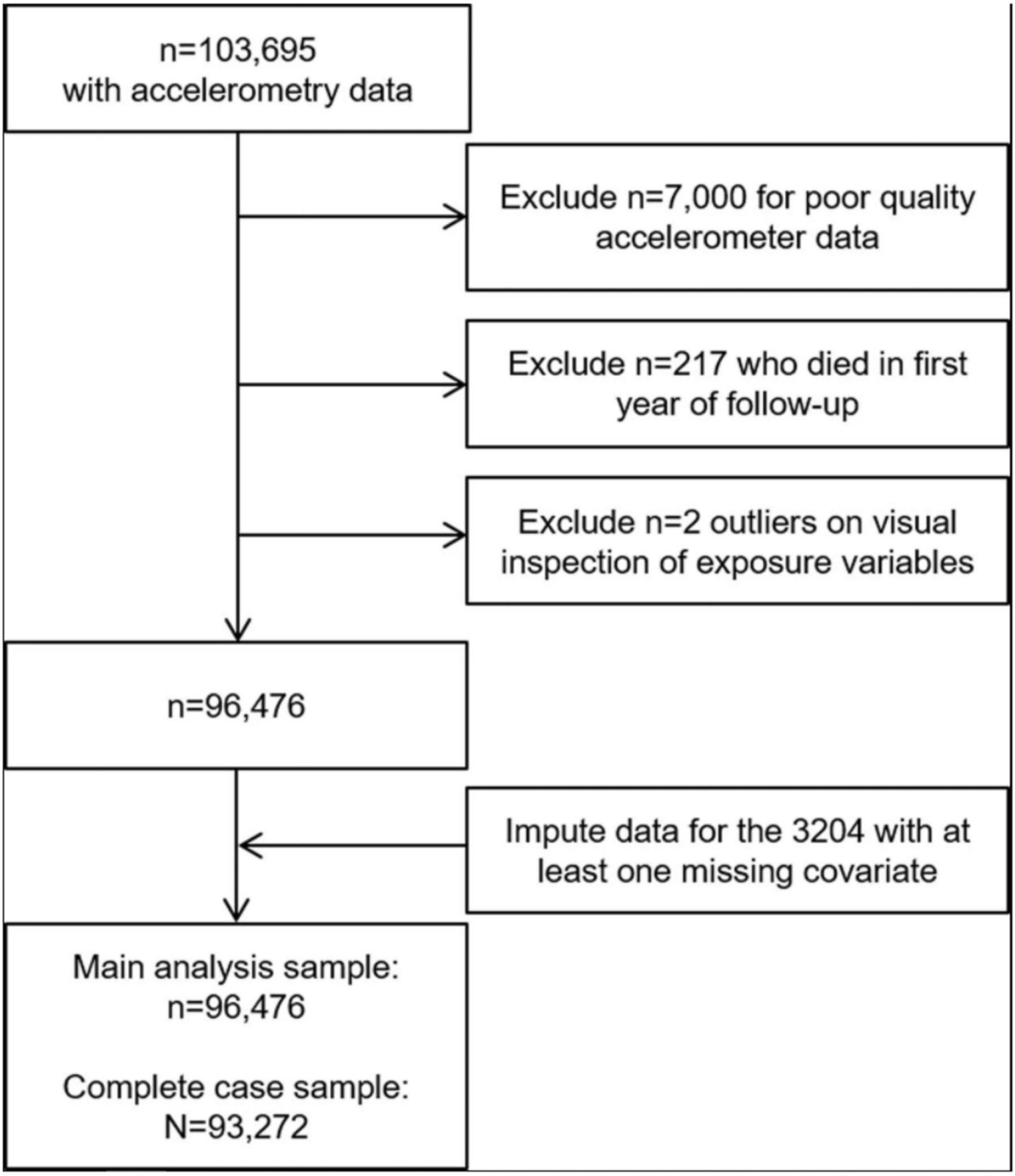
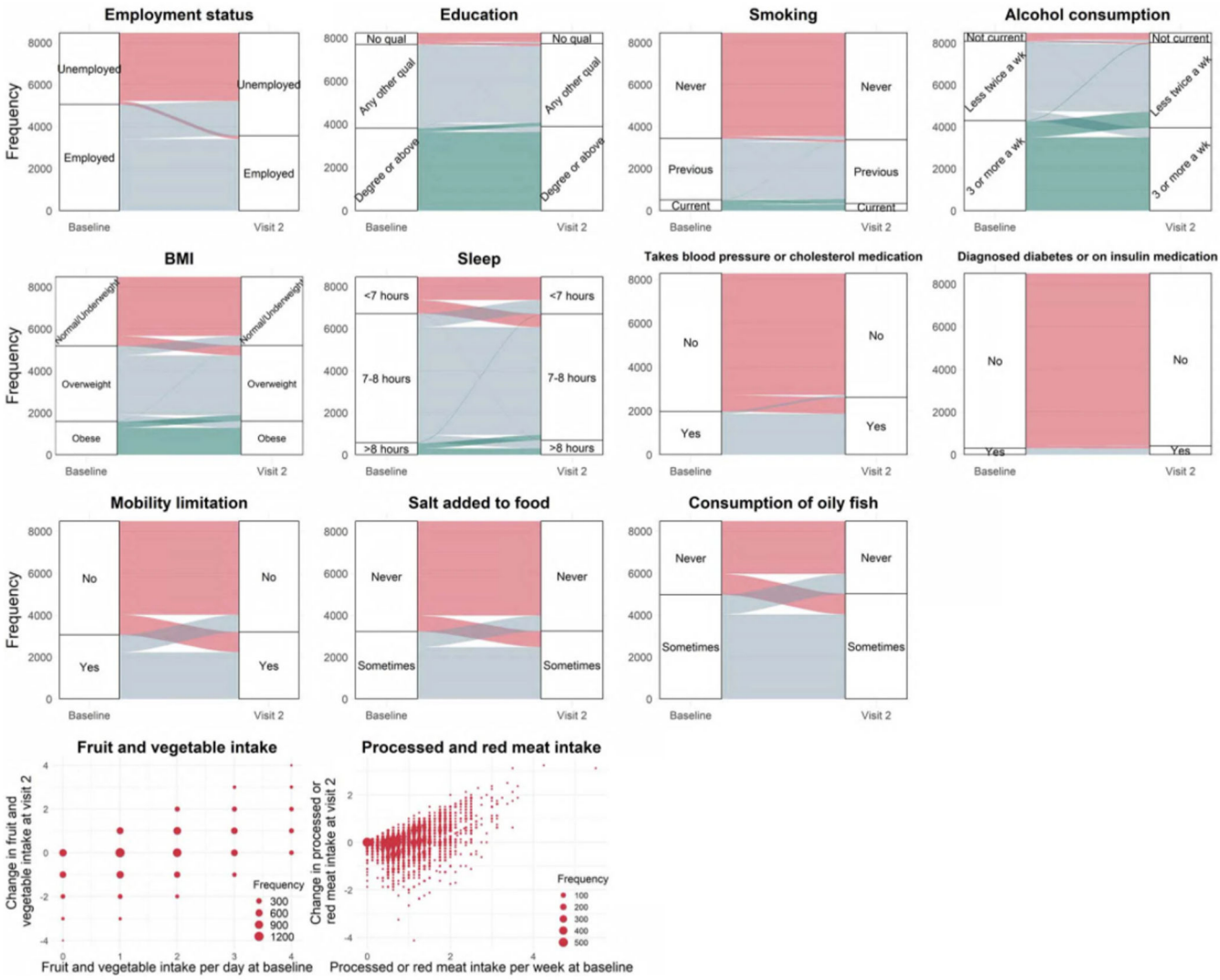
Extended Data





