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Reallocation of time between device-measured movement behaviours and risk of incident cardiovascular disease

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ABSTRACT

Objective To improve classification of movement behaviours in free-living accelerometer data using machine-learning methods, and to investigate the association between machine-learned movement behaviours and risk of incident cardiovascular disease (CVD) in adults.

Methods Using free-living data from 152 participants, we developed a machine-learning model to classify movement behaviours (moderate-to-vigorous physical activity behaviours (MVPA), light physical activity behaviours, sedentary behaviour, sleep) in wrist-worn accelerometer data. Participants in UK Biobank, a prospective cohort, were asked to wear an accelerometer for 7 days, and we applied our machine-learning model to classify their movement behaviours. Using compositional data analysis Cox regression, we investigated how reallocating time between movement behaviours was associated with CVD incidence.

Results In leave-one-participant-out analysis, our machine-learning method classified free-living movement behaviours with mean accuracy 88% (95% CI 87% to 89%) and Cohen's kappa 0.80 (95% CI 0.79 to 0.82). Among 87 498 UK Biobank participants, there were 4105 incident CVD events. Reallocating time from any behaviour to MVPA, or reallocating time from sedentary behaviour to any behaviour, was associated with lower CVD risk. For an average individual, reallocating 20 min/day to MVPA from all other behaviours proportionally was associated with 9% (95% CI 7% to 10%) lower risk, while reallocating 1 hour/day to sedentary behaviour from all other behaviours proportionally was associated with 5% (95% CI 3% to 7%) higher risk.

Conclusion Machine-learning methods classified movement behaviours accurately in free-living accelerometer data. Reallocating time from other behaviours to MVPA, and from sedentary behaviour to other behaviours, was associated with lower risk of incident CVD, and should be promoted by interventions and guidelines.

INTRODUCTION

Previous studies have shown low levels of light physical activity¹ and moderate-to-vigorous physical activity² and high levels of sedentary behaviour³ are associated with higher cardiovascular disease (CVD) risk, whereas for sleep a U-shaped association has been found.^{4 5} Due to challenges in measuring and analysing movement behaviours,

there is uncertainty about how different combinations of movement behaviours are related to CVD risk.

Recall and reporting bias affect self-reported measurements,⁶ and some behaviours (eg, light physical activity) are hard to capture.⁷ Device-based measurements address these concerns but introduce new challenges. Many studies use hip-worn devices, where mean wear time is typically <15 hours/day and sleep is not measured.⁸ Time in different behaviours has typically been identified using 'cut-point' based methods, which use an acceleration threshold to distinguish different intensities of activity.⁹ These methods can only distinguish behaviours based on intensity, and are prone to substantial misclassification,^{9–11} which may materially impact research findings.¹² As they use only a single metric of intensity to classify the behaviour, there may be substantial unused information in the accelerometer signal. Emerging machine-learning methods could, therefore, allow a wider range of behaviours to be classified accurately: these methods use many features of the data, capture non-linear relationships and can learn relationships from training data beyond what a researcher might hypothesise.^{9–11 13} Most behaviour classification methods have been developed using laboratory-based data.¹⁴ Using free-living data to develop and validate behaviour classification methods is important to ensure they perform well in practice.^{9–11 14 15}

There is uncertainty about how movement behaviours are associated with CVD, as analyses often neglect the fact that people engage in multiple movement behaviours over the course of a day (eg, an individual spending large amounts of time sedentary may also spend small amounts of time in light physical activity).¹⁶ Further complicating this, a person who increases time spent in one behaviour must compensate by decreasing time spent in others. This means that analyses should address the effect of reallocating time between behaviours.¹⁷ It also means that movement behaviour data are compositional data, whereby only the relative time spent in different behaviours (and not the absolute time in each behaviour) is informative.^{18 19} An individual cannot increase time spent in light physical activity while holding time in other behaviours fixed. However, they can increase time spent in light physical activity relative to other behaviours, while holding each of those



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behaviours fixed as a proportion of the remaining day. Methods for analysing compositional data aim to capture and model the relative values of variables.^{18 19} While there is a substantial and rapidly growing evidence base linking the movement behaviour composition to cardiovascular risk factors, evidence on incident disease outcomes is still lacking.²⁰ Evidence on how the relative time spent in different behaviours over the whole 24-hour day is associated with disease outcomes is important to inform interventions and guidance aimed at disease prevention.^{21 22} The objective of this study was to investigate the association between device-measured movement behaviours and risk of incident CVD in middle-aged to older-aged adults by:

1. Using free-living ‘ground truth’ data to develop and validate a machine-learning model to classify movement behaviours from wrist-worn accelerometer data.
2. Applying this new model to classify movement behaviours of 87 498 UK Biobank participants who wore an accelerometer.
3. Characterising the association between device-measured movement behaviours and incident CVD, accounting for the compositional nature of movement behaviours.

METHODS

UK Biobank: a large prospective cohort study

UK Biobank is a population-based prospective cohort study of over 500 000 participants in England, Scotland and Wales (protocol available at <https://www.ukbiobank.ac.uk/key-documents/>). Between 2006 and 2010, individuals aged 40–69 living within roughly 25 miles of an assessment centre were recruited by letter (all eligible individuals were identified from National Health Service records; response rate 5.5%).²³ At baseline, participants attended an assessment involving a touchscreen questionnaire, biological sampling, an interview by a trained interviewer and anthropometric measurements.²³

Device-based measures of movement behaviours in UK Biobank

Between June 2013 and December 2015, participants with a valid email address (excluding North West region due to participant burden concerns) were invited to wear an accelerometer. A total of 106 053 consenting participants were sent an Axivity AX3 wrist-worn triaxial accelerometer to be worn on the dominant wrist for 7 days.²⁴ A readable accelerometer dataset was obtained from 103 683 participants. Initial data processing followed established methods:²⁴ participants were excluded if the device could not be calibrated, if more than 1% of readings were ‘clipped’ (fell outside the device’s dynamic range of $\pm 8g$) before or after calibration, if they had less than 3 days of data or did not have data in each 1-hour period of the 24 hour cycle (with non-wear time defined as unbroken episodes of at least 60 min during which SD of each axis of acceleration was less than 13.0 mg),²⁴ or if the average acceleration was implausibly high ($>100 mg$).²⁴ Recording interruptions and non-wear time were imputed as the mean behaviour in the corresponding minute of the day on remaining days.

Classification of movement behaviours using machine-learning methods

CAPTURE-24

CAPTURE-24, an accelerometer validation study of 152 adults aged 18–91 recruited by advertisements in Oxford, UK, in 2014–2015,¹¹ was used to develop machine-learning classification methods. Participants were asked to wear an Axivity AX3 wrist-worn accelerometer for 24 hours, wear a Vicon

Autographer wearable camera while awake during that period, and keep a time use diary.¹⁰ Using camera images and time use diaries, trained annotators annotated accelerometer data with labels from the Compendium of Physical Activities.²⁵ Fine-grained labels were mapped to sleep, sedentary behaviour (eg, sitting working at a computer, watching television), light physical activity behaviours (eg, cooking, self-care) and moderate-to-vigorous physical activity behaviours (MVPA; eg, walking the dog, cycling) (see online supplemental methods and online supplemental table 1). Describing intensity in metabolic equivalent of task (METs), which measure energy expenditure relative to energy expenditure in quiet sitting, these behaviours were defined as:

1. Sleep: non-waking behaviour.
2. Sedentary behaviour: waking behaviour at ≤ 1.5 METs in a sitting, lying or reclining posture.²⁶
3. Light physical activity behaviours: waking behaviour at <3 METs not meeting the sedentary behaviour definition.
4. Moderate-to-vigorous physical activity behaviours: all behaviour at ≥ 3 METs.²⁵

Machine-learning for behaviour classification

Using this labelled data from the CAPTURE-24 study, a balanced Random Forest with 100 decision trees was trained to classify the behaviour in 30 s time windows using 50 rotation-invariant time and frequency domain features of the accelerometer signal (online supplemental table 2). As the Random Forest did not use time sequence information, the behaviour sequence was smoothed using a Hidden Markov model. This model treated the Random-Forest-predicted behaviours as ‘emissions’ from an underlying true behaviour sequence, and used the Viterbi algorithm to identify the most likely underlying true sequence given the observed sequence.²⁷ Transition probabilities between different behaviours were determined using camera validation data, and probability of the Random Forest predicting each behaviour conditional on the true behaviour was estimated using out-of-bag estimates from the Random Forest. This model structure closely followed our previous work,^{10 11} and more detail is given in online supplemental methods.

Performance was evaluated using leave-one-participant-out cross-validation. Accuracy was used to assess overall agreement between annotator-assigned ‘ground truth’ labels and model-assigned labels, and Cohen’s kappa was used to assess agreement beyond that expected by chance. Precision and recall were used to assess performance on each behaviour, and the confusion matrix was used to show classification patterns for examples of each behaviour. Accuracy, Cohen’s kappa, precision and recall were calculated for each participant individually, and we computed their mean (across participants). To examine how sensitive mean precision and recall were to the results of participants with few examples of a behaviour, the mean was recalculated excluding participants with up to 20 min of a particular behaviour (the online supplemental methods contains more detail on performance evaluation). To assess the performance of our model in the age group of interest, we also calculated mean per-participant accuracy and Cohen’s kappa in participants aged 38 years or older (age group as in a release version of this dataset). We also report a model trained in this age group only in online supplemental methods. Although overall comparison is precluded by the different behaviours classified, we compared precision and recall for MVPA using our model compared with using the standard cut-point of 100 mg.²⁸ Face validity of the behaviour classification method applied to UK Biobank data was

Table 1 Minute-wise confusion matrix for machine-learned classification of behaviours in accelerometer data from 152 CAPTURE-24 participants in leave-one-participant-out cross-validation

Model-assigned label	Sleep	Sedentary behaviour	Light physical activity behaviours	Moderate-to-vigorous physical activity behaviours
'Ground truth'				
Sleep	51 347	980	215	0
Sedentary behaviour	2322	53 052	5717	87
Light physical activity behaviours	54	4986	22 217	1533
Moderate-to-vigorous physical activity behaviours	6	158	2434	4978

assessed by plotting the behaviour profile of UK Biobank participants across the day.

Ascertainment of CVD endpoints

UK Biobank has ongoing passive follow-up via linkage to Hospital Episode Statistics (HES; hospital diagnoses from the National Health Service, the provider of almost all UK health-care) and the UK death register.²³ CVD was defined as ICD-10 codes I20–25 (ischaemic heart diseases) or I60–69 (cerebrovascular diseases) appearing in HES or on the death register. Participants with CVD prior to accelerometer wear, either HES-recorded or self-reported in the baseline questionnaire, were excluded. Participants who did not experience a CVD outcome were censored at death or the end of the study period as appropriate (28 February 2021 for participants in England and Scotland, 28 February 2018 for participants in Wales).

Compositional data analysis for movement behaviour data

A compositional data analysis approach was used in the statistical analyses. This approach uses log-ratios (log-transformed ratios between movement behaviours) to describe and adjust for the movement behaviour composition. By using ratios between behaviours, the relative time in different behaviours, rather than the absolute time in any given behaviour, is modelled. For this analysis, we used isometric log-ratio pivot coordinates, a particular set of log-ratios which is widely used in movement behaviour research (see online supplemental methods for more detail).^{19 29}

Our results are described by pairwise time reallocation plots, which show the HR associated with reallocating time from one behaviour to another behaviour, and by a plot showing the HR associated with particular reallocations of time between behaviours (eg, reallocating 1 hour/day to sedentary behaviour from all other behaviours proportionally).³⁰ All HRs are relative to the mean behaviour composition among included participants, so can be interpreted as showing the outcome associated with reallocating time between behaviours for a hypothetical average individual in our sample. Reallocation results are obtained by using the model to estimate the outcome associated with differences in values of the compositional exposure variables relative to the mean behaviour composition (ie, for different reallocations of time between behaviours; see online supplemental methods for more detail).^{12 30 31}

Statistical analyses

Multivariable-adjusted Cox proportional hazards regression models, with age as the timescale, were used to investigate the association between the movement behaviour composition, modelled using isometric log-ratio pivot coordinates, and incident CVD. A minimally adjusted analysis used age as the timescale and was stratified by sex but had no further adjustment for potential confounders. To address potential sources of

confounding, the main analysis used age as the timescale, was stratified by sex and was adjusted for ethnicity (Asian, black, other, white), smoking status (current, ex-smoker or never-smoker), frequency of alcohol consumption (never, <3 times/week, 3+ times/week), fresh fruit and vegetable consumption (<3, 3–4.9, 5–7.9, 8+ servings/day), frequency of red and processed meat consumption (<1, 1–2.9, 3–4.9, 5+ times/week), frequency of oily fish consumption (<1, 1, 2–4, >4 times/week), education (school leaver, further education, higher education) and deprivation (quarter of Townsend Deprivation Index in the study population). As body mass index (BMI) may mediate associations between movement behaviours and CVD, the main analysis was not adjusted for BMI. However, BMI may also act as a confounder for associations between movement behaviours and CVD. Therefore, an additional analysis was further adjusted for BMI. As there was evidence that BMI violated the proportional hazards assumption, this adjustment was performed by stratifying the Cox model by BMI (<25, 25–30, 30+ kg/m²).³² A further multivariable-adjusted analysis was performed with fatal cardiovascular events as the outcome. Separate analyses were also performed in women and men, and in those aged under 65 vs over 65 at the time of accelerometer wear. All adjustment variables were measured at baseline assessment (online supplemental table 3 gives more details on all variables used in the analysis), and variables were not adjusted for if they were likely mediators of the association between movement behaviours and CVD.

Participants with missing data in any adjustment variable were excluded. The proportional hazards assumption was tested component-wise and globally using the Grambsch-Therneau test with the Kaplan-Meier transformation,²⁹ and there was no evidence (at the 5% level) that it was violated in the main analysis. Plots of the Schoenfeld residuals were also examined. Results were reported according to Strengthening the Reporting of Observational Studies in Epidemiology guidelines (STROBE; see online supplemental material),³³ and all CIs are 95% CIs. Software is described in online supplemental methods.

Sensitivity analyses

The impact of reverse causality was assessed first by excluding the initial 2 years of follow-up and any events within it. A further analysis additionally excluded participants who self-reported poor health or use of diabetes or CVD-related medications at baseline or who had a prior hospital admission for any condition of the circulatory system (I00–I99 as a primary diagnosis, eg, admission for heart failure or aortic aneurysm).

To investigate unmeasured and residual confounding, we used a negative control outcome of accidents without a plausible mechanistic link to movement behaviours (accidents excluding falls, cycling accidents and intentional self-harm; see online supplemental table 3).³⁴ We also used E-values to assess the minimum strength of association that an unmeasured confounder

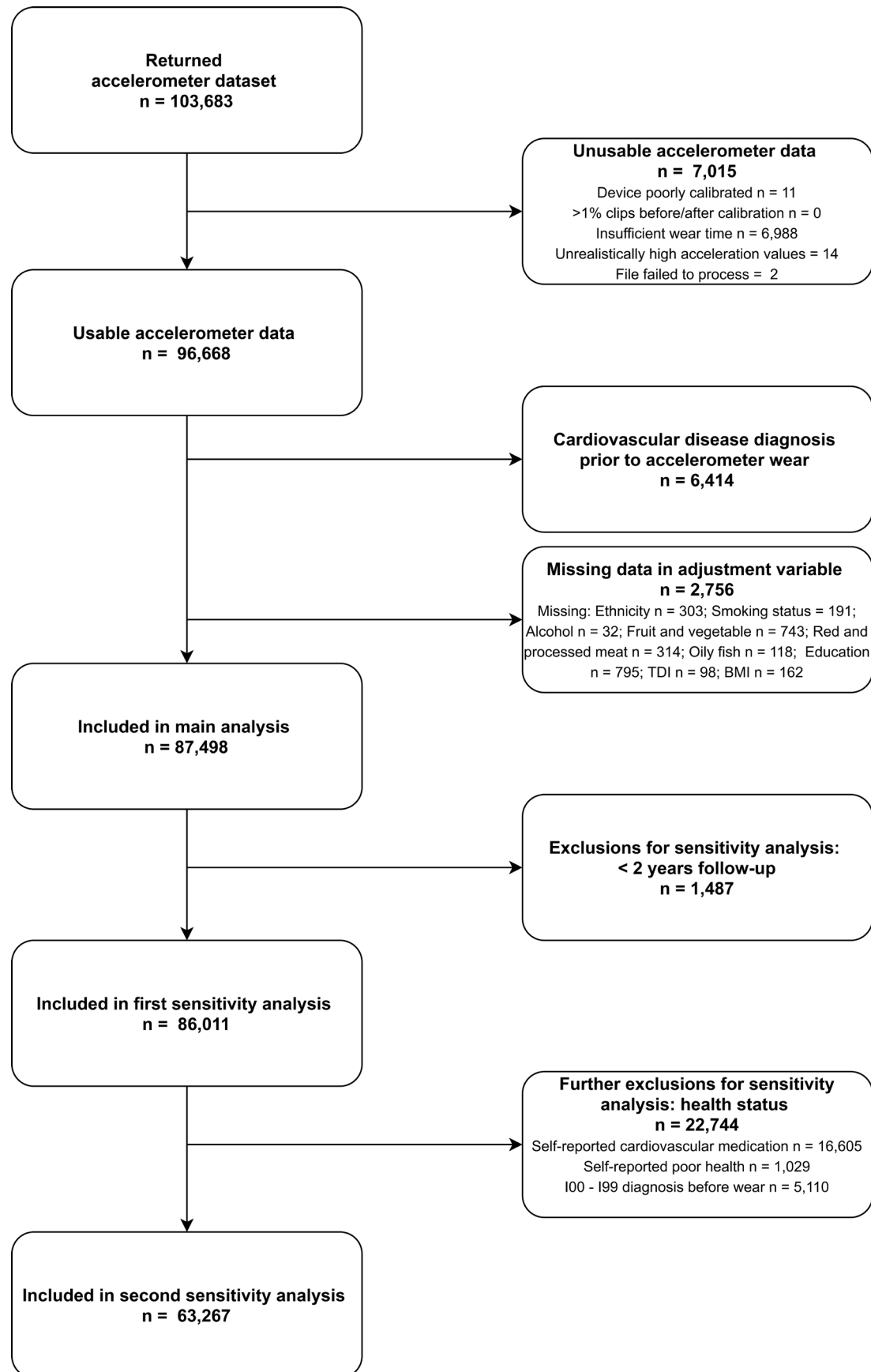


Figure 1 Participant flow diagram for the analysis of movement behaviours and incident cardiovascular disease in UK Biobank participants. BMI, Body Mass Index; TDI, Townsend Deprivation Index.

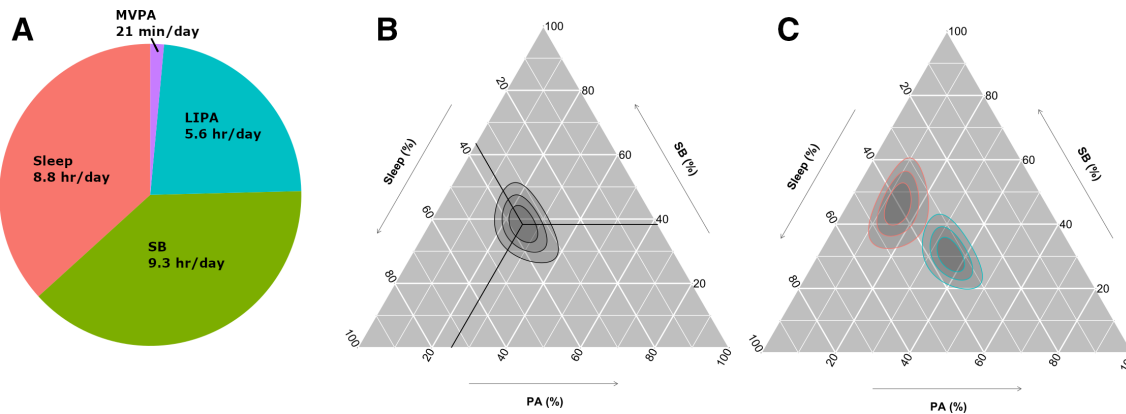


Figure 2 Distribution of movement behaviours in 87 498 UK Biobank participants. (A) Mean movement behaviour composition among UK Biobank participants. (B) Movement behaviours of UK Biobank participants on a ternary plot, showing sleep, sedentary behaviour (SB) and physical activity behaviours (PA; combines light and moderate-to-vigorous physical activity behaviours). The crosshair marks the compositional mean. Concentric rings represent the 25, 50% and 75% prediction regions for the data. The behaviour composition at a point can be found by tracing out (parallel to the white lines and crosshair) from the point to the axes. (C) Ternary plot showing the behaviour distribution of the 5% most active (blue) and 5% least active (red) UK Biobank participants by average acceleration. Concentric rings represent the 25, 50% and 75% prediction regions for each group. LIPA, light physical activity behaviours; MVPA, moderate-to-vigorous physical activity behaviours.

would need with both exposure and outcome to explain away the observed association (see online supplemental methods).^{35 36}

Two further sensitivity analyses, addressing the treatment of zero values and comparing with a linear isotemporal substitution approach, are reported in online supplemental methods.

Patient and public involvement

UK Biobank is a pre-existing resource, with public consultation in its design.³⁷ Patients and the public were not involved in the development of the research question or the design of the analysis in this study. Results of studies using UK Biobank data are disseminated to participants via UK Biobank's website and social media.

RESULTS

Movement behaviour classification in the training dataset

Our machine-learning method accurately classified movement behaviours in accelerometer data: when evaluated using leave-one-participant-out cross-validation in 2501 hours of free-living data from the CAPTURE-24 study (online supplemental table 4), mean per-participant accuracy was 88% (95% CI 87% to 89%) and mean per-participant Cohen's kappa was 0.80 (95% CI 0.79 to 0.82). This was consistent across age groups: in the 72 participants aged 38 years or older, mean per-participant accuracy was 86% (95% CI 85% to 88%) and mean per-participant Cohen's kappa was 0.79 (95% CI 0.76 to 0.82). Mean per-participant precision and recall for each behaviour show most examples of all behaviours were correctly classified, with highest performance for sleep (online supplemental figure 1). Misclassifications were most common between similar behaviours (table 1). As expected, classification performance was worse on individuals with very few true examples of a behaviour (online supplemental figure 1). While the different behaviours classified preclude an overall comparison, our model identified moderate-to-vigorous physical activity behaviours with substantially higher precision (overall precision 0.75 vs 0.37) and similar recall (overall recall both 0.66) compared with using the standard 100 mg cut-point, and had higher face validity in UK Biobank, with median 25 min/day in MVPA according to our model compared with 1.5 hours/day with the standard cutpoint. Overall, the behaviour classification showed high face validity when applied to UK Biobank participants' data (online supplemental figure 2).

Analyses in the UK Biobank

Baseline characteristics

After excluding participants with poor quality accelerometer data (defined in the Methods section: Device-based measures of movement behaviours in UK Biobank), participants with prevalent ischaemic heart disease or cerebrovascular disease in hospital records or baseline self-report, and participants with missing data, 87 498 UK Biobank participants were included in the Cox regression analysis for incident CVD (figure 1).

The mean composition of movement behaviours (the daily movement behaviours of a hypothetical average individual) was 8.8 hours/day sleep, 9.3 hours/day sedentary behaviour, 5.6 hours/day light physical activity behaviours and 21 min/day moderate-to-vigorous physical activity behaviours (figure 2). Time in physical activity behaviours and sedentary behaviour varied substantially among participants, while variation in sleep was more limited (figure 2). The least and most active participants by average acceleration differed in all dimensions of behaviour (figure 2).

When considering movement behaviours according to participant characteristics, notable differences included that women had higher levels of light physical activity behaviours than men, and lower sedentary time and MVPA (table 2). Older participants spent less time in MVPA than younger participants (table 2). Participants with higher BMI spent less time in light physical activity behaviours and MVPA than participants with lower BMI, and spent more time sedentary (table 2).

Associations with incident CVD

Over 524 919 person years of follow-up (median 6.2 years, maximum 7.7 years), there were 4105 incident CVD events. Reallocating time from sedentary behaviour to light physical activity behaviours was associated with a lower risk of CVD (figure 3): for an average individual in this sample, the HR associated with reallocating 1 hour/day from light physical activity behaviours to sedentary behaviour was 1.04 (95% CI 1.02 to 1.06), while the HR associated with reallocating 1 hour/day from sedentary behaviour to light physical activity behaviours was 0.96 (95% CI 0.95 to 0.98). Reallocating time from sedentary behaviour to MVPA was associated with more pronounced lower risk of

Table 2 Movement behaviours of 87 498 UK Biobank participants by participant characteristics

	N (%)*	Sleep† (hr/day)	Sedentary behaviour† (hr/day)	Light physical activity behaviour† (hr/day)	Moderate-to-vigorous physical activity behaviour† (min/day)
Overall	87 498 (100)	8.6 (7.9–9.3)	9.2 (8.0–10.3)	5.5 (4.5–6.7)	25 (12–44)
Age, years					
40–49	7767 (9)	8.5 (7.8–9.1)	9.4 (8.1–10.6)	5.4 (4.3–6.6)	30 (16–50)
50–59	26081 (30)	8.5 (7.8–9.2)	9.3 (8.1–10.5)	5.4 (4.4–6.7)	28 (14–47)
60–69	38774 (44)	8.6 (8.0–9.3)	9.0 (7.9–10.2)	5.6 (4.6–6.7)	25 (12–43)
70–79	14876 (17)	8.6 (7.9–9.4)	9.2 (8.1–10.3)	5.5 (4.5–6.7)	20 (9–36)
Sex					
Female	50882 (58)	8.6 (8.0–9.3)	8.9 (7.8–10.0)	5.8 (4.8–7.0)	22 (10–38)
Male	36616 (42)	8.4 (7.8–9.2)	9.6 (8.4–10.8)	5.1 (4.1–6.2)	31 (16–52)
Ethnicity					
Asian	756 (1)	8.4 (7.7–9.3)	9.3 (7.9–10.5)	5.6 (4.5–6.9)	19 (9–35)
Black	701 (1)	8.2 (7.3–9.0)	9.4 (8.0–10.6)	5.9 (4.8–7.2)	21 (10–35)
Other	1151 (1)	8.4 (7.6–9.1)	9.2 (8.0–10.5)	5.7 (4.5–7.0)	26 (13–44)
White	84890 (97)	8.6 (7.9–9.3)	9.2 (8.0–10.3)	5.5 (4.5–6.7)	25 (12–44)
Smoking status					
Never smoker	50888 (58)	8.6 (7.9–9.3)	9.2 (8.0–10.3)	5.5 (4.5–6.7)	26 (13–45)
Ex-smoker	30717 (35)	8.5 (7.9–9.3)	9.2 (8.0–10.3)	5.6 (4.5–6.7)	25 (12–44)
Current smoker	5893 (7)	8.6 (7.9–9.3)	9.4 (8.2–10.6)	5.4 (4.3–6.6)	21 (9–39)
Alcohol consumption					
Never drinker	4745 (5)	8.6 (7.9–9.4)	9.1 (7.8–10.3)	5.6 (4.5–6.9)	20 (9–39)
<3 times per week	39760 (45)	8.6 (7.9–9.3)	9.2 (8.0–10.3)	5.5 (4.5–6.7)	23 (11–41)
3+ times per week	42993 (49)	8.5 (7.9–9.2)	9.2 (8.0–10.4)	5.5 (4.5–6.7)	28 (14–47)
Fruit and vegetable consumption					
<3 servings/day	3595 (4)	8.6 (7.8–9.4)	9.7 (8.4–11.0)	5.0 (3.9–6.3)	21 (9–39)
3–4.9 servings/day	14293 (16)	8.6 (7.9–9.3)	9.4 (8.2–10.6)	5.3 (4.3–6.5)	24 (12–42)
5–7.9 servings/day	36991 (42)	8.6 (7.9–9.3)	9.2 (8.0–10.3)	5.5 (4.5–6.7)	26 (13–44)
8+ servings/day	32619 (37)	8.5 (7.9–9.2)	9.0 (7.8–10.1)	5.7 (4.7–6.9)	26 (13–45)
Townsend deprivation index					
Least deprived (< –3.8)	21913 (25)	8.6 (7.9–9.3)	9.1 (7.9–10.3)	5.6 (4.6–6.7)	24 (12–43)
Second least deprived (–3.8 to –2.5)	21839 (25)	8.6 (7.9–9.3)	9.1 (8.0–10.3)	5.6 (4.5–6.7)	24 (12–43)
Second most deprived (–2.5 to –0.2)	21872 (25)	8.6 (7.9–9.3)	9.2 (8.0–10.3)	5.6 (4.5–6.7)	25 (12–44)
Most deprived (> –0.2)	21874 (25)	8.5 (7.8–9.2)	9.3 (8.1–10.5)	5.4 (4.3–6.6)	27 (13–47)
Education					
School leaver	19535 (22)	8.7 (8.0–9.5)	8.9 (7.7–10.1)	5.7 (4.7–6.9)	20 (9–36)
Further education	29061 (33)	8.6 (7.9–9.3)	9.1 (7.9–10.3)	5.6 (4.6–6.8)	23 (11–41)
Higher education	38902 (44)	8.5 (7.8–9.1)	9.4 (8.2–10.5)	5.4 (4.4–6.5)	30 (16–50)
BMI					
Underweight (<18.5 kg/m ²)	511 (1)	8.5 (7.9–9.2)	8.5 (7.2–9.6)	6.3 (4.9–7.3)	34 (19–55)
Normal weight (18.5–24.9 kg/m ²)	35043 (40)	8.6 (8.0–9.2)	8.8 (7.7–10.0)	5.8 (4.7–6.9)	30 (16–50)
Overweight (25.0–29.9 kg/m ²)	35783 (41)	8.5 (7.9–9.3)	9.3 (8.1–10.4)	5.5 (4.4–6.6)	25 (12–43)
Obese (30+ kg/m ²)	16161 (18)	8.5 (7.8–9.3)	9.8 (8.5–10.9)	5.1 (4.1–6.3)	16 (7–31)

Movement behaviours are given as median (IQR).

*Percentages may not sum to 100% due to rounding.

†Presented as median (IQR).

BMI, body mass index.

CVD (figure 3): for an average individual, the HR associated with reallocating 15 min/day from MVPA to sedentary behaviour was 1.19 (95% CI 1.15 to 1.22), while the HR associated with reallocating 15 min/day from sedentary behaviour to MVPA was 0.92 (95% CI 0.91 to 0.94). Reallocating time from light physical activity behaviours or sleep to MVPA, and reallocating time from sedentary behaviour to sleep were also associated with a

lower risk of CVD, while reallocating time from sleep to LIPA was not associated with CVD risk (figure 3).

We found that, for an average individual in this sample, reallocating 20 min/day to MVPA from all other behaviours proportionally was associated with 9% (95% CI 7% to 10%) lower risk of CVD (figure 4; 28% of the study population exceeded this level of MVPA). Reallocating 1 hour/day to sedentary behaviour,

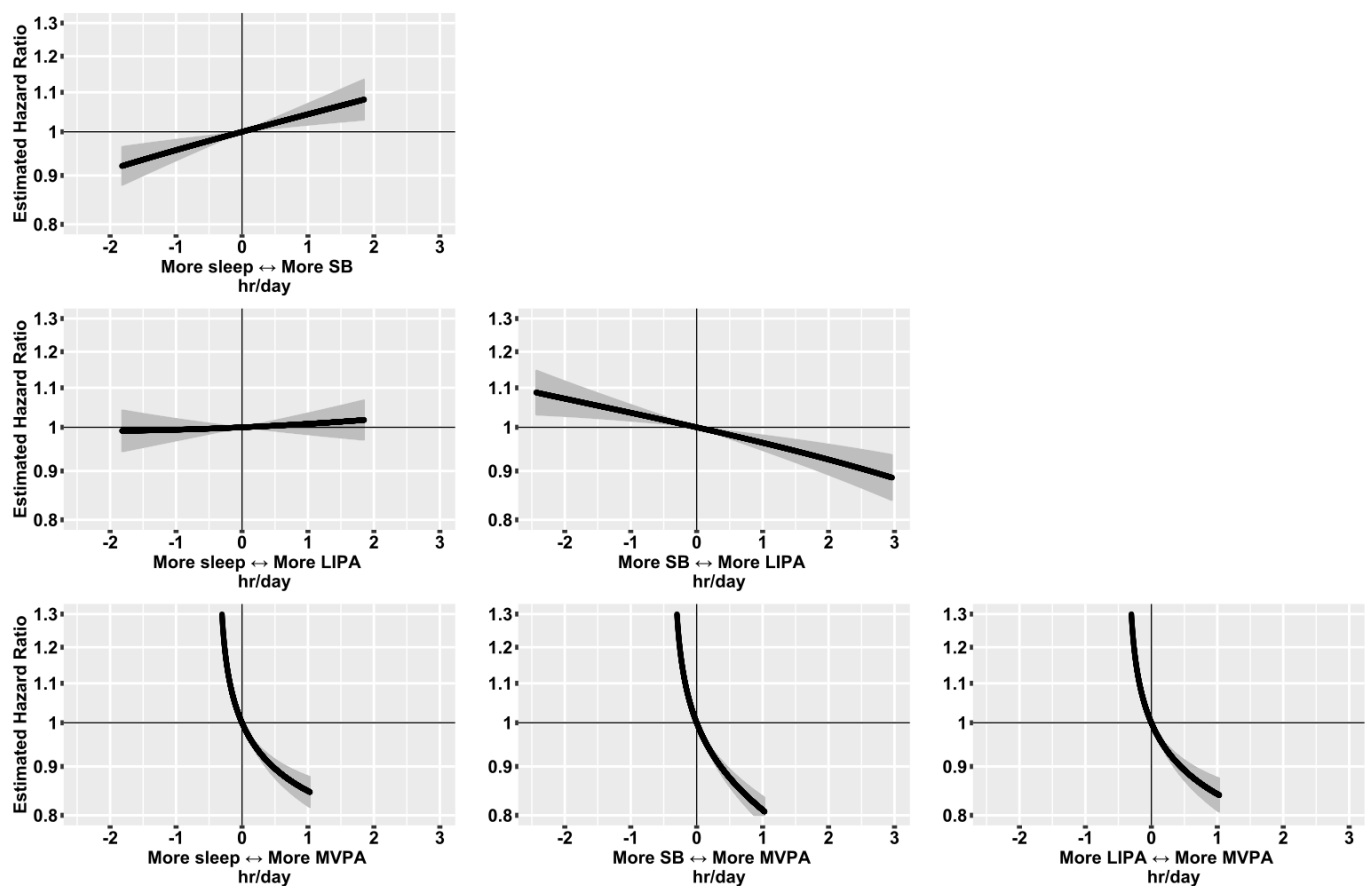


Figure 3 HRs for incident cardiovascular disease associated with balance between movement behaviours in 87 498 UK Biobank participants. Model based on 4105 events in 87 498 participants. All relative to the mean behaviour composition (8.8 hours/day sleep, 9.3 hours/day sedentary behaviour (SB), 5.6 hours/day light physical activity behaviours (LIPA), 0.35 hours/day (21 min/day) moderate-to-vigorous physical activity behaviours (MVPA)). Model used age as the timescale, was stratified by sex and was additionally adjusted for ethnicity, smoking status, alcohol consumption, fresh fruit and vegetable consumption, red and processed meat consumption, oily fish consumption, deprivation and education. 95% CIs shown.

from all other behaviours proportionally, was associated with 5% (95% CI 3% to 7%) higher risk of CVD (figure 4; 26% of the study population exceeded this level of sedentary behaviour).

Reallocating 1 hour/day to light physical activity behaviours, from sleep, sedentary behaviour and MVPA proportionally and reallocating 1 hour/day to sleep, from sedentary behaviour, light physical activity behaviours and MVPA proportionally, showed more modest and non-significant associations with lower risk of CVD (1% (95% CI -1% to 2%) and 2% (95% CI 0% to 4%), respectively; figure 4).

Results from the multivariable-adjusted model were only slightly attenuated compared with those from a minimally adjusted model (online supplemental figure 3, online supplemental table 6). Further adjustment for BMI, using a model stratified by BMI category, resulted in some attenuation of the association between movement behaviours and incident CVD (online supplemental figure 4, online supplemental table 6). For example, the 9% (95% CI 7% to 10%) lower risk of CVD relative to at the compositional mean associated with reallocating 20 min/day to MVPA was reduced to a 7% (95% CI 6% to 9%) lower risk after stratification by BMI. Associations for fatal cardiovascular events were similar to those for all cardiovascular events, with reallocating time from sedentary behaviour to light physical activity behaviours and sleep appearing more strongly associated with fatal events (online supplemental figure 5, online supplemental table 6). Results for women and men separately

were similar, with some associations appearing stronger for women (online supplemental figure 6, online supplemental table 6). Results for participants aged under and over 65 separately were similar, with some associations appearing stronger for older adults (online supplemental figure 7, online supplemental table 6).

Removing the first 2 years of follow-up attenuated all associations only minimally (online supplemental figure 8, online supplemental table 6). Further restricting to a healthy subgroup, associations for reallocating time into MVPA remained broadly similar, but associations for reallocating time from sedentary behaviour to light physical activity behaviours and to sleep were substantially attenuated (online supplemental figure 8, online supplemental table 6).

Analyses suggested residual and unmeasured confounding had a modest impact on the main findings. Specifically, some movement behaviours were associated with the negative control outcome, suggesting a small impact of residual confounding (online supplemental figure 9, online supplemental table 6). The E-values indicated that a substantial degree of unmeasured confounding would be required to reduce the observed associations to the null for MVPA and sedentary behaviour reallocated from other behaviours proportionally (online supplemental figure 10). For example, the E-value of 1.42 (for reallocating 20 min/day to MVPA, from all other behaviours) shows an unmeasured confounder would need to be associated with at

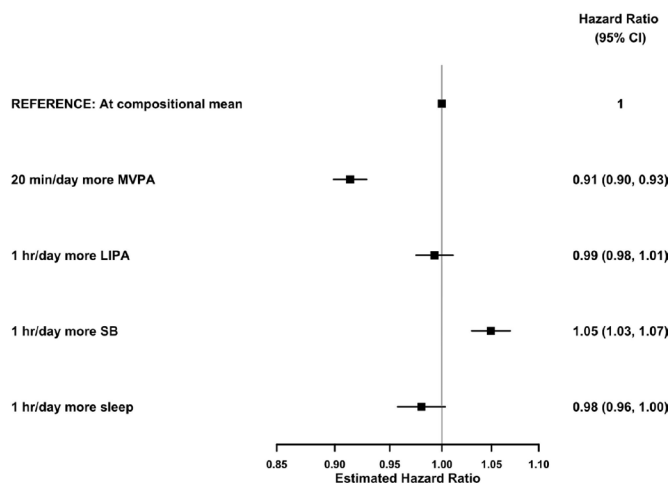


Figure 4 HRs for incident cardiovascular disease associated with reallocating time to named behaviour, from all other behaviours proportionally, in 87 498 UK Biobank participants. Model based on 4105 events in 87 498 participants. All relative to the mean behaviour composition (8.8 hours/day sleep, 9.3 hours/day sedentary behaviour (SB), 5.6 hours/day light physical activity behaviours (LIPA), 0.35 hours/day (21 min/day) moderate-to-vigorous physical activity behaviours (MVPA)) and more time in named behaviour reallocated from all other behaviours proportionally. Model used age as the timescale, was stratified by sex and was additionally adjusted for ethnicity, smoking status, alcohol consumption, fresh fruit and vegetable consumption, red and processed meat consumption, oily fish consumption, deprivation and education. 95% CIs shown.

least a 1.42-fold increase in risk for both exposure and outcome to explain away the observed association.

DISCUSSION

Using free-living ‘ground truth’ data, we showed that machine-learning methods were able to accurately classify movement behaviours in wrist-worn accelerometer data. By applying these methods, we were able to derive device-based measurements of movement behaviours in 87 498 UK Biobank participants. Using compositional data analysis Cox regression, we studied how the allocation of time between behaviours was associated with incident CVD events over a >6-year follow-up period. We found that reallocating time to MVPA from sleep, sedentary behaviour or light physical activity behaviours or reallocating time from sedentary behaviour to light physical activity behaviours or sleep was associated with lower risk of CVD. Per minute, the most pronounced differences in risk were seen for MVPA. BMI explained a modest proportion of the association between movement behaviours and incident CVD.

Our epidemiological findings extend previously reported results by showing how reallocating time between behaviours is associated with cardiovascular risk (after adjustment for other behaviours). The results of this study are consistent with our previous results, which showed a dose–response association across quartiles of device-measured moderate physical activity for cardiovascular events in the UK Biobank (with 42% lower risk in the highest quartile for moderate physical activity compared with the lowest).³⁸ Notably, the current study extends those previous results by measuring and adjusting for behaviours throughout the 24-hour day using a compositional data analysis approach. These results are also consistent with results from a study of community-dwelling older women in the USA, which

found 69% higher risk of incident CVD in the highest quartile for device-measured sedentary behaviour compared with the lowest,³⁹ and 22% lower risk of incident CVD in the highest quartile for light physical activity compared with the lowest.¹ Again, these studies only partially adjusted for other behaviours within the 24-hour day.¹ A recent pooled analysis of data from six cohort studies investigated the association between movement behaviours and all-cause mortality using a compositional data analysis approach and found associations broadly similar to those reported here.¹² However, they noted measurement challenges, including lack of device-measured sleep time in many studies and inaccurate classification using cut-points in wrist-worn accelerometer data, that hampered interpretation of some results.¹² The behaviour classification methods developed in this study support interpretable epidemiological analyses. For example, we were able to study device-measured sleep as part of the 24-hour day, and found suggestive results, including that reallocating time from sedentary behaviour to sleep was associated with a lower risk of incident CVD. However, in light of remaining challenges in validating sleep measurement and in studying sleep epidemiologically (eg, a fuller treatment may consider factors beyond duration, including sleep quality), these results are best considered as hypothesis generating.

The performance of our behaviour classification model represents an improvement on previously reported machine-learning approaches in free-living data (Cohen’s kappa 0.80 vs 0.68), likely due to careful curation of the behaviour classes in labelled data by two reviewers.¹¹ Our approach also performed better than traditional ‘cut-point’ approaches. While some characteristics of the CAPTURE-24 sample differ from UK Biobank, it is a large, varied dataset, and consistent performance of our methods across age groups suggests our methods are relatively robust. We encourage researchers to conduct studies similar to CAPTURE-24 embedded within prospective cohorts with accelerometer data in the future, and where possible to collect data on relevant participant characteristics. Although comparable with UK estimates from other sources,⁴⁰ sleep measurements should be interpreted cautiously: ‘ground truth’ labels for sleep came from a time use diary, which may identify time in bed rather than physiological sleep. In the future, sleep measurements require validation using polysomnography.

Strengths

This study has several strengths, notably including the use of device-based measurements to characterise movement behaviours in a large, comprehensive prospective study. Compared with self-reported measurements of behaviour, device-based measurements are at reduced risk of recall and reporting bias,⁶ and they can capture behaviours such as light physical activity well.⁷ The use of a wrist-worn device with a full 24-hour wear protocol (with high compliance) allowed the full day of behaviours to be measured.²⁴ The use of free-living data with ‘ground truth’ behaviour labels to develop and validate behaviour classification methods ensures they perform well in real-world settings. All methods used in this study are open-source and available for use in other wrist-worn accelerometer datasets. A major strength of the analysis in this study is the appropriate modelling of 24 hour behaviours using a compositional data analysis approach.^{18 19}

Limitations

An important limitation of any observational study is the possibility of reverse causality bias.⁴¹ After removing the first 2 years of follow-up, associations were only slightly attenuated. However,

What are the findings?