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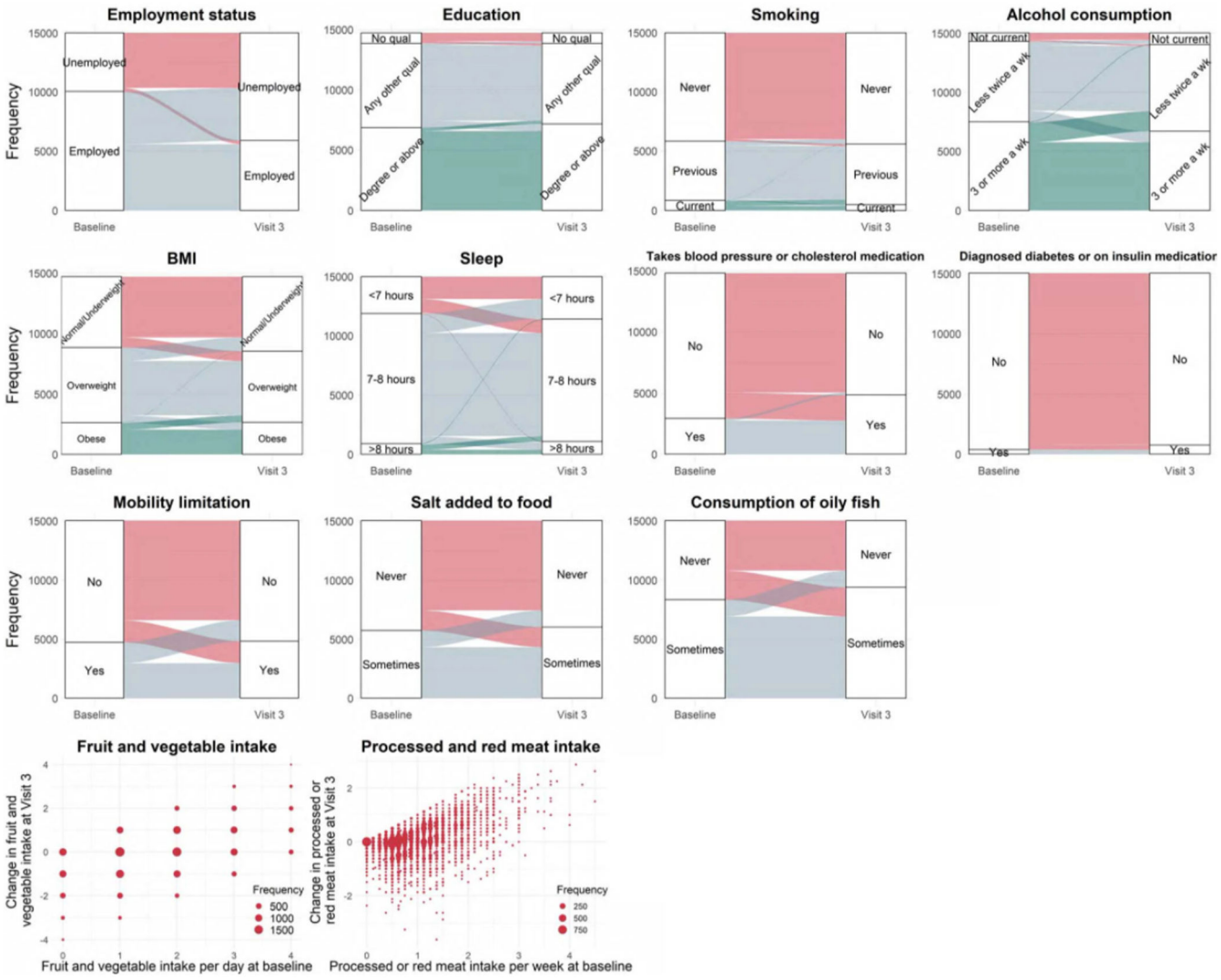

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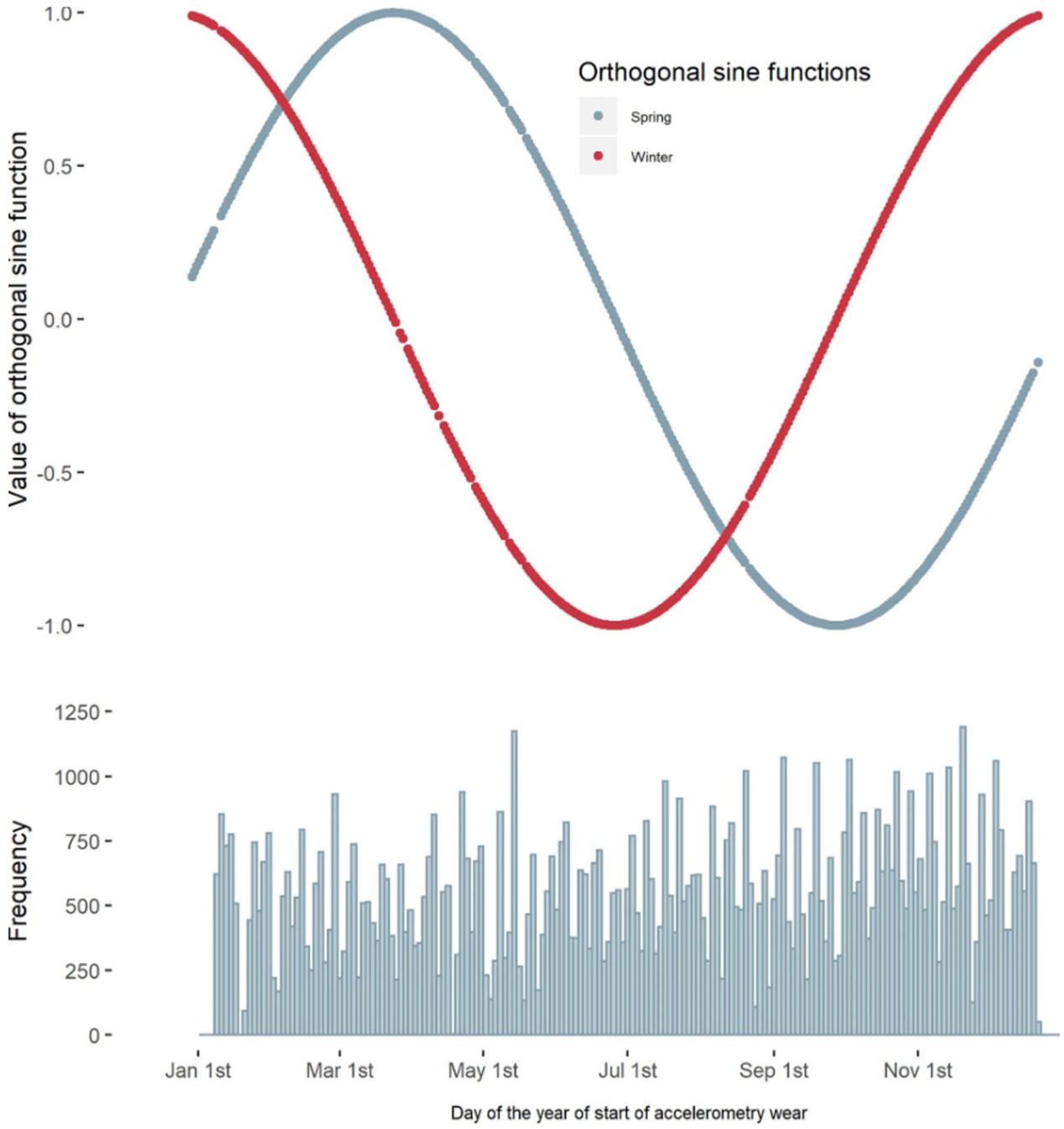

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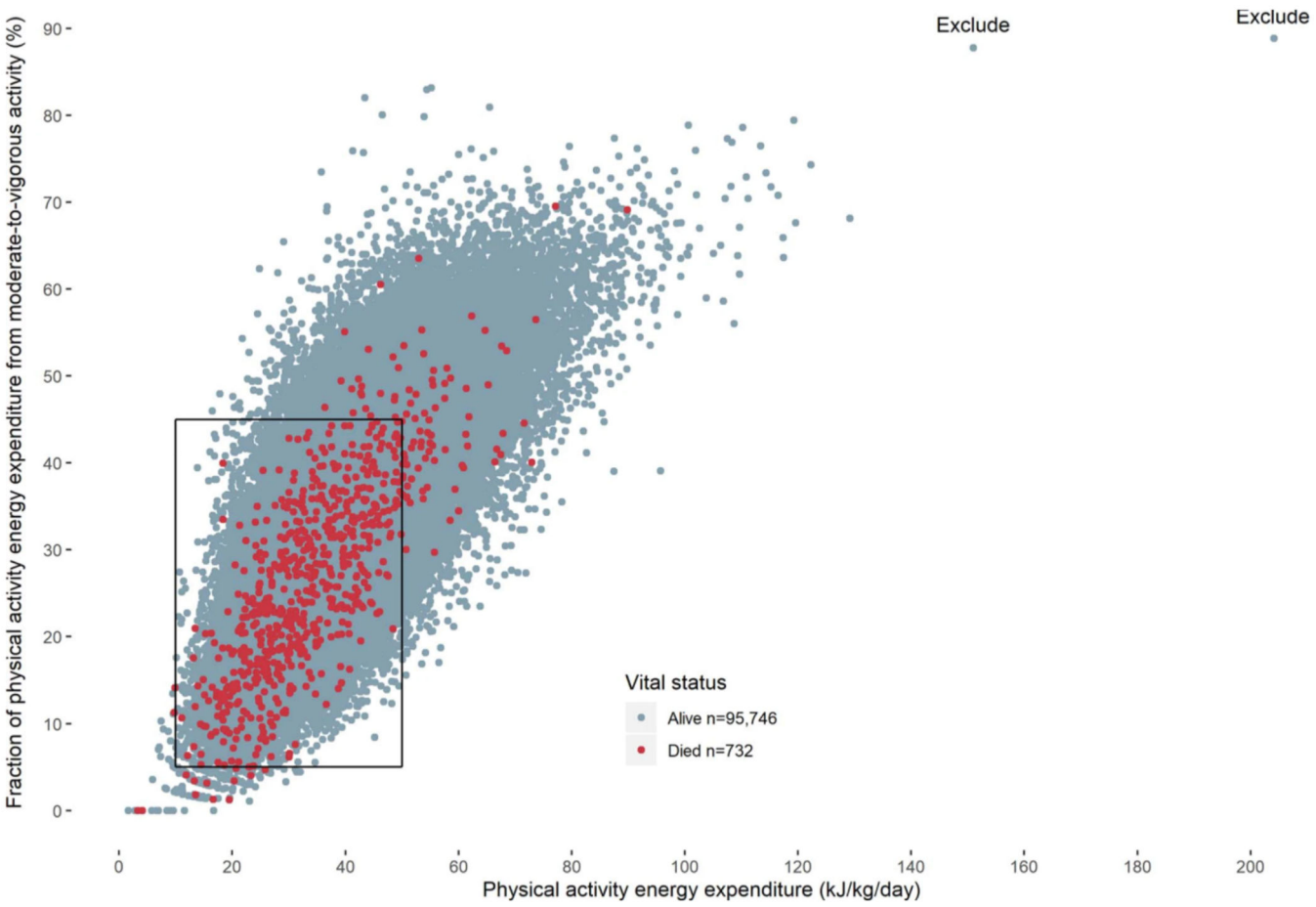