- ⇒ Emerging methods, including machine-learning for behaviour classification and statistical methods addressing the compositional nature of movement behaviours, can enhance epidemiological studies and lead to new health insights.
- ⇒ Machine-learning methods enabled accurate classification of movement behaviours from free-living wrist-worn device data (accuracy 88%, kappa 0.80).
- ⇒ Reallocating time to moderate-to-vigorous physical activity behaviours from light physical activity behaviours, sedentary behaviour or sleep was associated with lower risk of incident cardiovascular disease over >6 years of follow-up.
- ⇒ Reallocating time from sedentary behaviour to other behaviours was also associated with lower risk of incident cardiovascular disease.

How might it impact on clinical practice in the future?

- ⇒ Machine-learning methods for behaviour classification may be used to accurately classify movement behaviours from wrist-worn device data in free-living environments.
- ⇒ Our findings support existing public health guidance on reallocating time to moderate-to-vigorous physical activity from other behaviours and reallocating time from sedentary behaviour to light physical activity for population-based cardiovascular disease prevention.

further restricting analyses to a healthy subgroup attenuated the associations for reallocating time from sedentary behaviour to light physical activity behaviours and sleep. Associations for reallocating time to MVPA were attenuated slightly or not at all. Residual confounding also remains possible, although sensitivity analyses using a negative control outcome and E-values suggested its impact is likely to be modest. While results are presented for reallocations of time between behaviours, these are derived statistically across participants: each participant had a single measurement, so within-participant changes cannot be addressed directly. Validation of the machine-learning methods on another independent dataset would help to further understand their robustness.¹³ Finally, UK Biobank is not representative of the UK population²³ (eg, low socioeconomic status individuals are under-represented compared with the national population⁴²), though a previous study showed exposure–outcome associations found in UK Biobank were similar to results in more representative samples.⁴³

Conclusions

The use of machine-learning and compositional data analysis methods can enhance prospective cohort studies that collect wearable device data, leading to new health insights. The results of this study support the framing of current guidelines and interventions around increasing time spent in MVPA, and reallocating time from sedentary behaviour to light physical activity behaviours where that is infeasible.^{44–46}

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REFERENCES

- LaCroix AZ, Bellettiere J, Rillamas-Sun E, et al. Association of light physical activity measured by Accelerometry and incidence of coronary heart disease and cardiovascular disease in older women. *JAMA Netw Open* 2019;2:e190419.
- Lee I-M, Shiroma EJ, Lobelo F, et al. Effect of physical inactivity on major non-communicable diseases worldwide: an analysis of burden of disease and life expectancy. *Lancet* 2012;380:219–29.
- Pandey A, Salahuddin U, Garg S, et al. Continuous dose-response association between sedentary time and risk for cardiovascular disease: a meta-analysis. *JAMA Cardiol* 2016;1:575–83.
- Itani O, Jike M, Watanabe N, et al. Short sleep duration and health outcomes: a systematic review, meta-analysis, and meta-regression. *Sleep Med* 2017;32:246–56.
- Jike M, Itani O, Watanabe N, et al. Long sleep duration and health outcomes: a systematic review, meta-analysis and meta-regression. *Sleep Med Rev* 2018;39:25–36.
- Sabia S, van Hees VT, Shipley MJ, et al. Association between questionnaire- and accelerometer-assessed physical activity: the role of sociodemographic factors. *Am J Epidemiol* 2014;179:781–90.
- Lee I-M, Shiroma EJ. Using accelerometers to measure physical activity in large-scale epidemiological studies: issues and challenges. *Br J Sports Med* 2014;48:197–201.
- Ekelund U, Tarp J, Steene-Johannessen J, et al. Dose-response associations between accelerometer measured physical activity and sedentary time and all cause mortality: systematic review and harmonised meta-analysis. *BMJ* 2019;366:14570.
- Kerr J, Patterson RE, Ellis K. Objective assessment of physical activity: classifiers for public health. *Med Sci Sport Exerc* 2017;48:951–7.
- Willets M, Hollowell S, Aslett L, et al. Statistical machine learning of sleep and physical activity phenotypes from sensor data in 96,220 UK Biobank participants. *Sci Rep* 2018;8. doi:10.1038/s41598-018-26174-1. [Epub ahead of print: 21 05 2018].
- Doherty A, Smith-Byrne K, Ferreira T, et al. Gwas identifies 14 loci for device-measured physical activity and sleep duration. *Nat Commun* 2018;9:5257.
- Chastin S, McGregor D, Palarea-Albaladejo J, et al. Joint association between accelerometry-measured daily combination of time spent in physical activity, sedentary behaviour and sleep and all-cause mortality: a pooled analysis of six prospective cohorts using compositional analysis. *Br J Sports Med* 2021;55:1277–85.
- Montoye AHK, Westgate BS, Fonley MR, et al. Cross-Validation and out-of-sample testing of physical activity intensity predictions with a wrist-worn accelerometer. *J Appl Physiol* 2018;124:1284–93.
- Farrahi V, Niemelä M, Kangas M, et al. Calibration and validation of accelerometer-based activity monitors: a systematic review of machine-learning approaches. *Gait Posture* 2019;68:285–99.
- Narayanan A, Desai F, Stewart T, et al. Application of raw accelerometer data and machine-learning techniques to characterize human movement behavior: a systematic scoping review. *J Phys Act Health* 2020;17:360–83.
- DiPietro L, Al-Ansari SS, Biddle SJH, et al. Advancing the global physical activity agenda: recommendations for future research by the 2020 WHO physical activity and sedentary behavior guidelines development group. *Int J Behav Nutr Phys Act* 2020;17:1–11.
- Mekary RA, Willett WC, Hu FB, et al. Isotemporal substitution paradigm for physical activity epidemiology and weight change. *Am J Epidemiol* 2009;170:519–27.
- Chastin SFM, Palarea-Albaladejo J, Dontje ML, et al. Combined effects of time spent in physical activity, sedentary behaviors and sleep on obesity and cardio-metabolic health markers: a novel compositional data analysis approach. *PLoS One* 2015;10:e0139984.
- Dumuid D, Pedišić Željko, Palarea-Albaladejo J, et al. Compositional data analysis in time-use epidemiology: what, why, how. *Int J Environ Res Public Health* 2020;17:2220.
- Janssen I, Clarke AE, Carson V, et al. A systematic review of compositional data analysis studies examining associations between sleep, sedentary behaviour, and physical activity with health outcomes in adults. *Appl Physiol Nutr Metab* 2020;45:S248–57.
- Stamatakis E, Ekelund U, Ding D, et al. Is the time right for quantitative public health guidelines on sitting? A narrative review of sedentary behaviour research paradigms and findings. *Br J Sports Med* 2019;53:377–82.
- Stamatakis E, Ding D, Hamer M, et al. Any public health guidelines should always be developed from a consistent, clear evidence base. *Br J Sports Med* 2019;53:1555–6.
- Allen N, Sudlow C, Downey P, et al. UK Biobank: current status and what it means for epidemiology. *Health Policy Technol* 2012;1:123–6.
- Doherty A, Jackson D, Hammerla N, et al. Large scale population assessment of physical activity using wrist worn accelerometers: the UK Biobank study. *PLoS One* 2017;12:e0169649–14.
- Ainsworth BE, Haskell WL, Herrmann SD, et al. 2011 compendium of physical activities: a second update of codes and met values. *Med Sci Sports Exerc* 2011;43:1575–81.
- Tremblay MS, Aubert S, Barnes JD, et al. Sedentary behavior research network (SBRN) – terminology consensus project process and outcome. *Int J Behav Nutr Phys Act* 2017;14:1–17.
- Forney GD. The viterbi algorithm. *Proc IEEE Inst Electr Electron Eng* 1973;61:268–78.
- Hildebrand M, VAN Hees VT, Hansen BH, et al. Age group comparability of raw accelerometer output from wrist- and hip-worn monitors. *Med Sci Sports Exerc* 2014;46:1816–24.
- McGregor DE, Palarea-Albaladejo J, Dall PM, et al. Cox regression survival analysis with compositional covariates: application to modelling mortality risk from 24-h physical activity patterns. *Stat Methods Med Res* 2020;29:1447–65.
- Dumuid D, Pedišić Željko, Stanford TE, et al. The compositional isotemporal substitution model: a method for estimating changes in a health outcome for reallocation of time between sleep, physical activity and sedentary behaviour. *Stat Methods Med Res* 2019;28:846–57.
- Dumuid D, Stanford TE, Pedišić Željko, et al. Adiposity and the isotemporal substitution of physical activity, sedentary time and sleep among school-aged children: a compositional data analysis approach. *BMC Public Health* 2018;18:311.
- Woodward M. *Epidemiology: study design and data analysis*. Boca Raton, Florida ; London, England ; New York, New York: CRC Press, 2014.
- Von Elm E, Altman DG, Egger M. The strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. *PLoS Med* 2007.
- Hamer M, Bauman A, Bell JA, et al. Examining associations between physical activity and cardiovascular mortality using negative control outcomes. *Int J Epidemiol* 2019;48:1161–6.
- VanderWeele TJ, Ding P. Sensitivity analysis in observational research: introducing the E-Value. *Ann Intern Med* 2017;167:268–74.
- Mathur MB, Ding P, Riddell CA. Web site and R package for computing E-values. *Epidemiology* 2018;29:e45–7.
- UK Biobank, 2021. Available: <https://www.ukbiobank.ac.uk/> [Accessed 27 Jan 2021].
- Ramakrishnan R, Doherty A, Smith-Byrne K. Accelerometer measured physical activity and the incidence of cardiovascular disease : evidence from the UK biobank cohort study. *PLoS Med* 2021;2:1–16.
- Bellettiere J, LaMonte MJ, Evenson KR, et al. Sedentary behavior and cardiovascular disease in older women. *Circulation* 2019;139:1036–46.
- Lamote de Grignon Pérez J, Gershuny J, Foster R, et al. Sleep differences in the UK between 1974 and 2015: insights from detailed time diaries. *J Sleep Res* 2019;28:e12753.
- Strain T, Wijndaele K, Sharp SJ, et al. Impact of follow-up time and analytical approaches to account for reverse causality on the association between physical activity and health outcomes in UK Biobank. *Int J Epidemiol* 2020;49:162–72.
- Fry A, Littlejohns TJ, Sudlow C. Study design comparison of sociodemographic and health-related characteristics of UK Biobank participants with those of the general population 2017;186:1026–34.
- Batty GD, Gale CR, Kivimäki M, et al. Comparison of risk factor associations in UK Biobank against representative, general population based studies with conventional response rates: prospective cohort study and individual participant meta-analysis. *BMJ* 2020;368:m131–8.
- Davies DSC, Atherton F, McBride M. *UK chief medical officers' physical activity guidelines*. UK: Dep Heal Soc Care, 2019: 1–65. <https://www.gov.uk/government/publications/physical-activity-guidelines-uk-chief-medical-officers-report>
- Department of Human and Health Services. *Physical activity guidelines for Americans*. 2nd edn, 2018. <https://health.gov/paguidelines/about/>
- World Health Organization. *Who guidelines on physical activity and sedentary behaviour*. Geneva, 2020.

Supplementary Material

Supplementary material for **Reallocation of time between device-measured movement behaviours and risk of incident cardiovascular disease**

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Contents

Supplementary Methods	4
‘Ground truth’ labelling of movement behaviours in image data	4
Machine-learning methods	5
Machine-learning methods: Features	5
Machine-learning methods: Random Forest models	5
Machine-learning methods: Hidden Markov models	5
Machine-learning methods: Evaluation	5
Machine-learning methods: model in participants aged 38 years or older	6
A Compositional Data Analysis approach to movement behaviour data	7
Log-ratio transformation	7
Interpreting isometric log-ratio pivot coordinates	7
Zero values	8
Software	9
Sensitivity analyses: further details on E-values	10
Sensitivity analyses: linear isotemporal substitution	11
References	12
Supplementary Tables and Figures	14
Supplementary Table 1: Assignment of fine-grained camera image annotations from the Compendium of Physical Activities to broad movement behaviour classes.	14
Supplementary Table 2: Features of accelerometry signal used for behaviour classification.	22
Supplementary Table 3: Definition of variables from UK Biobank data included in statistical models.	24
Supplementary Table 4: Characteristics of CAPTURE-24 participants.	28
Supplementary Figure 1: Participant-wise mean (a) precision and (b) recall for classification of behaviours from accelerometer data calculated in Leave-One-Participant-Out Cross-Validation (with 95% confidence interval for the mean). The x-axis gives the minimum required recorded annotator-labelled time in the behaviour for inclusion in the calculation. For precision, participants with no model-labelled time in the behaviour were also excluded as precision is undefined in this case.	29
Supplementary Figure 2: Probability of being in sleep, sedentary behaviour (SB), light physical activity behaviours (LIPA) and moderate-to-vigorous physical activity behaviours (MVPA) among 87,498 UK Biobank participants according to machine-learned behaviour classification by hour of the day.	30
Supplementary Table 5: Coefficient of first isometric log-ratio pivot coordinate ^a for each movement behaviour estimated using a multivariable-adjusted Compositional Data Analysis Cox regression model.	31
Supplementary Table 6: Coefficient of first isometric log-ratio pivot coordinate for each movement behaviour estimated using all Compositional Data Analysis Cox regression models. ^a	32
Supplementary Figure 3: Hazard Ratios for cardiovascular disease for all behaviour pairs estimated using multivariable-adjusted (blue) and minimally adjusted (red) Cox regression models. ^a	33
Supplementary Figure 4: Hazard Ratios for incident cardiovascular disease estimated using a multivariable-adjusted Cox regression model before (blue) and after (red) stratification by BMI. ^a	34
Supplementary Figure 5: Hazard Ratios for all (blue) and fatal (red) incident cardiovascular disease for all behaviour pairs estimated using a multivariable-adjusted Cox regression model. ^a	35
Supplementary Figure 6: Hazard Ratios for incident cardiovascular disease for all behaviour pairs estimated using a multivariable-adjusted Cox regression model for women (blue) and men (red). ^a	36
Supplementary Figure 7: Hazard Ratios for incident cardiovascular disease for all behaviour pairs estimated using a multivariable-adjusted Cox regression model for participants aged under 65 (blue) and participants aged over 65 (red). ^a	37

Supplementary Figure 8: Hazard Ratios for incident cardiovascular disease for all behaviour pairs estimated using a multivariable-adjusted Cox regression model (blue), after removing the first two years of follow-up (red) and after additionally restricting to a healthy subgroup (green). ^a	38
Supplementary Figure 9: Hazard Ratios for cardiovascular disease (blue) and for non-activity-related accidents (red) for all behaviour pairs estimated using a multivariable-adjusted Cox regression model. ^a	39
Supplementary Figure 10: Hazard ratios and corresponding E-values for incident cardiovascular disease associated with reallocating time to named behaviour, from all other behaviours proportionally, in 87,498 UK Biobank participants. ^a	40
Supplementary Figure 11: An example of a decision tree to classify time windows using average acceleration vector magnitude (avm) and the 75 th percentile of acceleration vector magnitude (75thp).	41
Supplementary Figure 12: The structure of a Hidden Markov Model.....	42
Supplementary Figure 13: Hazard Ratios for incident cardiovascular disease for all behaviour pairs estimated using a multivariable-adjusted Cox regression model for all participants (blue) and in a sensitivity analysis excluding individuals with a zero value in any behaviour (red). ^a	43
Supplementary Figure 14: Hazard Ratios for incident cardiovascular disease estimated using a multivariable-adjusted Compositional Data Analysis Cox regression model (blue) and using a multivariable-adjusted linear isotemporal substitution Cox regression model (red). ^a	44
STROBE Statement—Checklist of items that should be included in reports of cohort studies.....	45

Supplementary Methods

'Ground truth' labelling of movement behaviours in image data

As described in the main text, to provide the 'ground truth' labels for machine-learning based behaviour classification, fine-grained behaviour annotations of image data were mapped to sleep, sedentary behaviour, light physical activity behaviours and moderate-to-vigorous physical activity behaviours based on the definition in the main text. In practice, this involved the following steps (the final mapping is given in **Supplementary Table 1**):

1. The fine-grained annotation for sleeping was assigned to sleep.
2. Behaviours at 3 or more METs (Metabolic Equivalent of Task, where 1 MET is energy expenditure in quiet sitting), as described in Compendium of Physical Activities [1], were assigned to moderate-to-vigorous physical activity behaviours.
3. For waking behaviours at <3 METs, if the fine-grained annotation indicated a sitting, lying or reclining posture, the behaviour was assigned to sedentary behaviour.
4. Waking behaviours at <3 METs not assigned to sedentary behaviour were assigned to light physical activity behaviours.
5. All labels were reviewed by two reviewers. Where reviewers agreed the fine-grained annotation was typically used by annotators for behaviours in a different category to the label given, the fine-grained annotation was recoded. This review was performed prior to model training, and no changes were made after results were obtained.

Machine-learning methods

As described in the main text, a Random Forest (RF) with 100 decision trees was developed to classify 30-second time windows as sleep, sedentary behaviour, light physical activity behaviours or moderate-to-vigorous physical activity behaviours using the time and frequency domain features outlined in **Supplementary Table 2**. A Hidden Markov model (HMM) was then employed to use time sequence information to improve on the RF-assigned label sequence. As described in the main text, models were trained using labelled data from the CAPTURE-24 study, in which participants wore wearable cameras and kept time use diaries alongside wearing an accelerometer.

Machine-learning methods: Features

Time windows of acceleration were classified using a list of features (variables) based on features used in the study of Willetts et al (this included time and frequency domain features e.g. mean and kurtosis of the acceleration vector magnitude, and power at different frequencies from the Fast Fourier Transform of acceleration vector magnitude) [2]. In the present study, only rotation-invariant features were used (see **Supplementary Table 2**). This addressed concerns about risk of overfitting and possible time trends in the data driven by sensitivity to device orientation within the wrist strap (orientation became more standardised over 2013-2015).

Machine-learning methods: Random Forest models

Random Forests are based on decision trees. Decision trees assign class labels based on splits of the data using feature value thresholds (as shown in the example in **Supplementary Figure 11**). They can be trained using the Classification and Regression Tree (CART) algorithm [3].

In a RF, many decision trees are used. When training the trees (using the CART algorithm), randomness is introduced by (i) training each tree on a set of data points picked randomly (with replacement) and (ii) at each split node, restricting the choice of splitting feature to a randomly picked subset of features.

To classify a data point using an RF, it is classified by each decision tree. Because they are trained on different subsets of data and use different features, different trees in the RF may classify data points differently. The overall classification given by the RF is the class that is assigned to the data point by the largest number of trees. This approach, whereby multiple randomly-differing instances are used in order to reduce variance on the output, is the technique of bootstrap-aggregating or ‘bagging’ [4].

For this application, a balanced RF was used. The fact some behaviours are much more common than others in the labelled data (e.g. sleep is much more common than moderate-to-vigorous physical activity behaviours) can cause a standard RF, which is trained by picking N examples at random with replacement, to favour assigning common labels at the expense of less common behaviours [2]. Using the balanced RF, if there were n_{rare} examples of the rarest behaviour, n_{rare} examples of each behaviour were picked with replacement to train each tree.

Machine-learning methods: Hidden Markov models

In a HMM, there is a sequence of unobserved hidden states, which is assumed to have the Markov property (i.e. future states only depend on past states through present states). This sequence is governed by transition probabilities, which determine the probability of transitioning between each pair of states. There is a sequence of observed states, which depend probabilistically on the sequence of hidden states (described as ‘emissions’ from the sequence of hidden states; **Supplementary Figure 12**).

Here, the hidden states were the true behaviours, and the emissions were the RF-assigned labels. The Viterbi algorithm, the standard approach to this problem, was used to estimate the most likely true behaviour sequence given the observed sequence of RF-assigned labels [5]. Applying the Viterbi algorithm required estimates of:

1. **Transition probabilities between hidden states:** Transition probabilities between behaviour pairs were estimated using the proportions of transitions that occurred between each behaviour pair in the labelled data.
2. **Emission probabilities of observed states from hidden states:** To estimate emission probabilities, time windows were first classified using out-of-bag predictions from the RF i.e. trees were used to classify data points on which they were not trained. This mimics use on unseen data, without requiring additional data. Emission probabilities were then estimated using the proportions of different pairs of true behaviour and RF out-of-bag estimate.

By using this HMM to estimate the most likely true behaviour sequence given the RF-assigned labels, a more plausible sequence of states was obtained. The HMM re-labelled behaviours which formed unrealistic sequences and were likely to be attributable to misclassification (e.g. short periods of moderate-to-vigorous physical activity behaviours during sleep time). Therefore, compared to the unadjusted RF-assigned labels, the labels after using the HMM gave improved measures of the behaviours of interest for subsequent epidemiological analyses.

Machine-learning methods: Evaluation

All metrics were calculated in Leave-One-Participant-Out Cross-Validation.

Leave-One-Participant-Out Cross-Validation involves, for each participant, a model trained on all other participants’ data (i.e. with this participant’s data left-out). The trained model is then used to label the left-out participant’s data and evaluation metrics are calculated. This is repeated for all participants, and metrics are aggregated or calculated across all participants.

Leave-One-Participant-Out Cross-Validation allows evaluation of the performance of the models on data not used in training, while retaining the maximal amount of data for use in training these models. Moreover, all of the data can then be used to train the final model used for classification.

For model performance, the following evaluation metrics were used:

1. We reported mean per-participant accuracy across all behaviours. This is a simple, intuitive metric of model performance, describing the proportion of 30-second time windows that were correctly classified. Using mean per-participant accuracy, rather than aggregate accuracy over all data, prevents the result being dominated by performance on a few participants with larger amounts of data (important as there may be inter-individual differences in classification performance).
2. We reported mean per-participant Cohen's kappa across all behaviours. This is a metric of interrater reliability. It evaluates how much higher the agreement between two raters (here, annotator-assigned 'ground truth' label and model-assigned label) is than that which would be achieved by chance, given the proportions in each class. It is preferable to accuracy, as it takes into account the proportions in each class (in particular, in data where some classes are dominant, a classifier assigning solely to the dominant classes can achieve high accuracy but not high Cohen's kappa).
3. We reported mean per-participant precision and recall for each behaviour. Precision for a given behaviour is the proportion of examples labelled by the model as that behaviour which are 'true' examples of that behaviour. Recall for a given behaviour is the proportion of 'true' examples of that behaviour labelled as that behaviour. Again, taking the mean across participants prevents performance being dominated by performance on participants with larger amounts of data. However, it also upweights the contribution of individuals with very small amounts of data for a given behaviour. Therefore, precision and recall were additionally calculated after excluding participants with up to 20 minutes in the behaviour.

Taken together, these metrics help to understand the validity of the model as a method to derive measures of movement behaviours for subsequent epidemiological analyses. After applying the model to derive measures of movement behaviours for UK Biobank participants, face validity was assessed by plotting behaviour profiles over the day.

Machine-learning methods: model in participants aged 38 years or older

We also carried out the above steps using only data from participants aged 38 years or older i.e. nearer to the age group represented in the UK Biobank sample. The age group 38+ years was used as this corresponds to the information available in a release version of this dataset.

In Leave-One-Participant-Out analysis, the mean per-participant accuracy was 86% (84, 88) and the mean per-participant Cohen's kappa was 0.79 (0.76, 0.81).

Given the results reported in the main text, showing that the model trained on all participants performed well when restricted to the age group of interest, we used the model trained on all participants for the main classification.

A Compositional Data Analysis approach to movement behaviour data

Log-ratio transformation

A Compositional Data Analysis approach is a set of methods for working with compositional data, based on the use of log-transformed ratios to describe the data [6–8]. Ratios between behaviours are used to describe compositional data as they capture the relative values of the different behaviours. Log-transforming ratios ensures the relationships and distances between different compositions are well-described: using log-transformed ratios is equivalent to working with compositional data in a ‘natural’ space for it, with operations which map compositions to genuine compositions and an appropriate distance metric [9,10]. For statistical purposes, log-transformed ratios are also typically more conveniently distributed than ratios [11].

While many different sets of log-transformed ratios can be used, isometric log-ratio pivot coordinates are widely used in movement behaviour research [12] and were used in this study. They were calculated as follows:

$$coordinate_1 = \sqrt{\frac{3}{4}} \ln \left(\frac{\text{sleep}}{\sqrt[3]{SB \times LIPA \times MVPA}} \right) = \sqrt{\frac{1}{12}} \ln \left(\frac{\text{sleep}}{SB} \right) + \sqrt{\frac{1}{12}} \ln \left(\frac{\text{sleep}}{LIPA} \right) + \sqrt{\frac{1}{12}} \ln \left(\frac{\text{sleep}}{MVPA} \right)$$

$$coordinate_2 = \sqrt{\frac{2}{3}} \ln \left(\frac{SB}{\sqrt[3]{LIPA \times MVPA}} \right) = \sqrt{\frac{1}{6}} \ln \left(\frac{SB}{LIPA} \right) + \sqrt{\frac{1}{6}} \ln \left(\frac{SB}{MVPA} \right)$$

$$coordinate_3 = \sqrt{\frac{1}{2}} \ln \left(\frac{LIPA}{MVPA} \right)$$

Interpreting isometric log-ratio pivot coordinates

As the coefficients in the model relate to the isometric log-ratio pivot coordinates, rather than the raw behaviour variables, interpreting them is not straightforward.

The first coordinate describes the balance between sleep and all other behaviours. Therefore, the coefficient of the first coordinate can be interpreted as the effect of reallocating time to sleep from all other behaviours proportionally i.e. if the coefficient of the first coordinate is greater than 0 (its exponent is greater than 1) reallocating time to sleep from all other behaviours proportionally is associated with higher risk of cardiovascular disease. However, the second and third coordinates are harder to interpret analogously. Therefore, to interpret individually the effect of reallocating time to each behaviour from all others proportionally, and following standard methods in movement behaviour research, one model per behaviour was produced (with different first coordinate). This approach was used to present the model parameters in **Supplementary Table 5** and **Supplementary Table 6** (note that, in consequence, they do not parametrise a single model).

However, even using this approach, the magnitudes of the coefficients are hard to interpret. Therefore, as described in the main text, and following established methods, model estimates of the hazard ratio at different compositions relative to the mean behaviour composition were reported e.g. using pairwise time reallocation plots.

In detail, suppose we have a Cox regression model in the isometric log-ratio pivot coordinates laid out above:

$$\ln \frac{h(t)}{h_0(t)} = \beta_1(\text{coordinate}_1) + \beta_2(\text{coordinate}_2) + \beta_3(\text{coordinate}_3) + \sum_{i=1}^k \gamma_i(\text{covariate}_i)$$

and that the value of the coordinates at the mean behaviour composition is $(m_coordinate_1, m_coordinate_2, m_coordinate_3)$. [This notation is not misleading: the value of the coordinates at the compositional mean behaviour composition is also the mean of the coordinate values.].

Then, we consider a new behaviour composition, which corresponds to isometric log-ratio pivot coordinate values $(coordinate_1, coordinate_2, coordinate_3)$. In particular, when considering a pairwise time reallocation plot we use would use a new composition where time in two behaviours remained at its value in the mean behaviour composition, a value was subtracted from time in one of the remaining behaviours, and that value added to the time in the other behaviour. The log hazard ratio, now relative to the mean behaviour composition, is then calculated as:

$$\ln(HR) = \beta_1(\text{coordinate}_1 - m_coordinate_1) + \beta_2(\text{coordinate}_2 - m_coordinate_2) + \beta_3(\text{coordinate}_3 - m_coordinate_3)$$

The standard error on this can be calculated using the variance-covariance matrix of the coefficients $\boldsymbol{\beta} = (\beta_1, \beta_2, \beta_3)$, denoted V . Writing $\mathbf{x} = (\text{coordinate}_1 - m_coordinate_1, \text{coordinate}_2 - m_coordinate_2, \text{coordinate}_3 - m_coordinate_3)^T$, then

$$SE = \sqrt{\mathbf{x}^T V \mathbf{x}}$$

This can be used to calculate the HR and an (approximate) 95% CI as:

$$\exp(\ln(HR)) (\exp(\ln(HR) - 1.96SE), \exp(\ln(HR) + 1.96SE)).$$

While here we follow an exposition similar to that of Dumuid et al in the context of linear regression [13] and Chastin et al [14], the approach is mathematically equivalent to that of McGregor et al.[15]

To ensure results were plotted within the range supported by the data, times plotted were truncated at the 5th and 95th centile for the behaviour in the pair for which this range was narrower.

Zero values

All participants recorded time in sleep, sedentary behaviour and light physical activity behaviours, but 1% of participants recorded no time in moderate-to-vigorous physical activity behaviours. As zero values cannot be incorporated directly into the coordinates above, different approaches to work with them have been developed. The appropriate method depends on the source of the zero values:

1. ‘Rounded’ zeroes relate to measurement precision: even where no time in a given behaviour was observed, had the wear time been long enough, or the time resolution of the measurement short enough, some time in the behaviour would be expected. If data contains rounded zeroes, they can be imputed as small positive values [16].
2. ‘True’ zeroes occur where no matter the precision of the measurement, no time in that behaviour would be observed. For example, this may occur in movement behaviour research if someone is physically unable to take part in certain behaviours. If data contains true zeroes, participants with a true zero in a particular behaviour should be excluded from the main analysis and analysed separately.

We followed established methods in movement behaviour research by considering zero values to be ‘rounded’ and imputing them using the log-ratio expectation maximization algorithm from the ‘zCompositions’ R package [8,15–17]. We used the smallest observed value in the data as the detection limit (0.0001 on the unitless scale, corresponding to 0.14 min/day). Sensitivity of results to the method of treating zero values (imputation or exclusion) under the Compositional Data Analysis approach was examined by performing an analysis restricted to participants with non-zero values in all behaviour variables. This did not materially impact the results (**Supplementary Figure 13**).

Software

Development of the machine-learning models and processing of accelerometer data used Python 3.6.6, with the ‘biobankAccelerometerAnalysis’ tool[2,18,19] for preparing accelerometer data and training machine-learning models.

Data preparation was performed in Python 3.6.6 and R 4.0.5, and used the ‘ukb_download_and_prep_template’ tool [20] for preparing covariate and outcome data.

Statistical analysis was performed in R 4.0.5[21] with ‘zCompositions’, ‘survival’, ‘forestplot’, ‘EValue’, ‘plyr’, ‘data.table’, ‘rlist’, ‘ggtern’, ‘ggplot2’, and ‘gtools’[16,22–32]. The R package ‘epicoda’ was developed for this analysis[33].

Code is available at github.com/activityMonitoring/manuscript_ml_behaviours_cvd_2021. For further directions, please contact Aiden Doherty.

Sensitivity analyses: further details on E-values

As described in the main text, E-values were reported alongside hazard ratios. The E-value for the estimate quantifies the minimum strength of association that an unmeasured confounder would need with both exposure and outcome to explain away the observed association. The E-value for the 95% confidence interval quantifies the minimum strength of association an unmeasured confounder would need with both exposure and outcome to reduce the interval to overlap the null [27,28]. As the exposure is continuous, in both cases the risk ratio would apply to hypothetical groups with either the specified behaviour composition or the reference (the mean behaviour composition) [28].

Sensitivity analyses: linear isotemporal substitution

For comparability with previous literature, a sensitivity analysis using a linear isotemporal substitution approach was conducted.

Under a linear isotemporal substitution approach, all but one of the movement behaviours are included in the model (so the included variables are not perfectly multicollinear). [In this study, as non-wear time was imputed all subjects had the same wear time. Therefore, a total time variable was not included, meaning the approach may be more properly called 'leave-one-out regression' than true linear isotemporal substitution [8].] Associations are modelled as linear (rather than linear in the log-ratios, as under a Compositional Data Analysis approach). The coefficient of each behaviour can be interpreted in terms of replacing time in the left-out behaviour with time in that behaviour. Linear isotemporal substitution has been widely used in movement behaviour epidemiology [34], but has been criticised for not addressing the fact movement behaviour data only conveys relative information [8].

While there were some differences in shape of the associations observed (due to the different assumptions), results using this approach were broadly similar to the results of the main analysis using Compositional Data Analysis (**Supplementary Figure 14**).

References

- 1 Ainsworth BE, Haskell WL, Herrmann SD, *et al.* 2011 compendium of physical activities: A second update of codes and MET values. *Med Sci Sports Exerc* 2011;**43**:1575–81. doi:10.1249/MSS.0b013e31821ece12
- 2 Willetts M, Hollowell S, Aslett L, *et al.* Statistical machine learning of sleep and physical activity phenotypes from sensor data in 96,220 UK Biobank participants. *Sci Rep* 2018;**8**:0–10. doi:10.1038/s41598-018-26174-1
- 3 Breiman L, Friedman JH, Olshen RA, *et al.* *Classification and regression trees*. 1984. doi:10.1201/9781315139470
- 4 Breiman L. Bagging predictors. *Mach Learn* 1996;**24**:123–40. doi:10.1007/bf00058655
- 5 Forney GD. The Viterbi Algorithm. *Proc IEEE* 1973;**61**:268–78. doi:10.1109/PROC.1973.9030
- 6 Pawlowsky-Glahn V, Egozcue JJ, Tolosana-Delgado R. Lecture notes on Compositional Data Analysis. 2011;:1–100. doi:10.13140/RG.2.1.1296.2728
- 7 Filzmoser P, Hron K, Templ M. *Applied Compositional Data Analysis*. 2018. doi:10.1007/978-3-319-96422-5
- 8 Dumuid D, Pedišić Ž, Palarea-Albaladejo J, *et al.* Compositional Data Analysis in Time-Use Epidemiology : What , Why , How. *Int J Environ Res Public Health* 2020;**17**:2220. doi:10.3390/ijerph17072220
- 9 Aitchison J, Egozcue JJ. Compositional data analysis: Where are we and where should we be heading? *Math Geol* Published Online First: 2005. doi:10.1007/s11004-005-7383-7
- 10 Egozcue JJ, Pawlowsky-Glahn V, Mateu-Figueras G, *et al.* Isometric Logratio Transformations for Compositional Data Analysis. *Math Geol* 2003;**35**:279–300. doi:10.1023/A:1023818214614
- 11 Aitchison J. The statistical analysis of compositional data. *Stat Anal Compos Data* 1982;**44**:139–77. doi:10.1007/978-94-009-4109-0
- 12 Dumuid D, Stanford TE, Martín-Fernández J-AA, *et al.* Compositional data analysis for physical activity, sedentary time and sleep research. *Stat Methods Med Res* 2017;**27**:096228021771083. doi:10.1177/0962280217710835
- 13 Dumuid D, Pedišić Ž, Stanford TE, *et al.* The compositional isotemporal substitution model: A method for estimating changes in a health outcome for reallocation of time between sleep, physical activity and sedentary behaviour. *Stat Methods Med Res* 2017;**28**:846–57. doi:10.1177/0962280217737805
- 14 Chastin S, McGregor D, Palarea-Albaladejo J, *et al.* Joint association between accelerometry-measured daily combination of time spent in physical activity, sedentary behaviour and sleep and all-cause mortality: a pooled analysis of six prospective cohorts using compositional analysis. *Br J Sports Med* 2021;:bjssports-2020-102345. doi:10.1136/bjssports-2020-102345
- 15 McGregor DE, Palarea-Albaladejo J, Dall PMP, *et al.* Cox regression survival analysis with compositional covariates: Application to modelling mortality risk from 24-h physical activity patterns. *Stat Methods Med Res* 2019;**29**:1447–65. doi:10.1177/0962280219864125
- 16 Palarea-Albaladejo J, Martín-Fernández JA. ZCompositions - R package for multivariate imputation of left-censored data under a compositional approach. *Chemom. Intell. Lab. Syst.* 2015;**143**:85–96. doi:10.1016/j.chemolab.2015.02.019
- 17 Rasmussen CL, Palarea-Albaladejo J, Johansson MS, *et al.* Zero problems with compositional data of physical behaviors: a comparison of three zero replacement methods. *Int J Behav Nutr Phys Act* 2020.
- 18 Doherty A, Jackson D, Hammerla N, *et al.* Large scale population assessment of physical activity using wrist worn accelerometers: The UK biobank study. *PLoS One* 2017;**12**:1–14. doi:10.1371/journal.pone.0169649
- 19 Doherty A, Smith-Byrne K, Ferreira T, *et al.* GWAS identifies 14 loci for device-measured physical activity and sleep duration. *Nat Commun* 2018;**9**. doi:10.1093/acrefore/9780190236557.013.204
- 20 Walmsley R, Chan S, Doherty A. `ukb_download_and_prep_template`. 2020.https://github.com/activityMonitoring/ukb_download_and_prep_template
- 21 R Core Team. R: A Language and Environment for Statistical Computing. *Vienna, Austria* Published Online First: 2019.<https://www.r-project.org/>
- 22 Therneau TM. A Package for Survival Analysis in R. 2021.<https://cran.r-project.org/package=survival>
- 23 Wickham H. *ggplot2: Elegant Graphics for Data Analysis*. New York: : Springer-Verlag 2016. <https://ggplot2.tidyverse.org>
- 24 Warnes GR, Bolker B, Lumley T. `gtools`: Various R Programming Tools. *R Packag version 381* 2018.
- 25 Terry M, Therneau, Patricia M. Grambsch. *Modeling Survival Data: Extending the Cox Model*. New York: : Springer 2000.
- 26 Max Gordon and Thomas Lumley. `forestplot`: Advanced Forest Plot Using ‘grid’ Graphics. R package version 1.9. 2019.<https://cran.r-project.org/package=forestplot>
- 27 Van Der Wee TJ, Ding P. Sensitivity analysis in observational research: Introducing the E-Value. *Ann Intern Med* 2017;**167**:268–74. doi:10.7326/M16-2607

- 28 Mathur MB, Ding P, Riddell CA, *et al.* Web Site and R Package for Computing E-values. *Epidemiology* 2018;**29**:e45. doi:10.1097/EDE.0000000000000864
- 29 Wickham H. The Split-Apply-Combine Strategy for Data Analysis. *J Stat Softw* 2011;**40**:1–29. <http://www.jstatsoft.org/v40/i01/>
- 30 Dowle M, Srinivasan A. data.table: Extension of `data.frame`. 2021. <https://cran.r-project.org/package=data.table>
- 31 Ren K. rlist: A Toolbox for Non-Tabular Data Manipulation. 2016. <https://cran.r-project.org/package=rlist>
- 32 Hamilton NE, Ferry M. Ggtern: Ternary diagrams using ggplot2. *J Stat Softw* 2018;**87**:1–17. doi:10.18637/jss.v087.c03
- 33 Walmsley R. epicoda. 2020. github.com/activityMonitoring/epicoda
- 34 Mekary RA, Ding EL. Isotemporal substitution as the gold standard model for physical activity epidemiology: Why it is the most appropriate for activity time research. *Int J Environ Res Public Health* 2019;**16**:11–3. doi:10.3390/ijerph16050797

Supplementary Tables and Figures

Supplementary Table 1: Assignment of fine-grained camera image annotations from the Compendium of Physical Activities to broad movement behaviour classes.