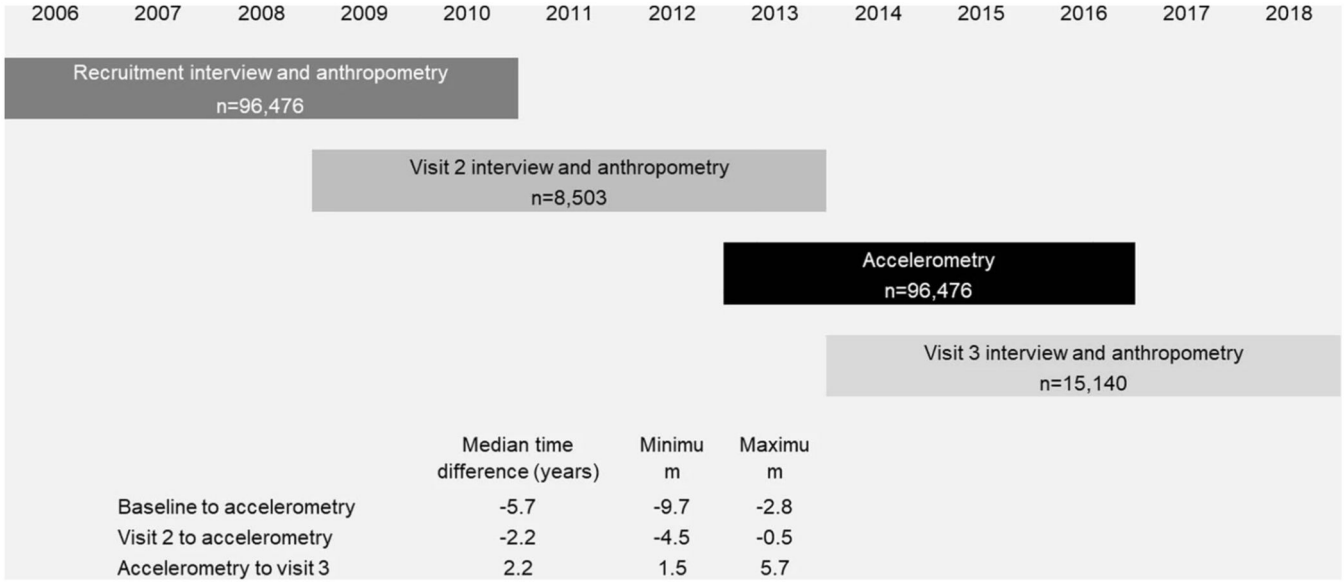

	Median time difference (years)	Minimum	Maximum
Baseline to accelerometry	-5.7	-9.7	-2.8
Visit 2 to accelerometry	-2.2	-4.5	-0.5
Accelerometry to visit 3	2.2	1.5	5.7

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Acknowledgments

We are grateful to the participants of the UK Biobank Study and those who collected and managed the data. This work was conducted under UK Biobank application number 20684. TS, KW, SB, SJS, TL, PCD, MP, JJ and NJW are supported by the UK Medical Research Council (unit programme numbers MC_UU_12015/1 and MC_UU_12015/3). PCD is supported by a National Health and Medical Research Council of Australia research fellowship (#1142685). TL is supported by Cambridge Trust and St Catharine's College.

Data Availability

The UK Biobank data that support the findings of this study can be accessed by researchers on application (https://www.ukbiobank.ac.uk/register-apply/). Variables derived specifically for this study will be returned along with the code to the UK Biobank for future applicants to request.

Code Availability

Analysis code available on request.

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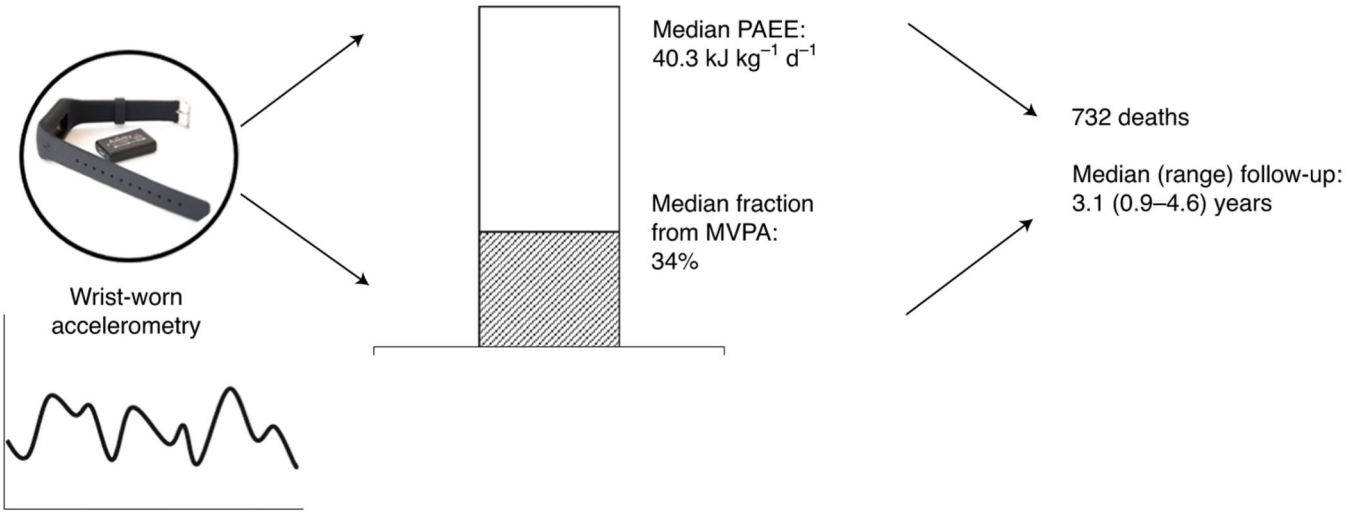

Figure 1.
Overview of methods with selected descriptive statistics. MVPA: moderate-to-vigorous physical activity.

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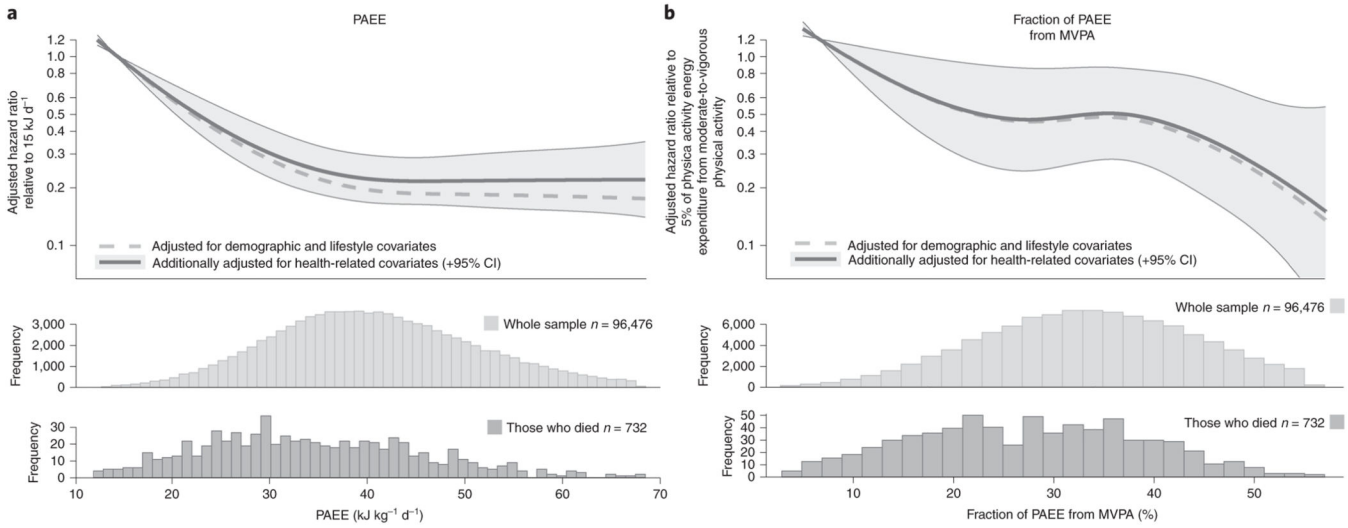

Figure 2.

Adjusted hazard ratios of all-cause mortality comparing (a) different volumes of physical activity energy expenditure and (b) different fractions of physical activity energy expenditure from moderate-to-vigorous physical activity, adjusted for physical activity energy expenditure. Adjusted hazard ratios and histogram data shown for values inside the 1st or 99th percentiles of the physical activity energy expenditure distribution amongst those who died.

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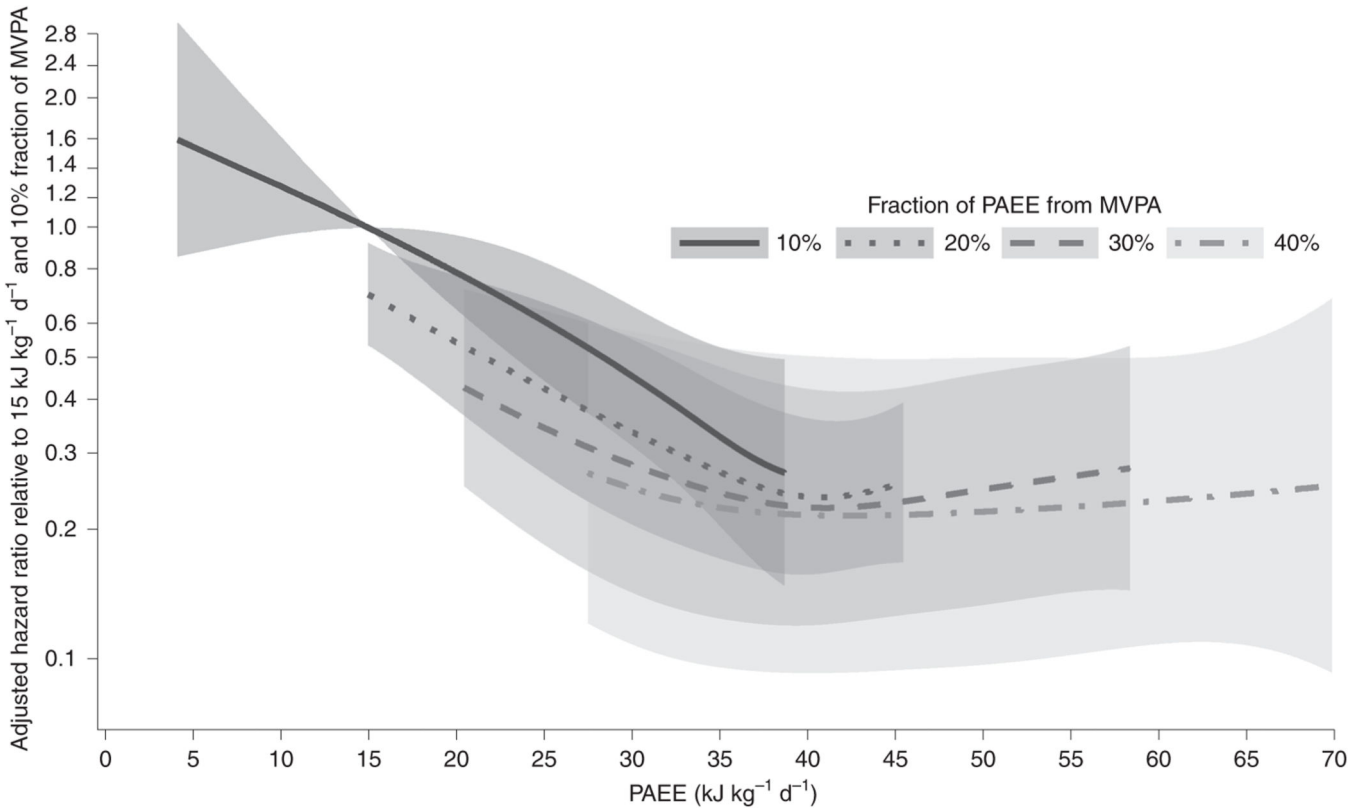

Figure 3.