<p><u>Sleep</u></p> <p>7030 sleeping</p>
<p><u>Sedentary behaviour</u></p> <p>occupation;office and administrative support;11580 office/computer work general</p> <p>occupation;office and administrative support;11580 office wok/computer work general</p> <p>home activity;miscellaneous;sitting;9060 sitting/lying reading or without observable/identifiable activities</p> <p>leisure;miscellaneous;sitting;0010 sitting / lying dialysis</p> <p>transportation;private transportation;16010 driving automobile or light truck (not a semi)</p> <p>home activity;miscellaneous;sitting;7010 sitting/lying and watching television with TV on as the primary activity</p> <p>home activity;miscellaneous;sitting;11580 office/computer work general</p> <p>home activity;miscellaneous;sitting;9055 sitting/lying talking in person/using a mobile phone/smartphone/tablet or talking on the phone/computer (skype chatting)</p> <p>home activity;miscellaneous;sitting;11580 office work such as writing and typing (with or without eating at the same time)</p> <p>home activity;eating;13030 eating sitting alone or with someone</p> <p>home activity;miscellaneous;sitting;9030 sitting desk entertainment/hobby (with or without eating at the same time)</p> <p>home activity;miscellaneous;sitting;5080 sitting non-desk work (with or without eating at the same time)</p> <p>occupation;interruption;sitting;11585 sitting meeting/talking to colleagues with or without eating</p> <p>leisure;miscellaneous;sitting;9060 (generic) sitting/lying reading or without observable/identifiable activities</p> <p>occupation;interruption;11585 sitting meeting/talking to colleages with or without eating</p> <p>home activity;leisure;activities for maintenance of a household;miscellaneous;9100 retreat/family reunion activities involving sitting eating relaxing talking with more than one person</p> <p>home activity;miscellaneous;sitting;9060 sitting/lying reading or without observable activities</p> <p>leisure;eating;social;13030 eating sitting indoor/outdoor</p> <p>home activity;leisure;activities for maintenance of a household;miscellaneous;9100 retreat/family reunion activities involving sitting eating relaxing talking with more than one person</p> <p>occupation;public admin/education/health;education;9065 students/attending seminars or talks</p> <p>home activity;miscellaneous;sitting;9030 sitting desk work (with or without eating at the same time)</p> <p>occupation;interruption;sitting;9060 sitting without observable/identifiable activities</p>

leisure;miscellaneous;sitting;9055 sitting talking to person/using the phone
transportation;private transportation;16015 riding in a car or truck
leisure;eating;13030 eating sitting indoor/outdoor
occupation;interruption;13030 eating sitting
home activity;miscellaneous;sitting;9045 sitting playing traditional video game computer game
home activity;miscellaneous;sitting;9030 sitting desk work (with or without eating at the same time)
occupation;interruption;sitting;13030 eating sitting
home activity;leisure;individual activities;9075 sitting arts and crafts carving/wood weaving/spinning wool
home activity;household chores;washing/ironing/mending clothes;5080 knitting sewing sitting
occupation;interruption;sitting;9055 sitting using a mobile phone/smartphone/tablet or talking on the phone/computer (skype meeting etc.)
leisure;miscellaneous;sitting;21000 sitting meeting
leisure;miscellaneous;sitting;21005 (generic) sitting light office writing typing work
occupation;office and administrative support;11580 office work/computer work general
home activity;miscellaneous;sitting;7010 lying and watching television with TV on as the primary activity
leisure;miscellaneous;sitting;9060 (generic) sitting/lying reading or without observable activities
transportation;waiting;7021 sitting
occupation;interruption;11585 sitting meeting/talking to colleagues with or without eating
leisure;religious activities;20000 sitting in church in service attending a ceremony sitting quietly
transportation;private transportation;16030 motor scooter motorcycle
occupation;interruption;9055 sitting using a mobile phone/smartphone/tablet or talking on the phone/computer (skype meeting etc.)
leisure;miscellaneous;21005 (generic) sitting light office writing typing work
home activity;miscellaneous;sitting;7021 sitting without observable activities
home activity;leisure;activities for maintenance of a household;with children;5170 sitting playing with child(ren)
home activity;leisure;activities for maintenance of a household;with children;5170 sitting playing with child(ren)
occupation;interruption;9060 (generic) sitting without observable activities
home activity;child/elderly/pet care;child care;5185 child care sitting/kneeling
home activity;miscellaneous;sitting;21010 sitting non-desk work (with or without eating at the same time)
leisure;eating;not-social;13030 eating sitting indoor/outdoor
leisure;miscellaneous;sitting;5080 sitting non-desk work (with or without eating at the same time)
home activity;leisure;activities for maintenance of a household;9100 retreat/family reunion activities involving sitting eating relaxing talking with more than one person

leisure;miscellaneous;sitting;21016 sitting child care only active periods
 home activity;leisure;activities for maintenance of a household;5170 sitting playing with child(ren)
 home activity;lawn and garden;gardening service;8055 driving tractor
 occupation;interruption;9060 (generic) sitting without observable/identifiable activities
 home activity;self care;13036 taking medication
 leisure;miscellaneous;21000 sitting meeting or talking with others
 home activity;self care;13046 having hair or nails done by someone else sitting
 home activity;household chores;washing/ironing/mending clothes;5080 knitting sewing wrapping presents sitting
 home activity;miscellaneous;sitting;9060 sitting reading or using a mobile phone/smartphone/tablet or talking on the phone/computer (skype chatting)
 leisure;miscellaneous;21010 sitting non-desk work (with or without eating at the same time)
 occupation;interruption;9060 sitting using a mobile phone/smartphone/tablet or talking on the phone/computer (skype meeting etc.)
 leisure;religious activities;20005 sitting in church talking or singing attending a ceremony sitting active
 home activity;child/elderly/pet care;child care;5185 child care sitting/kneeling occasional lifting
 leisure;miscellaneous;21016 sitting child care only active periods
 home activity;miscellaneous;sitting;7021 sitting without observable activities
 home activity;leisure;activities for maintenance of a household;with animals;5190 sitting playing with animals active periods
 transportation;public transportation;16016 riding in a bus or train
 leisure;sports;water activities;18012 boating power passenger

Light physical activity behaviours

home activity;household chores;preparing meals/cooking/washing dishes;5035 kitchen activity general cooking/washing/dishes/cleaning up
 home activity;miscellaneous;walking;17150 walking household without observable loads
 home activity;miscellaneous;walking;5165 (generic) walking non-cleaning task such as closing windows lock door putting away items
 leisure;miscellaneous;walking;21070 (generic) walking and occasional standing (no more than two consecutive images)
 transportation;walking;17161 walking not as the single means of transports e.g.from house to transports or vice versa/from car to places or vice versa/between transports
 leisure;miscellaneous;walking;5060 shopping miscellaneous
 occupation;interruption;11791 walking on job in office or lab area
 home activity;miscellaneous;standing;9050 standing talking in person/on the phone/computer (skype chatting) or using a mobile phone/smartphone/tablet
 home activity;household chores;washing/ironing/mending clothes;5090 folding or hanging clothes/put clothes in or out of washer or dryer/packing suitcase limited walking

home activity;miscellaneous;standing;9070 standing reading or without observable/identifiable activities
occupation;interruption;walking;11791 walking on job in office or lab area
occupation;manufacturing;11115 chef
home activity;self care;13040 (generic) self care such as grooming/washing hands/shaving/brushing teeth/putting on make-up not eliminating and bathing (not necessary in the toilet)
occupation;office and administrative support;11600 (generic) standing tasks such as store clerk/librarian/packing boxes/repair heavy parts
leisure;miscellaneous;5060 shopping miscellaneous
home activity;household chores;washing/ironing/mending clothes;5070 ironing
leisure;miscellaneous;standing;9050 standing talking in person/using a phone/smartphone/tablet
home activity;miscellaneous;walking;5147 walking moving away light items (pens/papers/keys not included)
occupation;miscellaneous;11475 (generic) manual labour
occupation;interruption;standing;9050 standing talking in person/using a phone/smartphone/tablet
occupation;personal services;11413 kitchen maid
home activity;household chores;grocery shopping;5060 shopping
home activity;home repair;indoor;6126 home repair miscellaneous
leisure;miscellaneous;standing;9070 standing reading or without observable/identifiable activities
transportation;waiting;7040 standing in a line
home activity;child/elderly/pet care;child care;5185 child care sitting/kneeling occasional lifting
home activity;miscellaneous;standing;9071 (generic) standing miscellaneous
leisure;miscellaneous;standing;9071 (generic) standing miscellaneous
occupation;interruption;standing;9070 standing reading or without observable/identifiable activities
home activity;miscellaneous;standing;9020 standing writing/drawing/painting
home activity;leisure;individual activities;10074 playing musical instruments
occupation;interruption;5041 kitchen activity in the working place
home activity;miscellaneous;walking;17140 using crutches or frame
occupation;interruption;9050 standing talking in person/using a phone/smartphone/tablet
home activity;leisure;individual activities;9085 standing arts and crafts/sand painting/carving weaving
home activity;miscellaneous;5025 (generic) multiple household tasks all at once including standing/lifting/sitting
home activity;miscellaneous;standing;9070 standing reading or without obvious activities
home activity;household chores;washing/ironing/mending clothes;5095 putting away /gathering clothes involving walking
home activity;lawn and garden;lawn care service;8135 planting potting transplanting seedlings or plants

occupation;interruption;standing;9071 (generic) standing miscellaneous
transportation;walking;9050 standing miscellaneous (talking to others etc.)
occupation;interruption;miscellaneous;5041 kitchen activity in the working place
home activity;household chores;house cleaning;miscellaneous;5100 making bed/changing linens
occupation;interruption;standing;9015 standing scanning documents
home activity;household chores;house cleaning;furniture;5032 dusting or polishing furniture
home activity;eating;13035 eating standing alone or with others
occupation;miscellaneous;11870 working in scene shop theatre actor backstage employee
occupation;office and administrative support;11600 (generic) standing tasks such as store clerk/librarian/packing boxes/repair heavy parts
home activity;miscellaneous;standing;9050 standing talking in person on the phone/computer (skype chatting) or using a mobile phone/smartphone/tablet
home activity;household chores;house cleaning;floors;5010 cleaning sweeping carpet or floors
leisure;sports;ball games;15090 bowling
home activity;self care;13020 dressing/undressing
occupation;interruption;9070 standing reading or without observable/identifiable activities
leisure;music playing;10074 playing musical instruments
home activity;home repair;indoor;6205 sharpening tools
home activity;home repair;indoor;6124 hammering nails
home activity;child/elderly/pet care;child care;5186 child care standing occasional lifting
occupation;interruption;13035 eating standing
home activity;child/elderly/pet care;pet care;5197 household animal care aside from feeding
leisure;recreation;outdoor;5171 standing playing with child(ren)
occupation;interruption;miscellaneous;13009 toilet break
home activity;household chores;house cleaning;miscellaneous;5148 watering plants
occupation;miscellaneous;11475 (generic) manual or unskilled labour
occupation;interruption;standing;9020 standing writing/drawing/painting
leisure;eating;social;13035 eating standing indoor/outdoor
home activity;household chores;house cleaning;floors;5131 scrubbing floors on hands and knees scrubbing bathroom bathtub
occupation;public admin/education/health;education;09071 teaching standing
home activity;household chores;preparing meals/cooking/washing dishes;5051 serving food/setting table implied walking and standing
home activity;household chores;preparing meals/cooking/washing dishes;5035 cleaning up table after meal implied walking (e.g. leaving from eating table to the kitchen)

leisure;eating;not-social;5060 buying foods or drinks as a takeaway
leisure;miscellaneous;21070 (generic) walking/standing combination indoor
home activity;self care;13009 toilet eliminating or squatting
home activity;self care;13045 hairstyling standing
home activity;lawn and garden;gardening service;8230 watering garden
occupation;interruption;13009 toilet break
leisure;miscellaneous;standing;9070 standing reading or without obvious activities
home activity;leisure;activities for maintenance of a household;miscellaneous;9101 retreat/family reunion activities playing games with more than one person
occupation;interruption;9015 standing scanning documents
home activity;child/elderly/pet care;child care;5183 standing holding child
occupation;interruption;9070 standing reading or without obvious activities
leisure;miscellaneous;standing;9020 standing writing/drawing/painting
leisure;religious activities;20039 walking/standing combination for religious purposes usher
leisure;recreation;indoor;9020 drawing writing painting standing
leisure;miscellaneous;21017 standing child care only active periods
home activity;child/elderly/pet care;pet care;5053 feeding household animals
leisure;eating;13035 eating standing indoor/outdoor
leisure;miscellaneous;9071 (generic) standing miscellaneous indoor or outdoor
leisure;sports;conditioning;2115 upper body exercise arm ergometer
occupation;interruption;standing;9050 standing talking in person/using a phone/smartphone/tablet
home activity;self care;13000 getting ready for bed standing
leisure;eating;social;5060 buying foods or drinks as a takeaway
home activity;home repair;indoor;5160 standing light effort tasks
transportation;walking;9071 standing miscellaneous (talking to others etc.)
occupation;interruption;standing;13035 eating standing
occupation;interruption;9020 standing writing/drawing/painting
home activity;lawn and garden;gardening service;8220 walking applying fertilizer or seeding a lawn push applicator
leisure;eating;5060 buying foods or drinks as a takeaway
leisure;religious activities;20030 standing talking in church
leisure;eating;not-social;13035 eating standing indoor/outdoor

occupation;public admin/education/health;education;9071 teaching standing
home activity;household chores;washing/ironing/mending clothes;5082 sewing with a machine

Moderate-to-vigorous physical activity behaviours

transportation;private transportation;1010 bicycling
transportation;walking;17165 walking the dog
occupation;interruption;17133 walking upstairs
leisure;miscellaneous;walking;17031 loading /unloading a car implied walking
home activity;child/elderly/pet care;child care;5181 walking and carrying child
home activity;lawn and garden;gardening service;8050 digging spading filling garden compositing
leisure;sports;miscellaneous;17082 hiking or walking at a normal pace through fields and hillsides
home activity;lawn and garden;tree and shrub service;8025 clearing light brush thinning garden
home activity;lawn and garden;lawn care service;8165 raking lawn
occupation;interruption;walking;11795 walking on job and carrying light objects such as boxes or pushing trolleys
leisure;sports;water activities;18070 canoeing/rowing
home activity;lawn and garden;lawn care service;8080 laying crushed rock
leisure;sports;gymnasium and athletics;athletics;12150 running
leisure;sports;ball games;15235 football or baseball playing catch
home activity;miscellaneous;standing;5146 standing packing/unpacking household items occasional lifting
home activity;lawn and garden;gardening service;8245 gardening/picking up fruits vegetables flowers
leisure;miscellaneous;walking;17105 pushing a wheelchair non-occupational
leisure;sports;ball games;15680 tennis doubles
home activity;lawn and garden;gardening service;8192 shovelling dirt or mud
leisure;sports;miscellaneous;17082 hiking or walking at a normal pace through fields and hillsides
leisure;dancing;3010 ballet modern or jazz general rehearsal or class
leisure;sports;conditioning;2060 health club exercise
leisure;sports;ball games;15690 tennis singles
home activity;lawn and garden;lawn care service;8095 mowing lawn
occupation;public admin/education/health;health;11615 nursing patient care

occupation;miscellaneous;11615 (generic) standing lifting items continuously with limited walking
leisure;miscellaneous;17031 loading /unloading a car implied walking
leisure;sports;conditioning;2019 bicycling stationary RPM/Spin bike class
home activity;leisure;activities for maintenance of a household;with animals;5192 walking/running playing with animals active periods
home activity;lawn and garden;gardening service;8192 shoveling dirt or mud
home activity;household chores;house cleaning;furniture;5020 cleaning heavy such as car/windows/garage
leisure;sports;conditioning;2048 elliptical trainer
occupation;interruption;11795 walking on job and carrying light objects such as boxes or pushing trolleys
leisure;sports;conditioning;2050 resistance training
leisure;sports;conditioning;2070 rowing stationary ergometer
leisure;recreation;outdoor;5175 walking/running playing with child(ren)
leisure;sports;conditioning;2010 bicycling stationary
leisure;sports;conditioning;2120 water aerobics water calisthenics water exercise
home activity;home repair;outdoor;6020 automobile body work
occupation;agriculture/forestry/fishing;11192 taking care of animals
leisure;miscellaneous;standing;21017 standing child care only active periods
leisure;sports;conditioning;2065 stair-treadmill ergometer general
home activity;household chores;washing/ironing/mending clothes;5092 washing clothes by hand (with or without hanging wash)
leisure;miscellaneous;walking;17133 walking upstairs
transportation;walking;12150 running
occupation;interruption;walking;17070 walking downstairs
home activity;household chores;house cleaning;floors;5140 sweeping garage sidewalk or outside of house
occupation;interruption;walking;17133 walking upstairs
occupation;agriculture/forestry/fishing;11540 shovelling digging ditches
occupation;construction;11050 carrying heavy loads
transportation;walking;17250 walking as the single means to a destination not to work or class
leisure;miscellaneous;walking;17070 descending stairs
home activity;miscellaneous;walking;5121 walking with moving and lifting loads such as bikes and furniture
transportation;walking;17270 walking as the single means to work or class (not from)

Supplementary Table 2: Features of accelerometry signal used for behaviour classification.

Feature	Description
enmoTrunc	Euclidean Norm Minus One truncated below at 0
mean	Mean
sd	Standard Deviation
coefvariation	Coefficient of Variation
median	Median
min	Minimum
max	Maximum
25thp	25 th percentile
75thp	75 th percentile
autocorr	Autocorrelation
fmax	Frequency of signal with highest power
pmax	Maximal power of signal
fmaxband	Frequency of signal with highest power between 0.3 and 3 Hz
pmaxband	Maximal power of signal between 0.3 and 3 Hz
entropy	Entropy
fft1	Power at 1Hz
fft2	Power at 2Hz
fft3	Power at 3Hz
fft4	Power at 4Hz
fft5	Power at 5Hz
fft6	Power at 6Hz
fft7	Power at 7Hz
fft8	Power at 8Hz
fft9	Power at 9Hz
fft10	Power at 10Hz
fft11	Power at 11Hz
fft12	Power at 12Hz

Feature	Description
MAD	Mean Amplitude Deviation
MPD	Mean Power Deviation
skew	Skew
kurt	Kurtosis
f1	Frequency of signal with highest power between 0.3 and 15 Hz
p1	Maximal power of signal between 0.3 and 15 Hz
f2	Frequency of signal with second highest power between 0.3 and 15 Hz
p2	Second highest power of signal between 0.3 and 15 Hz
f625	Frequency of signal with highest power between 0.6 and 2.5 Hz
p625	Maximal power of signal between 0.6 and 2.5 Hz
totalPower	Total power for frequencies between 0.3 and 15 Hz
vmfft1	Power at 1/30 Hz
vmfft2	Power at 2/30 Hz
vmfft3	Power at 3/30 Hz
vmfft4	Power at 4/30 Hz
vmfft5	Power at 5/30 Hz
vmfft6	Power at 6/30 Hz
vmfft7	Power at 7/30 Hz
vmfft8	Power at 8/30 Hz
vmfft9	Power at 9/30 Hz
vmfft10	Power at 10/30 Hz
vmfft11	Power at 11/30 Hz
vmfft12	Power at 12/30 Hz

Supplementary Table 3: Definition of variables from UK Biobank data included in statistical models.

Characteristic	Source	Notes	UK Biobank field	Coding
OUTCOME				
Age at first cardiovascular disease event	Death Registry, HES.	First appearance of ICD-10 codes I20-25 (ischaemic heart disease) or I60-69 (cerebrovascular disease) in either HES or death register data.	Derived from Category 100093, Category 2000.	
Age at loss-to-follow-up	Death Registry.	Earliest of: date of latest study data available and date of non-cardiovascular disease death.	Derived from Category 100093.	
EXPOSURE				
Sleep	Accelerometry.	Derived using machine-learning methods described in main text.	Derived from 90001.	
Sedentary behaviour	Accelerometry.	Derived using machine-learning methods described in main text.	Derived from 90001.	
Light physical activity behaviours	Accelerometry.	Derived using machine-learning methods described in main text.	Derived from 90001.	
Moderate-to-vigorous physical activity behaviours	Accelerometry.	Derived using machine-learning methods described in main text.	Derived from 90001.	
EXCLUSION VARIABLES – MAIN ANALYSIS				
Prior HES-recorded cardiovascular disease	HES.	Appearance of ICD-10 codes I20-25 (ischaemic heart disease) or I60-69 (cerebrovascular disease) or ICD-9 codes 410 – 414 or 430 – 438 in HES data prior to accelerometer wear.	Derived from Category 2000.	

Characteristic	Source	Notes	UK Biobank field	Coding
Prior self-reported cardiovascular disease	Baseline.	Self-reported heart attack or stroke.	Derived from 6150.	
ADJUSTMENT VARIABLES – MAIN ANALYSIS				
Age	Baseline.	Age used as the timescale in Cox regression analysis; participants entered study at the end of accelerometer wear.	Derived from 90011, 34, 52.	
Sex	Baseline.	Used to stratify analysis.	31	Female, Male.
Ethnicity	Baseline.		Derived from 21000.	Asian, Black, Other, White. (Categorised as in Resource 100336; Other includes Mixed, Chinese and Other due to small numbers).
Smoking status	Baseline.		20116	Never smoker, Ex-smoker, Current smoker.
Frequency of alcohol consumption	Baseline.		Derived from 1558.	Never, <3 times/week, 3+ times/week.
Education	Baseline.		Derived from 6138.	School leaver, Further education (education beyond O-Levels/CSEs, excluding college/ university degree) and Higher education (college/university degree).
Townsend Deprivation Index	Baseline.	Townsend Deprivation Index of address at time of UKB baseline assessment.	Derived from 189.	Divided by quartile in the study population.
Daily servings of fresh fruit and vegetables.	Baseline.		Derived from 1289, 1299, 1309.	Less than one coded as 0·5, then sum of 1289, 1299, 1309. Categorised as < 3, 3-4·9, 5-7·9, 8+ servings/ day.

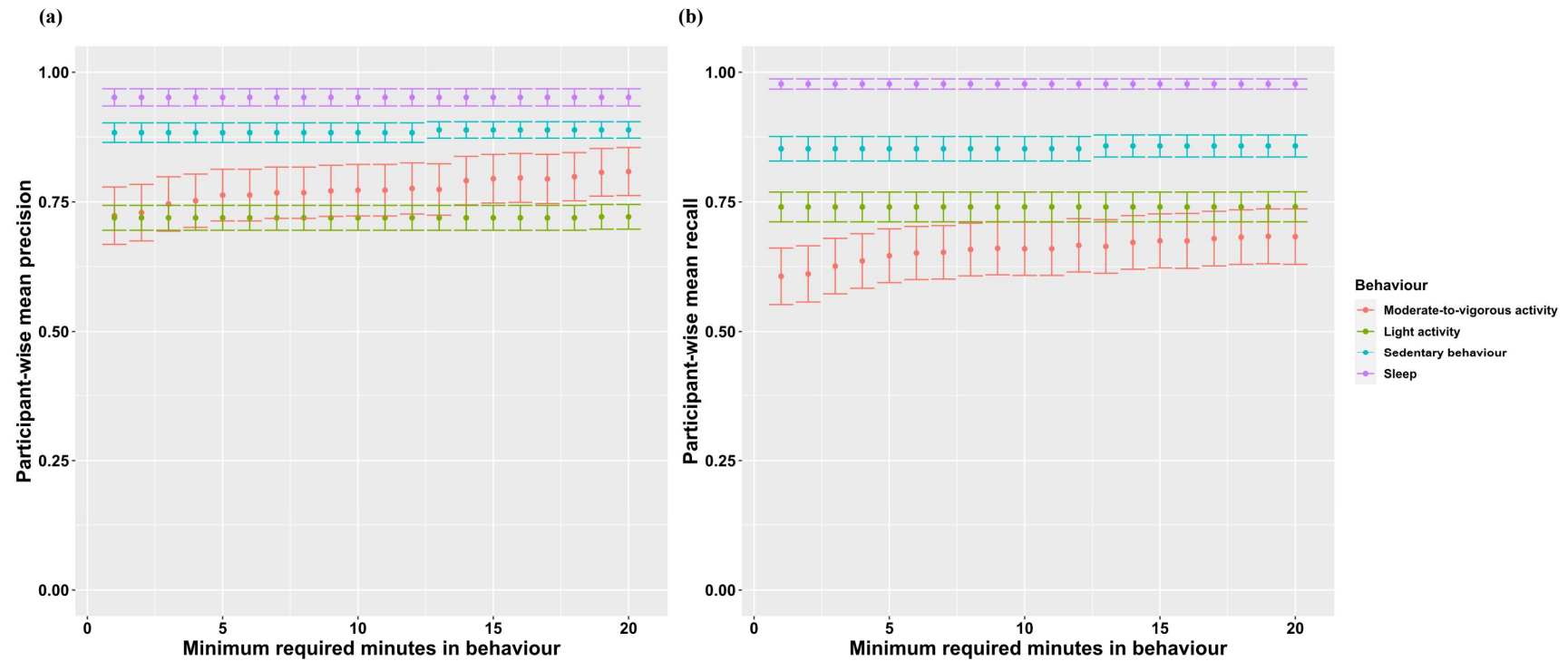
Characteristic	Source	Notes	UK Biobank field	Coding
Frequency of red and processed meat consumption.	Baseline.		Derived from 1369, 1379, 1389, 1349.	Less than one coded as 0·5, then sum of 1369, 1379, 1389. Categorised as <1, 1-2·9, 3-4·9, 5+ times/ week.
Frequency of oily fish consumption.	Baseline.		Derived from 1329.	< 1, 1, 2-4, >4 times/week.
ADJUSTMENT VARIABLES – ADDITIONAL				
BMI	Baseline.		Derived from 21001.	For descriptive analyses: Underweight (<18·5kgm ⁻²), Normal weight (18·5 -24·9 kgm ⁻²), Overweight (25 -29·9 kgm ⁻²), Obese (30+ kgm ⁻²). For BMI-stratified analysis, Underweight and Normal weight categories combined.
EXCLUSION VARIABLES – SENSITIVITY ANALYSIS FOR REVERSE CAUSALITY				
Medication for diabetes, cholesterol or blood pressure	Baseline.		Derived from 6177, 6153.	
Self-reported overall health rating	Baseline.		2178	
Prior primary admission for disease of the circulatory system.	HES.	Hospital admission with primary diagnosis of I00-I99 before accelerometer wear.	Derived from Category 2000.	
NEGATIVE CONTROL OUTCOME – SENSITIVITY ANALYSIS FOR RESIDUAL CONFOUNDING				
Age at first accident unrelated to movement behaviour.	Death Registry, HES.	First appearance of ICD-10 codes V00-09, V20-99, W20-W99, X00-X59.	Derived from Category 100093, Category 2000.	
Age at loss-to-follow-up	Death Registry.	Earliest of: date of latest study data available and date of death.	Derived from Category 100093.	

Characteristic	Source	Notes	UK Biobank field	Coding
Prior HES-recorded accident unrelated to movement behaviour.	HES.	First appearance of ICD-10 codes V00-09, V20-99, W20-W99, X00-X59.	Derived from Category 2000.	

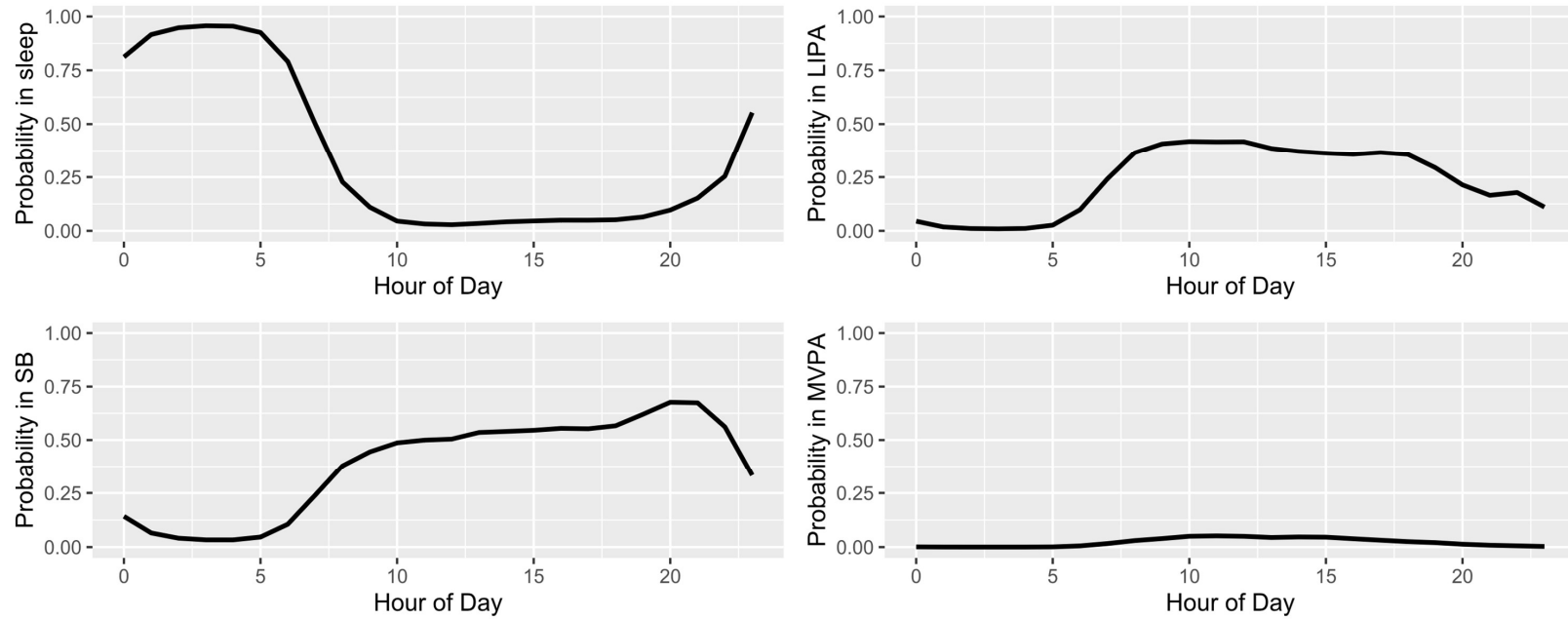
Supplementary Table 4: Characteristics of CAPTURE-24 participants.

	n (%)
Overall	152
Age, years	
18-29	39 (26)
30-39	41 (27)
40-49	24 (16)
50-59	21 (14)
60-69	17 (11)
70-79	7 (5)
80-91	2 (1)
Not recorded	1 (1)
Sex	
Female	99 (65)
Male	53 (35)

Supplementary Figure 1: Participant-wise mean (a) precision and (b) recall for classification of behaviours from accelerometer data calculated in Leave-One-Participant-Out Cross-Validation (with 95% confidence interval for the mean). The x-axis gives the minimum required recorded annotator-labelled time in the behaviour for inclusion in the calculation. For precision, participants with no model-labelled time in the behaviour were also excluded as precision is undefined in this case.



Supplementary Figure 2: Probability of being in sleep, sedentary behaviour (SB), light physical activity behaviours (LIPA) and moderate-to-vigorous physical activity behaviours (MVPA) among 87,498 UK Biobank participants according to machine-learned behaviour classification by hour of the day.



Supplementary Table 5: Coefficient of first isometric log-ratio pivot coordinate^a for each movement behaviour estimated using a multivariable-adjusted Compositional Data Analysis Cox regression model.

Movement behaviour variable	$exp(\hat{\beta})$ (95% CI)
Pivot coordinate: Sleep vs All other behaviours	0.88 (0.75, 1.02)
Pivot coordinate: SB vs All other behaviours	1.38 (1.22, 1.57)
Pivot coordinate: LIPA vs All other behaviours	0.96 (0.88, 1.06)
Pivot coordinate: MVPA vs All other behaviours	0.86 (0.84, 0.88)

^aSee **Supplementary Methods**. Model based on 4,105 events in 87,498 participants. Model used age as the timescale, was stratified by sex and was additionally adjusted for ethnicity, smoking status, alcohol consumption, fresh fruit and vegetable consumption, red and processed meat consumption, oily fish consumption, deprivation and education.

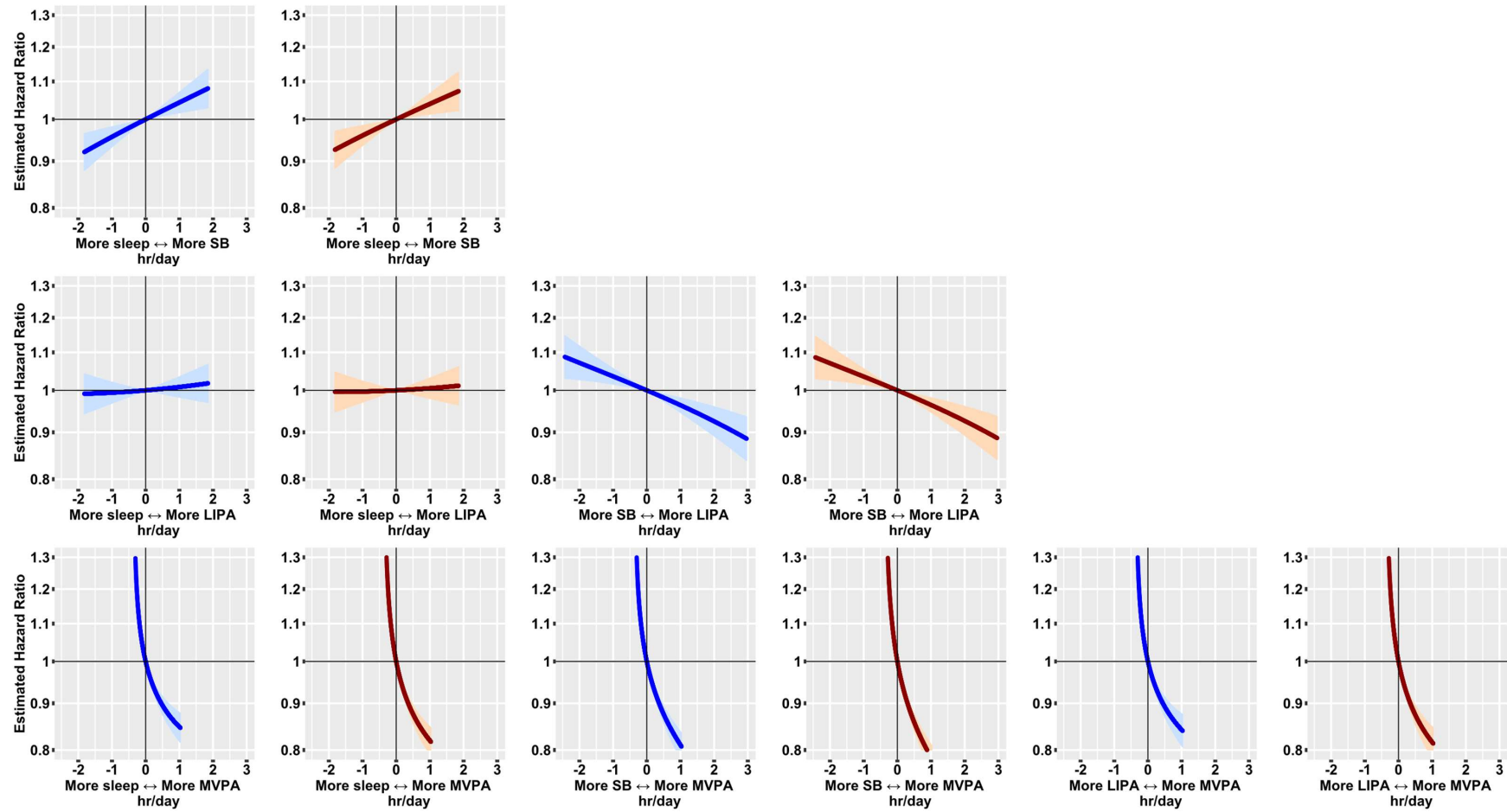
Supplementary Table 6: Coefficient of first isometric log-ratio pivot coordinate for each movement behaviour estimated using all Compositional Data Analysis Cox regression models.^a

Movement behaviour variable	Main analysis	Minimally adjusted	Additionally stratified by BMI	Fatal events	Women only	Men only
Pivot coordinate: sleep vs All other behaviours	0.88 (0.75, 1.02)	0.90 (0.77, 1.05)	0.90 (0.77, 1.05)	0.79 (0.48, 1.29)	0.78 (0.60, 1.02)	0.93 (0.77, 1.13)
Pivot coordinate: SB vs All other behaviours	1.38 (1.22, 1.57)	1.37 (1.21, 1.56)	1.29 (1.13, 1.46)	2.13 (1.40, 3.22)	1.57 (1.28, 1.94)	1.28 (1.09, 1.50)
Pivot coordinate: LIPA vs All other behaviours	0.96 (0.88, 1.06)	0.96 (0.88, 1.06)	0.98 (0.89, 1.08)	0.71 (0.52, 0.95)	0.95 (0.81, 1.11)	0.97 (0.86, 1.09)
Pivot coordinate: MVPA vs All other behaviours	0.86 (0.84, 0.88)	0.84 (0.81, 0.86)	0.88 (0.85, 0.90)	0.85 (0.78, 0.92)	0.85 (0.82, 0.89)	0.86 (0.83, 0.90)

Movement behaviour variable	Main analysis	Under 65s only	Over 65s only	First 2 years of follow-up removed	Follow-up removed + healthy subgroup	Excluding zero values	Negative control: accidents
Pivot coordinate: sleep vs All other behaviours	0.88 (0.75, 1.02)	0.98 (0.75, 1.28)	0.83 (0.69, 1.00)	0.88 (0.73, 1.06)	1.01 (0.77, 1.31)	0.86 (0.73, 1.01)	0.91 (0.69, 1.20)
Pivot coordinate: SB vs All other behaviours	1.38 (1.22, 1.57)	1.17 (0.95, 1.45)	1.52 (1.30, 1.77)	1.33 (1.15, 1.55)	1.09 (0.89, 1.35)	1.38 (1.21, 1.57)	1.09 (0.87, 1.36)
Pivot coordinate: LIPA vs All other behaviours	0.96 (0.88, 1.06)	1.01 (0.86, 1.18)	0.93 (0.82, 1.04)	0.98 (0.88, 1.10)	1.04 (0.88, 1.21)	0.99 (0.89, 1.09)	1.10 (0.93, 1.30)
Pivot coordinate: MVPA vs All other behaviours	0.86 (0.84, 0.88)	0.86 (0.82, 0.91)	0.86 (0.83, 0.89)	0.87 (0.84, 0.90)	0.88 (0.83, 0.92)	0.86 (0.83, 0.89)	0.92 (0.87, 0.97)

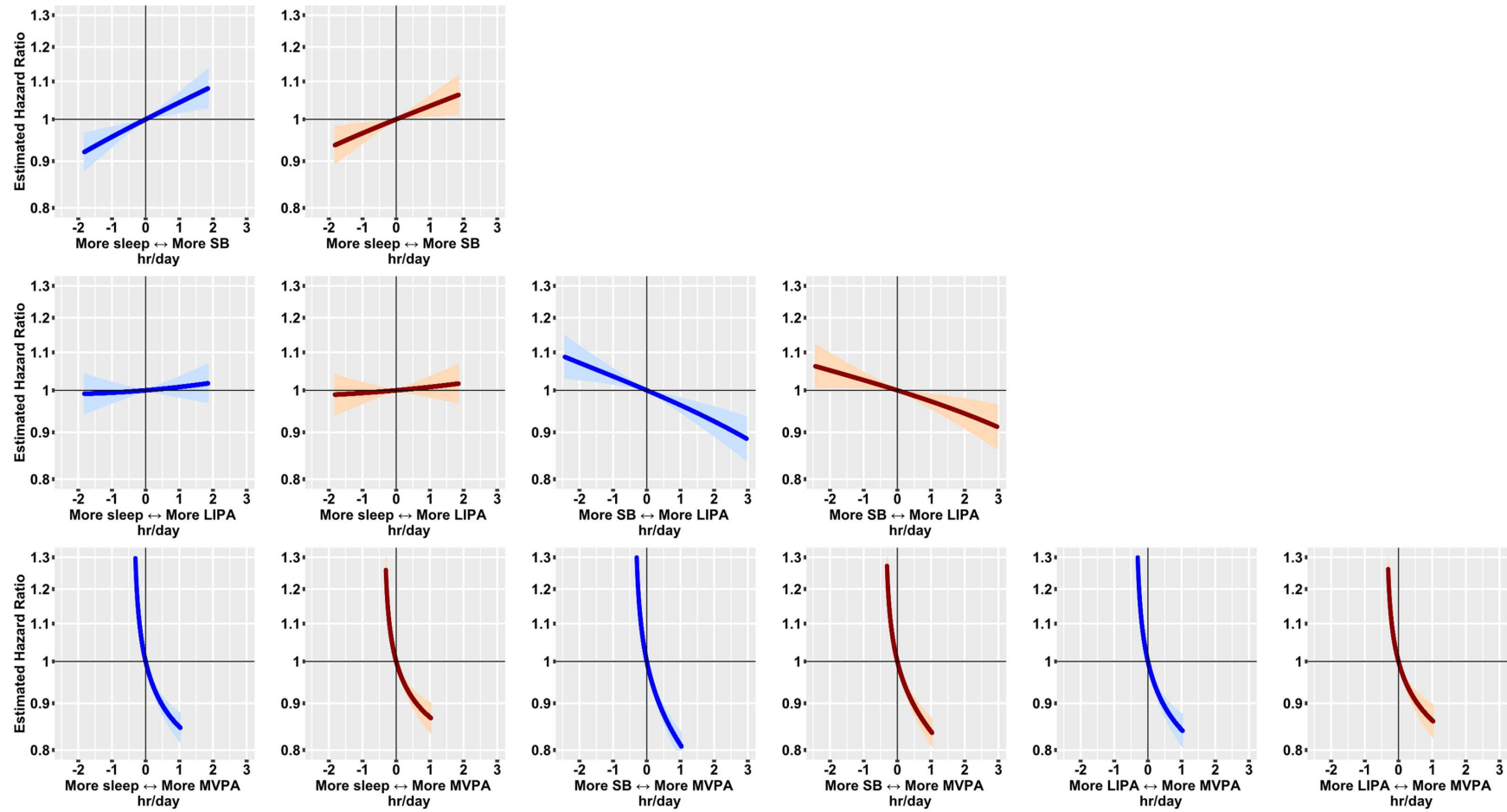
^aSee Methods, Results and Supplementary Figures 3-13 for more details of models. All columns report $\exp(\hat{\beta})$ (95% CI).

Supplementary Figure 3: Hazard Ratios for cardiovascular disease for all behaviour pairs estimated using multivariable-adjusted (blue) and minimally adjusted (red) Cox regression models.^a



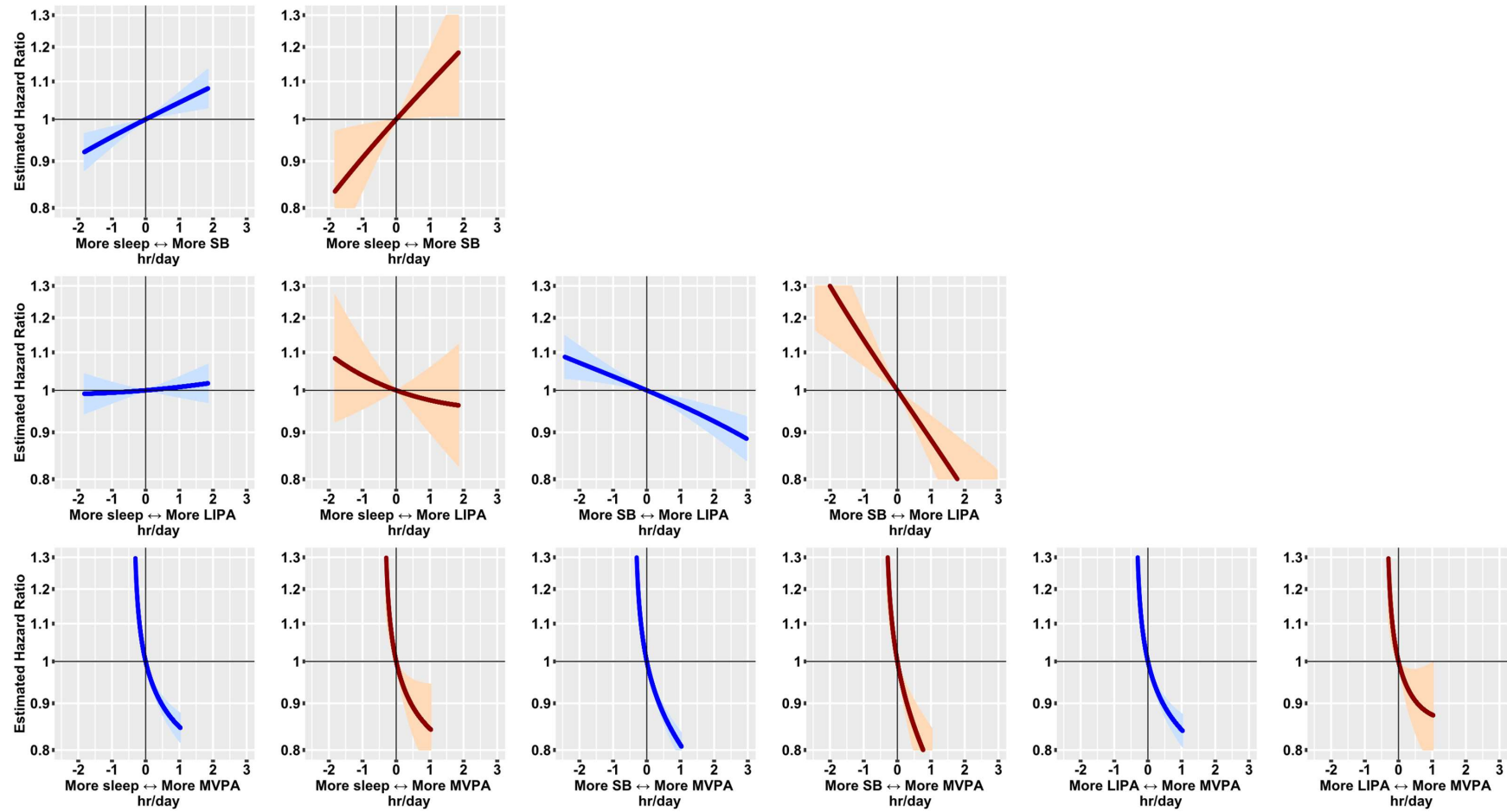
^aModel based on 4,105 events in 87,498 participants. All relative to the mean behaviour composition: 8.8 hours/day sleep, 9.3 hours/day sedentary behaviour, 5.6 hours/day light physical activity behaviours, 0.35 hours/day (21 minutes/day) moderate-to-vigorous physical activity behaviours. Multivariable-adjusted model used age as the timescale, was stratified by sex and was additionally adjusted for ethnicity, smoking status, alcohol consumption, fresh fruit and vegetable consumption, red and processed meat consumption, oily fish consumption, deprivation and education. Minimally-adjusted model used age as the timescale and was stratified by sex.