Hazard ratios of all-cause mortality according to the joint distribution of physical activity energy expenditure and the fraction from moderate-to-vigorous physical activity, relative to a physical activity energy expenditure of 15kJ/kg/day and 10% fraction of moderate-to-vigorous physical activity. MVPA: moderate-to-vigorous physical activity. (n=96,476).

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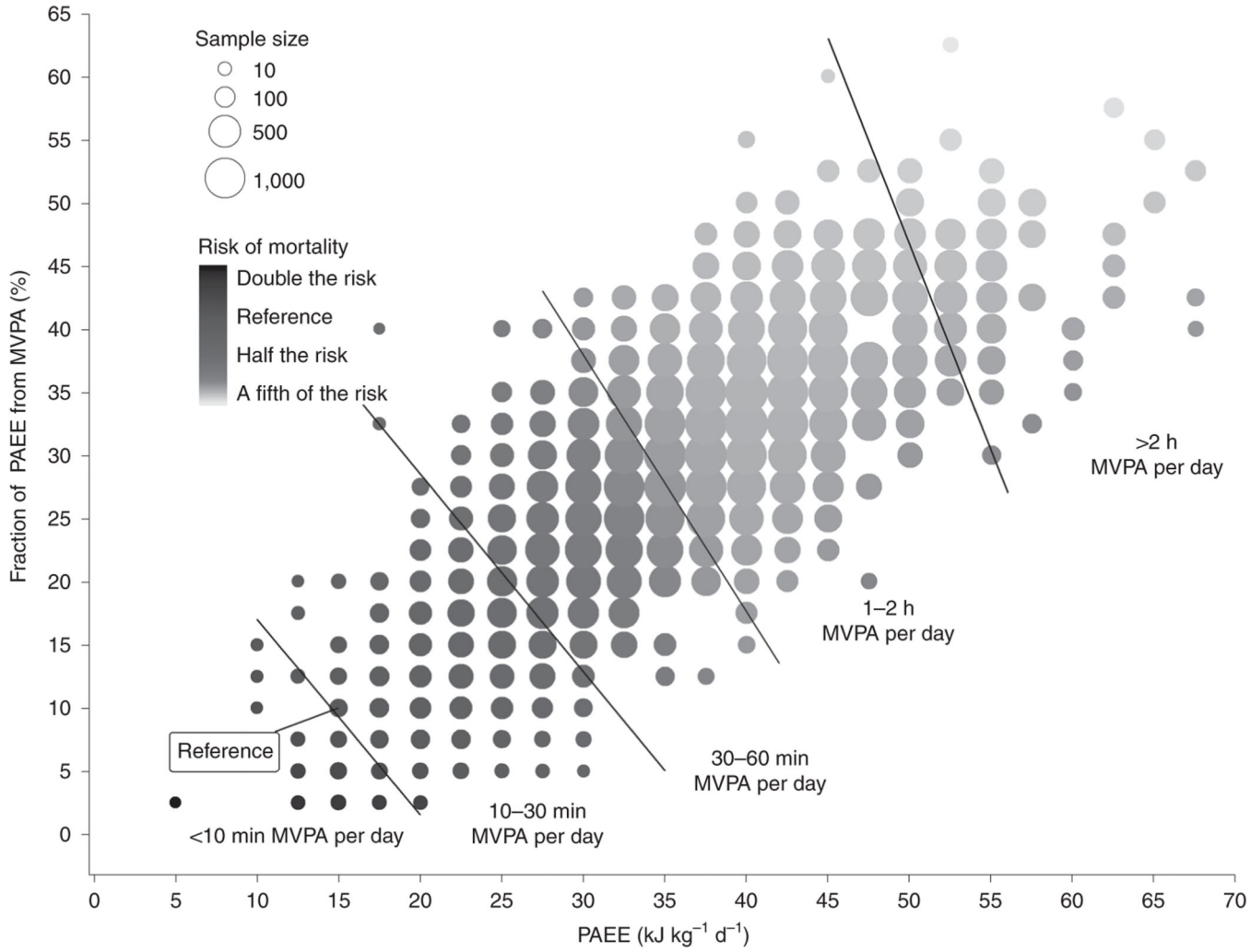

Figure 4.

The relative risk of mortality for combinations of physical activity energy expenditure and the fraction that came from moderate-to-vigorous physical activity. MVPA: Moderate-to-vigorous physical activity. Adjusted hazard ratio for mortality represented by the colour gradient with 15 kJ/kg/day and 10% as reference values. Size of the points represents sample size and segments indicate the average minutes of unbouted MVPA for each combination. Lines divide groups of similar observed median values of MVPA time, as indicated by the text. Each data point represents categories of dimensions 2.5 kJ/kg/day * 2.5%. Data points are placed at the midpoint of these categories. Points are not shown if there were no deaths for that combination. (n=96,476).

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Table 1

Descriptive characteristics of the sample, by quartiles of physical activity energy expenditure

	Physical Activity Energy Expenditure				Main analysis sample, n=96476
	Quartile 1, n=24119	Quartile 2, n=24119	Quartile 3, n=24119	Quartile 4, n=24119	
PAEE in kJ/kg/day, median (range)	28.87 (1.67-33.38)	36.90 (33.38-40.27)	43.81 (40.27-48.04)	54.20 (48.04-129.17)	40.27 (1.67-129.17)
Proportion of PAEE from MVPA, median (range)	0.24 (0.00-0.65)	0.31 (0.06-0.73)	0.36 (0.08-0.82)	0.45 (0.12-0.83)	0.34 (0.00-0.83)
Deaths, No. (%)	363 (1.5)	141 (0.6)	129 (0.5)	99 (0.4)	732 (0.8)
Age at accelerometry, mean (sd), y	65.00 (7.35)	63.07 (7.68)	61.68 (7.74)	59.82 (7.66)	62.39 (7.84)
Female sex, No. (%)	11690 (48.5)	13544 (56.2)	14288 (59.2)	14838 (61.5)	54360 (56.3)
White ethnicity, No. (%)	23416 (97.1)	23337 (96.8)	23288 (96.6)	23125 (95.9)	93166 (96.6)
Missing	102 (0.4)	82 (0.3)	75 (0.3)	76 (0.3)	335 (0.3)
Highest educational level achieved, No. (%)					
Degree or above	2588 (10.7)	1935 (8.0)	1660 (6.9)	1572 (6.5)	7755 (8.0)
Any other qualification	11558 (47.9)	11335 (47.0)	11531 (47.8)	11679 (48.4)	46103 (47.8)
No qualification	9777 (40.5)	10714 (44.4)	10813 (44.8)	10741 (44.5)	42045 (43.6)
Missing	196 (0.8)	135 (0.6)	115 (0.5)	127 (0.5)	573 (0.6)
Townsend indicator of multiple deprivation[a], median (IQR)	-2.35 (-3.75-0.07)	-2.49 (-3.84--0.29)	-2.51 (-3.85--0.30)	-2.45 (-3.82--0.19)	-2.44 (-3.81--0.17)
Missing	35 (0.1)	30 (0.1)	22 (0.1)	23 (0.1)	110 (0.1)
In employment, No. (%)	10993 (45.6)	13156 (54.5)	14550 (60.3)	15882 (65.8)	54581 (56.6)
Missing	46 (0.2)	37 (0.2)	41 (0.2)	58 (0.2)	182 (0.2)
Smoking, No. (%)					
Never	12691 (52.6)	13762 (57.1)	14004 (58.1)	14315 (59.4)	54772 (56.8)
Previous	9351 (38.8)	8818 (36.6)	8675 (36.0)	8410 (34.9)	35254 (36.5)
Current	2017 (8.4)	1484 (6.2)	1393 (5.8)	1337 (5.5)	6231 (6.5)
Missing	60 (0.2)	55 (0.2)	47 (0.2)	57 (0.2)	219 (0.2)
Alcohol consumption, No. (%)					
Never	1744 (7.2)	1376 (5.7)	1291 (5.4)	1361 (5.6)	5772 (6.0)
Previous drinker	11721 (48.6)	11030 (45.7)	10947 (45.4)	10807 (44.8)	44505 (46.1)
Current drinker	10638 (44.1)	11693 (48.5)	11870 (49.2)	11927 (49.5)	46128 (47.8)
Missing	16 (0.1)	20 (0.1)	11 (0.0)	24 (0.1)	71 (0.1)
Sometimes add salt to food, No. (%)	9987 (41.4)	9595 (39.8)	9751 (40.4)	9521 (39.5)	38854 (40.3)
Missing	8 (0.0)	11 (0.0)	8 (0.0)	15 (0.1)	42 (0.0)
Sometimes consume oily fish, No. (%)	13866 (57.5)	14093 (58.4)	13885 (57.6)	13652 (56.6)	55496 (57.5)

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	Physical Activity Energy Expenditure				Main analysis sample, n=96476
	Quartile 1, n=24119	Quartile 2, n=24119	Quartile 3, n=24119	Quartile 4, n=24119	
Missing	69 (0.3)	47 (0.2)	50 (0.2)	49 (0.2)	215 (0.2)
Fruit and vegetable intake score, median (IQR)	1 (1-2)	2 (1-2)	2 (1-3)	2 (1-3)	2 (1-2)
Missing	23 (0.1)	13 (0.1)	13 (0.1)	24 (0.1)	73 (0.1)
Weekly frequency of red or processed meat intake, median (IQR)	0.75 (0.50-1.25)	0.75 (0.50-1.13)	0.75 (0.50-1.13)	0.63 (0.50-1.13)	0.75 (0.50-1.13)
Missing	11 (0.0)	14 (0.1)	14 (0.1)	18 (0.1)	57 (0.1)
Mean sleep duration, No. (%)					
<7 hours/day	5393 (22.4)	5352 (22.2)	5335 (22.1)	5546 (23.0)	21626 (22.4)
7-8 hours/day	16287 (67.5)	17071 (70.8)	17368 (72.0)	17534 (72.7)	68260 (70.8)
>8 hours/day	2354 (9.8)	1637 (6.8)	1371 (5.7)	986 (4.1)	6348 (6.6)
Missing	85 (0.4)	59 (0.2)	45 (0.2)	53 (0.2)	242 (0.3)
Parental history of cardiovascular disease or cancer, No. (%)	17876 (74.1)	17920 (74.3)	17576 (72.9)	17198 (71.3)	16557 (68.6)
Missing	379 (1.6)	336 (1.4)	299 (1.2)	325 (1.3)	1339 (1.4)
Body Mass Index, No. (%)					
Normal/Underweight <25kg/m^2	6191 (25.7)	8775 (36.4)	10302 (42.7)	12941 (53.7)	38209 (39.6)
Overweight 25-30kg/m^2	10276 (42.6)	10413 (43.2)	10021 (41.5)	8643 (35.8)	39353 (40.8)
Obese ≥30kg/m^2	7560 (31.3)	4896 (20.3)	3763 (15.6)	2512 (10.4)	18731 (19.4)
Missing	92 (0.4)	35 (0.1)	33 (0.1)	23 (0.1)	183 (0.2)
Current prescription of blood pressure or cholesterol medicine, No. (%)	9138 (37.9)	9194 (38.1)	6499 (26.9)	5058 (21.0)	3623 (15.0)
Missing	74 (0.3)	59 (0.2)	43 (0.2)	61 (0.3)	237 (0.2)
Diagnosis of diabetes or insulin prescription, No. (%)	1885 (7.8)	1880 (7.8)	839 (3.5)	639 (2.6)	412 (1.7)
Missing	10 (0.0)	13 (0.1)	11 (0.0)	17 (0.1)	51 (0.1)
Previous diagnosis of cardiovascular disease, No. (%)	2966 (12.3)	2982 (12.4)	1724 (7.1)	1239 (5.1)	829 (3.4)
Missing	25 (0.1)	26 (0.1)	17 (0.1)	13 (0.1)	81 (0.1)
Previous diagnosis of cancer disease, No. (%)	3551 (14.7)	3578 (14.8)	3036 (12.6)	2581 (10.7)	2209 (9.2)
Missing	15 (0.1)	13 (0.1)	10 (0.0)	16 (0.1)	54 (0.1)
Mobility limitation, No. (%)	11276 (46.8)	11279 (46.8)	8832 (36.6)	7774 (32.2)	6655 (27.6)
Missing	38 (0.2)	29 (0.1)	24 (0.1)	29 (0.1)	120 (0.1)