Supplementary Figure 4: Hazard Ratios for incident cardiovascular disease estimated using a multivariable-adjusted Cox regression model before (blue) and after (red) stratification by BMI.^a



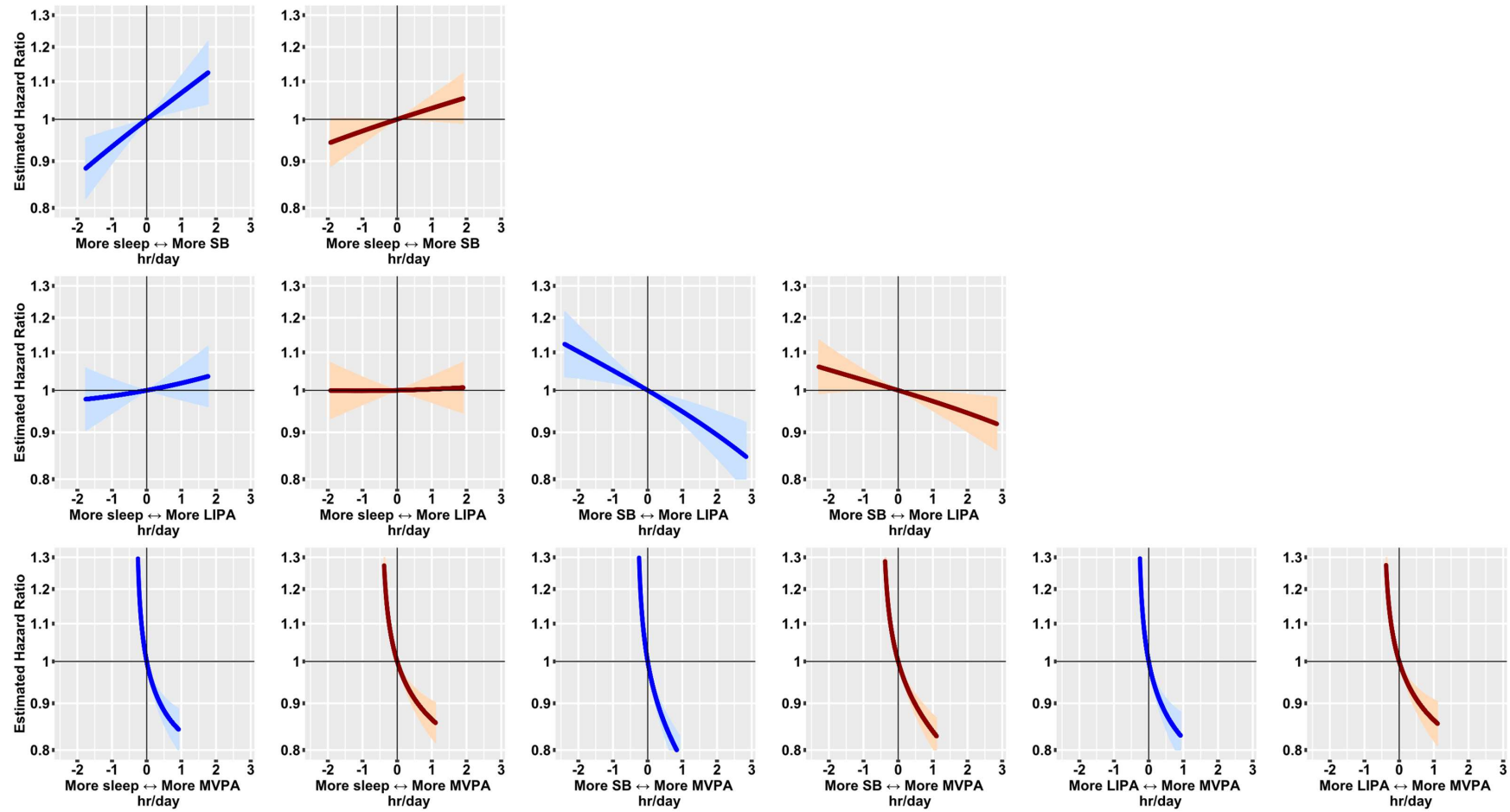
^aModel based on 4,105 events in 87,498 participants. All relative to the mean behaviour composition: 8.8 hours/day sleep, 9.3 hours/day sedentary behaviour, 5.6 hours/day light physical activity behaviours, 0.35 hours/day (21 minutes/day) moderate-to-vigorous physical activity behaviours. Models used age as the timescale, were stratified by sex and were additionally adjusted for ethnicity, smoking status, alcohol consumption, fresh fruit and vegetable consumption, red and processed meat consumption, oily fish consumption, deprivation and education.

Supplementary Figure 5: Hazard Ratios for all (blue) and fatal (red) incident cardiovascular disease for all behaviour pairs estimated using a multivariable-adjusted Cox regression model.^a



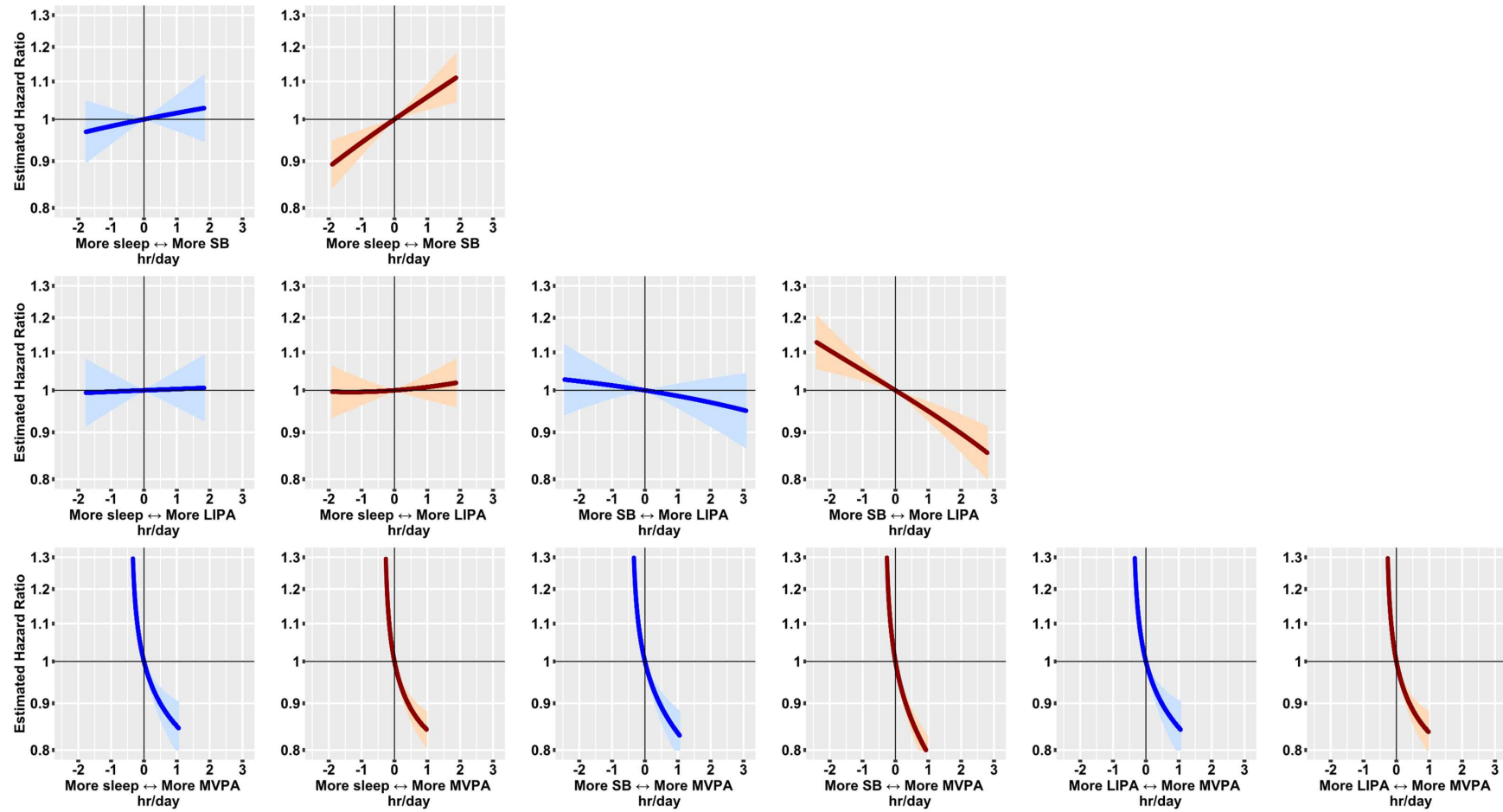
^aModels based on 4,105 events and 348 cardiovascular deaths in 87,498 participants. All relative to the mean behaviour composition: 8.8 hours/day sleep, 9.3 hours/day sedentary behaviour, 5.6 hours/day light physical activity behaviours, 0.35 hours/day (21 minutes/day) moderate-to-vigorous physical activity behaviours. Models used age as the timescale, were stratified by sex and were additionally adjusted for ethnicity, smoking status, alcohol consumption, fresh fruit and vegetable consumption, red and processed meat consumption, oily fish consumption, deprivation and education.

Supplementary Figure 6: Hazard Ratios for incident cardiovascular disease for all behaviour pairs estimated using a multivariable-adjusted Cox regression model for women (blue) and men (red).^a



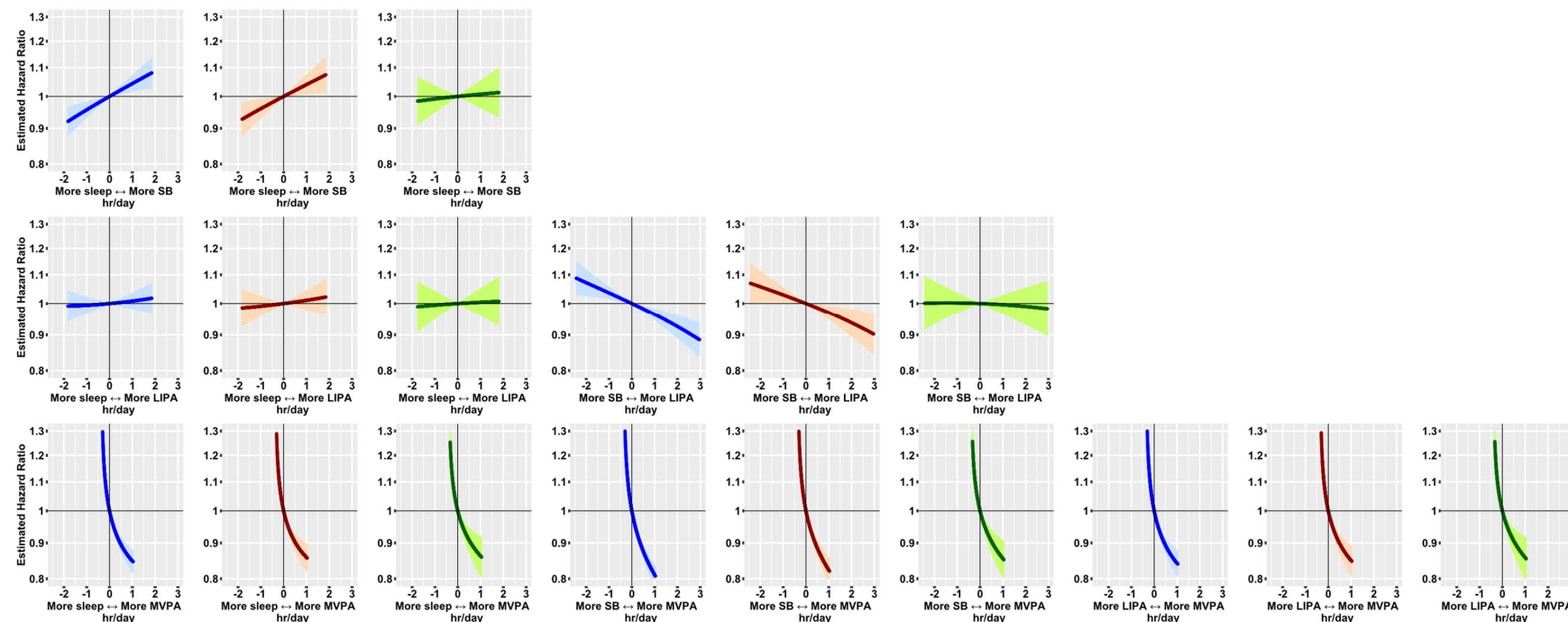
^aModels based on 1,654 events in 50,882 women and 2,451 events in 36,616 men. All relative to the mean behaviour composition in each case (women – 8.9 hours/day sleep, 9.0 hours/day sedentary behaviour, 5.9 hours/day light physical activity behaviours, 0.30 hours/day (18 minutes/day) moderate-to-vigorous physical activity behaviours; men – 8.7 hours/day sleep, 9.7 hours/day sedentary behaviour, 5.1 hours/day light physical activity behaviours, 0.45 hours/day (27 minutes/day) moderate-to-vigorous physical activity behaviours). Models used age as the timescale and were additionally adjusted for ethnicity, smoking status, alcohol consumption, fresh fruit and vegetable consumption, red and processed meat consumption, oily fish consumption, deprivation and education.

Supplementary Figure 7: Hazard Ratios for incident cardiovascular disease for all behaviour pairs estimated using a multivariable-adjusted Cox regression model for participants aged under 65 (blue) and participants aged over 65 (red).^a



^aModels based on 1,425 events in 51,180 participants aged under 65 and 2,680 events in 36,318 participants aged over 65. All relative to the mean behaviour composition in each case (participants aged under 65 – 8.8 hours/day sleep, 9.3 hours/day sedentary behaviour, 5.5 hours/day light physical activity behaviours, 0.39 hours/day (23 minutes/day) moderate-to-vigorous physical activity behaviours; participants aged over 65 – 8.9 hours/day sleep, 9.2 hours/day sedentary behaviour, 5.6 hours/day light physical activity behaviours, 0.30 hours/day (18 minutes/day) moderate-to-vigorous physical activity behaviours). Models used age as the timescale, were stratified by sex and were additionally adjusted for ethnicity, smoking status, alcohol consumption, fresh fruit and vegetable consumption, red and processed meat consumption, oily fish consumption, deprivation and education.

Supplementary Figure 8: Hazard Ratios for incident cardiovascular disease for all behaviour pairs estimated using a multivariable-adjusted Cox regression model (blue), after removing the first two years of follow-up (red) and after additionally restricting to a healthy subgroup (green).^a



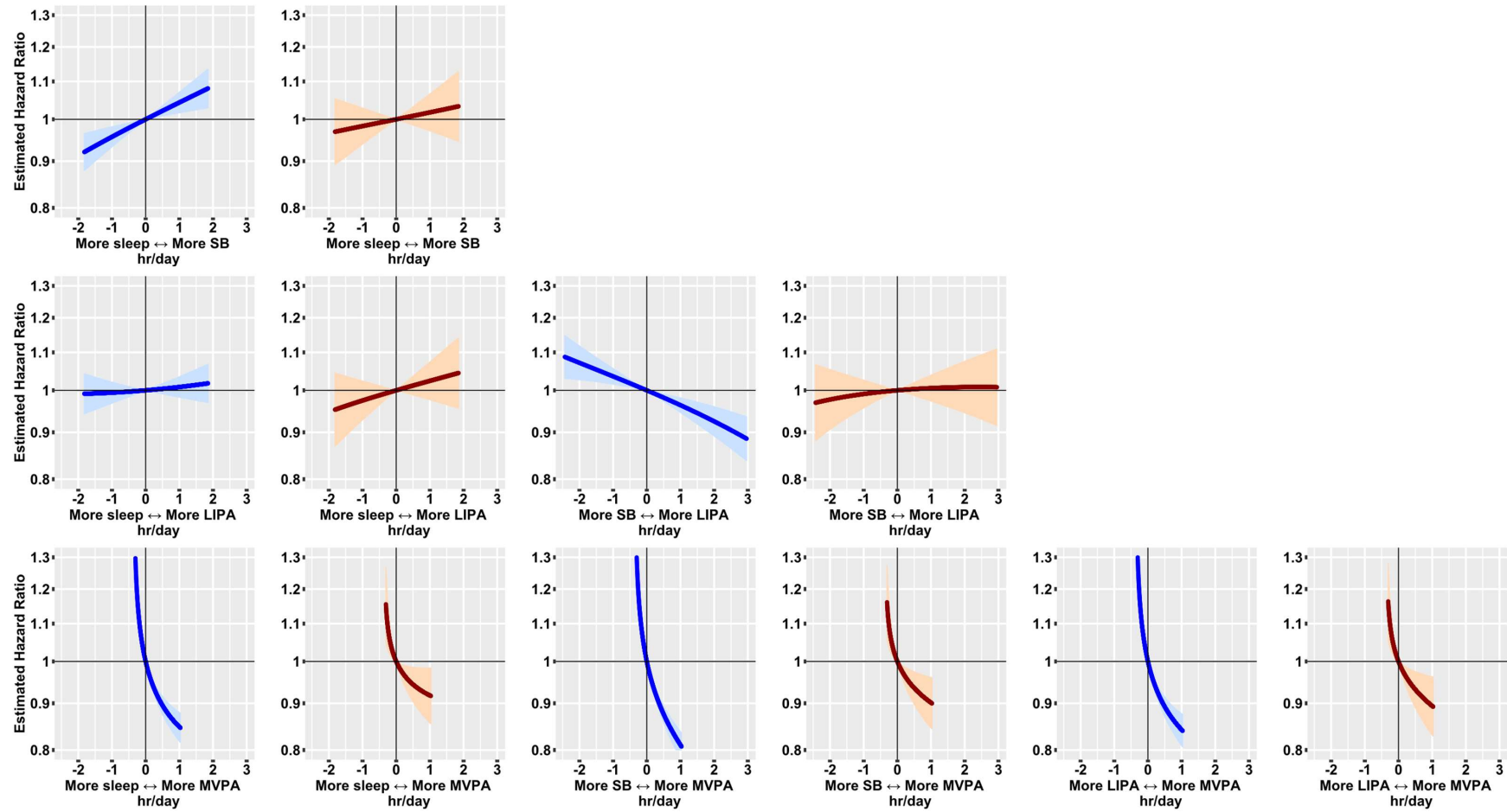
^aMain analysis based on 4,105 events in 87,498 participants. First sensitivity analysis based on 2,947 events in 86,011 participants. Second sensitivity analysis based on 1,597 events in 63,267 participants. Models used age as the timescale, were stratified by sex and were additionally adjusted for ethnicity, smoking status, alcohol consumption, fresh fruit and vegetable consumption, red and processed meat consumption, oily fish consumption, deprivation and education. All values reported relative to the mean behaviour composition in each case:

Main analysis - 8.8 hours/day sleep, 9.3 hours/day sedentary behaviour, 5.6 hours/day light physical activity behaviours, 0.35 hours/day (21 minutes/day) moderate-to-vigorous physical activity behaviours

1st sensitivity - 8.8 hours/day sleep, 9.3 hours/day sedentary behaviour, 5.6 hours/day light physical activity behaviours, 0.35 hours/day (21 minutes/day) moderate-to-vigorous physical activity behaviours

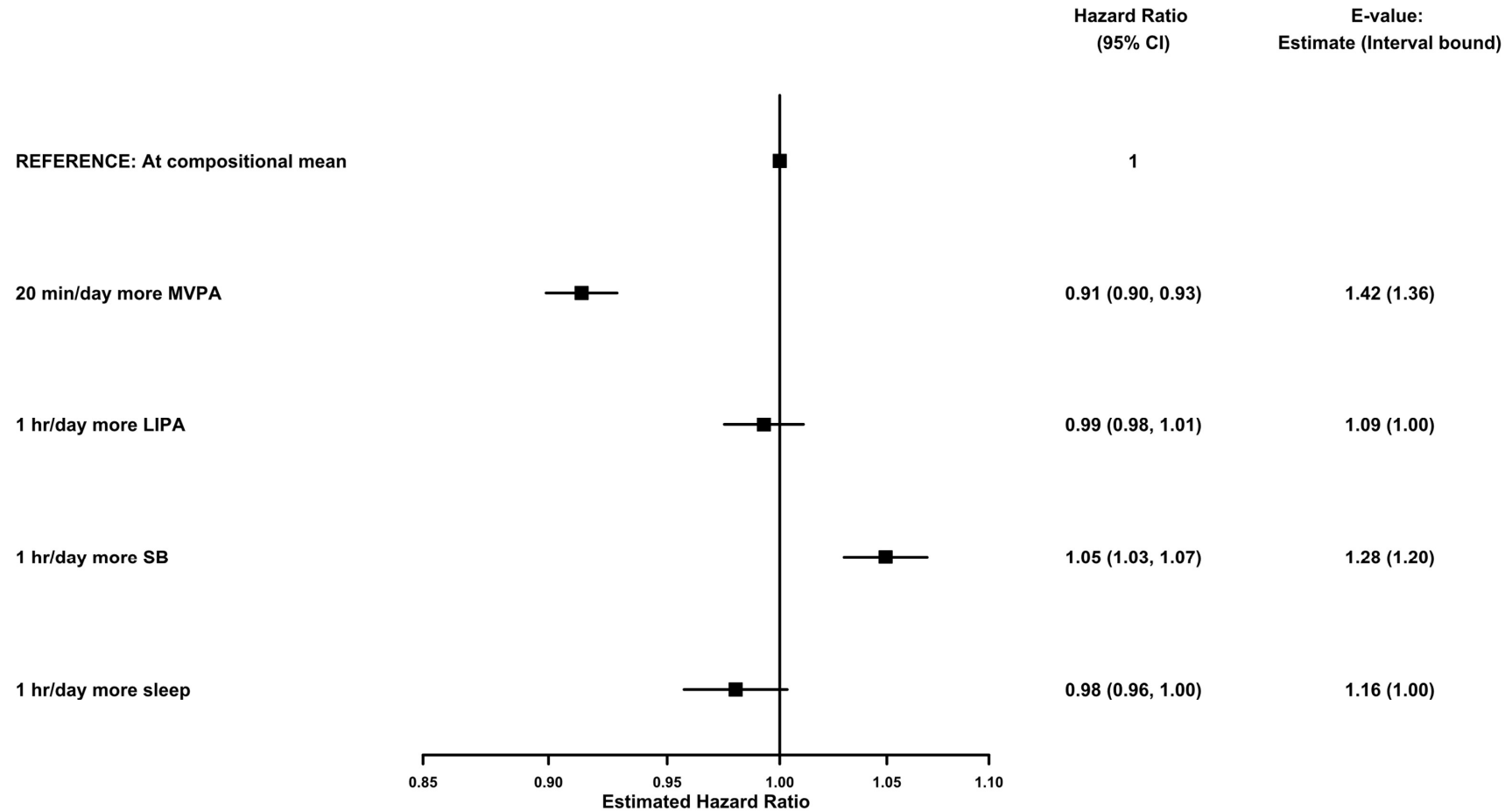
2nd sensitivity - 8.8 hours/day sleep, 9.2 hours/day sedentary behaviour, 5.6 hours/day light physical activity behaviours, 0.39 hours/day (23 minutes/day) moderate-to-vigorous physical activity behaviours.

Supplementary Figure 9: Hazard Ratios for cardiovascular disease (blue) and for non-activity-related accidents (red) for all behaviour pairs estimated using a multivariable-adjusted Cox regression model.^a



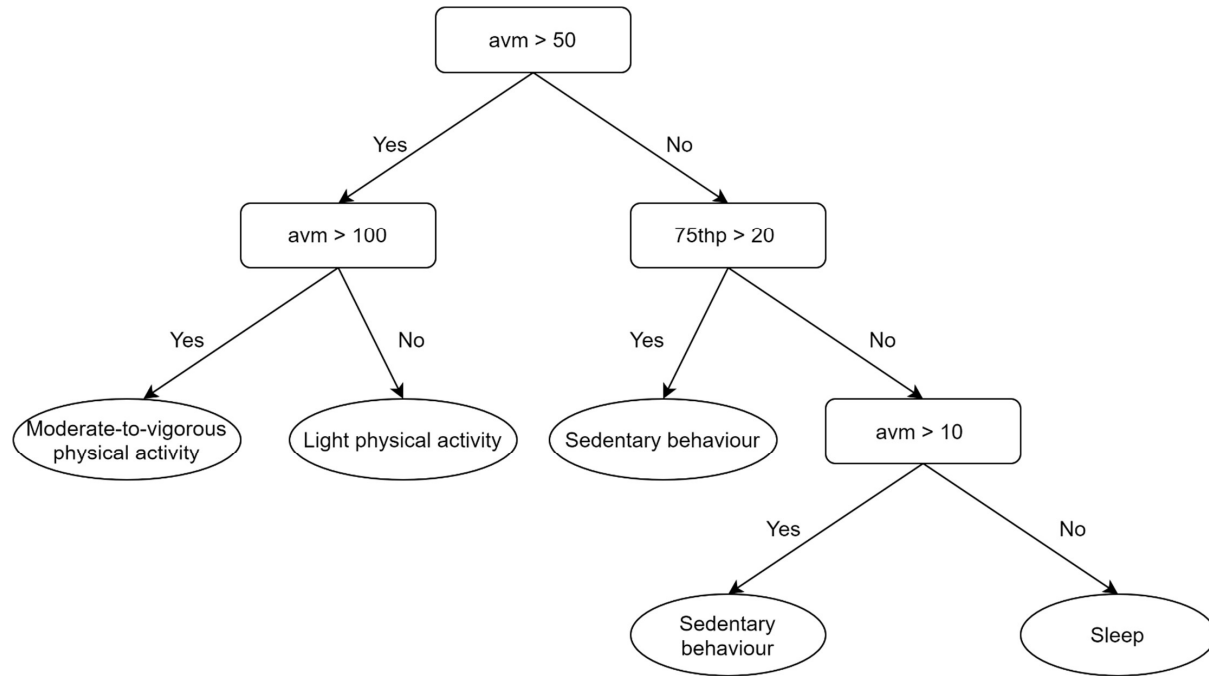
^aMain model based on 4,105 events in 87,498 participants. Negative control model based on 1,375 events in 84,552 participants (participants with prior accident additionally excluded). All relative to the mean behaviour composition in each case (both 8.8 hours/day sleep, 9.3 hours/day sedentary behaviour, 5.6 hours/day light physical activity behaviours, 0.35 hours/day (21 minutes/day) moderate-to-vigorous physical activity behaviours). Models used age as the timescale, were stratified by sex and were additionally adjusted for ethnicity, smoking status, alcohol consumption, fresh fruit and vegetable consumption, red and processed meat consumption, oily fish consumption, deprivation and education.

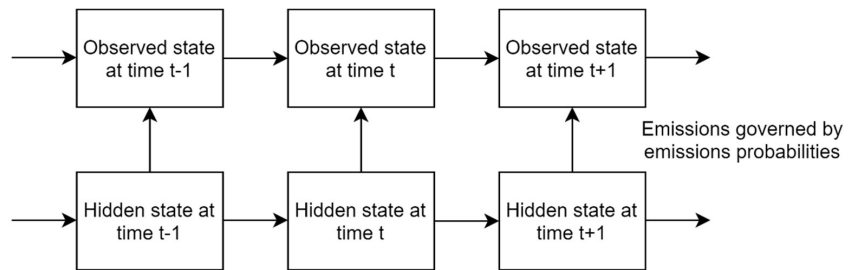
Supplementary Figure 10: Hazard ratios and corresponding E-values for incident cardiovascular disease associated with reallocating time to named behaviour, from all other behaviours proportionally, in 87,498 UK Biobank participants.^a



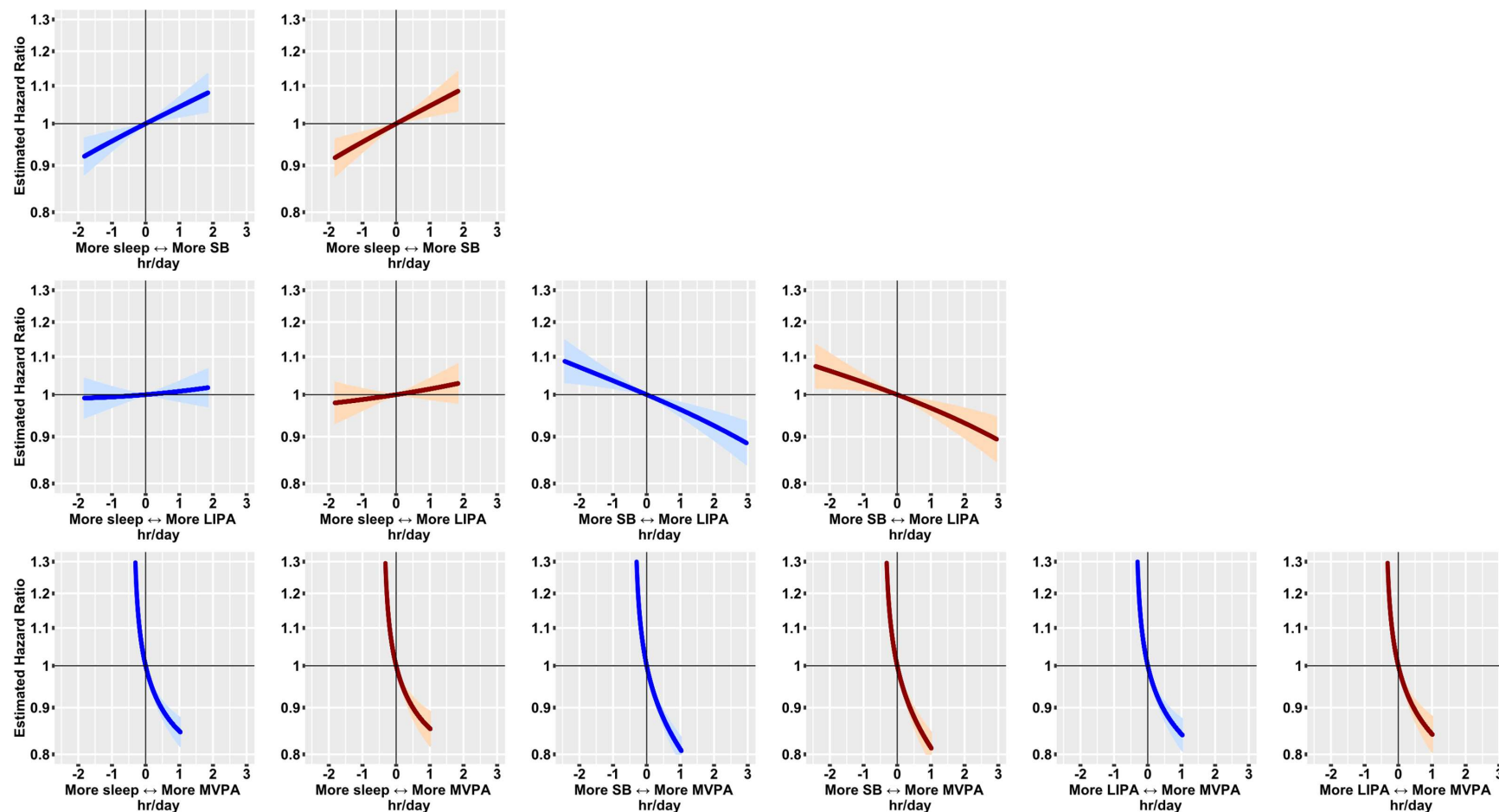
^aModel based on 4,105 events in 87,498 participants. All relative to the mean behaviour composition (8.8 hours/day sleep, 9.3 hours/day sedentary behaviour, 5.6 hours/day light physical activity behaviours, 0.35 hours/day (21 minutes/day) moderate-to-vigorous physical activity behaviours) and more time in named behaviour reallocated from all other behaviours proportionally. Model used age as the timescale, was stratified by sex and was additionally adjusted for ethnicity, smoking status, alcohol consumption, fresh fruit and vegetable consumption, red and processed meat consumption, oily fish consumption, deprivation and education.

Supplementary Figure 11: An example of a decision tree to classify time windows using average acceleration vector magnitude (avm) and the 75th percentile of acceleration vector magnitude (75thp).



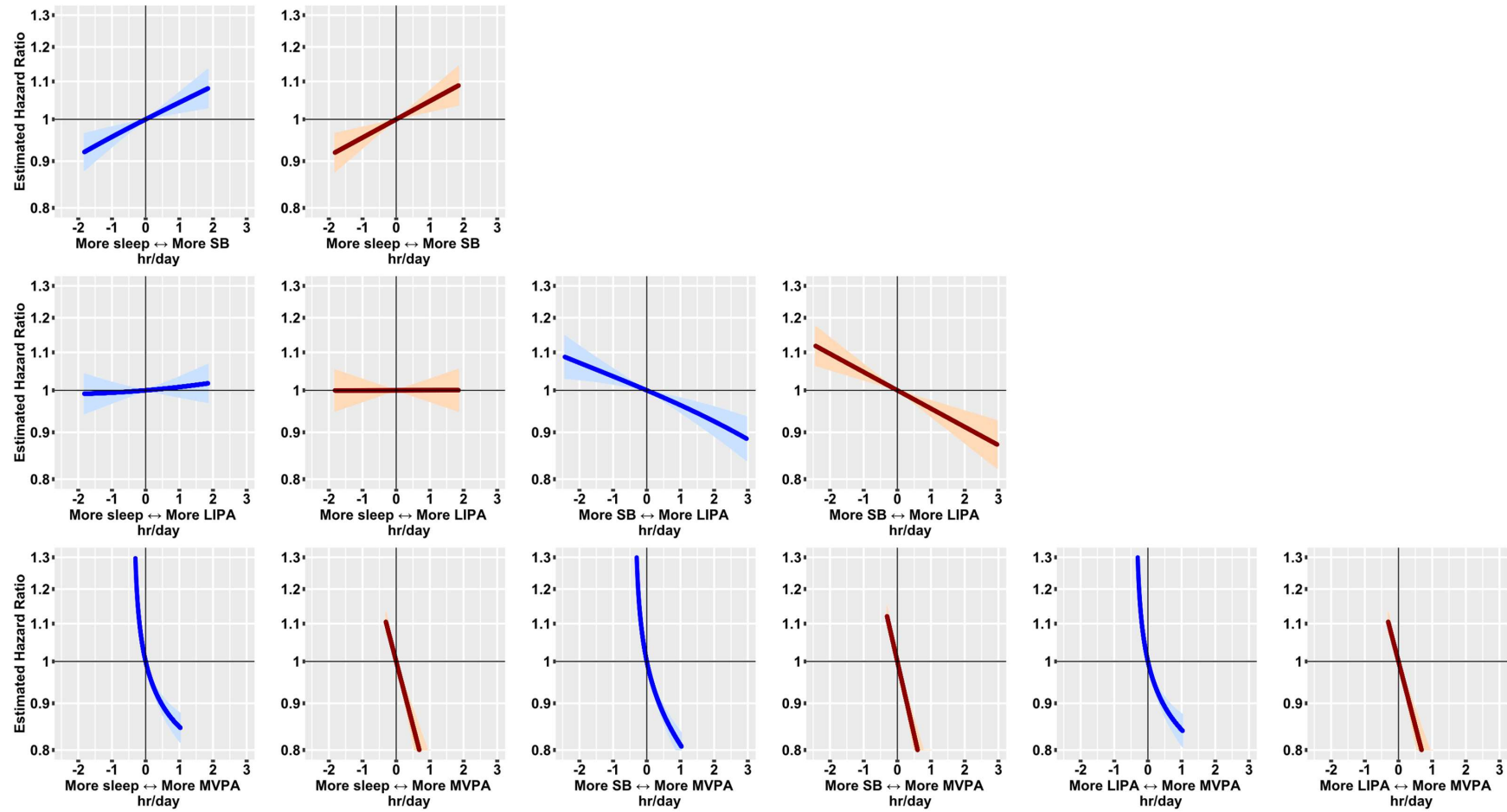
Supplementary Figure 12: The structure of a Hidden Markov Model.

Supplementary Figure 13: Hazard Ratios for incident cardiovascular disease for all behaviour pairs estimated using a multivariable-adjusted Cox regression model for all participants (blue) and in a sensitivity analysis excluding individuals with a zero value in any behaviour (red).^a



^aMain model based on 4,105 events in 87,498 participants. Model excluding individuals with zero values based on 4,017 events in 86,696 participants. All relative to the mean behaviour composition in each case (main analysis – 8.8 hours/day sleep, 9.3 hours/day sedentary behaviour, 5.6 hours/day light physical activity behaviours, 0.35 hours/day (21 minutes/day) moderate-to-vigorous physical activity behaviours; analysis excluding individuals with zero values – 8.8 hours/day sleep, 9.3 hours/day sedentary behaviour, 5.6 hours/day light physical activity behaviours, 0.37 hours/day (22 minutes/day) moderate-to-vigorous physical activity behaviours). Models used age as the timescale, were stratified by sex and were additionally adjusted for ethnicity, smoking status, alcohol consumption, fresh fruit and vegetable consumption, red and processed meat consumption, oily fish consumption, deprivation and education.

Supplementary Figure 14: Hazard Ratios for incident cardiovascular disease estimated using a multivariable-adjusted Compositional Data Analysis Cox regression model (blue) and using a multivariable-adjusted linear isotemporal substitution Cox regression model (red).^a



^aModel based on 4,105 events in 87,498 participants. All relative to the mean behaviour composition: 8.8 hours/day sleep, 9.3 hours/day sedentary behaviour, 5.6 hours/day light physical activity behaviours, 0.35 hours/day (21 minutes/day) moderate-to-vigorous physical activity behaviours. Models used age as the timescale, were stratified by sex and were additionally adjusted for ethnicity, smoking status, alcohol consumption, fresh fruit and vegetable consumption, red and processed meat consumption, oily fish consumption, deprivation and education.

STROBE Statement—Checklist of items that should be included in reports of cohort studies

	Item No	Recommendation	Included
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	Yes
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	Yes
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	Yes
Objectives	3	State specific objectives, including any prespecified hypotheses	Yes, No pre-specified hypotheses
Methods			
Study design	4	Present key elements of study design early in the paper	Yes
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Yes
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	Yes
		(b) For matched studies, give matching criteria and number of exposed and unexposed	NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	Yes
Data sources/measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	Yes
Bias	9	Describe any efforts to address potential sources of bias	Yes
Study size	10	Explain how the study size was arrived at	Yes
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Yes
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	Yes
		(b) Describe any methods used to examine subgroups and interactions	Yes
		(c) Explain how missing data were addressed	Yes
		(d) If applicable, explain how loss to follow-up was addressed	Yes
		(e) Describe any sensitivity analyses	Yes
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Yes
		(b) Give reasons for non-participation at each stage	Yes
		(c) Consider use of a flow diagram	Yes
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Yes
		(b) Indicate number of participants with missing data for each variable of interest	Yes
		(c) Summarise follow-up time (eg, average and total amount)	Yes
Outcome data	15*	Report numbers of outcome events or summary measures over time	Yes
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Yes: confounder-adjusted estimates and estimates adjusted for only age and sex given.
		(b) Report category boundaries when continuous variables were categorized	Yes.
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Not included.
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Yes.
Discussion			
Key results	18	Summarise key results with reference to study objectives	Yes.
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	Yes.
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Yes.
Generalisability	21	Discuss the generalisability (external validity) of the study results	Yes.
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	Yes.

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at <http://www.strobe-statement.org>.

Supplementary Material

Supplementary material for **Reallocation of time between device-measured movement behaviours and risk of incident cardiovascular disease**

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Contents

Supplementary Methods	4
‘Ground truth’ labelling of movement behaviours in image data	4
Machine-learning methods	5
Machine-learning methods: Features	5
Machine-learning methods: Random Forest models	5
Machine-learning methods: Hidden Markov models	5
Machine-learning methods: Evaluation	5
Machine-learning methods: model in participants aged 38 years or older	6
A Compositional Data Analysis approach to movement behaviour data	7
Log-ratio transformation	7
Interpreting isometric log-ratio pivot coordinates	7
Zero values	8
Software	9
Sensitivity analyses: further details on E-values	10
Sensitivity analyses: linear isotemporal substitution	11
References	12
Supplementary Tables and Figures	14
Supplementary Table 1: Assignment of fine-grained camera image annotations from the Compendium of Physical Activities to broad movement behaviour classes.	14
Supplementary Table 2: Features of accelerometry signal used for behaviour classification.	22
Supplementary Table 3: Definition of variables from UK Biobank data included in statistical models.	24
Supplementary Table 4: Characteristics of CAPTURE-24 participants.	28
Supplementary Figure 1: Participant-wise mean (a) precision and (b) recall for classification of behaviours from accelerometer data calculated in Leave-One-Participant-Out Cross-Validation (with 95% confidence interval for the mean). The x-axis gives the minimum required recorded annotator-labelled time in the behaviour for inclusion in the calculation. For precision, participants with no model-labelled time in the behaviour were also excluded as precision is undefined in this case.	29
Supplementary Figure 2: Probability of being in sleep, sedentary behaviour (SB), light physical activity behaviours (LIPA) and moderate-to-vigorous physical activity behaviours (MVPA) among 87,498 UK Biobank participants according to machine-learned behaviour classification by hour of the day.	30
Supplementary Table 5: Coefficient of first isometric log-ratio pivot coordinate ^a for each movement behaviour estimated using a multivariable-adjusted Compositional Data Analysis Cox regression model.	31
Supplementary Table 6: Coefficient of first isometric log-ratio pivot coordinate for each movement behaviour estimated using all Compositional Data Analysis Cox regression models. ^a	32
Supplementary Figure 3: Hazard Ratios for cardiovascular disease for all behaviour pairs estimated using multivariable-adjusted (blue) and minimally adjusted (red) Cox regression models. ^a	33
Supplementary Figure 4: Hazard Ratios for incident cardiovascular disease estimated using a multivariable-adjusted Cox regression model before (blue) and after (red) stratification by BMI. ^a	34
Supplementary Figure 5: Hazard Ratios for all (blue) and fatal (red) incident cardiovascular disease for all behaviour pairs estimated using a multivariable-adjusted Cox regression model. ^a	35
Supplementary Figure 6: Hazard Ratios for incident cardiovascular disease for all behaviour pairs estimated using a multivariable-adjusted Cox regression model for women (blue) and men (red). ^a	36
Supplementary Figure 7: Hazard Ratios for incident cardiovascular disease for all behaviour pairs estimated using a multivariable-adjusted Cox regression model for participants aged under 65 (blue) and participants aged over 65 (red). ^a	37

Supplementary Figure 8: Hazard Ratios for incident cardiovascular disease for all behaviour pairs estimated using a multivariable-adjusted Cox regression model (blue), after removing the first two years of follow-up (red) and after additionally restricting to a healthy subgroup (green). ^a	38
Supplementary Figure 9: Hazard Ratios for cardiovascular disease (blue) and for non-activity-related accidents (red) for all behaviour pairs estimated using a multivariable-adjusted Cox regression model. ^a	39
Supplementary Figure 10: Hazard ratios and corresponding E-values for incident cardiovascular disease associated with reallocating time to named behaviour, from all other behaviours proportionally, in 87,498 UK Biobank participants. ^a	40
Supplementary Figure 11: An example of a decision tree to classify time windows using average acceleration vector magnitude (avm) and the 75 th percentile of acceleration vector magnitude (75thp).	41
Supplementary Figure 12: The structure of a Hidden Markov Model.....	42
Supplementary Figure 13: Hazard Ratios for incident cardiovascular disease for all behaviour pairs estimated using a multivariable-adjusted Cox regression model for all participants (blue) and in a sensitivity analysis excluding individuals with a zero value in any behaviour (red). ^a	43
Supplementary Figure 14: Hazard Ratios for incident cardiovascular disease estimated using a multivariable-adjusted Compositional Data Analysis Cox regression model (blue) and using a multivariable-adjusted linear isotemporal substitution Cox regression model (red). ^a	44
STROBE Statement—Checklist of items that should be included in reports of cohort studies.....	45

Supplementary Methods

'Ground truth' labelling of movement behaviours in image data

As described in the main text, to provide the 'ground truth' labels for machine-learning based behaviour classification, fine-grained behaviour annotations of image data were mapped to sleep, sedentary behaviour, light physical activity behaviours and moderate-to-vigorous physical activity behaviours based on the definition in the main text. In practice, this involved the following steps (the final mapping is given in **Supplementary Table 1**):

1. The fine-grained annotation for sleeping was assigned to sleep.
2. Behaviours at 3 or more METs (Metabolic Equivalent of Task, where 1 MET is energy expenditure in quiet sitting), as described in Compendium of Physical Activities [1], were assigned to moderate-to-vigorous physical activity behaviours.
3. For waking behaviours at <3 METs, if the fine-grained annotation indicated a sitting, lying or reclining posture, the behaviour was assigned to sedentary behaviour.
4. Waking behaviours at <3 METs not assigned to sedentary behaviour were assigned to light physical activity behaviours.
5. All labels were reviewed by two reviewers. Where reviewers agreed the fine-grained annotation was typically used by annotators for behaviours in a different category to the label given, the fine-grained annotation was recoded. This review was performed prior to model training, and no changes were made after results were obtained.