PAEE: physical activity energy expenditure. MVPA: moderate-to-vigorous physical activity. Season of wear is described in Extended Data 4..

[a] Townsend deprivation score: higher score indicates higher deprivation.

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Table 2

Adjusted hazard ratios of all-cause mortality according to the joint distribution of physical activity energy expenditure and the fraction from moderate-to-vigorous physical activity.

Physical activity energy expenditure (kJ/kg/day)	Fraction of physical activity energy expenditure from MVPA	Model 2	Model 2 in sub-sample[a] with lower correlation between exposures	Model 2 with no interaction terms between exposures	Model 2 excluding those with prevalent disease[b]	Model 2 Complete-case analysis
n		96476	70609	96476	79205	93272
Person-years		302526	220948	302526	248914	292447
Deaths		732	623	732	421	703
15	10% (median 7 mins)	1 (reference)	1 (reference)	1 (reference)	1 (reference)	1 (reference)
	20% (median 16 mins)	0.70 (0.53-0.92)	0.67 (0.51-0.89)	0.74 (0.64-0.86)	0.79 (0.56-1.13)	0.68 (0.51-0.90)
	30%	N/A	0.53 (0.34-0.83)	N/A	N/A	0.54 (0.35-0.84)
	40%	N/A	N/A	N/A	N/A	N/A
20	10% (median 13 mins)	0.79 (0.65-0.96)	0.94 (0.69-1.28)	0.74 (0.62-0.88)	0.71 (0.54-0.94)	0.78 (0.64-0.96)
	20% (median 23 mins)	0.54 (0.38-0.78)	0.63 (0.42-0.95)	0.55 (0.47-0.64)	0.48 (0.30-0.76)	0.53 (0.37-0.76)
	30% (median 33 mins)	0.44 (0.26-0.73)	0.50 (0.27-0.92)	0.46 (0.38-0.57)	N/A	0.42 (0.25-0.71)
	40%	N/A	N/A	N/A	N/A	N/A
30	10% (median 20 mins)	0.46 (0.31-0.66)	0.48 (0.29-0.81)	0.46 (0.32-0.66)	0.33 (0.20-0.55)	0.44 (0.30-0.65)
	20% (median 33 mins)	0.34 (0.21-0.55)	0.39 (0.22-0.70)	0.34 (0.26-0.46)	0.22 (0.11-0.41)	0.33 (0.20-0.55)
	30% (median 48 mins)	0.28 (0.14-0.56)	0.35 (0.14-0.87)	0.29 (0.22-0.38)	0.17 (0.07-0.42)	0.28 (0.14-0.56)
	40% (median 62 mins)	0.25 (0.11-0.58)	0.32 (0.10-1.04)	0.26 (0.19-0.34)	0.14 (0.04-0.44)	0.24 (0.10-0.57)
40	10%	N/A	N/A	N/A	0.15 (0.06-0.34)	N/A
	20% (median 46 mins)	0.24 (0.16-0.36)	0.34 (0.19-0.61)	0.27 (0.20-0.37)	0.15 (0.09-0.26)	0.24 (0.15-0.36)
	30% (median 62 mins)	0.23 (0.12-0.42)	0.28 (0.12-0.65)	0.23 (0.17-0.30)	0.15 (0.07-0.35)	0.22 (0.12-0.43)
	40% (median 79 mins)	0.22 (0.09-0.50)	0.24 (0.08-0.73)	0.20 (0.15-0.27)	0.15 (0.05-0.47)	0.22 (0.09-0.51)
50	10%	N/A	N/A	N/A	N/A	N/A
	20%	N/A	N/A	N/A	N/A	N/A
	30% (median 78 mins)	0.25 (0.13-0.46)	N/A	0.24 (0.18-0.34)	0.17 (0.08-0.39)	0.25 (0.13-0.47)
	40% (median 101 mins)	0.22 (0.10-0.50)	0.33 (0.10-1.11)	0.22 (0.16-0.29)	0.16 (0.06-0.47)	0.22 (0.10-0.51)

N/A indicates value not between the 1st and 99th percentiles of the physical activity energy expenditure distribution amongst those who died for that fraction of moderate-to-vigorous physical activity. See Figure 3 footnotes for more details. Median values are for the main analysis sample

included in Model 2. Models adjusted for age, sex, ethnicity, education level, employment status, Townsend index of deprivation, season of accelerometer wear, fruit and vegetable intake, processed and red meat intake, oily fish intake, regularity of adding salt to food, alcohol intake, smoking status, average sleep duration, and parental history of cardiovascular disease or cancer, blood pressure or cholesterol medication use, diabetes diagnosis or insulin prescription, body mass index, mobility limitation, prevalent cardiovascular disease and prevalent cancer. Model 2 is displayed on Figure 3.

[a] Subsample restricted to values of 10-50 kJ/kg/day for physical activity energy expenditure and between 5-45% fraction of moderate-to-vigorous physical activity. See Supplementary Table 2 for details on the correlation calculations.

[b] did not adjust for prevalent cardiovascular disease of cancer.

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