Machine-learning methods

As described in the main text, a Random Forest (RF) with 100 decision trees was developed to classify 30-second time windows as sleep, sedentary behaviour, light physical activity behaviours or moderate-to-vigorous physical activity behaviours using the time and frequency domain features outlined in **Supplementary Table 2**. A Hidden Markov model (HMM) was then employed to use time sequence information to improve on the RF-assigned label sequence. As described in the main text, models were trained using labelled data from the CAPTURE-24 study, in which participants wore wearable cameras and kept time use diaries alongside wearing an accelerometer.

Machine-learning methods: Features

Time windows of acceleration were classified using a list of features (variables) based on features used in the study of Willetts et al (this included time and frequency domain features e.g. mean and kurtosis of the acceleration vector magnitude, and power at different frequencies from the Fast Fourier Transform of acceleration vector magnitude) [2]. In the present study, only rotation-invariant features were used (see **Supplementary Table 2**). This addressed concerns about risk of overfitting and possible time trends in the data driven by sensitivity to device orientation within the wrist strap (orientation became more standardised over 2013-2015).

Machine-learning methods: Random Forest models

Random Forests are based on decision trees. Decision trees assign class labels based on splits of the data using feature value thresholds (as shown in the example in **Supplementary Figure 11**). They can be trained using the Classification and Regression Tree (CART) algorithm [3].

In a RF, many decision trees are used. When training the trees (using the CART algorithm), randomness is introduced by (i) training each tree on a set of data points picked randomly (with replacement) and (ii) at each split node, restricting the choice of splitting feature to a randomly picked subset of features.

To classify a data point using an RF, it is classified by each decision tree. Because they are trained on different subsets of data and use different features, different trees in the RF may classify data points differently. The overall classification given by the RF is the class that is assigned to the data point by the largest number of trees. This approach, whereby multiple randomly-differing instances are used in order to reduce variance on the output, is the technique of bootstrap-aggregating or ‘bagging’ [4].

For this application, a balanced RF was used. The fact some behaviours are much more common than others in the labelled data (e.g. sleep is much more common than moderate-to-vigorous physical activity behaviours) can cause a standard RF, which is trained by picking N examples at random with replacement, to favour assigning common labels at the expense of less common behaviours [2]. Using the balanced RF, if there were n_{rare} examples of the rarest behaviour, n_{rare} examples of each behaviour were picked with replacement to train each tree.

Machine-learning methods: Hidden Markov models

In an HMM, there is a sequence of unobserved hidden states, which is assumed to have the Markov property (i.e. future states only depend on past states through present states). This sequence is governed by transition probabilities, which determine the probability of transitioning between each pair of states. There is a sequence of observed states, which depend probabilistically on the sequence of hidden states (described as ‘emissions’ from the sequence of hidden states; **Supplementary Figure 12**).

Here, the hidden states were the true behaviours, and the emissions were the RF-assigned labels. The Viterbi algorithm, the standard approach to this problem, was used to estimate the most likely true behaviour sequence given the observed sequence of RF-assigned labels [5]. Applying the Viterbi algorithm required estimates of:

1. **Transition probabilities between hidden states:** Transition probabilities between behaviour pairs were estimated using the proportions of transitions that occurred between each behaviour pair in the labelled data.
2. **Emission probabilities of observed states from hidden states:** To estimate emission probabilities, time windows were first classified using out-of-bag predictions from the RF i.e. trees were used to classify data points on which they were not trained. This mimics use on unseen data, without requiring additional data. Emission probabilities were then estimated using the proportions of different pairs of true behaviour and RF out-of-bag estimate.

By using this HMM to estimate the most likely true behaviour sequence given the RF-assigned labels, a more plausible sequence of states was obtained. The HMM re-labelled behaviours which formed unrealistic sequences and were likely to be attributable to misclassification (e.g. short periods of moderate-to-vigorous physical activity behaviours during sleep time). Therefore, compared to the unadjusted RF-assigned labels, the labels after using the HMM gave improved measures of the behaviours of interest for subsequent epidemiological analyses.

Machine-learning methods: Evaluation

All metrics were calculated in Leave-One-Participant-Out Cross-Validation.

Leave-One-Participant-Out Cross-Validation involves, for each participant, a model trained on all other participants’ data (i.e. with this participant’s data left-out). The trained model is then used to label the left-out participant’s data and evaluation metrics are calculated. This is repeated for all participants, and metrics are aggregated or calculated across all participants.

Leave-One-Participant-Out Cross-Validation allows evaluation of the performance of the models on data not used in training, while retaining the maximal amount of data for use in training these models. Moreover, all of the data can then be used to train the final model used for classification.

For model performance, the following evaluation metrics were used:

1. We reported mean per-participant accuracy across all behaviours. This is a simple, intuitive metric of model performance, describing the proportion of 30-second time windows that were correctly classified. Using mean per-participant accuracy, rather than aggregate accuracy over all data, prevents the result being dominated by performance on a few participants with larger amounts of data (important as there may be inter-individual differences in classification performance).
2. We reported mean per-participant Cohen's kappa across all behaviours. This is a metric of interrater reliability. It evaluates how much higher the agreement between two raters (here, annotator-assigned 'ground truth' label and model-assigned label) is than that which would be achieved by chance, given the proportions in each class. It is preferable to accuracy, as it takes into account the proportions in each class (in particular, in data where some classes are dominant, a classifier assigning solely to the dominant classes can achieve high accuracy but not high Cohen's kappa).
3. We reported mean per-participant precision and recall for each behaviour. Precision for a given behaviour is the proportion of examples labelled by the model as that behaviour which are 'true' examples of that behaviour. Recall for a given behaviour is the proportion of 'true' examples of that behaviour labelled as that behaviour. Again, taking the mean across participants prevents performance being dominated by performance on participants with larger amounts of data. However, it also upweights the contribution of individuals with very small amounts of data for a given behaviour. Therefore, precision and recall were additionally calculated after excluding participants with up to 20 minutes in the behaviour.

Taken together, these metrics help to understand the validity of the model as a method to derive measures of movement behaviours for subsequent epidemiological analyses. After applying the model to derive measures of movement behaviours for UK Biobank participants, face validity was assessed by plotting behaviour profiles over the day.

Machine-learning methods: model in participants aged 38 years or older

We also carried out the above steps using only data from participants aged 38 years or older i.e. nearer to the age group represented in the UK Biobank sample. The age group 38+ years was used as this corresponds to the information available in a release version of this dataset.

In Leave-One-Participant-Out analysis, the mean per-participant accuracy was 86% (84, 88) and the mean per-participant Cohen's kappa was 0.79 (0.76, 0.81).

Given the results reported in the main text, showing that the model trained on all participants performed well when restricted to the age group of interest, we used the model trained on all participants for the main classification.

A Compositional Data Analysis approach to movement behaviour data

Log-ratio transformation

A Compositional Data Analysis approach is a set of methods for working with compositional data, based on the use of log-transformed ratios to describe the data [6–8]. Ratios between behaviours are used to describe compositional data as they capture the relative values of the different behaviours. Log-transforming ratios ensures the relationships and distances between different compositions are well-described: using log-transformed ratios is equivalent to working with compositional data in a ‘natural’ space for it, with operations which map compositions to genuine compositions and an appropriate distance metric [9,10]. For statistical purposes, log-transformed ratios are also typically more conveniently distributed than ratios [11].

While many different sets of log-transformed ratios can be used, isometric log-ratio pivot coordinates are widely used in movement behaviour research [12] and were used in this study. They were calculated as follows:

$$coordinate_1 = \sqrt{\frac{3}{4}} \ln \left(\frac{\text{sleep}}{\sqrt[3]{\text{SB} \times \text{LIPA} \times \text{MVPA}}} \right) = \sqrt{\frac{1}{12}} \ln \left(\frac{\text{sleep}}{\text{SB}} \right) + \sqrt{\frac{1}{12}} \ln \left(\frac{\text{sleep}}{\text{LIPA}} \right) + \sqrt{\frac{1}{12}} \ln \left(\frac{\text{sleep}}{\text{MVPA}} \right)$$

$$coordinate_2 = \sqrt{\frac{2}{3}} \ln \left(\frac{\text{SB}}{\sqrt[3]{\text{LIPA} \times \text{MVPA}}} \right) = \sqrt{\frac{1}{6}} \ln \left(\frac{\text{SB}}{\text{LIPA}} \right) + \sqrt{\frac{1}{6}} \ln \left(\frac{\text{SB}}{\text{MVPA}} \right)$$

$$coordinate_3 = \sqrt{\frac{1}{2}} \ln \left(\frac{\text{LIPA}}{\text{MVPA}} \right)$$

Interpreting isometric log-ratio pivot coordinates

As the coefficients in the model relate to the isometric log-ratio pivot coordinates, rather than the raw behaviour variables, interpreting them is not straightforward.

The first coordinate describes the balance between sleep and all other behaviours. Therefore, the coefficient of the first coordinate can be interpreted as the effect of reallocating time to sleep from all other behaviours proportionally i.e. if the coefficient of the first coordinate is greater than 0 (its exponent is greater than 1) reallocating time to sleep from all other behaviours proportionally is associated with higher risk of cardiovascular disease. However, the second and third coordinates are harder to interpret analogously. Therefore, to interpret individually the effect of reallocating time to each behaviour from all others proportionally, and following standard methods in movement behaviour research, one model per behaviour was produced (with different first coordinate). This approach was used to present the model parameters in **Supplementary Table 5** and **Supplementary Table 6** (note that, in consequence, they do not parametrise a single model).

However, even using this approach, the magnitudes of the coefficients are hard to interpret. Therefore, as described in the main text, and following established methods, model estimates of the hazard ratio at different compositions relative to the mean behaviour composition were reported e.g. using pairwise time reallocation plots.

In detail, suppose we have a Cox regression model in the isometric log-ratio pivot coordinates laid out above:

$$\ln \frac{h(t)}{h_0(t)} = \beta_1(\text{coordinate}_1) + \beta_2(\text{coordinate}_2) + \beta_3(\text{coordinate}_3) + \sum_{i=1}^k \gamma_i(\text{covariate}_i)$$

and that the value of the coordinates at the mean behaviour composition is $(m_coordinate_1, m_coordinate_2, m_coordinate_3)$. [This notation is not misleading: the value of the coordinates at the compositional mean behaviour composition is also the mean of the coordinate values.].

Then, we consider a new behaviour composition, which corresponds to isometric log-ratio pivot coordinate values $(coordinate_1, coordinate_2, coordinate_3)$. In particular, when considering a pairwise time reallocation plot we use would use a new composition where time in two behaviours remained at its value in the mean behaviour composition, a value was subtracted from time in one of the remaining behaviours, and that value added to the time in the other behaviour. The log hazard ratio, now relative to the mean behaviour composition, is then calculated as:

$$\ln(HR) = \beta_1(\text{coordinate}_1 - m_coordinate_1) + \beta_2(\text{coordinate}_2 - m_coordinate_2) + \beta_3(\text{coordinate}_3 - m_coordinate_3)$$

The standard error on this can be calculated using the variance-covariance matrix of the coefficients $\boldsymbol{\beta} = (\beta_1, \beta_2, \beta_3)$, denoted V . Writing $\mathbf{x} = (\text{coordinate}_1 - m_coordinate_1, \text{coordinate}_2 - m_coordinate_2, \text{coordinate}_3 - m_coordinate_3)^T$, then

$$SE = \sqrt{\mathbf{x}^T V \mathbf{x}}$$

This can be used to calculate the HR and an (approximate) 95% CI as:

$$\exp(\ln(HR)) (\exp(\ln(HR) - 1.96SE), \exp(\ln(HR) + 1.96SE)).$$

While here we follow an exposition similar to that of Dumuid et al in the context of linear regression [13] and Chastin et al [14], the approach is mathematically equivalent to that of McGregor et al.[15]

To ensure results were plotted within the range supported by the data, times plotted were truncated at the 5th and 95th centile for the behaviour in the pair for which this range was narrower.

Zero values

All participants recorded time in sleep, sedentary behaviour and light physical activity behaviours, but 1% of participants recorded no time in moderate-to-vigorous physical activity behaviours. As zero values cannot be incorporated directly into the coordinates above, different approaches to work with them have been developed. The appropriate method depends on the source of the zero values:

1. ‘Rounded’ zeroes relate to measurement precision: even where no time in a given behaviour was observed, had the wear time been long enough, or the time resolution of the measurement short enough, some time in the behaviour would be expected. If data contains rounded zeroes, they can be imputed as small positive values [16].
2. ‘True’ zeroes occur where no matter the precision of the measurement, no time in that behaviour would be observed. For example, this may occur in movement behaviour research if someone is physically unable to take part in certain behaviours. If data contains true zeroes, participants with a true zero in a particular behaviour should be excluded from the main analysis and analysed separately.

We followed established methods in movement behaviour research by considering zero values to be ‘rounded’ and imputing them using the log-ratio expectation maximization algorithm from the ‘zCompositions’ R package [8,15–17]. We used the smallest observed value in the data as the detection limit (0.0001 on the unitless scale, corresponding to 0.14 min/day). Sensitivity of results to the method of treating zero values (imputation or exclusion) under the Compositional Data Analysis approach was examined by performing an analysis restricted to participants with non-zero values in all behaviour variables. This did not materially impact the results (**Supplementary Figure 13**).

Software

Development of the machine-learning models and processing of accelerometer data used Python 3.6.6, with the ‘biobankAccelerometerAnalysis’ tool[2,18,19] for preparing accelerometer data and training machine-learning models.

Data preparation was performed in Python 3.6.6 and R 4.0.5, and used the ‘ukb_download_and_prep_template’ tool [20] for preparing covariate and outcome data.

Statistical analysis was performed in R 4.0.5[21] with ‘zCompositions’, ‘survival’, ‘forestplot’, ‘EValue’, ‘plyr’, ‘data.table’, ‘rlist’, ‘ggtern’, ‘ggplot2’, and ‘gtools’[16,22–32]. The R package ‘epicoda’ was developed for this analysis[33].

Code is available at github.com/activityMonitoring/manuscript_ml_behaviours_cvd_2021. For further directions, please contact Aiden Doherty.

Sensitivity analyses: further details on E-values

As described in the main text, E-values were reported alongside hazard ratios. The E-value for the estimate quantifies the minimum strength of association that an unmeasured confounder would need with both exposure and outcome to explain away the observed association. The E-value for the 95% confidence interval quantifies the minimum strength of association an unmeasured confounder would need with both exposure and outcome to reduce the interval to overlap the null [27,28]. As the exposure is continuous, in both cases the risk ratio would apply to hypothetical groups with either the specified behaviour composition or the reference (the mean behaviour composition) [28].

Sensitivity analyses: linear isotemporal substitution

For comparability with previous literature, a sensitivity analysis using a linear isotemporal substitution approach was conducted.

Under a linear isotemporal substitution approach, all but one of the movement behaviours are included in the model (so the included variables are not perfectly multicollinear). [In this study, as non-wear time was imputed all subjects had the same wear time. Therefore, a total time variable was not included, meaning the approach may be more properly called 'leave-one-out regression' than true linear isotemporal substitution [8].] Associations are modelled as linear (rather than linear in the log-ratios, as under a Compositional Data Analysis approach). The coefficient of each behaviour can be interpreted in terms of replacing time in the left-out behaviour with time in that behaviour. Linear isotemporal substitution has been widely used in movement behaviour epidemiology [34], but has been criticised for not addressing the fact movement behaviour data only conveys relative information [8].

While there were some differences in shape of the associations observed (due to the different assumptions), results using this approach were broadly similar to the results of the main analysis using Compositional Data Analysis (**Supplementary Figure 14**).

References

- 1 Ainsworth BE, Haskell WL, Herrmann SD, *et al.* 2011 compendium of physical activities: A second update of codes and MET values. *Med Sci Sports Exerc* 2011;**43**:1575–81. doi:10.1249/MSS.0b013e31821ece12
- 2 Willetts M, Hollowell S, Aslett L, *et al.* Statistical machine learning of sleep and physical activity phenotypes from sensor data in 96,220 UK Biobank participants. *Sci Rep* 2018;**8**:0–10. doi:10.1038/s41598-018-26174-1
- 3 Breiman L, Friedman JH, Olshen RA, *et al.* *Classification and regression trees*. 1984. doi:10.1201/9781315139470
- 4 Breiman L. Bagging predictors. *Mach Learn* 1996;**24**:123–40. doi:10.1007/bf00058655
- 5 Forney GD. The Viterbi Algorithm. *Proc IEEE* 1973;**61**:268–78. doi:10.1109/PROC.1973.9030
- 6 Pawlowsky-Glahn V, Egozcue JJ, Tolosana-Delgado R. Lecture notes on Compositional Data Analysis. 2011;:1–100. doi:10.13140/RG.2.1.1296.2728
- 7 Filzmoser P, Hron K, Templ M. *Applied Compositional Data Analysis*. 2018. doi:10.1007/978-3-319-96422-5
- 8 Dumuid D, Pedišić Ž, Palarea-Albaladejo J, *et al.* Compositional Data Analysis in Time-Use Epidemiology : What , Why , How. *Int J Environ Res Public Health* 2020;**17**:2220. doi:10.3390/ijerph17072220
- 9 Aitchison J, Egozcue JJ. Compositional data analysis: Where are we and where should we be heading? *Math Geol* Published Online First: 2005. doi:10.1007/s11004-005-7383-7
- 10 Egozcue JJ, Pawlowsky-Glahn V, Mateu-Figueras G, *et al.* Isometric Logratio Transformations for Compositional Data Analysis. *Math Geol* 2003;**35**:279–300. doi:10.1023/A:1023818214614
- 11 Aitchison J. The statistical analysis of compositional data. *Stat Anal Compos Data* 1982;**44**:139–77. doi:10.1007/978-94-009-4109-0
- 12 Dumuid D, Stanford TE, Martín-Fernández J-AA, *et al.* Compositional data analysis for physical activity, sedentary time and sleep research. *Stat Methods Med Res* 2017;**27**:096228021771083. doi:10.1177/0962280217710835
- 13 Dumuid D, Pedišić Ž, Stanford TE, *et al.* The compositional isotemporal substitution model: A method for estimating changes in a health outcome for reallocation of time between sleep, physical activity and sedentary behaviour. *Stat Methods Med Res* 2017;**28**:846–57. doi:10.1177/0962280217737805
- 14 Chastin S, McGregor D, Palarea-Albaladejo J, *et al.* Joint association between accelerometry-measured daily combination of time spent in physical activity, sedentary behaviour and sleep and all-cause mortality: a pooled analysis of six prospective cohorts using compositional analysis. *Br J Sports Med* 2021;:bjssports-2020-102345. doi:10.1136/bjssports-2020-102345
- 15 McGregor DE, Palarea-Albaladejo J, Dall PMP, *et al.* Cox regression survival analysis with compositional covariates: Application to modelling mortality risk from 24-h physical activity patterns. *Stat Methods Med Res* 2019;**29**:1447–65. doi:10.1177/0962280219864125
- 16 Palarea-Albaladejo J, Martín-Fernández JA. ZCompositions - R package for multivariate imputation of left-censored data under a compositional approach. *Chemom. Intell. Lab. Syst.* 2015;**143**:85–96. doi:10.1016/j.chemolab.2015.02.019
- 17 Rasmussen CL, Palarea-Albaladejo J, Johansson MS, *et al.* Zero problems with compositional data of physical behaviors: a comparison of three zero replacement methods. *Int J Behav Nutr Phys Act* 2020.
- 18 Doherty A, Jackson D, Hammerla N, *et al.* Large scale population assessment of physical activity using wrist worn accelerometers: The UK biobank study. *PLoS One* 2017;**12**:1–14. doi:10.1371/journal.pone.0169649
- 19 Doherty A, Smith-Byrne K, Ferreira T, *et al.* GWAS identifies 14 loci for device-measured physical activity and sleep duration. *Nat Commun* 2018;**9**. doi:10.1093/acrefore/9780190236557.013.204
- 20 Walmsley R, Chan S, Doherty A. `ukb_download_and_prep_template`. 2020.https://github.com/activityMonitoring/ukb_download_and_prep_template
- 21 R Core Team. R: A Language and Environment for Statistical Computing. *Vienna, Austria* Published Online First: 2019.<https://www.r-project.org/>
- 22 Therneau TM. A Package for Survival Analysis in R. 2021.<https://cran.r-project.org/package=survival>
- 23 Wickham H. *ggplot2: Elegant Graphics for Data Analysis*. New York: : Springer-Verlag 2016. <https://ggplot2.tidyverse.org>
- 24 Warnes GR, Bolker B, Lumley T. `gtools`: Various R Programming Tools. *R Packag version 381* 2018.
- 25 Terry M, Therneau, Patricia M. Grambsch. *Modeling Survival Data: Extending the Cox Model*. New York: : Springer 2000.
- 26 Max Gordon and Thomas Lumley. `forestplot`: Advanced Forest Plot Using ‘grid’ Graphics. R package version 1.9. 2019.<https://cran.r-project.org/package=forestplot>
- 27 Van Der Wee TJ, Ding P. Sensitivity analysis in observational research: Introducing the E-Value. *Ann Intern Med* 2017;**167**:268–74. doi:10.7326/M16-2607

- 28 Mathur MB, Ding P, Riddell CA, *et al.* Web Site and R Package for Computing E-values. *Epidemiology* 2018;**29**:e45. doi:10.1097/EDE.0000000000000864
- 29 Wickham H. The Split-Apply-Combine Strategy for Data Analysis. *J Stat Softw* 2011;**40**:1–29. <http://www.jstatsoft.org/v40/i01/>
- 30 Dowle M, Srinivasan A. data.table: Extension of `data.frame`. 2021. <https://cran.r-project.org/package=data.table>
- 31 Ren K. rlist: A Toolbox for Non-Tabular Data Manipulation. 2016. <https://cran.r-project.org/package=rlist>
- 32 Hamilton NE, Ferry M. Ggtern: Ternary diagrams using ggplot2. *J Stat Softw* 2018;**87**:1–17. doi:10.18637/jss.v087.c03
- 33 Walmsley R. epicoda. 2020. github.com/activityMonitoring/epicoda
- 34 Mekary RA, Ding EL. Isotemporal substitution as the gold standard model for physical activity epidemiology: Why it is the most appropriate for activity time research. *Int J Environ Res Public Health* 2019;**16**:11–3. doi:10.3390/ijerph16050797

Supplementary Tables and Figures

Supplementary Table 1: Assignment of fine-grained camera image annotations from the Compendium of Physical Activities to broad movement behaviour classes.

<p><u>Sleep</u></p> <p>7030 sleeping</p>
<p><u>Sedentary behaviour</u></p> <p>occupation;office and administrative support;11580 office/computer work general</p> <p>occupation;office and administrative support;11580 office wok/computer work general</p> <p>home activity;miscellaneous;sitting;9060 sitting/lying reading or without observable/identifiable activities</p> <p>leisure;miscellaneous;sitting;0010 sitting / lying dialysis</p> <p>transportation;private transportation;16010 driving automobile or light truck (not a semi)</p> <p>home activity;miscellaneous;sitting;7010 sitting/lying and watching television with TV on as the primary activity</p> <p>home activity;miscellaneous;sitting;11580 office/computer work general</p> <p>home activity;miscellaneous;sitting;9055 sitting/lying talking in person/using a mobile phone/smartphone/tablet or talking on the phone/computer (skype chatting)</p> <p>home activity;miscellaneous;sitting;11580 office work such as writing and typing (with or without eating at the same time)</p> <p>home activity;eating;13030 eating sitting alone or with someone</p> <p>home activity;miscellaneous;sitting;9030 sitting desk entertainment/hobby (with or without eating at the same time)</p> <p>home activity;miscellaneous;sitting;5080 sitting non-desk work (with or without eating at the same time)</p> <p>occupation;interruption;sitting;11585 sitting meeting/talking to colleagues with or without eating</p> <p>leisure;miscellaneous;sitting;9060 (generic) sitting/lying reading or without observable/identifiable activities</p> <p>occupation;interruption;11585 sitting meeting/talking to colleages with or without eating</p> <p>home activity;leisure;activities for maintenance of a household;miscellaneous;9100 retreat/family reunion activities involving sitting eating relaxing talking with more than one person</p> <p>home activity;miscellaneous;sitting;9060 sitting/lying reading or without observable activities</p> <p>leisure;eating;social;13030 eating sitting indoor/outdoor</p> <p>home activity;leisure;activities for maintenance of a household;miscellaneous;9100 retreat/family reunion activities involving sitting eating relaxing talking with more than one person</p> <p>occupation;public admin/education/health;education;9065 students/attending seminars or talks</p> <p>home activity;miscellaneous;sitting;9030 sitting desk work (with or without eating at the same time)</p> <p>occupation;interruption;sitting;9060 sitting without observable/identifiable activities</p>

leisure;miscellaneous;sitting;9055 sitting talking to person/using the phone
transportation;private transportation;16015 riding in a car or truck
leisure;eating;13030 eating sitting indoor/outdoor
occupation;interruption;13030 eating sitting
home activity;miscellaneous;sitting;9045 sitting playing traditional video game computer game
home activity;miscellaneous;sitting;9030 sitting desk work (with or without eating at the same time)
occupation;interruption;sitting;13030 eating sitting
home activity;leisure;individual activities;9075 sitting arts and crafts carving/wood weaving/spinning wool
home activity;household chores;washing/ironing/mending clothes;5080 knitting sewing sitting
occupation;interruption;sitting;9055 sitting using a mobile phone/smartphone/tablet or talking on the phone/computer (skype meeting etc.)
leisure;miscellaneous;sitting;21000 sitting meeting
leisure;miscellaneous;sitting;21005 (generic) sitting light office writing typing work
occupation;office and administrative support;11580 office work/computer work general
home activity;miscellaneous;sitting;7010 lying and watching television with TV on as the primary activity
leisure;miscellaneous;sitting;9060 (generic) sitting/lying reading or without observable activities
transportation;waiting;7021 sitting
occupation;interruption;11585 sitting meeting/talking to colleagues with or without eating
leisure;religious activities;20000 sitting in church in service attending a ceremony sitting quietly
transportation;private transportation;16030 motor scooter motorcycle
occupation;interruption;9055 sitting using a mobile phone/smartphone/tablet or talking on the phone/computer (skype meeting etc.)
leisure;miscellaneous;21005 (generic) sitting light office writing typing work
home activity;miscellaneous;sitting;7021 sitting without observable activities
home activity;leisure;activities for maintenance of a household;with children;5170 sitting playing with child(ren)
home activity;leisure;activities for maintenance of a household;with children;5170 sitting playing with child(ren)
occupation;interruption;9060 (generic) sitting without observable activities
home activity;child/elderly/pet care;child care;5185 child care sitting/kneeling
home activity;miscellaneous;sitting;21010 sitting non-desk work (with or without eating at the same time)
leisure;eating;not-social;13030 eating sitting indoor/outdoor
leisure;miscellaneous;sitting;5080 sitting non-desk work (with or without eating at the same time)
home activity;leisure;activities for maintenance of a household;9100 retreat/family reunion activities involving sitting eating relaxing talking with more than one person

leisure;miscellaneous;sitting;21016 sitting child care only active periods
 home activity;leisure;activities for maintenance of a household;5170 sitting playing with child(ren)
 home activity;lawn and garden;gardening service;8055 driving tractor
 occupation;interruption;9060 (generic) sitting without observable/identifiable activities
 home activity;self care;13036 taking medication
 leisure;miscellaneous;21000 sitting meeting or talking with others
 home activity;self care;13046 having hair or nails done by someone else sitting
 home activity;household chores;washing/ironing/mending clothes;5080 knitting sewing wrapping presents sitting
 home activity;miscellaneous;sitting;9060 sitting reading or using a mobile phone/smartphone/tablet or talking on the phone/computer (skype chatting)
 leisure;miscellaneous;21010 sitting non-desk work (with or without eating at the same time)
 occupation;interruption;9060 sitting using a mobile phone/smartphone/tablet or talking on the phone/computer (skype meeting etc.)
 leisure;religious activities;20005 sitting in church talking or singing attending a ceremony sitting active
 home activity;child/elderly/pet care;child care;5185 child care sitting/kneeling occasional lifting
 leisure;miscellaneous;21016 sitting child care only active periods
 home activity;miscellaneous;sitting;7021 sitting without observable activities
 home activity;leisure;activities for maintenance of a household;with animals;5190 sitting playing with animals active periods
 transportation;public transportation;16016 riding in a bus or train
 leisure;sports;water activities;18012 boating power passenger

Light physical activity behaviours

home activity;household chores;preparing meals/cooking/washing dishes;5035 kitchen activity general cooking/washing/dishes/cleaning up
 home activity;miscellaneous;walking;17150 walking household without observable loads
 home activity;miscellaneous;walking;5165 (generic) walking non-cleaning task such as closing windows lock door putting away items
 leisure;miscellaneous;walking;21070 (generic) walking and occasional standing (no more than two consecutive images)
 transportation;walking;17161 walking not as the single means of transports e.g.from house to transports or vice versa/from car to places or vice versa/between transports
 leisure;miscellaneous;walking;5060 shopping miscellaneous
 occupation;interruption;11791 walking on job in office or lab area
 home activity;miscellaneous;standing;9050 standing talking in person/on the phone/computer (skype chatting) or using a mobile phone/smartphone/tablet
 home activity;household chores;washing/ironing/mending clothes;5090 folding or hanging clothes/put clothes in or out of washer or dryer/packing suitcase limited walking

home activity;miscellaneous;standing;9070 standing reading or without observable/identifiable activities
occupation;interruption;walking;11791 walking on job in office or lab area
occupation;manufacturing;11115 chef
home activity;self care;13040 (generic) self care such as grooming/washing hands/shaving/brushing teeth/putting on make-up not eliminating and bathing (not necessary in the toilet)
occupation;office and administrative support;11600 (generic) standing tasks such as store clerk/librarian/packing boxes/repair heavy parts
leisure;miscellaneous;5060 shopping miscellaneous
home activity;household chores;washing/ironing/mending clothes;5070 ironing
leisure;miscellaneous;standing;9050 standing talking in person/using a phone/smartphone/tablet
home activity;miscellaneous;walking;5147 walking moving away light items (pens/papers/keys not included)
occupation;miscellaneous;11475 (generic) manual labour
occupation;interruption;standing;9050 standing talking in person/using a phone/smartphone/tablet
occupation;personal services;11413 kitchen maid
home activity;household chores;grocery shopping;5060 shopping
home activity;home repair;indoor;6126 home repair miscellaneous
leisure;miscellaneous;standing;9070 standing reading or without observable/identifiable activities
transportation;waiting;7040 standing in a line
home activity;child/elderly/pet care;child care;5185 child care sitting/kneeling occasional lifting
home activity;miscellaneous;standing;9071 (generic) standing miscellaneous
leisure;miscellaneous;standing;9071 (generic) standing miscellaneous
occupation;interruption;standing;9070 standing reading or without observable/identifiable activities
home activity;miscellaneous;standing;9020 standing writing/drawing/painting
home activity;leisure;individual activities;10074 playing musical instruments
occupation;interruption;5041 kitchen activity in the working place
home activity;miscellaneous;walking;17140 using crutches or frame
occupation;interruption;9050 standing talking in person/using a phone/smartphone/tablet
home activity;leisure;individual activities;9085 standing arts and crafts/sand painting/carving weaving
home activity;miscellaneous;5025 (generic) multiple household tasks all at once including standing/lifting/sitting
home activity;miscellaneous;standing;9070 standing reading or without obvious activities
home activity;household chores;washing/ironing/mending clothes;5095 putting away /gathering clothes involving walking
home activity;lawn and garden;lawn care service;8135 planting potting transplanting seedlings or plants

occupation;interruption;standing;9071 (generic) standing miscellaneous
transportation;walking;9050 standing miscellaneous (talking to others etc.)
occupation;interruption;miscellaneous;5041 kitchen activity in the working place
home activity;household chores;house cleaning;miscellaneous;5100 making bed/changing linens
occupation;interruption;standing;9015 standing scanning documents
home activity;household chores;house cleaning;furniture;5032 dusting or polishing furniture
home activity;eating;13035 eating standing alone or with others
occupation;miscellaneous;11870 working in scene shop theatre actor backstage employee
occupation;office and administrative support;11600 (generic) standing tasks such as store clerk/librarian/packing boxes/repair heavy parts
home activity;miscellaneous;standing;9050 standing talking in person on the phone/computer (skype chatting) or using a mobile phone/smartphone/tablet
home activity;household chores;house cleaning;floors;5010 cleaning sweeping carpet or floors
leisure;sports;ball games;15090 bowling
home activity;self care;13020 dressing/undressing
occupation;interruption;9070 standing reading or without observable/identifiable activities
leisure;music playing;10074 playing musical instruments
home activity;home repair;indoor;6205 sharpening tools
home activity;home repair;indoor;6124 hammering nails
home activity;child/elderly/pet care;child care;5186 child care standing occasional lifting
occupation;interruption;13035 eating standing
home activity;child/elderly/pet care;pet care;5197 household animal care aside from feeding
leisure;recreation;outdoor;5171 standing playing with child(ren)
occupation;interruption;miscellaneous;13009 toilet break
home activity;household chores;house cleaning;miscellaneous;5148 watering plants
occupation;miscellaneous;11475 (generic) manual or unskilled labour
occupation;interruption;standing;9020 standing writing/drawing/painting
leisure;eating;social;13035 eating standing indoor/outdoor
home activity;household chores;house cleaning;floors;5131 scrubbing floors on hands and knees scrubbing bathroom bathtub
occupation;public admin/education/health;education;09071 teaching standing
home activity;household chores;preparing meals/cooking/washing dishes;5051 serving food/setting table implied walking and standing
home activity;household chores;preparing meals/cooking/washing dishes;5035 cleaning up table after meal implied walking (e.g. leaving from eating table to the kitchen)

leisure;eating;not-social;5060 buying foods or drinks as a takeaway
leisure;miscellaneous;21070 (generic) walking/standing combination indoor
home activity;self care;13009 toilet eliminating or squatting
home activity;self care;13045 hairstyling standing
home activity;lawn and garden;gardening service;8230 watering garden
occupation;interruption;13009 toilet break
leisure;miscellaneous;standing;9070 standing reading or without obvious activities
home activity;leisure;activities for maintenance of a household;miscellaneous;9101 retreat/family reunion activities playing games with more than one person
occupation;interruption;9015 standing scanning documents
home activity;child/elderly/pet care;child care;5183 standing holding child
occupation;interruption;9070 standing reading or without obvious activities
leisure;miscellaneous;standing;9020 standing writing/drawing/painting
leisure;religious activities;20039 walking/standing combination for religious purposes usher
leisure;recreation;indoor;9020 drawing writing painting standing
leisure;miscellaneous;21017 standing child care only active periods
home activity;child/elderly/pet care;pet care;5053 feeding household animals
leisure;eating;13035 eating standing indoor/outdoor
leisure;miscellaneous;9071 (generic) standing miscellaneous indoor or outdoor
leisure;sports;conditioning;2115 upper body exercise arm ergometer
occupation;interruption;standing;9050 standing talking in person/using a phone/smartphone/tablet
home activity;self care;13000 getting ready for bed standing
leisure;eating;social;5060 buying foods or drinks as a takeaway
home activity;home repair;indoor;5160 standing light effort tasks
transportation;walking;9071 standing miscellaneous (talking to others etc.)
occupation;interruption;standing;13035 eating standing
occupation;interruption;9020 standing writing/drawing/painting
home activity;lawn and garden;gardening service;8220 walking applying fertilizer or seeding a lawn push applicator
leisure;eating;5060 buying foods or drinks as a takeaway
leisure;religious activities;20030 standing talking in church
leisure;eating;not-social;13035 eating standing indoor/outdoor

occupation;public admin/education/health;education;9071 teaching standing
home activity;household chores;washing/ironing/mending clothes;5082 sewing with a machine

Moderate-to-vigorous physical activity behaviours

transportation;private transportation;1010 bicycling
transportation;walking;17165 walking the dog
occupation;interruption;17133 walking upstairs
leisure;miscellaneous;walking;17031 loading /unloading a car implied walking
home activity;child/elderly/pet care;child care;5181 walking and carrying child
home activity;lawn and garden;gardening service;8050 digging spading filling garden compositing
leisure;sports;miscellaneous;17082 hiking or walking at a normal pace through fields and hillsides
home activity;lawn and garden;tree and shrub service;8025 clearing light brush thinning garden
home activity;lawn and garden;lawn care service;8165 raking lawn
occupation;interruption;walking;11795 walking on job and carrying light objects such as boxes or pushing trolleys
leisure;sports;water activities;18070 canoeing/rowing
home activity;lawn and garden;lawn care service;8080 laying crushed rock
leisure;sports;gymnasium and athletics;athletics;12150 running
leisure;sports;ball games;15235 football or baseball playing catch
home activity;miscellaneous;standing;5146 standing packing/unpacking household items occasional lifting
home activity;lawn and garden;gardening service;8245 gardening/picking up fruits vegetables flowers
leisure;miscellaneous;walking;17105 pushing a wheelchair non-occupational
leisure;sports;ball games;15680 tennis doubles
home activity;lawn and garden;gardening service;8192 shovelling dirt or mud
leisure;sports;miscellaneous;17082 hiking or walking at a normal pace through fields and hillsides
leisure;dancing;3010 ballet modern or jazz general rehearsal or class
leisure;sports;conditioning;2060 health club exercise
leisure;sports;ball games;15690 tennis singles
home activity;lawn and garden;lawn care service;8095 mowing lawn
occupation;public admin/education/health;health;11615 nursing patient care

occupation;miscellaneous;11615 (generic) standing lifting items continuously with limited walking
leisure;miscellaneous;17031 loading /unloading a car implied walking
leisure;sports;conditioning;2019 bicycling stationary RPM/Spin bike class
home activity;leisure;activities for maintenance of a household;with animals;5192 walking/running playing with animals active periods
home activity;lawn and garden;gardening service;8192 shoveling dirt or mud
home activity;household chores;house cleaning;furniture;5020 cleaning heavy such as car/windows/garage
leisure;sports;conditioning;2048 elliptical trainer
occupation;interruption;11795 walking on job and carrying light objects such as boxes or pushing trolleys
leisure;sports;conditioning;2050 resistance training
leisure;sports;conditioning;2070 rowing stationary ergometer
leisure;recreation;outdoor;5175 walking/running playing with child(ren)
leisure;sports;conditioning;2010 bicycling stationary
leisure;sports;conditioning;2120 water aerobics water calisthenics water exercise
home activity;home repair;outdoor;6020 automobile body work
occupation;agriculture/forestry/fishing;11192 taking care of animals
leisure;miscellaneous;standing;21017 standing child care only active periods
leisure;sports;conditioning;2065 stair-treadmill ergometer general
home activity;household chores;washing/ironing/mending clothes;5092 washing clothes by hand (with or without hanging wash)
leisure;miscellaneous;walking;17133 walking upstairs
transportation;walking;12150 running
occupation;interruption;walking;17070 walking downstairs
home activity;household chores;house cleaning;floors;5140 sweeping garage sidewalk or outside of house
occupation;interruption;walking;17133 walking upstairs
occupation;agriculture/forestry/fishing;11540 shovelling digging ditches
occupation;construction;11050 carrying heavy loads
transportation;walking;17250 walking as the single means to a destination not to work or class
leisure;miscellaneous;walking;17070 descending stairs
home activity;miscellaneous;walking;5121 walking with moving and lifting loads such as bikes and furniture
transportation;walking;17270 walking as the single means to work or class (not from)

Supplementary Table 2: Features of accelerometry signal used for behaviour classification.

Feature	Description
enmoTrunc	Euclidean Norm Minus One truncated below at 0
mean	Mean
sd	Standard Deviation
coefvariation	Coefficient of Variation
median	Median
min	Minimum
max	Maximum
25thp	25 th percentile
75thp	75 th percentile
autocorr	Autocorrelation
fmax	Frequency of signal with highest power
pmax	Maximal power of signal
fmaxband	Frequency of signal with highest power between 0.3 and 3 Hz
pmaxband	Maximal power of signal between 0.3 and 3 Hz
entropy	Entropy
fft1	Power at 1Hz
fft2	Power at 2Hz
fft3	Power at 3Hz
fft4	Power at 4Hz
fft5	Power at 5Hz
fft6	Power at 6Hz
fft7	Power at 7Hz
fft8	Power at 8Hz
fft9	Power at 9Hz
fft10	Power at 10Hz
fft11	Power at 11Hz
fft12	Power at 12Hz

Feature	Description
MAD	Mean Amplitude Deviation
MPD	Mean Power Deviation
skew	Skew
kurt	Kurtosis
f1	Frequency of signal with highest power between 0.3 and 15 Hz
p1	Maximal power of signal between 0.3 and 15 Hz
f2	Frequency of signal with second highest power between 0.3 and 15 Hz
p2	Second highest power of signal between 0.3 and 15 Hz
f625	Frequency of signal with highest power between 0.6 and 2.5 Hz
p625	Maximal power of signal between 0.6 and 2.5 Hz
totalPower	Total power for frequencies between 0.3 and 15 Hz
vmfft1	Power at 1/30 Hz
vmfft2	Power at 2/30 Hz
vmfft3	Power at 3/30 Hz
vmfft4	Power at 4/30 Hz
vmfft5	Power at 5/30 Hz
vmfft6	Power at 6/30 Hz
vmfft7	Power at 7/30 Hz
vmfft8	Power at 8/30 Hz
vmfft9	Power at 9/30 Hz
vmfft10	Power at 10/30 Hz
vmfft11	Power at 11/30 Hz
vmfft12	Power at 12/30 Hz

Supplementary Table 3: Definition of variables from UK Biobank data included in statistical models.

Characteristic	Source	Notes	UK Biobank field	Coding
OUTCOME				
Age at first cardiovascular disease event	Death Registry, HES.	First appearance of ICD-10 codes I20-25 (ischaemic heart disease) or I60-69 (cerebrovascular disease) in either HES or death register data.	Derived from Category 100093, Category 2000.	
Age at loss-to-follow-up	Death Registry.	Earliest of: date of latest study data available and date of non-cardiovascular disease death.	Derived from Category 100093.	
EXPOSURE				
Sleep	Accelerometry.	Derived using machine-learning methods described in main text.	Derived from 90001.	
Sedentary behaviour	Accelerometry.	Derived using machine-learning methods described in main text.	Derived from 90001.	
Light physical activity behaviours	Accelerometry.	Derived using machine-learning methods described in main text.	Derived from 90001.	
Moderate-to-vigorous physical activity behaviours	Accelerometry.	Derived using machine-learning methods described in main text.	Derived from 90001.	
EXCLUSION VARIABLES – MAIN ANALYSIS				
Prior HES-recorded cardiovascular disease	HES.	Appearance of ICD-10 codes I20-25 (ischaemic heart disease) or I60-69 (cerebrovascular disease) or ICD-9 codes 410 – 414 or 430 – 438 in HES data prior to accelerometer wear.	Derived from Category 2000.	

Characteristic	Source	Notes	UK Biobank field	Coding
Prior self-reported cardiovascular disease	Baseline.	Self-reported heart attack or stroke.	Derived from 6150.	
ADJUSTMENT VARIABLES – MAIN ANALYSIS				
Age	Baseline.	Age used as the timescale in Cox regression analysis; participants entered study at the end of accelerometer wear.	Derived from 90011, 34, 52.	
Sex	Baseline.	Used to stratify analysis.	31	Female, Male.
Ethnicity	Baseline.		Derived from 21000.	Asian, Black, Other, White. (Categorised as in Resource 100336; Other includes Mixed, Chinese and Other due to small numbers).
Smoking status	Baseline.		20116	Never smoker, Ex-smoker, Current smoker.
Frequency of alcohol consumption	Baseline.		Derived from 1558.	Never, <3 times/week, 3+ times/week.
Education	Baseline.		Derived from 6138.	School leaver, Further education (education beyond O-Levels/CSEs, excluding college/ university degree) and Higher education (college/university degree).
Townsend Deprivation Index	Baseline.	Townsend Deprivation Index of address at time of UKB baseline assessment.	Derived from 189.	Divided by quartile in the study population.
Daily servings of fresh fruit and vegetables.	Baseline.		Derived from 1289, 1299, 1309.	Less than one coded as 0·5, then sum of 1289, 1299, 1309. Categorised as < 3, 3-4·9, 5-7·9, 8+ servings/ day.

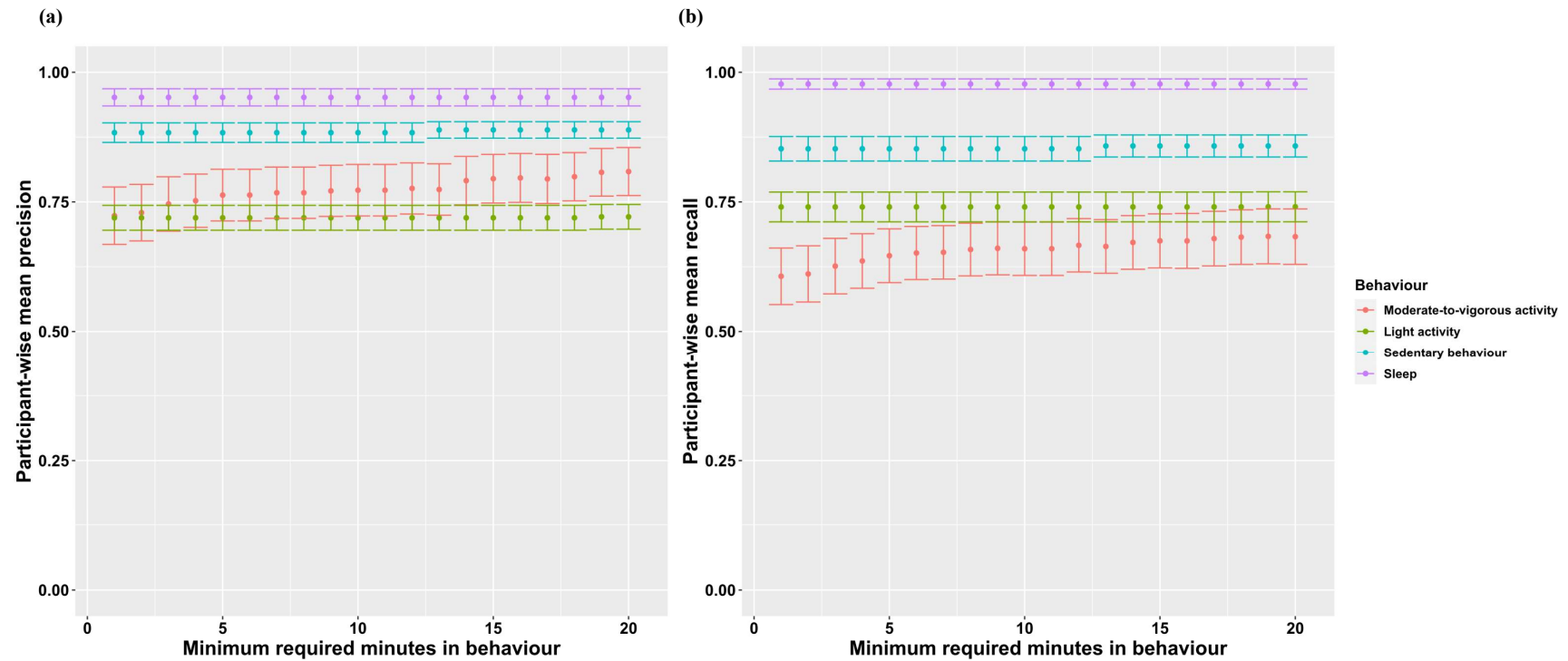
Characteristic	Source	Notes	UK Biobank field	Coding
Frequency of red and processed meat consumption.	Baseline.		Derived from 1369, 1379, 1389, 1349.	Less than one coded as 0·5, then sum of 1369, 1379, 1389. Categorised as <1, 1-2·9, 3-4·9, 5+ times/ week.
Frequency of oily fish consumption.	Baseline.		Derived from 1329.	< 1, 1, 2-4, >4 times/week.
ADJUSTMENT VARIABLES – ADDITIONAL				
BMI	Baseline.		Derived from 21001.	For descriptive analyses: Underweight (<18·5kgm ⁻²), Normal weight (18·5 -24·9 kgm ⁻²), Overweight (25 -29·9 kgm ⁻²), Obese (30+ kgm ⁻²). For BMI-stratified analysis, Underweight and Normal weight categories combined.
EXCLUSION VARIABLES – SENSITIVITY ANALYSIS FOR REVERSE CAUSALITY				
Medication for diabetes, cholesterol or blood pressure	Baseline.		Derived from 6177, 6153.	
Self-reported overall health rating	Baseline.		2178	
Prior primary admission for disease of the circulatory system.	HES.	Hospital admission with primary diagnosis of I00-I99 before accelerometer wear.	Derived from Category 2000.	
NEGATIVE CONTROL OUTCOME – SENSITIVITY ANALYSIS FOR RESIDUAL CONFOUNDING				
Age at first accident unrelated to movement behaviour.	Death Registry, HES.	First appearance of ICD-10 codes V00-09, V20-99, W20-W99, X00-X59.	Derived from Category 100093, Category 2000.	
Age at loss-to-follow-up	Death Registry.	Earliest of: date of latest study data available and date of death.	Derived from Category 100093.	

Characteristic	Source	Notes	UK Biobank field	Coding
Prior HES-recorded accident unrelated to movement behaviour.	HES.	First appearance of ICD-10 codes V00-09, V20-99, W20-W99, X00-X59.	Derived from Category 2000.	

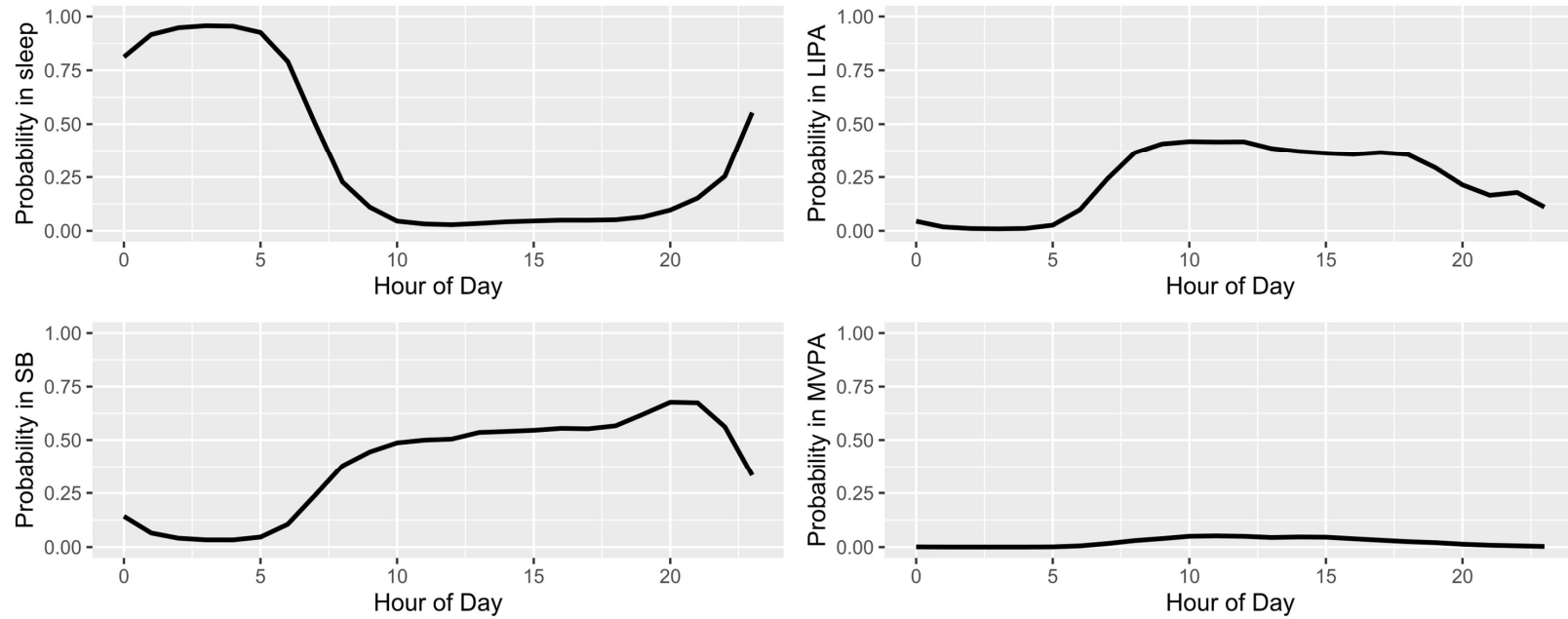
Supplementary Table 4: Characteristics of CAPTURE-24 participants.

	n (%)
Overall	152
Age, years	
18-29	39 (26)
30-39	41 (27)
40-49	24 (16)
50-59	21 (14)
60-69	17 (11)
70-79	7 (5)
80-91	2 (1)
Not recorded	1 (1)
Sex	
Female	99 (65)
Male	53 (35)

Supplementary Figure 1: Participant-wise mean (a) precision and (b) recall for classification of behaviours from accelerometer data calculated in Leave-One-Participant-Out Cross-Validation (with 95% confidence interval for the mean). The x-axis gives the minimum required recorded annotator-labelled time in the behaviour for inclusion in the calculation. For precision, participants with no model-labelled time in the behaviour were also excluded as precision is undefined in this case.



Supplementary Figure 2: Probability of being in sleep, sedentary behaviour (SB), light physical activity behaviours (LIPA) and moderate-to-vigorous physical activity behaviours (MVPA) among 87,498 UK Biobank participants according to machine-learned behaviour classification by hour of the day.



Supplementary Table 5: Coefficient of first isometric log-ratio pivot coordinate^a for each movement behaviour estimated using a multivariable-adjusted Compositional Data Analysis Cox regression model.

Movement behaviour variable	$exp(\hat{\beta})$ (95% CI)
Pivot coordinate: Sleep vs All other behaviours	0.88 (0.75, 1.02)
Pivot coordinate: SB vs All other behaviours	1.38 (1.22, 1.57)
Pivot coordinate: LIPA vs All other behaviours	0.96 (0.88, 1.06)
Pivot coordinate: MVPA vs All other behaviours	0.86 (0.84, 0.88)

^aSee **Supplementary Methods**. Model based on 4,105 events in 87,498 participants. Model used age as the timescale, was stratified by sex and was additionally adjusted for ethnicity, smoking status, alcohol consumption, fresh fruit and vegetable consumption, red and processed meat consumption, oily fish consumption, deprivation and education.

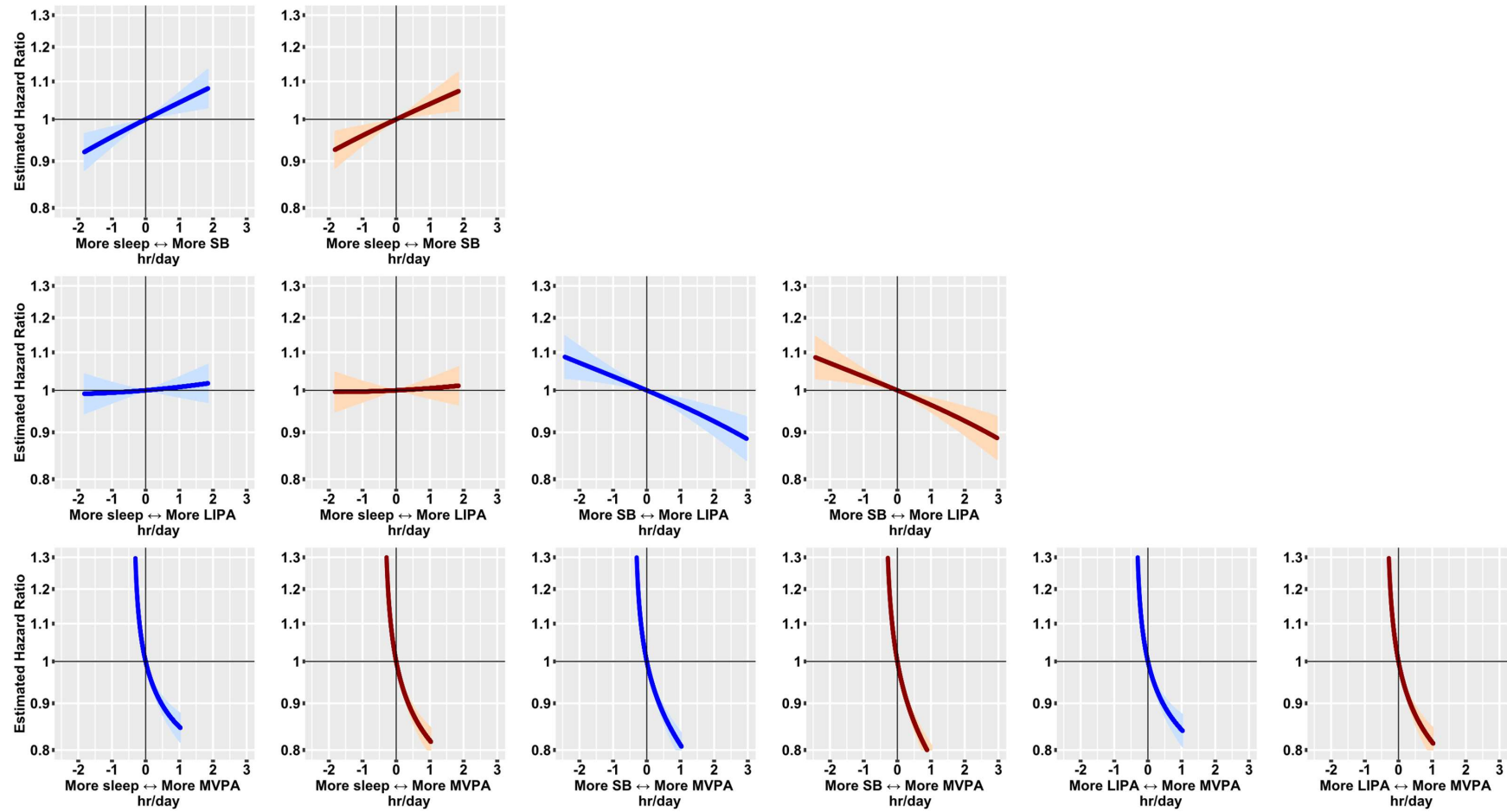
Supplementary Table 6: Coefficient of first isometric log-ratio pivot coordinate for each movement behaviour estimated using all Compositional Data Analysis Cox regression models.^a

Movement behaviour variable	Main analysis	Minimally adjusted	Additionally stratified by BMI	Fatal events	Women only	Men only
Pivot coordinate: sleep vs All other behaviours	0.88 (0.75, 1.02)	0.90 (0.77, 1.05)	0.90 (0.77, 1.05)	0.79 (0.48, 1.29)	0.78 (0.60, 1.02)	0.93 (0.77, 1.13)
Pivot coordinate: SB vs All other behaviours	1.38 (1.22, 1.57)	1.37 (1.21, 1.56)	1.29 (1.13, 1.46)	2.13 (1.40, 3.22)	1.57 (1.28, 1.94)	1.28 (1.09, 1.50)
Pivot coordinate: LIPA vs All other behaviours	0.96 (0.88, 1.06)	0.96 (0.88, 1.06)	0.98 (0.89, 1.08)	0.71 (0.52, 0.95)	0.95 (0.81, 1.11)	0.97 (0.86, 1.09)
Pivot coordinate: MVPA vs All other behaviours	0.86 (0.84, 0.88)	0.84 (0.81, 0.86)	0.88 (0.85, 0.90)	0.85 (0.78, 0.92)	0.85 (0.82, 0.89)	0.86 (0.83, 0.90)

Movement behaviour variable	Main analysis	Under 65s only	Over 65s only	First 2 years of follow-up removed	Follow-up removed + healthy subgroup	Excluding zero values	Negative control: accidents
Pivot coordinate: sleep vs All other behaviours	0.88 (0.75, 1.02)	0.98 (0.75, 1.28)	0.83 (0.69, 1.00)	0.88 (0.73, 1.06)	1.01 (0.77, 1.31)	0.86 (0.73, 1.01)	0.91 (0.69, 1.20)
Pivot coordinate: SB vs All other behaviours	1.38 (1.22, 1.57)	1.17 (0.95, 1.45)	1.52 (1.30, 1.77)	1.33 (1.15, 1.55)	1.09 (0.89, 1.35)	1.38 (1.21, 1.57)	1.09 (0.87, 1.36)
Pivot coordinate: LIPA vs All other behaviours	0.96 (0.88, 1.06)	1.01 (0.86, 1.18)	0.93 (0.82, 1.04)	0.98 (0.88, 1.10)	1.04 (0.88, 1.21)	0.99 (0.89, 1.09)	1.10 (0.93, 1.30)
Pivot coordinate: MVPA vs All other behaviours	0.86 (0.84, 0.88)	0.86 (0.82, 0.91)	0.86 (0.83, 0.89)	0.87 (0.84, 0.90)	0.88 (0.83, 0.92)	0.86 (0.83, 0.89)	0.92 (0.87, 0.97)

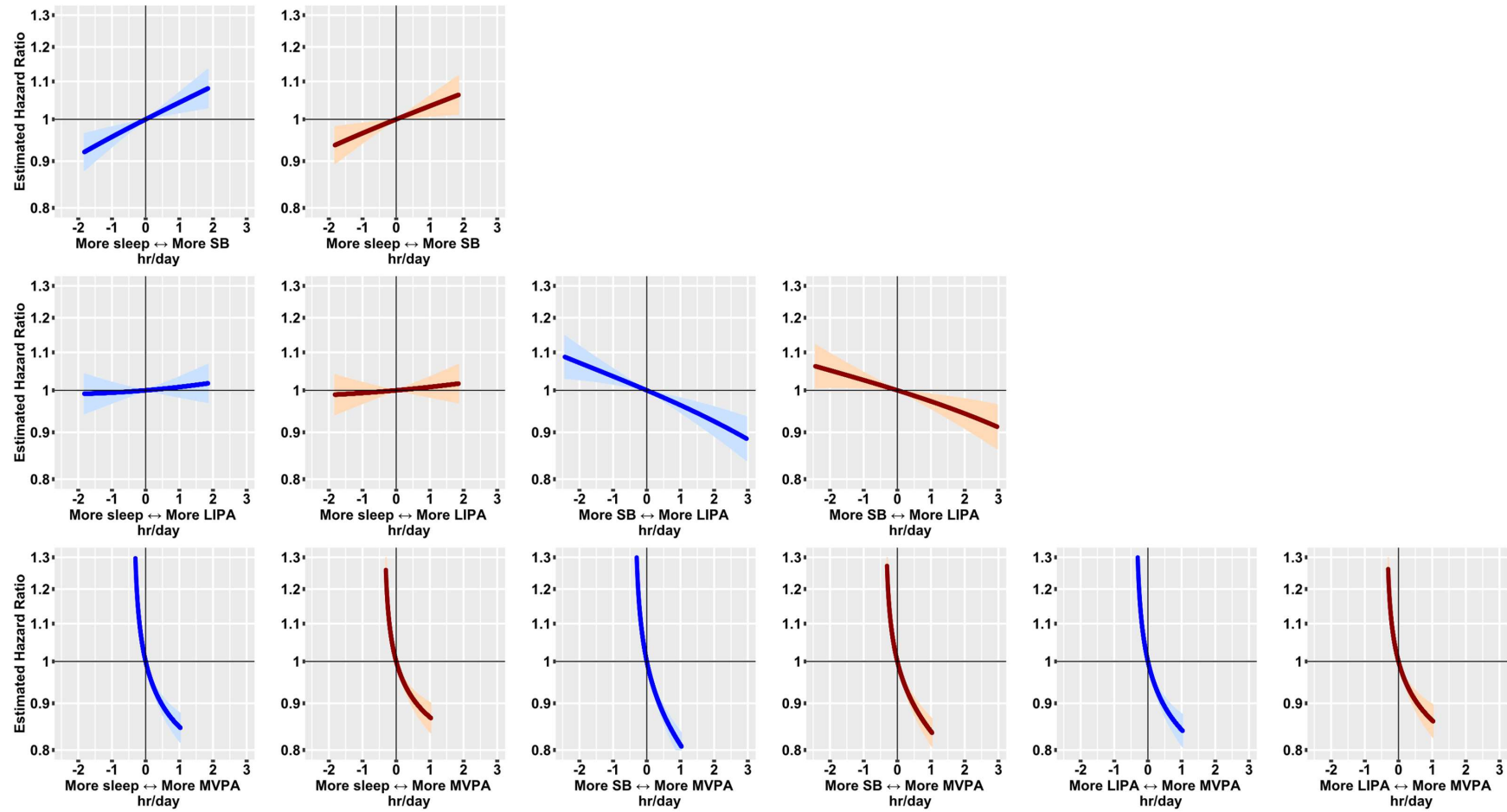
^aSee Methods, Results and Supplementary Figures 3-13 for more details of models. All columns report $\exp(\hat{\beta})$ (95% CI).

Supplementary Figure 3: Hazard Ratios for cardiovascular disease for all behaviour pairs estimated using multivariable-adjusted (blue) and minimally adjusted (red) Cox regression models.^a



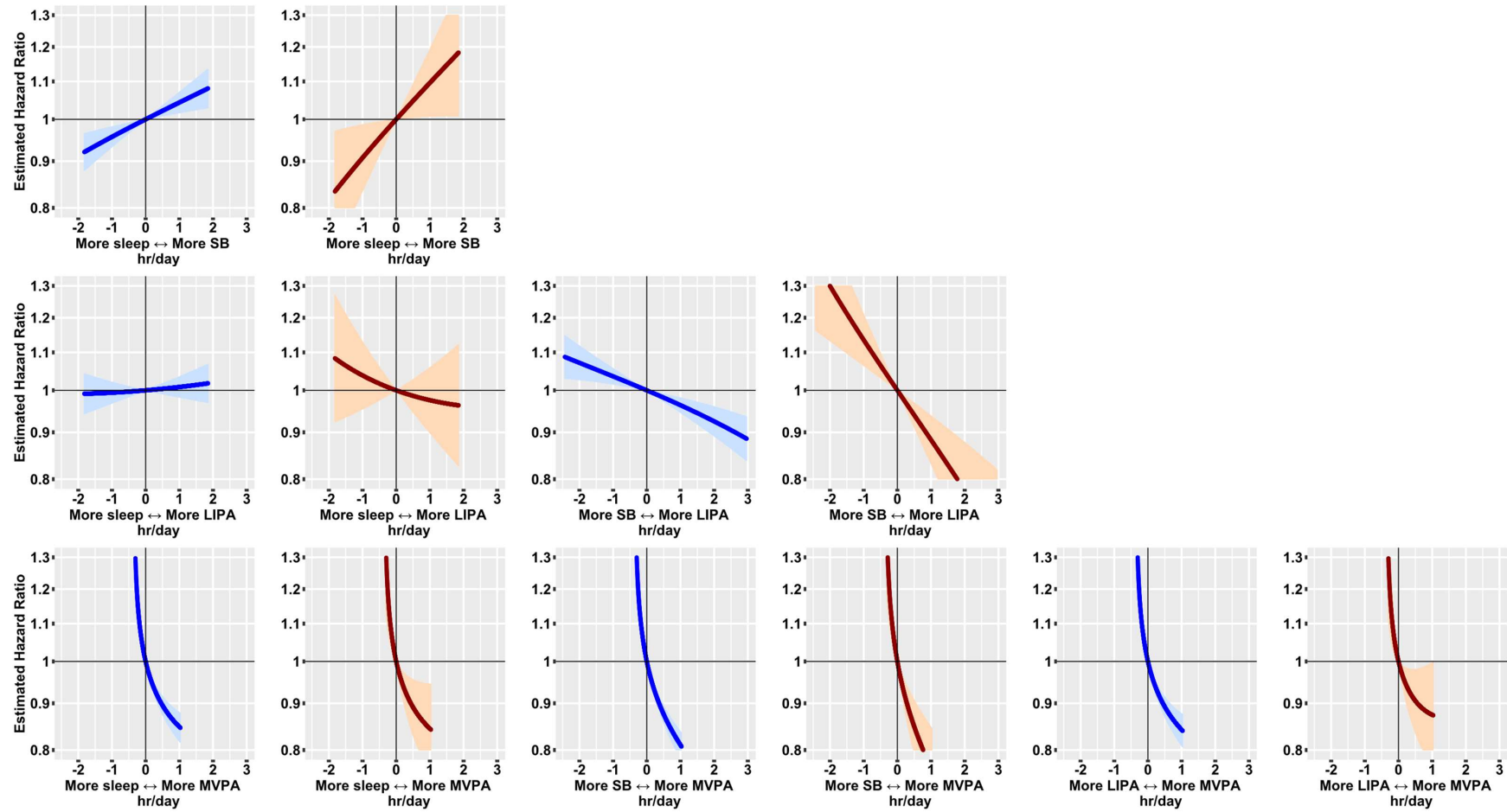
^aModel based on 4,105 events in 87,498 participants. All relative to the mean behaviour composition: 8.8 hours/day sleep, 9.3 hours/day sedentary behaviour, 5.6 hours/day light physical activity behaviours, 0.35 hours/day (21 minutes/day) moderate-to-vigorous physical activity behaviours. Multivariable-adjusted model used age as the timescale, was stratified by sex and was additionally adjusted for ethnicity, smoking status, alcohol consumption, fresh fruit and vegetable consumption, red and processed meat consumption, oily fish consumption, deprivation and education. Minimally-adjusted model used age as the timescale and was stratified by sex.

Supplementary Figure 4: Hazard Ratios for incident cardiovascular disease estimated using a multivariable-adjusted Cox regression model before (blue) and after (red) stratification by BMI.^a



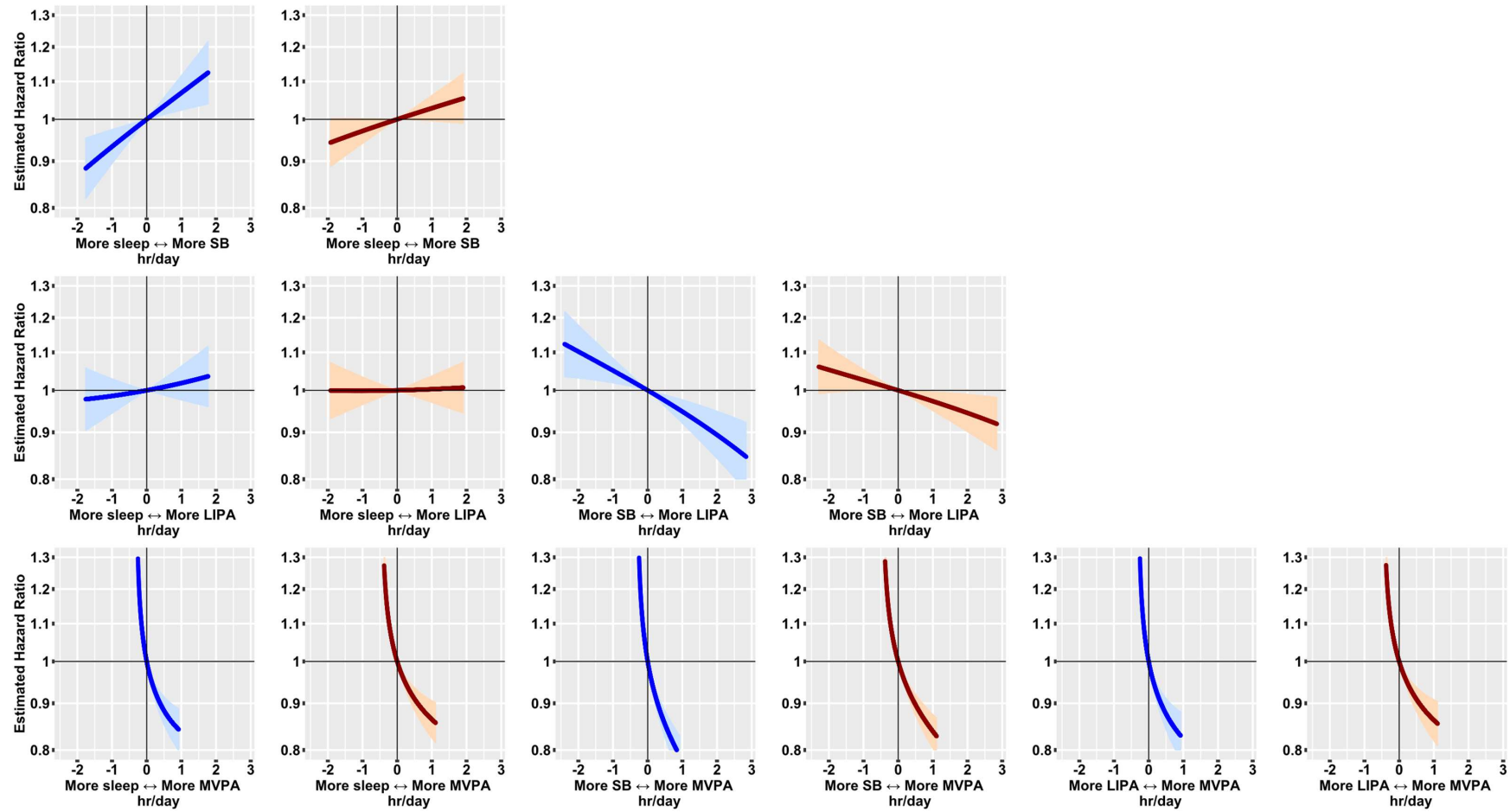
^aModel based on 4,105 events in 87,498 participants. All relative to the mean behaviour composition: 8.8 hours/day sleep, 9.3 hours/day sedentary behaviour, 5.6 hours/day light physical activity behaviours, 0.35 hours/day (21 minutes/day) moderate-to-vigorous physical activity behaviours. Models used age as the timescale, were stratified by sex and were additionally adjusted for ethnicity, smoking status, alcohol consumption, fresh fruit and vegetable consumption, red and processed meat consumption, oily fish consumption, deprivation and education.

Supplementary Figure 5: Hazard Ratios for all (blue) and fatal (red) incident cardiovascular disease for all behaviour pairs estimated using a multivariable-adjusted Cox regression model.^a



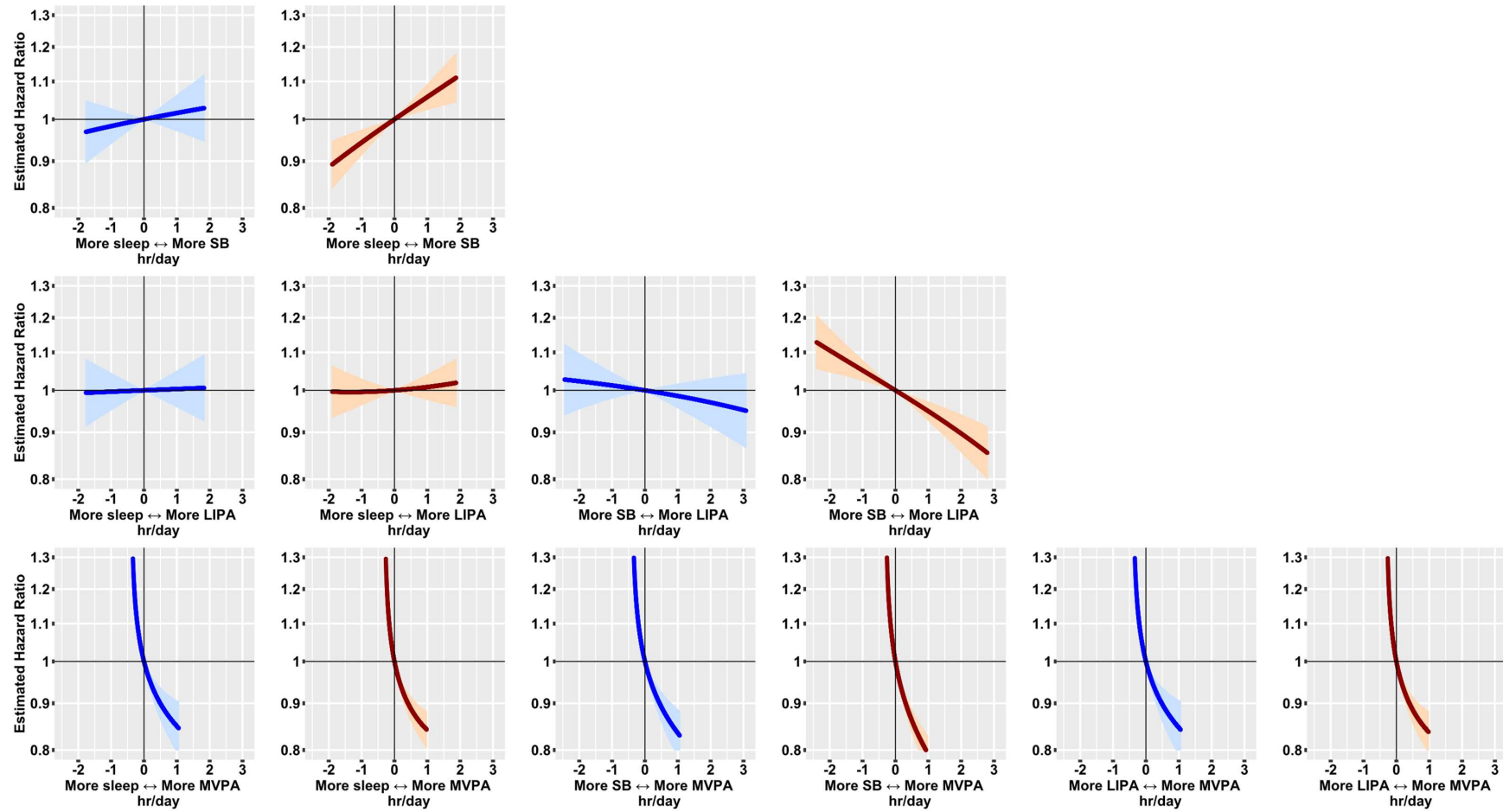
^aModels based on 4,105 events and 348 cardiovascular deaths in 87,498 participants. All relative to the mean behaviour composition: 8.8 hours/day sleep, 9.3 hours/day sedentary behaviour, 5.6 hours/day light physical activity behaviours, 0.35 hours/day (21 minutes/day) moderate-to-vigorous physical activity behaviours. Models used age as the timescale, were stratified by sex and were additionally adjusted for ethnicity, smoking status, alcohol consumption, fresh fruit and vegetable consumption, red and processed meat consumption, oily fish consumption, deprivation and education.

Supplementary Figure 6: Hazard Ratios for incident cardiovascular disease for all behaviour pairs estimated using a multivariable-adjusted Cox regression model for women (blue) and men (red).^a



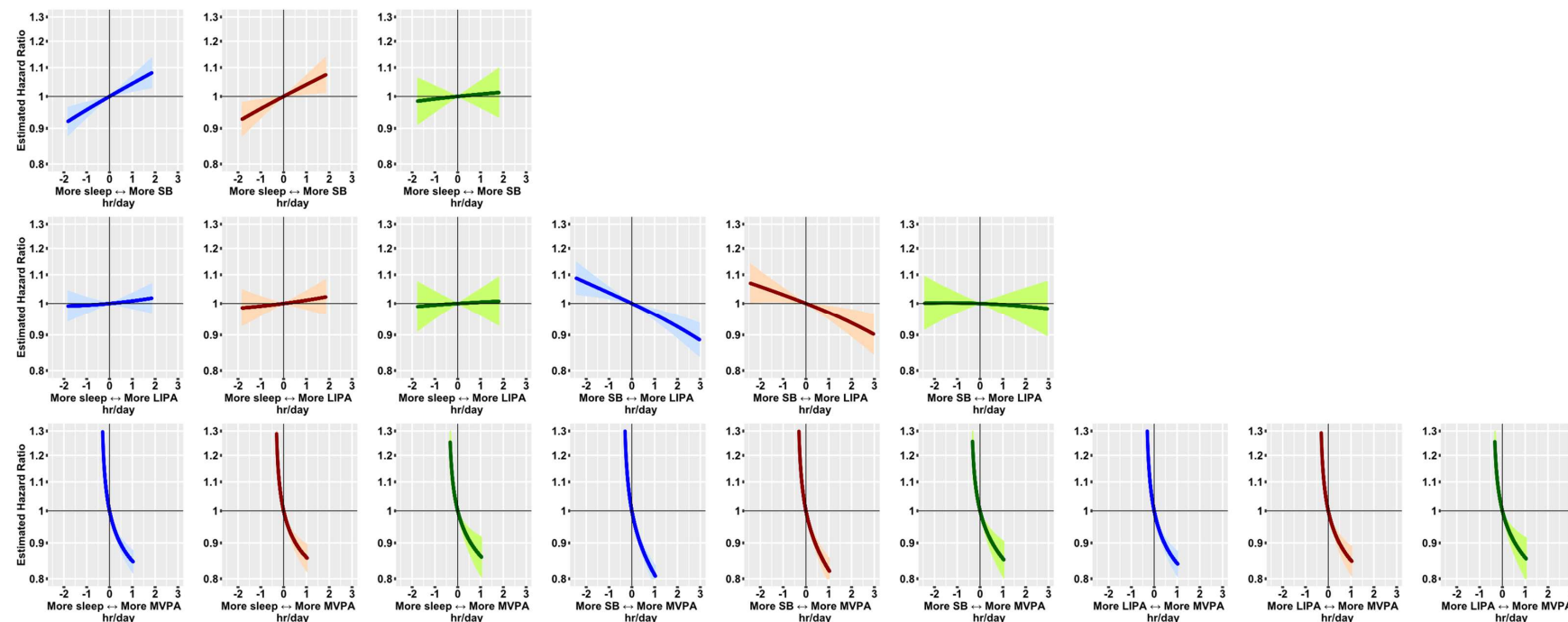
^aModels based on 1,654 events in 50,882 women and 2,451 events in 36,616 men. All relative to the mean behaviour composition in each case (women – 8.9 hours/day sleep, 9.0 hours/day sedentary behaviour, 5.9 hours/day light physical activity behaviours, 0.30 hours/day (18 minutes/day) moderate-to-vigorous physical activity behaviours; men – 8.7 hours/day sleep, 9.7 hours/day sedentary behaviour, 5.1 hours/day light physical activity behaviours, 0.45 hours/day (27 minutes/day) moderate-to-vigorous physical activity behaviours). Models used age as the timescale and were additionally adjusted for ethnicity, smoking status, alcohol consumption, fresh fruit and vegetable consumption, red and processed meat consumption, oily fish consumption, deprivation and education.

Supplementary Figure 7: Hazard Ratios for incident cardiovascular disease for all behaviour pairs estimated using a multivariable-adjusted Cox regression model for participants aged under 65 (blue) and participants aged over 65 (red).^a



^aModels based on 1,425 events in 51,180 participants aged under 65 and 2,680 events in 36,318 participants aged over 65. All relative to the mean behaviour composition in each case (participants aged under 65 – 8.8 hours/day sleep, 9.3 hours/day sedentary behaviour, 5.5 hours/day light physical activity behaviours, 0.39 hours/day (23 minutes/day) moderate-to-vigorous physical activity behaviours; participants aged over 65 – 8.9 hours/day sleep, 9.2 hours/day sedentary behaviour, 5.6 hours/day light physical activity behaviours, 0.30 hours/day (18 minutes/day) moderate-to-vigorous physical activity behaviours). Models used age as the timescale, were stratified by sex and were additionally adjusted for ethnicity, smoking status, alcohol consumption, fresh fruit and vegetable consumption, red and processed meat consumption, oily fish consumption, deprivation and education.

Supplementary Figure 8: Hazard Ratios for incident cardiovascular disease for all behaviour pairs estimated using a multivariable-adjusted Cox regression model (blue), after removing the first two years of follow-up (red) and after additionally restricting to a healthy subgroup (green).^a



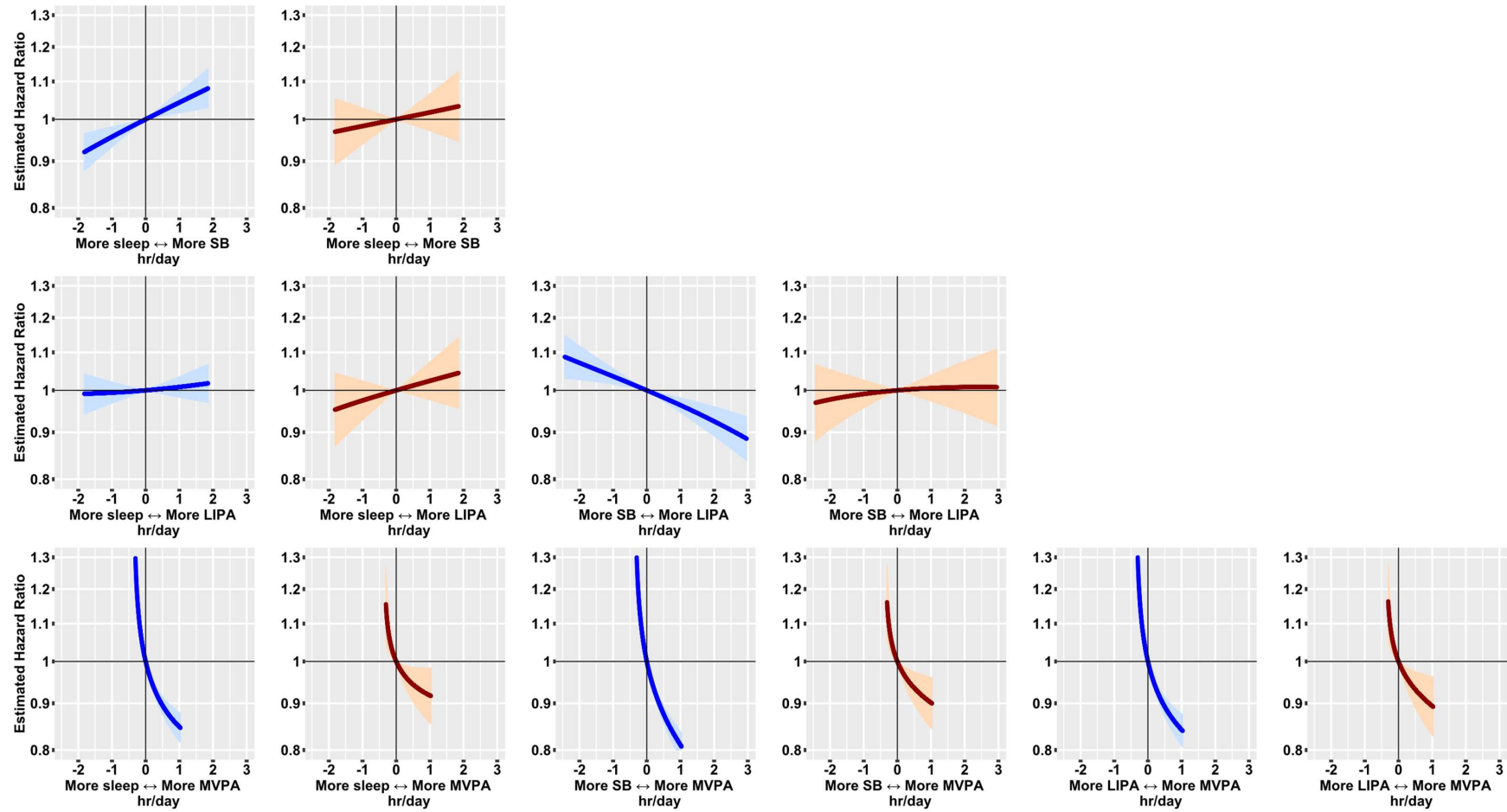
^aMain analysis based on 4,105 events in 87,498 participants. First sensitivity analysis based on 2,947 events in 86,011 participants. Second sensitivity analysis based on 1,597 events in 63,267 participants. Models used age as the timescale, were stratified by sex and were additionally adjusted for ethnicity, smoking status, alcohol consumption, fresh fruit and vegetable consumption, red and processed meat consumption, oily fish consumption, deprivation and education. All values reported relative to the mean behaviour composition in each case:

Main analysis - 8.8 hours/day sleep, 9.3 hours/day sedentary behaviour, 5.6 hours/day light physical activity behaviours, 0.35 hours/day (21 minutes/day) moderate-to-vigorous physical activity behaviours

1st sensitivity - 8.8 hours/day sleep, 9.3 hours/day sedentary behaviour, 5.6 hours/day light physical activity behaviours, 0.35 hours/day (21 minutes/day) moderate-to-vigorous physical activity behaviours

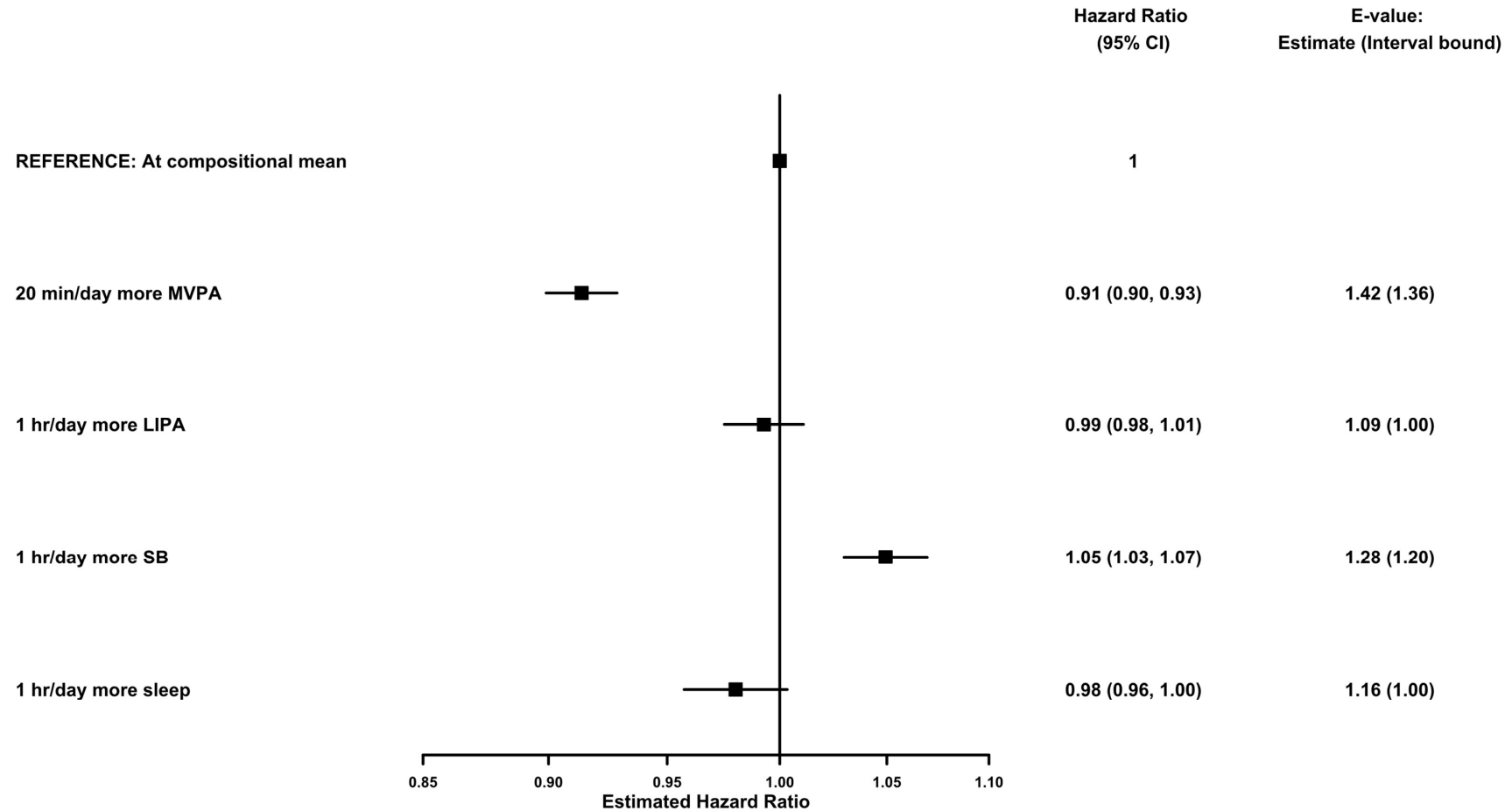
2nd sensitivity - 8.8 hours/day sleep, 9.2 hours/day sedentary behaviour, 5.6 hours/day light physical activity behaviours, 0.39 hours/day (23 minutes/day) moderate-to-vigorous physical activity behaviours.

Supplementary Figure 9: Hazard Ratios for cardiovascular disease (blue) and for non-activity-related accidents (red) for all behaviour pairs estimated using a multivariable-adjusted Cox regression model.^a



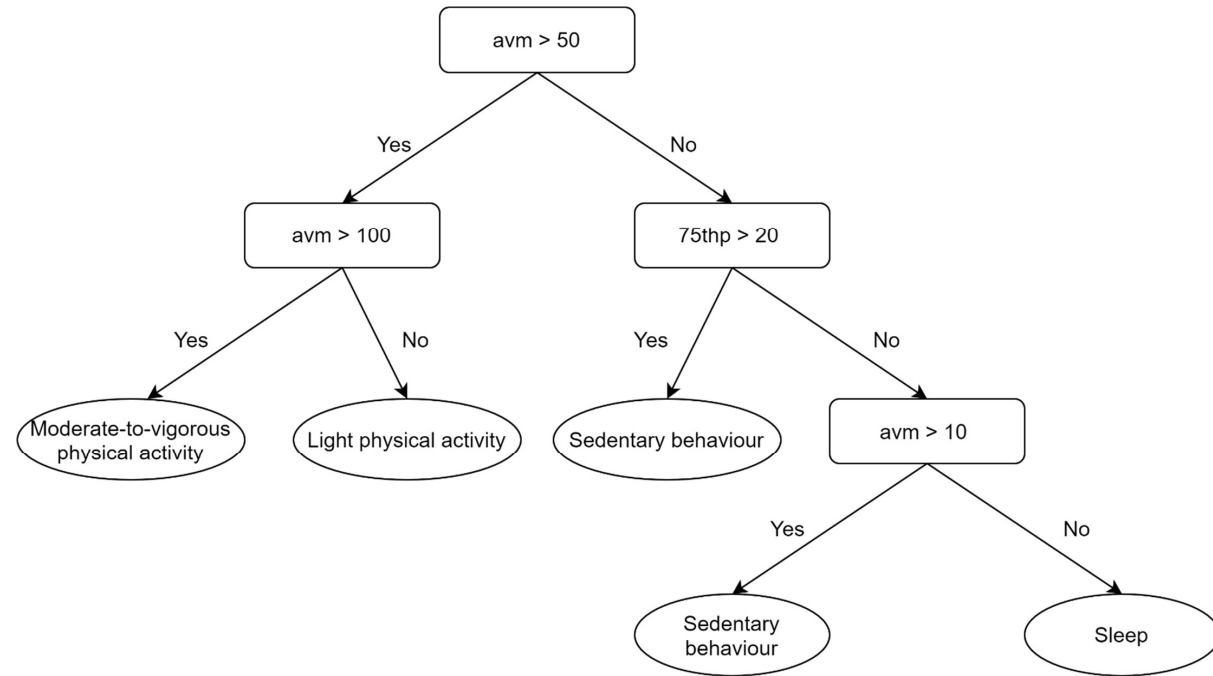
^aMain model based on 4,105 events in 87,498 participants. Negative control model based on 1,375 events in 84,552 participants (participants with prior accident additionally excluded). All relative to the mean behaviour composition in each case (both 8.8 hours/day sleep, 9.3 hours/day sedentary behaviour, 5.6 hours/day light physical activity behaviours, 0.35 hours/day (21 minutes/day) moderate-to-vigorous physical activity behaviours). Models used age as the timescale, were stratified by sex and were additionally adjusted for ethnicity, smoking status, alcohol consumption, fresh fruit and vegetable consumption, red and processed meat consumption, oily fish consumption, deprivation and education.

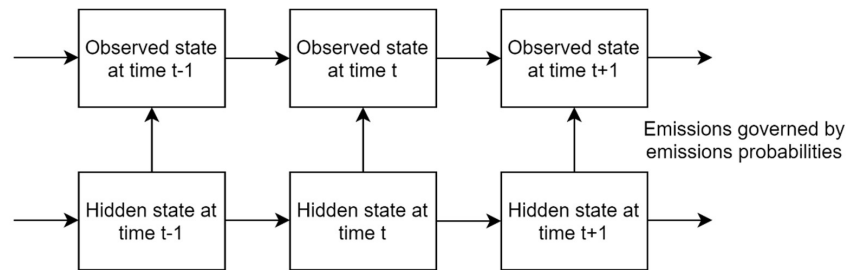
Supplementary Figure 10: Hazard ratios and corresponding E-values for incident cardiovascular disease associated with reallocating time to named behaviour, from all other behaviours proportionally, in 87,498 UK Biobank participants.^a



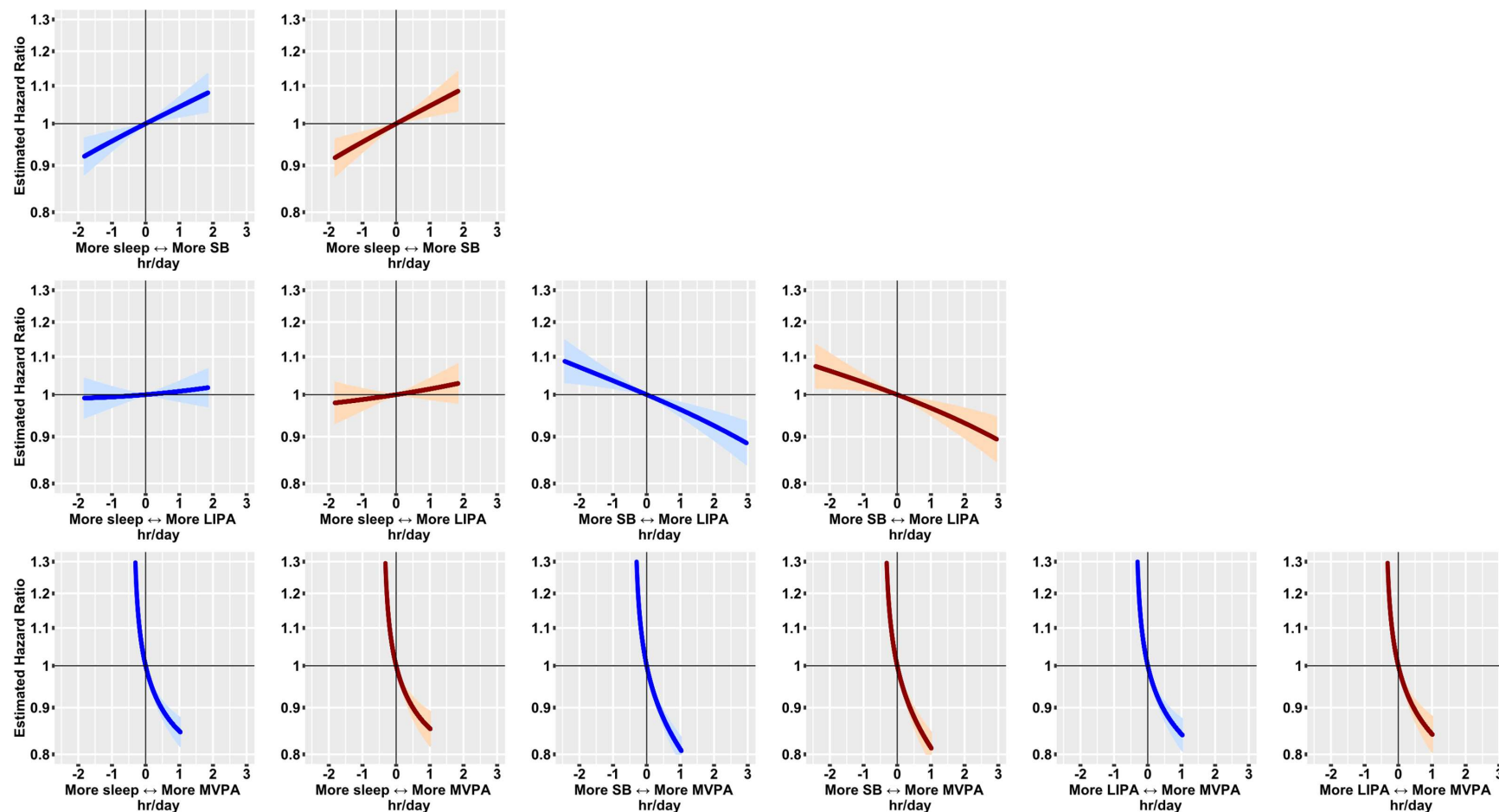
^aModel based on 4,105 events in 87,498 participants. All relative to the mean behaviour composition (8.8 hours/day sleep, 9.3 hours/day sedentary behaviour, 5.6 hours/day light physical activity behaviours, 0.35 hours/day (21 minutes/day) moderate-to-vigorous physical activity behaviours) and more time in named behaviour reallocated from all other behaviours proportionally. Model used age as the timescale, was stratified by sex and was additionally adjusted for ethnicity, smoking status, alcohol consumption, fresh fruit and vegetable consumption, red and processed meat consumption, oily fish consumption, deprivation and education.

Supplementary Figure 11: An example of a decision tree to classify time windows using average acceleration vector magnitude (avm) and the 75th percentile of acceleration vector magnitude (75thp).



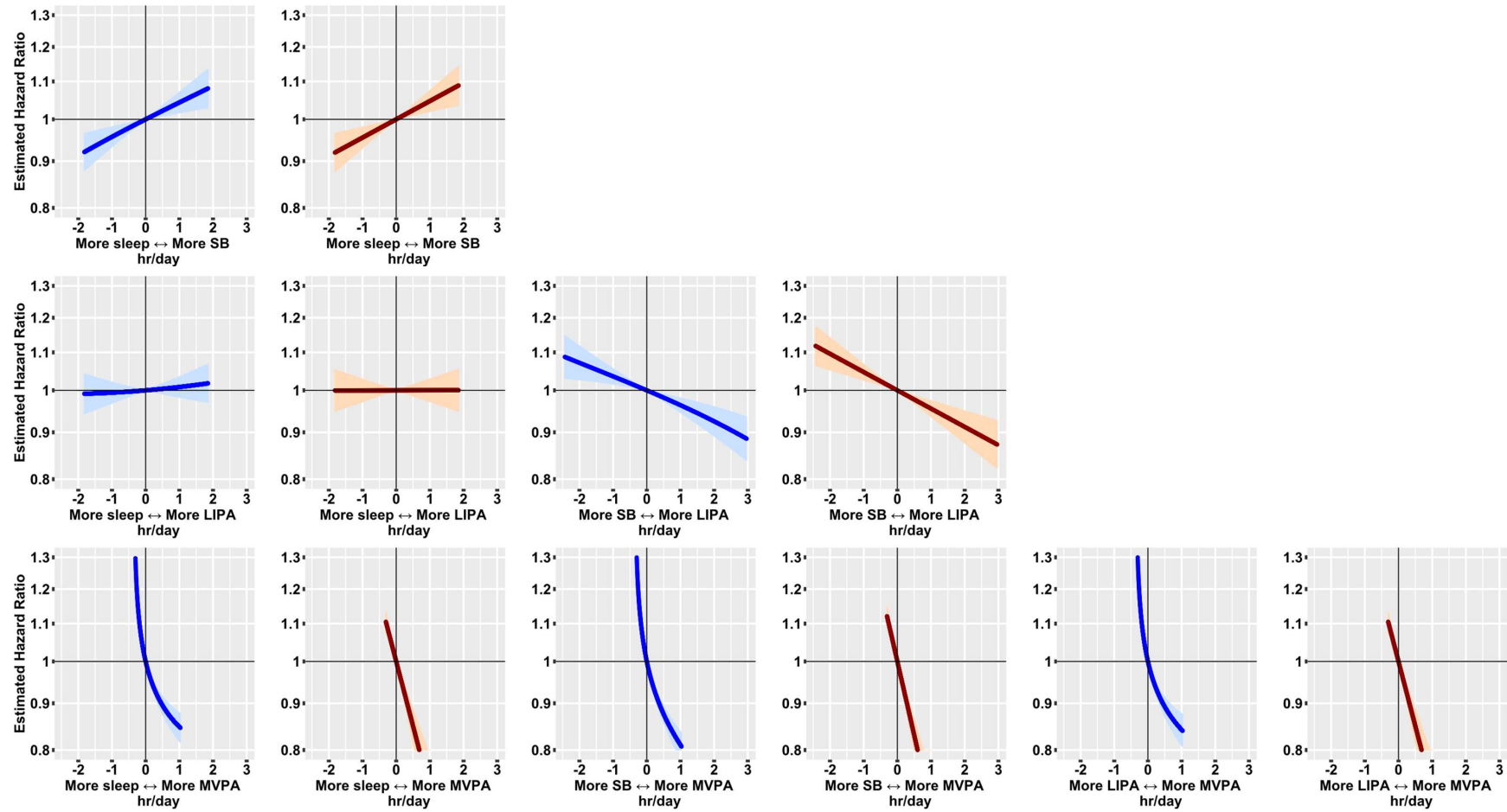
Supplementary Figure 12: The structure of a Hidden Markov Model.

Supplementary Figure 13: Hazard Ratios for incident cardiovascular disease for all behaviour pairs estimated using a multivariable-adjusted Cox regression model for all participants (blue) and in a sensitivity analysis excluding individuals with a zero value in any behaviour (red).^a



^aMain model based on 4,105 events in 87,498 participants. Model excluding individuals with zero values based on 4,017 events in 86,696 participants. All relative to the mean behaviour composition in each case (main analysis – 8.8 hours/day sleep, 9.3 hours/day sedentary behaviour, 5.6 hours/day light physical activity behaviours, 0.35 hours/day (21 minutes/day) moderate-to-vigorous physical activity behaviours; analysis excluding individuals with zero values – 8.8 hours/day sleep, 9.3 hours/day sedentary behaviour, 5.6 hours/day light physical activity behaviours, 0.37 hours/day (22 minutes/day) moderate-to-vigorous physical activity behaviours). Models used age as the timescale, were stratified by sex and were additionally adjusted for ethnicity, smoking status, alcohol consumption, fresh fruit and vegetable consumption, red and processed meat consumption, oily fish consumption, deprivation and education.

Supplementary Figure 14: Hazard Ratios for incident cardiovascular disease estimated using a multivariable-adjusted Compositional Data Analysis Cox regression model (blue) and using a multivariable-adjusted linear isotemporal substitution Cox regression model (red).^a



^aModel based on 4,105 events in 87,498 participants. All relative to the mean behaviour composition: 8.8 hours/day sleep, 9.3 hours/day sedentary behaviour, 5.6 hours/day light physical activity behaviours, 0.35 hours/day (21 minutes/day) moderate-to-vigorous physical activity behaviours. Models used age as the timescale, were stratified by sex and were additionally adjusted for ethnicity, smoking status, alcohol consumption, fresh fruit and vegetable consumption, red and processed meat consumption, oily fish consumption, deprivation and education.

STROBE Statement—Checklist of items that should be included in reports of cohort studies

	Item No	Recommendation	Included
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	Yes
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	Yes
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	Yes
Objectives	3	State specific objectives, including any prespecified hypotheses	Yes, No pre-specified hypotheses
Methods			
Study design	4	Present key elements of study design early in the paper	Yes
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Yes
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	Yes
		(b) For matched studies, give matching criteria and number of exposed and unexposed	NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	Yes
Data sources/measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	Yes
Bias	9	Describe any efforts to address potential sources of bias	Yes
Study size	10	Explain how the study size was arrived at	Yes
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Yes
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	Yes
		(b) Describe any methods used to examine subgroups and interactions	Yes
		(c) Explain how missing data were addressed	Yes
		(d) If applicable, explain how loss to follow-up was addressed	Yes
		(e) Describe any sensitivity analyses	Yes

Results

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Yes
		(b) Give reasons for non-participation at each stage	Yes
		(c) Consider use of a flow diagram	Yes
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Yes
		(b) Indicate number of participants with missing data for each variable of interest	Yes
		(c) Summarise follow-up time (eg, average and total amount)	Yes
Outcome data	15*	Report numbers of outcome events or summary measures over time	Yes
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Yes: confounder-adjusted estimates and estimates adjusted for only age and sex given.
		(b) Report category boundaries when continuous variables were categorized	Yes.
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Not included.
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Yes.
Discussion			
Key results	18	Summarise key results with reference to study objectives	Yes.
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	Yes.
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Yes.
Generalisability	21	Discuss the generalisability (external validity) of the study results	Yes.
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	Yes.

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at <http://www.strobe-statement.org>.

Supplementary Material

Supplementary material for **Reallocation of time between device-measured movement behaviours and risk of incident cardiovascular disease**

Rosemary Walmsley MMathPhil, Shing Chan PhD, Karl Smith-Byrne DPhil, Rema Ramakrishnan PhD, Mark Woodward PhD, Kazem Rahimi FRCP, Terence Dwyer MD, Derrick Bennett PhD, Aiden Doherty PhD

Contents

Supplementary Methods	4
‘Ground truth’ labelling of movement behaviours in image data	4
Machine-learning methods	5
Machine-learning methods: Features	5
Machine-learning methods: Random Forest models	5
Machine-learning methods: Hidden Markov models	5
Machine-learning methods: Evaluation	5
Machine-learning methods: model in participants aged 38 years or older	6
A Compositional Data Analysis approach to movement behaviour data	7
Log-ratio transformation	7
Interpreting isometric log-ratio pivot coordinates	7
Zero values	8
Software	9
Sensitivity analyses: further details on E-values	10
Sensitivity analyses: linear isotemporal substitution	11
References	12
Supplementary Tables and Figures	14
Supplementary Table 1: Assignment of fine-grained camera image annotations from the Compendium of Physical Activities to broad movement behaviour classes.	14
Supplementary Table 2: Features of accelerometry signal used for behaviour classification.	22
Supplementary Table 3: Definition of variables from UK Biobank data included in statistical models.	24
Supplementary Table 4: Characteristics of CAPTURE-24 participants.	27
Supplementary Figure 1: Participant-wise mean (a) precision and (b) recall for classification of behaviours from accelerometer data calculated in Leave-One-Participant-Out Cross-Validation (with 95% confidence interval for the mean). The x-axis gives the minimum required recorded annotator-labelled time in the behaviour for inclusion in the calculation. For precision, participants with no model-labelled time in the behaviour were also excluded as precision is undefined in this case.	28
Supplementary Figure 2: Probability of being in sleep, sedentary behaviour (SB), light physical activity behaviours (LIPA) and moderate-to-vigorous physical activity behaviours (MVPA) among 87,498 UK Biobank participants according to machine-learned behaviour classification by hour of the day.	29
Supplementary Table 5: Coefficient of first isometric log-ratio pivot coordinate ^a for each movement behaviour estimated using a multivariable-adjusted Compositional Data Analysis Cox regression model.	30
Supplementary Table 6: Coefficient of first isometric log-ratio pivot coordinate for each movement behaviour estimated using all Compositional Data Analysis Cox regression models. ^a	31
Supplementary Figure 3: Hazard Ratios for cardiovascular disease for all behaviour pairs estimated using multivariable-adjusted (blue) and minimally adjusted (red) Cox regression models. ^a	32
Supplementary Figure 4: Hazard Ratios for incident cardiovascular disease estimated using a multivariable-adjusted Cox regression model before (blue) and after (red) stratification by BMI. ^a	33
Supplementary Figure 5: Hazard Ratios for all (blue) and fatal (red) incident cardiovascular disease for all behaviour pairs estimated using a multivariable-adjusted Cox regression model. ^a	34
Supplementary Figure 6: Hazard Ratios for incident cardiovascular disease for all behaviour pairs estimated using a multivariable-adjusted Cox regression model for women (blue) and men (red). ^a	35
Supplementary Figure 7: Hazard Ratios for incident cardiovascular disease for all behaviour pairs estimated using a multivariable-adjusted Cox regression model for participants aged under 65 (blue) and participants aged over 65 (red). ^a	36

Supplementary Figure 8: Hazard Ratios for incident cardiovascular disease for all behaviour pairs estimated using a multivariable-adjusted Cox regression model (blue), after removing the first two years of follow-up (red) and after additionally restricting to a healthy subgroup (green). ^a	37
Supplementary Figure 9: Hazard Ratios for cardiovascular disease (blue) and for non-activity-related accidents (red) for all behaviour pairs estimated using a multivariable-adjusted Cox regression model. ^a	38
Supplementary Figure 10: Hazard ratios and corresponding E-values for incident cardiovascular disease associated with reallocating time to named behaviour, from all other behaviours proportionally, in 87,498 UK Biobank participants. ^a	39
Supplementary Figure 11: An example of a decision tree to classify time windows using average acceleration vector magnitude (avm) and the 75 th percentile of acceleration vector magnitude (75thp).	40
Supplementary Figure 12: The structure of a Hidden Markov Model.....	41
Supplementary Figure 13: Hazard Ratios for incident cardiovascular disease for all behaviour pairs estimated using a multivariable-adjusted Cox regression model for all participants (blue) and in a sensitivity analysis excluding individuals with a zero value in any behaviour (red). ^a	42
Supplementary Figure 14: Hazard Ratios for incident cardiovascular disease estimated using a multivariable-adjusted Compositional Data Analysis Cox regression model (blue) and using a multivariable-adjusted linear isotemporal substitution Cox regression model (red). ^a	43
STROBE Statement—Checklist of items that should be included in reports of cohort studies.....	44

Supplementary Methods

'Ground truth' labelling of movement behaviours in image data

As described in the main text, to provide the 'ground truth' labels for machine-learning based behaviour classification, fine-grained behaviour annotations of image data were mapped to sleep, sedentary behaviour, light physical activity behaviours and moderate-to-vigorous physical activity behaviours based on the definition in the main text. In practice, this involved the following steps (the final mapping is given in **Supplementary Table 1**):

1. The fine-grained annotation for sleeping was assigned to sleep.
2. Behaviours at 3 or more METs (Metabolic Equivalent of Task, where 1 MET is energy expenditure in quiet sitting), as described in Compendium of Physical Activities [1], were assigned to moderate-to-vigorous physical activity behaviours.
3. For waking behaviours at <3 METs, if the fine-grained annotation indicated a sitting, lying or reclining posture, the behaviour was assigned to sedentary behaviour.
4. Waking behaviours at <3 METs not assigned to sedentary behaviour were assigned to light physical activity behaviours.
5. All labels were reviewed by two reviewers. Where reviewers agreed the fine-grained annotation was typically used by annotators for behaviours in a different category to the label given, the fine-grained annotation was recoded. This review was performed prior to model training, and no changes were made after results were obtained.

Machine-learning methods

As described in the main text, a Random Forest (RF) with 100 decision trees was developed to classify 30-second time windows as sleep, sedentary behaviour, light physical activity behaviours or moderate-to-vigorous physical activity behaviours using the time and frequency domain features outlined in **Supplementary Table 2**. A Hidden Markov model (HMM) was then employed to use time sequence information to improve on the RF-assigned label sequence. As described in the main text, models were trained using labelled data from the CAPTURE-24 study, in which participants wore wearable cameras and kept time use diaries alongside wearing an accelerometer.

Machine-learning methods: Features

Time windows of acceleration were classified using a list of features (variables) based on features used in the study of Willetts et al (this included time and frequency domain features e.g. mean and kurtosis of the acceleration vector magnitude, and power at different frequencies from the Fast Fourier Transform of acceleration vector magnitude) [2]. In the present study, only rotation-invariant features were used (see **Supplementary Table 2**). This addressed concerns about risk of overfitting and possible time trends in the data driven by sensitivity to device orientation within the wrist strap (orientation became more standardised over 2013-2015).

Machine-learning methods: Random Forest models

Random Forests are based on decision trees. Decision trees assign class labels based on splits of the data using feature value thresholds (as shown in the example in **Supplementary Figure 11**). They can be trained using the Classification and Regression Tree (CART) algorithm [3].

In a RF, many decision trees are used. When training the trees (using the CART algorithm), randomness is introduced by (i) training each tree on a set of data points picked randomly (with replacement) and (ii) at each split node, restricting the choice of splitting feature to a randomly picked subset of features.

To classify a data point using an RF, it is classified by each decision tree. Because they are trained on different subsets of data and use different features, different trees in the RF may classify data points differently. The overall classification given by the RF is the class that is assigned to the data point by the largest number of trees. This approach, whereby multiple randomly-differing instances are used in order to reduce variance on the output, is the technique of bootstrap-aggregating or ‘bagging’ [4].

For this application, a balanced RF was used. The fact some behaviours are much more common than others in the labelled data (e.g. sleep is much more common than moderate-to-vigorous physical activity behaviours) can cause a standard RF, which is trained by picking N examples at random with replacement, to favour assigning common labels at the expense of less common behaviours [2]. Using the balanced RF, if there were n_{rare} examples of the rarest behaviour, n_{rare} examples of each behaviour were picked with replacement to train each tree.

Machine-learning methods: Hidden Markov models

In an HMM, there is a sequence of unobserved hidden states, which is assumed to have the Markov property (i.e. future states only depend on past states through present states). This sequence is governed by transition probabilities, which determine the probability of transitioning between each pair of states. There is a sequence of observed states, which depend probabilistically on the sequence of hidden states (described as ‘emissions’ from the sequence of hidden states; **Supplementary Figure 12**).

Here, the hidden states were the true behaviours, and the emissions were the RF-assigned labels. The Viterbi algorithm, the standard approach to this problem, was used to estimate the most likely true behaviour sequence given the observed sequence of RF-assigned labels [5]. Applying the Viterbi algorithm required estimates of:

1. **Transition probabilities between hidden states:** Transition probabilities between behaviour pairs were estimated using the proportions of transitions that occurred between each behaviour pair in the labelled data.
2. **Emission probabilities of observed states from hidden states:** To estimate emission probabilities, time windows were first classified using out-of-bag predictions from the RF i.e. trees were used to classify data points on which they were not trained. This mimics use on unseen data, without requiring additional data. Emission probabilities were then estimated using the proportions of different pairs of true behaviour and RF out-of-bag estimate.

By using this HMM to estimate the most likely true behaviour sequence given the RF-assigned labels, a more plausible sequence of states was obtained. The HMM re-labelled behaviours which formed unrealistic sequences and were likely to be attributable to misclassification (e.g. short periods of moderate-to-vigorous physical activity behaviours during sleep time). Therefore, compared to the unadjusted RF-assigned labels, the labels after using the HMM gave improved measures of the behaviours of interest for subsequent epidemiological analyses.

Machine-learning methods: Evaluation

All metrics were calculated in Leave-One-Participant-Out Cross-Validation.

Leave-One-Participant-Out Cross-Validation involves, for each participant, a model trained on all other participants’ data (i.e. with this participant’s data left-out). The trained model is then used to label the left-out participant’s data and evaluation metrics are calculated. This is repeated for all participants, and metrics are aggregated or calculated across all participants.

Leave-One-Participant-Out Cross-Validation allows evaluation of the performance of the models on data not used in training, while retaining the maximal amount of data for use in training these models. Moreover, all of the data can then be used to train the final model used for classification.

For model performance, the following evaluation metrics were used:

1. We reported mean per-participant accuracy across all behaviours. This is a simple, intuitive metric of model performance, describing the proportion of 30-second time windows that were correctly classified. Using mean per-participant accuracy, rather than aggregate accuracy over all data, prevents the result being dominated by performance on a few participants with larger amounts of data (important as there may be inter-individual differences in classification performance).
2. We reported mean per-participant Cohen's kappa across all behaviours. This is a metric of interrater reliability. It evaluates how much higher the agreement between two raters (here, annotator-assigned 'ground truth' label and model-assigned label) is than that which would be achieved by chance, given the proportions in each class. It is preferable to accuracy, as it takes into account the proportions in each class (in particular, in data where some classes are dominant, a classifier assigning solely to the dominant classes can achieve high accuracy but not high Cohen's kappa).
3. We reported mean per-participant precision and recall for each behaviour. Precision for a given behaviour is the proportion of examples labelled by the model as that behaviour which are 'true' examples of that behaviour. Recall for a given behaviour is the proportion of 'true' examples of that behaviour labelled as that behaviour. Again, taking the mean across participants prevents performance being dominated by performance on participants with larger amounts of data. However, it also upweights the contribution of individuals with very small amounts of data for a given behaviour. Therefore, precision and recall were additionally calculated after excluding participants with up to 20 minutes in the behaviour.

Taken together, these metrics help to understand the validity of the model as a method to derive measures of movement behaviours for subsequent epidemiological analyses. After applying the model to derive measures of movement behaviours for UK Biobank participants, face validity was assessed by plotting behaviour profiles over the day.

Machine-learning methods: model in participants aged 38 years or older

We also carried out the above steps using only data from participants aged 38 years or older i.e. nearer to the age group represented in the UK Biobank sample. The age group 38+ years was used as this corresponds to the information available in a release version of this dataset.

In Leave-One-Participant-Out analysis, the mean per-participant accuracy was 86% (84, 88) and the mean per-participant Cohen's kappa was 0.79 (0.76, 0.81).

Given the results reported in the main text, showing that the model trained on all participants performed well when restricted to the age group of interest, we used the model trained on all participants for the main classification.

A Compositional Data Analysis approach to movement behaviour data

Log-ratio transformation

A Compositional Data Analysis approach is a set of methods for working with compositional data, based on the use of log-transformed ratios to describe the data [6–8]. Ratios between behaviours are used to describe compositional data as they capture the relative values of the different behaviours. Log-transforming ratios ensures the relationships and distances between different compositions are well-described: using log-transformed ratios is equivalent to working with compositional data in a ‘natural’ space for it, with operations which map compositions to genuine compositions and an appropriate distance metric [9,10]. For statistical purposes, log-transformed ratios are also typically more conveniently distributed than ratios [11].

While many different sets of log-transformed ratios can be used, isometric log-ratio pivot coordinates are widely used in movement behaviour research [12] and were used in this study. They were calculated as follows:

$$coordinate_1 = \sqrt{\frac{3}{4}} \ln \left(\frac{\text{sleep}}{\sqrt[3]{SB \times LIPA \times MVPA}} \right) = \sqrt{\frac{1}{12}} \ln \left(\frac{\text{sleep}}{SB} \right) + \sqrt{\frac{1}{12}} \ln \left(\frac{\text{sleep}}{LIPA} \right) + \sqrt{\frac{1}{12}} \ln \left(\frac{\text{sleep}}{MVPA} \right)$$

$$coordinate_2 = \sqrt{\frac{2}{3}} \ln \left(\frac{SB}{\sqrt[3]{LIPA \times MVPA}} \right) = \sqrt{\frac{1}{6}} \ln \left(\frac{SB}{LIPA} \right) + \sqrt{\frac{1}{6}} \ln \left(\frac{SB}{MVPA} \right)$$

$$coordinate_3 = \sqrt{\frac{1}{2}} \ln \left(\frac{LIPA}{MVPA} \right)$$

Interpreting isometric log-ratio pivot coordinates

As the coefficients in the model relate to the isometric log-ratio pivot coordinates, rather than the raw behaviour variables, interpreting them is not straightforward.

The first coordinate describes the balance between sleep and all other behaviours. Therefore, the coefficient of the first coordinate can be interpreted as the effect of reallocating time to sleep from all other behaviours proportionally i.e. if the coefficient of the first coordinate is greater than 0 (its exponent is greater than 1) reallocating time to sleep from all other behaviours proportionally is associated with higher risk of cardiovascular disease. However, the second and third coordinates are harder to interpret analogously. Therefore, to interpret individually the effect of reallocating time to each behaviour from all others proportionally, and following standard methods in movement behaviour research, one model per behaviour was produced (with different first coordinate). This approach was used to present the model parameters in **Supplementary Table 5** and **Supplementary Table 6** (note that, in consequence, they do not parametrise a single model).

However, even using this approach, the magnitudes of the coefficients are hard to interpret. Therefore, as described in the main text, and following established methods, model estimates of the hazard ratio at different compositions relative to the mean behaviour composition were reported e.g. using pairwise time reallocation plots.

In detail, suppose we have a Cox regression model in the isometric log-ratio pivot coordinates laid out above:

$$\ln \frac{h(t)}{h_0(t)} = \beta_1(\text{coordinate}_1) + \beta_2(\text{coordinate}_2) + \beta_3(\text{coordinate}_3) + \sum_{i=1}^k \gamma_i(\text{covariate}_i)$$

and that the value of the coordinates at the mean behaviour composition is $(m_coordinate_1, m_coordinate_2, m_coordinate_3)$. [This notation is not misleading: the value of the coordinates at the compositional mean behaviour composition is also the mean of the coordinate values.].

Then, we consider a new behaviour composition, which corresponds to isometric log-ratio pivot coordinate values $(coordinate_1, coordinate_2, coordinate_3)$. In particular, when considering a pairwise time reallocation plot we use would use a new composition where time in two behaviours remained at its value in the mean behaviour composition, a value was subtracted from time in one of the remaining behaviours, and that value added to the time in the other behaviour. The log hazard ratio, now relative to the mean behaviour composition, is then calculated as:

$$\ln(HR) = \beta_1(\text{coordinate}_1 - m_coordinate_1) + \beta_2(\text{coordinate}_2 - m_coordinate_2) + \beta_3(\text{coordinate}_3 - m_coordinate_3)$$

The standard error on this can be calculated using the variance-covariance matrix of the coefficients $\boldsymbol{\beta} = (\beta_1, \beta_2, \beta_3)$, denoted V . Writing $\mathbf{x} = (\text{coordinate}_1 - m_coordinate_1, \text{coordinate}_2 - m_coordinate_2, \text{coordinate}_3 - m_coordinate_3)^T$, then

$$SE = \sqrt{\mathbf{x}^T V \mathbf{x}}$$

This can be used to calculate the HR and an (approximate) 95% CI as:

$$\exp(\ln(HR)) (\exp(\ln(HR) - 1.96SE), \exp(\ln(HR) + 1.96SE)).$$

While here we follow an exposition similar to that of Dumuid et al in the context of linear regression [13] and Chastin et al [14], the approach is mathematically equivalent to that of McGregor et al.[15]

To ensure results were plotted within the range supported by the data, times plotted were truncated at the 5th and 95th centile for the behaviour in the pair for which this range was narrower.

Zero values

All participants recorded time in sleep, sedentary behaviour and light physical activity behaviours, but 1% of participants recorded no time in moderate-to-vigorous physical activity behaviours. As zero values cannot be incorporated directly into the coordinates above, different approaches to work with them have been developed. The appropriate method depends on the source of the zero values:

1. ‘Rounded’ zeroes relate to measurement precision: even where no time in a given behaviour was observed, had the wear time been long enough, or the time resolution of the measurement short enough, some time in the behaviour would be expected. If data contains rounded zeroes, they can be imputed as small positive values [16].
2. ‘True’ zeroes occur where no matter the precision of the measurement, no time in that behaviour would be observed. For example, this may occur in movement behaviour research if someone is physically unable to take part in certain behaviours. If data contains true zeroes, participants with a true zero in a particular behaviour should be excluded from the main analysis and analysed separately.

We followed established methods in movement behaviour research by considering zero values to be ‘rounded’ and imputing them using the log-ratio expectation maximization algorithm from the ‘zCompositions’ R package [8,15–17]. We used the smallest observed value in the data as the detection limit (0.0001 on the unitless scale, corresponding to 0.14 min/day). Sensitivity of results to the method of treating zero values (imputation or exclusion) under the Compositional Data Analysis approach was examined by performing an analysis restricted to participants with non-zero values in all behaviour variables. This did not materially impact the results (**Supplementary Figure 13**).

Software

Development of the machine-learning models and processing of accelerometer data used Python 3.6.6, with the ‘biobankAccelerometerAnalysis’ tool[2,18,19] for preparing accelerometer data and training machine-learning models.

Data preparation was performed in Python 3.6.6 and R 4.0.5, and used the ‘ukb_download_and_prep_template’ tool [20] for preparing covariate and outcome data.

Statistical analysis was performed in R 4.0.5[21] with ‘zCompositions’, ‘survival’, ‘forestplot’, ‘EValue’, ‘plyr’, ‘data.table’, ‘rlist’, ‘ggtern’, ‘ggplot2’, and ‘gtools’[16,22–32]. The R package ‘epicoda’ was developed for this analysis[33].

For directions to the code used, please contact Aiden Doherty.

Sensitivity analyses: further details on E-values

As described in the main text, E-values were reported alongside hazard ratios. The E-value for the estimate quantifies the minimum strength of association that an unmeasured confounder would need with both exposure and outcome to explain away the observed association. The E-value for the 95% confidence interval quantifies the minimum strength of association an unmeasured confounder would need with both exposure and outcome to reduce the interval to overlap the null [27,28]. As the exposure is continuous, in both cases the risk ratio would apply to hypothetical groups with either the specified behaviour composition or the reference (the mean behaviour composition) [28].

Sensitivity analyses: linear isotemporal substitution

For comparability with previous literature, a sensitivity analysis using a linear isotemporal substitution approach was conducted.

Under a linear isotemporal substitution approach, all but one of the movement behaviours are included in the model (so the included variables are not perfectly multicollinear). [In this study, as non-wear time was imputed all subjects had the same wear time. Therefore, a total time variable was not included, meaning the approach may be more properly called 'leave-one-out regression' than true linear isotemporal substitution [8].] Associations are modelled as linear (rather than linear in the log-ratios, as under a Compositional Data Analysis approach). The coefficient of each behaviour can be interpreted in terms of replacing time in the left-out behaviour with time in that behaviour. Linear isotemporal substitution has been widely used in movement behaviour epidemiology [34], but has been criticised for not addressing the fact movement behaviour data only conveys relative information [8].

While there were some differences in shape of the associations observed (due to the different assumptions), results using this approach were broadly similar to the results of the main analysis using Compositional Data Analysis (**Supplementary Figure 14**).

References

- 1 Ainsworth BE, Haskell WL, Herrmann SD, *et al.* 2011 compendium of physical activities: A second update of codes and MET values. *Med Sci Sports Exerc* 2011;**43**:1575–81. doi:10.1249/MSS.0b013e31821ece12
- 2 Willetts M, Hollowell S, Aslett L, *et al.* Statistical machine learning of sleep and physical activity phenotypes from sensor data in 96,220 UK Biobank participants. *Sci Rep* 2018;**8**:0–10. doi:10.1038/s41598-018-26174-1
- 3 Breiman L, Friedman JH, Olshen RA, *et al.* *Classification and regression trees*. 1984. doi:10.1201/9781315139470
- 4 Breiman L. Bagging predictors. *Mach Learn* 1996;**24**:123–40. doi:10.1007/bf00058655
- 5 Forney GD. The Viterbi Algorithm. *Proc IEEE* 1973;**61**:268–78. doi:10.1109/PROC.1973.9030
- 6 Pawlowsky-Glahn V, Egozcue JJ, Tolosana-Delgado R. Lecture notes on Compositional Data Analysis. 2011;:1–100. doi:10.13140/RG.2.1.1296.2728
- 7 Filzmoser P, Hron K, Templ M. *Applied Compositional Data Analysis*. 2018. doi:10.1007/978-3-319-96422-5
- 8 Dumuid D, Pedišić Ž, Palarea-Albaladejo J, *et al.* Compositional Data Analysis in Time-Use Epidemiology : What , Why , How. *Int J Environ Res Public Health* 2020;**17**:2220. doi:10.3390/ijerph17072220
- 9 Aitchison J, Egozcue JJ. Compositional data analysis: Where are we and where should we be heading? *Math Geol* Published Online First: 2005. doi:10.1007/s11004-005-7383-7
- 10 Egozcue JJ, Pawlowsky-Glahn V, Mateu-Figueras G, *et al.* Isometric Logratio Transformations for Compositional Data Analysis. *Math Geol* 2003;**35**:279–300. doi:10.1023/A:1023818214614
- 11 Aitchison J. The statistical analysis of compositional data. *Stat Anal Compos Data* 1982;**44**:139–77. doi:10.1007/978-94-009-4109-0
- 12 Dumuid D, Stanford TE, Martín-Fernández J-AA, *et al.* Compositional data analysis for physical activity, sedentary time and sleep research. *Stat Methods Med Res* 2017;**27**:096228021771083. doi:10.1177/0962280217710835
- 13 Dumuid D, Pedišić Ž, Stanford TE, *et al.* The compositional isotemporal substitution model: A method for estimating changes in a health outcome for reallocation of time between sleep, physical activity and sedentary behaviour. *Stat Methods Med Res* 2017;**28**:846–57. doi:10.1177/0962280217737805
- 14 Chastin S, McGregor D, Palarea-Albaladejo J, *et al.* Joint association between accelerometry-measured daily combination of time spent in physical activity, sedentary behaviour and sleep and all-cause mortality: a pooled analysis of six prospective cohorts using compositional analysis. *Br J Sports Med* 2021;:bjssports-2020-102345. doi:10.1136/bjssports-2020-102345
- 15 McGregor DE, Palarea-Albaladejo J, Dall PMP, *et al.* Cox regression survival analysis with compositional covariates: Application to modelling mortality risk from 24-h physical activity patterns. *Stat Methods Med Res* 2019;**29**:1447–65. doi:10.1177/0962280219864125
- 16 Palarea-Albaladejo J, Martín-Fernández JA. ZCompositions - R package for multivariate imputation of left-censored data under a compositional approach. *Chemom. Intell. Lab. Syst.* 2015;**143**:85–96. doi:10.1016/j.chemolab.2015.02.019
- 17 Rasmussen CL, Palarea-Albaladejo J, Johansson MS, *et al.* Zero problems with compositional data of physical behaviors: a comparison of three zero replacement methods. *Int J Behav Nutr Phys Act* 2020.
- 18 Doherty A, Jackson D, Hammerla N, *et al.* Large scale population assessment of physical activity using wrist worn accelerometers: The UK biobank study. *PLoS One* 2017;**12**:1–14. doi:10.1371/journal.pone.0169649
- 19 Doherty A, Smith-Byrne K, Ferreira T, *et al.* GWAS identifies 14 loci for device-measured physical activity and sleep duration. *Nat Commun* 2018;**9**. doi:10.1093/acrefore/9780190236557.013.204
- 20 Walmsley R, Chan S, Doherty A. `ukb_download_and_prep_template`. 2020.https://github.com/activityMonitoring/ukb_download_and_prep_template
- 21 R Core Team. R: A Language and Environment for Statistical Computing. *Vienna, Austria* Published Online First: 2019.<https://www.r-project.org/>
- 22 Therneau TM. A Package for Survival Analysis in R. 2021.<https://cran.r-project.org/package=survival>
- 23 Wickham H. *ggplot2: Elegant Graphics for Data Analysis*. New York: : Springer-Verlag 2016. <https://ggplot2.tidyverse.org>
- 24 Warnes GR, Bolker B, Lumley T. `gtools`: Various R Programming Tools. *R Packag version 381* 2018.
- 25 Terry M, Therneau, Patricia M. Grambsch. *Modeling Survival Data: Extending the Cox Model*. New York: : Springer 2000.
- 26 Max Gordon and Thomas Lumley. `forestplot`: Advanced Forest Plot Using ‘grid’ Graphics. R package version 1.9. 2019.<https://cran.r-project.org/package=forestplot>
- 27 Van Der Wee TJ, Ding P. Sensitivity analysis in observational research: Introducing the E-Value. *Ann Intern Med* 2017;**167**:268–74. doi:10.7326/M16-2607

- 28 Mathur MB, Ding P, Riddell CA, *et al.* Web Site and R Package for Computing E-values. *Epidemiology* 2018;**29**:e45. doi:10.1097/EDE.0000000000000864
- 29 Wickham H. The Split-Apply-Combine Strategy for Data Analysis. *J Stat Softw* 2011;**40**:1–29. <http://www.jstatsoft.org/v40/i01/>
- 30 Dowle M, Srinivasan A. data.table: Extension of `data.frame`. 2021. <https://cran.r-project.org/package=data.table>
- 31 Ren K. rlist: A Toolbox for Non-Tabular Data Manipulation. 2016. <https://cran.r-project.org/package=rlist>
- 32 Hamilton NE, Ferry M. Ggtern: Ternary diagrams using ggplot2. *J Stat Softw* 2018;**87**:1–17. doi:10.18637/jss.v087.c03
- 33 Walmsley R. epicoda. 2020. github.com/activityMonitoring/epicoda
- 34 Mekary RA, Ding EL. Isotemporal substitution as the gold standard model for physical activity epidemiology: Why it is the most appropriate for activity time research. *Int J Environ Res Public Health* 2019;**16**:11–3. doi:10.3390/ijerph16050797

Supplementary Tables and Figures

Supplementary Table 1: Assignment of fine-grained camera image annotations from the Compendium of Physical Activities to broad movement behaviour classes.

<p><u>Sleep</u></p> <p>7030 sleeping</p>
<p><u>Sedentary behaviour</u></p> <p>occupation;office and administrative support;11580 office/computer work general</p> <p>occupation;office and administrative support;11580 office wok/computer work general</p> <p>home activity;miscellaneous;sitting;9060 sitting/lying reading or without observable/identifiable activities</p> <p>leisure;miscellaneous;sitting;0010 sitting / lying dialysis</p> <p>transportation;private transportation;16010 driving automobile or light truck (not a semi)</p> <p>home activity;miscellaneous;sitting;7010 sitting/lying and watching television with TV on as the primary activity</p> <p>home activity;miscellaneous;sitting;11580 office/computer work general</p> <p>home activity;miscellaneous;sitting;9055 sitting/lying talking in person/using a mobile phone/smartphone/tablet or talking on the phone/computer (skype chatting)</p> <p>home activity;miscellaneous;sitting;11580 office work such as writing and typing (with or without eating at the same time)</p> <p>home activity;eating;13030 eating sitting alone or with someone</p> <p>home activity;miscellaneous;sitting;9030 sitting desk entertainment/hobby (with or without eating at the same time)</p> <p>home activity;miscellaneous;sitting;5080 sitting non-desk work (with or without eating at the same time)</p> <p>occupation;interruption;sitting;11585 sitting meeting/talking to colleagues with or without eating</p> <p>leisure;miscellaneous;sitting;9060 (generic) sitting/lying reading or without observable/identifiable activities</p> <p>occupation;interruption;11585 sitting meeting/talking to colleages with or without eating</p> <p>home activity;leisure;activities for maintenance of a household;miscellaneous;9100 retreat/family reunion activities involving sitting eating relaxing talking with more than one person</p> <p>home activity;miscellaneous;sitting;9060 sitting/lying reading or without observable activities</p> <p>leisure;eating;social;13030 eating sitting indoor/outdoor</p> <p>home activity;leisure;activities for maintenance of a household;miscellaneous;9100 retreat/family reunion activities involving sitting eating relaxing talking with more than one person</p> <p>occupation;public admin/education/health;education;9065 students/attending seminars or talks</p> <p>home activity;miscellaneous;sitting;9030 sitting desk work (with or without eating at the same time)</p> <p>occupation;interruption;sitting;9060 sitting without observable/identifiable activities</p>

leisure;miscellaneous;sitting;9055 sitting talking to person/using the phone
transportation;private transportation;16015 riding in a car or truck
leisure;eating;13030 eating sitting indoor/outdoor
occupation;interruption;13030 eating sitting
home activity;miscellaneous;sitting;9045 sitting playing traditional video game computer game
home activity;miscellaneous;sitting;9030 sitting desk work (with or without eating at the same time)
occupation;interruption;sitting;13030 eating sitting
home activity;leisure;individual activities;9075 sitting arts and crafts carving/wood weaving/spinning wool
home activity;household chores;washing/ironing/mending clothes;5080 knitting sewing sitting
occupation;interruption;sitting;9055 sitting using a mobile phone/smartphone/tablet or talking on the phone/computer (skype meeting etc.)
leisure;miscellaneous;sitting;21000 sitting meeting
leisure;miscellaneous;sitting;21005 (generic) sitting light office writing typing work
occupation;office and administrative support;11580 office work/computer work general
home activity;miscellaneous;sitting;7010 lying and watching television with TV on as the primary activity
leisure;miscellaneous;sitting;9060 (generic) sitting/lying reading or without observable activities
transportation;waiting;7021 sitting
occupation;interruption;11585 sitting meeting/talking to colleagues with or without eating
leisure;religious activities;20000 sitting in church in service attending a ceremony sitting quietly
transportation;private transportation;16030 motor scooter motorcycle
occupation;interruption;9055 sitting using a mobile phone/smartphone/tablet or talking on the phone/computer (skype meeting etc.)
leisure;miscellaneous;21005 (generic) sitting light office writing typing work
home activity;miscellaneous;sitting;7021 sitting without observable activities
home activity;leisure;activities for maintenance of a household;with children;5170 sitting playing with child(ren)
home activity;leisure;activities for maintenance of a household;with children;5170 sitting playing with child(ren)
occupation;interruption;9060 (generic) sitting without observable activities
home activity;child/elderly/pet care;child care;5185 child care sitting/kneeling
home activity;miscellaneous;sitting;21010 sitting non-desk work (with or without eating at the same time)
leisure;eating;not-social;13030 eating sitting indoor/outdoor
leisure;miscellaneous;sitting;5080 sitting non-desk work (with or without eating at the same time)
home activity;leisure;activities for maintenance of a household;9100 retreat/family reunion activities involving sitting eating relaxing talking with more than one person

leisure;miscellaneous;sitting;21016 sitting child care only active periods
 home activity;leisure;activities for maintenance of a household;5170 sitting playing with child(ren)
 home activity;lawn and garden;gardening service;8055 driving tractor
 occupation;interruption;9060 (generic) sitting without observable/identifiable activities
 home activity;self care;13036 taking medication
 leisure;miscellaneous;21000 sitting meeting or talking with others
 home activity;self care;13046 having hair or nails done by someone else sitting
 home activity;household chores;washing/ironing/mending clothes;5080 knitting sewing wrapping presents sitting
 home activity;miscellaneous;sitting;9060 sitting reading or using a mobile phone/smartphone/tablet or talking on the phone/computer (skype chatting)
 leisure;miscellaneous;21010 sitting non-desk work (with or without eating at the same time)
 occupation;interruption;9060 sitting using a mobile phone/smartphone/tablet or talking on the phone/computer (skype meeting etc.)
 leisure;religious activities;20005 sitting in church talking or singing attending a ceremony sitting active
 home activity;child/elderly/pet care;child care;5185 child care sitting/kneeling occasional lifting
 leisure;miscellaneous;21016 sitting child care only active periods
 home activity;miscellaneous;sitting;7021 sitting without observable activities
 home activity;leisure;activities for maintenance of a household;with animals;5190 sitting playing with animals active periods
 transportation;public transportation;16016 riding in a bus or train
 leisure;sports;water activities;18012 boating power passenger

Light physical activity behaviours

home activity;household chores;preparing meals/cooking/washing dishes;5035 kitchen activity general cooking/washing/dishes/cleaning up
 home activity;miscellaneous;walking;17150 walking household without observable loads
 home activity;miscellaneous;walking;5165 (generic) walking non-cleaning task such as closing windows lock door putting away items
 leisure;miscellaneous;walking;21070 (generic) walking and occasional standing (no more than two consecutive images)
 transportation;walking;17161 walking not as the single means of transports e.g.from house to transports or vice versa/from car to places or vice versa/between transports
 leisure;miscellaneous;walking;5060 shopping miscellaneous
 occupation;interruption;11791 walking on job in office or lab area
 home activity;miscellaneous;standing;9050 standing talking in person/on the phone/computer (skype chatting) or using a mobile phone/smartphone/tablet
 home activity;household chores;washing/ironing/mending clothes;5090 folding or hanging clothes/put clothes in or out of washer or dryer/packing suitcase limited walking

home activity;miscellaneous;standing;9070 standing reading or without observable/identifiable activities
occupation;interruption;walking;11791 walking on job in office or lab area
occupation;manufacturing;11115 chef
home activity;self care;13040 (generic) self care such as grooming/washing hands/shaving/brushing teeth/putting on make-up not eliminating and bathing (not necessary in the toilet)
occupation;office and administrative support;11600 (generic) standing tasks such as store clerk/librarian/packing boxes/repair heavy parts
leisure;miscellaneous;5060 shopping miscellaneous
home activity;household chores;washing/ironing/mending clothes;5070 ironing
leisure;miscellaneous;standing;9050 standing talking in person/using a phone/smartphone/tablet
home activity;miscellaneous;walking;5147 walking moving away light items (pens/papers/keys not included)
occupation;miscellaneous;11475 (generic) manual labour
occupation;interruption;standing;9050 standing talking in person/using a phone/smartphone/tablet
occupation;personal services;11413 kitchen maid
home activity;household chores;grocery shopping;5060 shopping
home activity;home repair;indoor;6126 home repair miscellaneous
leisure;miscellaneous;standing;9070 standing reading or without observable/identifiable activities
transportation;waiting;7040 standing in a line
home activity;child/elderly/pet care;child care;5185 child care sitting/kneeling occasional lifting
home activity;miscellaneous;standing;9071 (generic) standing miscellaneous
leisure;miscellaneous;standing;9071 (generic) standing miscellaneous
occupation;interruption;standing;9070 standing reading or without observable/identifiable activities
home activity;miscellaneous;standing;9020 standing writing/drawing/painting
home activity;leisure;individual activities;10074 playing musical instruments
occupation;interruption;5041 kitchen activity in the working place
home activity;miscellaneous;walking;17140 using crutches or frame
occupation;interruption;9050 standing talking in person/using a phone/smartphone/tablet
home activity;leisure;individual activities;9085 standing arts and crafts/sand painting/carving weaving
home activity;miscellaneous;5025 (generic) multiple household tasks all at once including standing/lifting/sitting
home activity;miscellaneous;standing;9070 standing reading or without obvious activities
home activity;household chores;washing/ironing/mending clothes;5095 putting away /gathering clothes involving walking
home activity;lawn and garden;lawn care service;8135 planting potting transplanting seedlings or plants

occupation;interruption;standing;9071 (generic) standing miscellaneous
transportation;walking;9050 standing miscellaneous (talking to others etc.)
occupation;interruption;miscellaneous;5041 kitchen activity in the working place
home activity;household chores;house cleaning;miscellaneous;5100 making bed/changing linens
occupation;interruption;standing;9015 standing scanning documents
home activity;household chores;house cleaning;furniture;5032 dusting or polishing furniture
home activity;eating;13035 eating standing alone or with others
occupation;miscellaneous;11870 working in scene shop theatre actor backstage employee
occupation;office and administrative support;11600 (generic) standing tasks such as store clerk/librarian/packing boxes/repair heavy parts
home activity;miscellaneous;standing;9050 standing talking in person on the phone/computer (skype chatting) or using a mobile phone/smartphone/tablet
home activity;household chores;house cleaning;floors;5010 cleaning sweeping carpet or floors
leisure;sports;ball games;15090 bowling
home activity;self care;13020 dressing/undressing
occupation;interruption;9070 standing reading or without observable/identifiable activities
leisure;music playing;10074 playing musical instruments
home activity;home repair;indoor;6205 sharpening tools
home activity;home repair;indoor;6124 hammering nails
home activity;child/elderly/pet care;child care;5186 child care standing occasional lifting
occupation;interruption;13035 eating standing
home activity;child/elderly/pet care;pet care;5197 household animal care aside from feeding
leisure;recreation;outdoor;5171 standing playing with child(ren)
occupation;interruption;miscellaneous;13009 toilet break
home activity;household chores;house cleaning;miscellaneous;5148 watering plants
occupation;miscellaneous;11475 (generic) manual or unskilled labour
occupation;interruption;standing;9020 standing writing/drawing/painting
leisure;eating;social;13035 eating standing indoor/outdoor
home activity;household chores;house cleaning;floors;5131 scrubbing floors on hands and knees scrubbing bathroom bathtub
occupation;public admin/education/health;education;09071 teaching standing
home activity;household chores;preparing meals/cooking/washing dishes;5051 serving food/setting table implied walking and standing
home activity;household chores;preparing meals/cooking/washing dishes;5035 cleaning up table after meal implied walking (e.g. leaving from eating table to the kitchen)

leisure;eating;not-social;5060 buying foods or drinks as a takeaway
leisure;miscellaneous;21070 (generic) walking/standing combination indoor
home activity;self care;13009 toilet eliminating or squatting
home activity;self care;13045 hairstyling standing
home activity;lawn and garden;gardening service;8230 watering garden
occupation;interruption;13009 toilet break
leisure;miscellaneous;standing;9070 standing reading or without obvious activities
home activity;leisure;activities for maintenance of a household;miscellaneous;9101 retreat/family reunion activities playing games with more than one person
occupation;interruption;9015 standing scanning documents
home activity;child/elderly/pet care;child care;5183 standing holding child
occupation;interruption;9070 standing reading or without obvious activities
leisure;miscellaneous;standing;9020 standing writing/drawing/painting
leisure;religious activities;20039 walking/standing combination for religious purposes usher
leisure;recreation;indoor;9020 drawing writing painting standing
leisure;miscellaneous;21017 standing child care only active periods
home activity;child/elderly/pet care;pet care;5053 feeding household animals
leisure;eating;13035 eating standing indoor/outdoor
leisure;miscellaneous;9071 (generic) standing miscellaneous indoor or outdoor
leisure;sports;conditioning;2115 upper body exercise arm ergometer
occupation;interruption;standing;9050 standing talking in person/using a phone/smartphone/tablet
home activity;self care;13000 getting ready for bed standing
leisure;eating;social;5060 buying foods or drinks as a takeaway
home activity;home repair;indoor;5160 standing light effort tasks
transportation;walking;9071 standing miscellaneous (talking to others etc.)
occupation;interruption;standing;13035 eating standing
occupation;interruption;9020 standing writing/drawing/painting
home activity;lawn and garden;gardening service;8220 walking applying fertilizer or seeding a lawn push applicator
leisure;eating;5060 buying foods or drinks as a takeaway
leisure;religious activities;20030 standing talking in church
leisure;eating;not-social;13035 eating standing indoor/outdoor

occupation;public admin/education/health;education;9071 teaching standing
home activity;household chores;washing/ironing/mending clothes;5082 sewing with a machine

Moderate-to-vigorous physical activity behaviours

transportation;private transportation;1010 bicycling
transportation;walking;17165 walking the dog
occupation;interruption;17133 walking upstairs
leisure;miscellaneous;walking;17031 loading /unloading a car implied walking
home activity;child/elderly/pet care;child care;5181 walking and carrying child
home activity;lawn and garden;gardening service;8050 digging spading filling garden compositing
leisure;sports;miscellaneous;17082 hiking or walking at a normal pace through fields and hillsides
home activity;lawn and garden;tree and shrub service;8025 clearing light brush thinning garden
home activity;lawn and garden;lawn care service;8165 raking lawn
occupation;interruption;walking;11795 walking on job and carrying light objects such as boxes or pushing trolleys
leisure;sports;water activities;18070 canoeing/rowing
home activity;lawn and garden;lawn care service;8080 laying crushed rock
leisure;sports;gymnasium and athletics;athletics;12150 running
leisure;sports;ball games;15235 football or baseball playing catch
home activity;miscellaneous;standing;5146 standing packing/unpacking household items occasional lifting
home activity;lawn and garden;gardening service;8245 gardening/picking up fruits vegetables flowers
leisure;miscellaneous;walking;17105 pushing a wheelchair non-occupational
leisure;sports;ball games;15680 tennis doubles
home activity;lawn and garden;gardening service;8192 shovelling dirt or mud
leisure;sports;miscellaneous;17082 hiking or walking at a normal pace through fields and hillsides
leisure;dancing;3010 ballet modern or jazz general rehearsal or class
leisure;sports;conditioning;2060 health club exercise
leisure;sports;ball games;15690 tennis singles
home activity;lawn and garden;lawn care service;8095 mowing lawn
occupation;public admin/education/health;health;11615 nursing patient care

occupation;miscellaneous;11615 (generic) standing lifting items continuously with limited walking
leisure;miscellaneous;17031 loading /unloading a car implied walking
leisure;sports;conditioning;2019 bicycling stationary RPM/Spin bike class
home activity;leisure;activities for maintenance of a household;with animals;5192 walking/running playing with animals active periods
home activity;lawn and garden;gardening service;8192 shoveling dirt or mud
home activity;household chores;house cleaning;furniture;5020 cleaning heavy such as car/windows/garage
leisure;sports;conditioning;2048 elliptical trainer
occupation;interruption;11795 walking on job and carrying light objects such as boxes or pushing trolleys
leisure;sports;conditioning;2050 resistance training
leisure;sports;conditioning;2070 rowing stationary ergometer
leisure;recreation;outdoor;5175 walking/running playing with child(ren)
leisure;sports;conditioning;2010 bicycling stationary
leisure;sports;conditioning;2120 water aerobics water calisthenics water exercise
home activity;home repair;outdoor;6020 automobile body work
occupation;agriculture/forestry/fishing;11192 taking care of animals
leisure;miscellaneous;standing;21017 standing child care only active periods
leisure;sports;conditioning;2065 stair-treadmill ergometer general
home activity;household chores;washing/ironing/mending clothes;5092 washing clothes by hand (with or without hanging wash)
leisure;miscellaneous;walking;17133 walking upstairs
transportation;walking;12150 running
occupation;interruption;walking;17070 walking downstairs
home activity;household chores;house cleaning;floors;5140 sweeping garage sidewalk or outside of house
occupation;interruption;walking;17133 walking upstairs
occupation;agriculture/forestry/fishing;11540 shovelling digging ditches
occupation;construction;11050 carrying heavy loads
transportation;walking;17250 walking as the single means to a destination not to work or class
leisure;miscellaneous;walking;17070 descending stairs
home activity;miscellaneous;walking;5121 walking with moving and lifting loads such as bikes and furniture
transportation;walking;17270 walking as the single means to work or class (not from)

Supplementary Table 2: Features of accelerometry signal used for behaviour classification.

Feature	Description
enmoTrunc	Euclidean Norm Minus One truncated below at 0
mean	Mean
sd	Standard Deviation
coefvariation	Coefficient of Variation
median	Median
min	Minimum
max	Maximum
25thp	25 th percentile
75thp	75 th percentile
autocorr	Autocorrelation
fmax	Frequency of signal with highest power
pmax	Maximal power of signal
fmaxband	Frequency of signal with highest power between 0.3 and 3 Hz
pmaxband	Maximal power of signal between 0.3 and 3 Hz
entropy	Entropy
fft1	Power at 1Hz
fft2	Power at 2Hz
fft3	Power at 3Hz
fft4	Power at 4Hz
fft5	Power at 5Hz
fft6	Power at 6Hz
fft7	Power at 7Hz
fft8	Power at 8Hz
fft9	Power at 9Hz
fft10	Power at 10Hz
fft11	Power at 11Hz
fft12	Power at 12Hz

Feature	Description
MAD	Mean Amplitude Deviation
MPD	Mean Power Deviation
skew	Skew
kurt	Kurtosis
f1	Frequency of signal with highest power between 0.3 and 15 Hz
p1	Maximal power of signal between 0.3 and 15 Hz
f2	Frequency of signal with second highest power
p2	Second highest power of signal
f625	Frequency of signal with highest power between 0.6 and 2.5 Hz
p625	Maximal power of signal between 0.6 and 2.5 Hz
totalPower	Total power for frequencies between 0.3 and 15 Hz
vmfft1	Power at 1/30 Hz
vmfft2	Power at 2/30 Hz
vmfft3	Power at 3/30 Hz
vmfft4	Power at 4/30 Hz
vmfft5	Power at 5/30 Hz
vmfft6	Power at 6/30 Hz
vmfft7	Power at 7/30 Hz
vmfft8	Power at 8/30 Hz
vmfft9	Power at 9/30 Hz
vmfft10	Power at 10/30 Hz
vmfft11	Power at 11/30 Hz
vmfft12	Power at 12/30 Hz

Supplementary Table 3: Definition of variables from UK Biobank data included in statistical models.

Characteristic	Source	Notes	UK Biobank field	Coding
OUTCOME				
Age at first cardiovascular disease event	Death Registry, HES.	First appearance of ICD-10 codes I20-25 (ischaemic heart disease) or I60-69 (cerebrovascular disease) in either HES or death register data.	Derived from Category 100093, Category 2000.	
Age at loss-to-follow-up	Death Registry.	Earliest of: date of latest study data available and date of non-cardiovascular disease death.	Derived from Category 100093.	
EXPOSURE				
Sleep	Accelerometry.	Derived using machine-learning methods described in main text.	Derived from 90001.	
Sedentary behaviour	Accelerometry.	Derived using machine-learning methods described in main text.	Derived from 90001.	
Light physical activity behaviours	Accelerometry.	Derived using machine-learning methods described in main text.	Derived from 90001.	
Moderate-to-vigorous physical activity behaviours	Accelerometry.	Derived using machine-learning methods described in main text.	Derived from 90001.	
EXCLUSION VARIABLES – MAIN ANALYSIS				
Prior HES-recorded cardiovascular disease	HES.	Appearance of ICD-10 codes I20-25 (ischaemic heart disease) or I60-69 (cerebrovascular disease) or ICD-9 codes 410 – 414 or 430 – 438 in HES data prior to accelerometer wear.	Derived from Category 2000.	

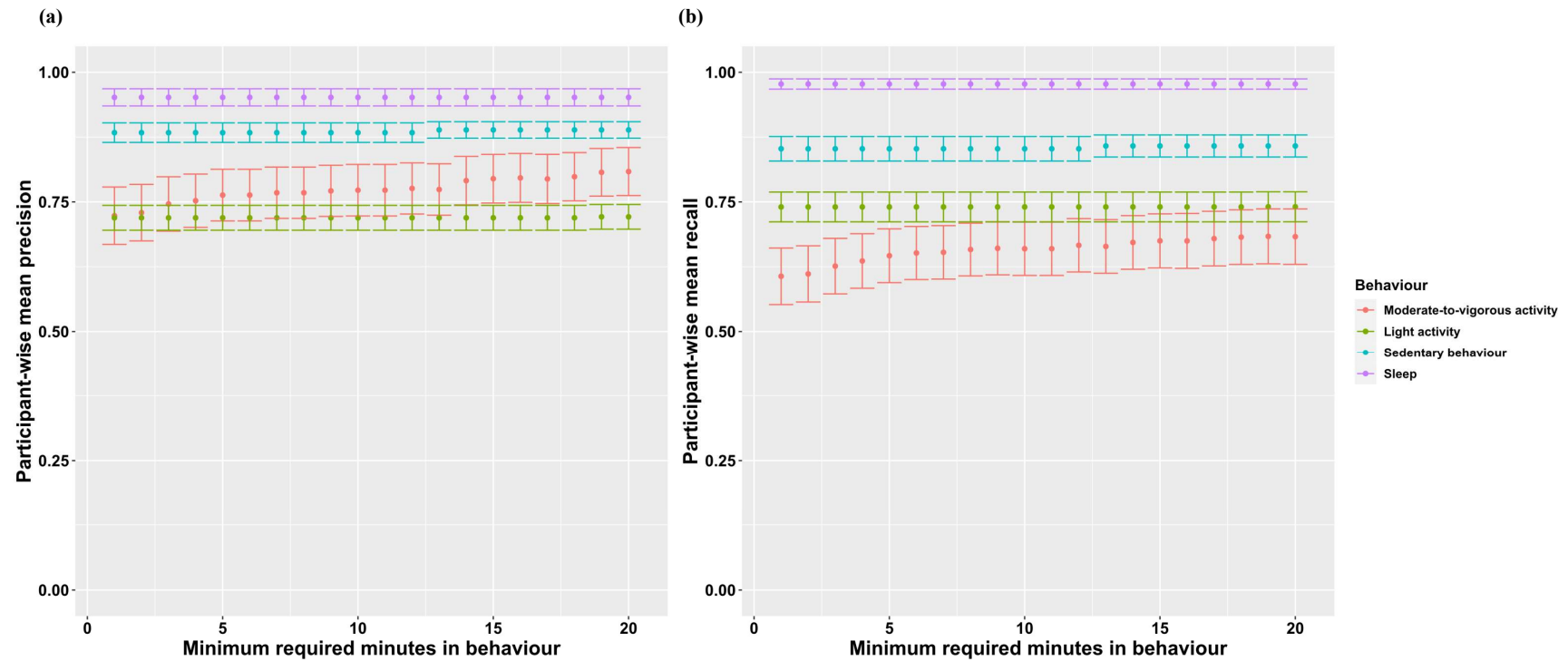
Characteristic	Source	Notes	UK Biobank field	Coding
Prior self-reported cardiovascular disease	Baseline.	Self-reported heart attack or stroke.	Derived from 6150.	
ADJUSTMENT VARIABLES – MAIN ANALYSIS				
Age	Baseline.	Age used as the timescale in Cox regression analysis; participants entered study at the end of accelerometer wear.	Derived from 90011, 34, 52.	
Sex	Baseline.	Used to stratify analysis.	31	Female, Male.
Ethnicity	Baseline.		Derived from 21000.	Asian, Black, Other, White. (Categorised as in Resource 100336; Other includes Mixed, Chinese and Other due to small numbers).
Smoking status	Baseline.		20116	Never smoker, Ex-smoker, Current smoker.
Frequency of alcohol consumption	Baseline.		Derived from 1558.	Never, <3 times/week, 3+ times/week.
Education	Baseline.		Derived from 6138.	School leaver, Further education (education beyond O-Levels/CSEs, excluding college/ university degree) and Higher education (college/university degree).
Townsend Deprivation Index	Baseline.	Townsend Deprivation Index of address at time of UKB baseline assessment.	Derived from 189.	Divided by quartile in the study population.
Daily servings of fresh fruit and vegetables.	Baseline.		Derived from 1289, 1299, 1309.	Less than one coded as 0·5, then sum of 1289, 1299, 1309. Categorised as < 3, 3-4·9, 5-7·9, 8+ servings/ day.

Characteristic	Source	Notes	UK Biobank field	Coding
Frequency of red and processed meat consumption.	Baseline.		Derived from 1369, 1379, 1389, 1349.	Less than one coded as 0·5, then sum of 1369, 1379, 1389. Categorised as <1, 1-2·9, 3-4·9, 5+ times/ week.
Frequency of oily fish consumption.	Baseline.		Derived from 1329.	< 1, 1, 2-4, >4 times/week.
ADJUSTMENT VARIABLES – ADDITIONAL				
BMI	Baseline.		Derived from 21001.	For descriptive analyses: Underweight (<18·5kgm ⁻²), Normal weight (18·5 -24·9 kgm ⁻²), Overweight (25 -29·9 kgm ⁻²), Obese (30+ kgm ⁻²). For BMI-stratified analysis, Underweight and Normal weight categories combined.
EXCLUSION VARIABLES – SENSITIVITY ANALYSIS FOR REVERSE CAUSALITY				
Medication for diabetes, cholesterol or blood pressure	Baseline.		Derived from 6177, 6153.	
Self-reported overall health rating	Baseline.		2178	
Prior primary admission for disease of the circulatory system.	HES.	Hospital admission with primary diagnosis of I00-I99 before accelerometer wear.	Derived from Category 2000.	
NEGATIVE CONTROL OUTCOME – SENSITIVITY ANALYSIS FOR RESIDUAL CONFOUNDING				
Age at first accident unrelated to movement behaviour.	HES.	First appearance of ICD-10 codes V00-09, V20-99, W20-W99, X00-X99, Y00- Y09.	Derived from, Category 2000.	
Age at loss-to-follow-up	Death Registry.	Earliest of: date of latest study data available and date of death.	Derived from Category 100093.	

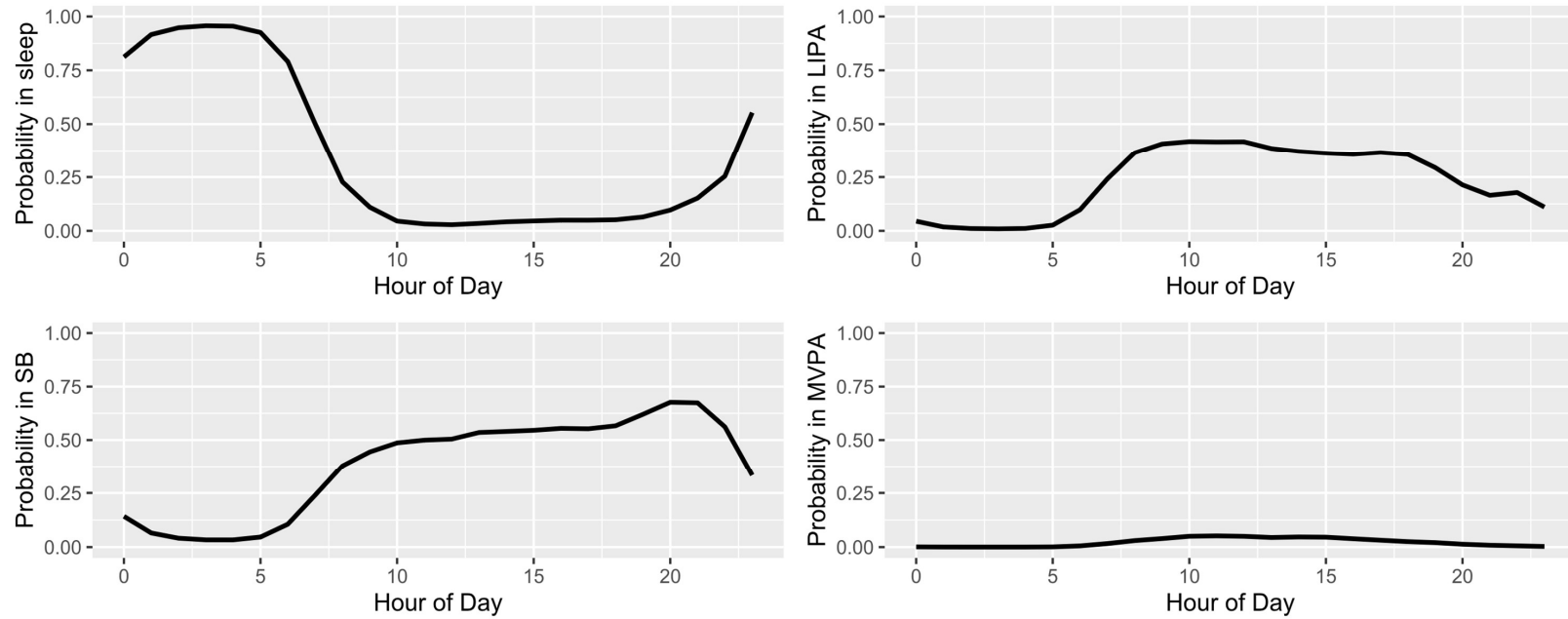
Supplementary Table 4: Characteristics of CAPTURE-24 participants.

	n (%)
Overall	152
Age, years	
18-29	39 (26)
30-39	41 (27)
40-49	24 (16)
50-59	21 (14)
60-69	17 (11)
70-79	7 (5)
80-91	2 (1)
Not recorded	1 (1)
Sex	
Female	99 (65)
Male	53 (35)

Supplementary Figure 1: Participant-wise mean (a) precision and (b) recall for classification of behaviours from accelerometer data calculated in Leave-One-Participant-Out Cross-Validation (with 95% confidence interval for the mean). The x-axis gives the minimum required recorded annotator-labelled time in the behaviour for inclusion in the calculation. For precision, participants with no model-labelled time in the behaviour were also excluded as precision is undefined in this case.



Supplementary Figure 2: Probability of being in sleep, sedentary behaviour (SB), light physical activity behaviours (LIPA) and moderate-to-vigorous physical activity behaviours (MVPA) among 87,498 UK Biobank participants according to machine-learned behaviour classification by hour of the day.



Supplementary Table 5: Coefficient of first isometric log-ratio pivot coordinate^a for each movement behaviour estimated using a multivariable-adjusted Compositional Data Analysis Cox regression model.

Movement behaviour variable	$exp(\hat{\beta})$ (95% CI)
Pivot coordinate: Sleep vs All other behaviours	0.88 (0.75, 1.02)
Pivot coordinate: SB vs All other behaviours	1.38 (1.22, 1.57)
Pivot coordinate: LIPA vs All other behaviours	0.96 (0.88, 1.06)
Pivot coordinate: MVPA vs All other behaviours	0.86 (0.84, 0.88)

^aSee **Supplementary Methods**. Model based on 4,105 events in 87,498 participants. Model used age as the timescale, was stratified by sex and was additionally adjusted for ethnicity, smoking status, alcohol consumption, fresh fruit and vegetable consumption, red and processed meat consumption, oily fish consumption, deprivation and education.

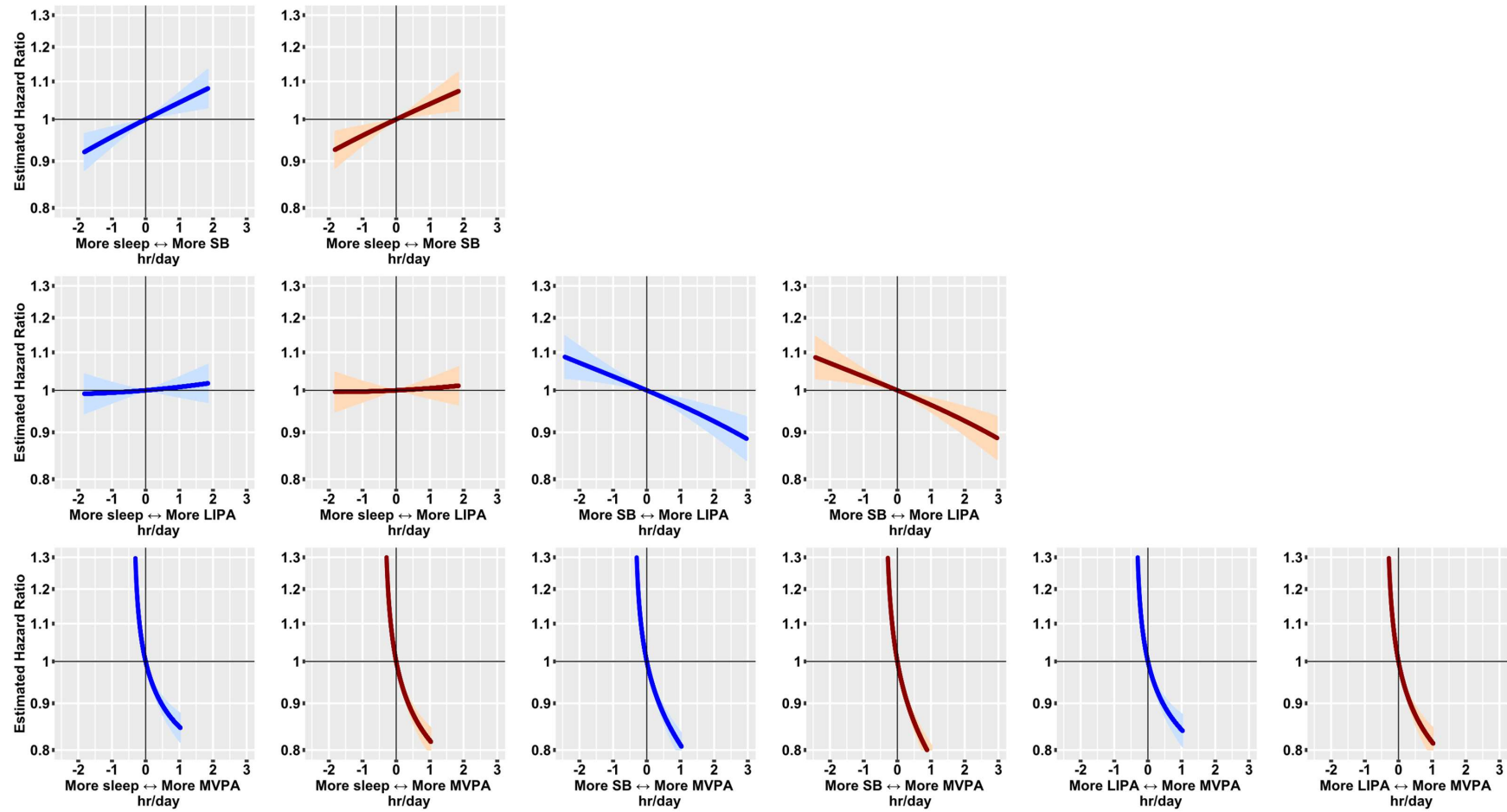
Supplementary Table 6: Coefficient of first isometric log-ratio pivot coordinate for each movement behaviour estimated using all Compositional Data Analysis Cox regression models.^a

Movement behaviour variable	Main analysis	Minimally adjusted	Additionally stratified by BMI	Fatal events	Women only	Men only
Pivot coordinate: sleep vs All other behaviours	0.88 (0.75, 1.02)	0.90 (0.77, 1.05)	0.90 (0.77, 1.05)	0.79 (0.48, 1.29)	0.78 (0.60, 1.02)	0.93 (0.77, 1.13)
Pivot coordinate: SB vs All other behaviours	1.38 (1.22, 1.57)	1.37 (1.21, 1.56)	1.29 (1.13, 1.46)	2.13 (1.40, 3.22)	1.57 (1.28, 1.94)	1.28 (1.09, 1.50)
Pivot coordinate: LIPA vs All other behaviours	0.96 (0.88, 1.06)	0.96 (0.88, 1.06)	0.98 (0.89, 1.08)	0.71 (0.52, 0.95)	0.95 (0.81, 1.11)	0.97 (0.86, 1.09)
Pivot coordinate: MVPA vs All other behaviours	0.86 (0.84, 0.88)	0.84 (0.81, 0.86)	0.88 (0.85, 0.90)	0.85 (0.78, 0.92)	0.85 (0.82, 0.89)	0.86 (0.83, 0.90)

Movement behaviour variable	Main analysis	Under 65s only	Over 65s only	First 2 years of follow-up removed	Follow-up removed + healthy subgroup	Excluding zero values	Negative control: accidents
Pivot coordinate: sleep vs All other behaviours	0.88 (0.75, 1.02)	0.98 (0.75, 1.28)	0.83 (0.69, 1.00)	0.88 (0.73, 1.06)	1.01 (0.77, 1.31)	0.86 (0.73, 1.01)	0.93 (0.70, 1.22)
Pivot coordinate: SB vs All other behaviours	1.38 (1.22, 1.57)	1.17 (0.95, 1.45)	1.52 (1.30, 1.77)	1.33 (1.15, 1.55)	1.09 (0.89, 1.35)	1.38 (1.21, 1.57)	1.08 (0.86, 1.34)
Pivot coordinate: LIPA vs All other behaviours	0.96 (0.88, 1.06)	1.01 (0.86, 1.18)	0.93 (0.82, 1.04)	0.98 (0.88, 1.10)	1.04 (0.88, 1.21)	0.99 (0.89, 1.09)	1.09 (0.92, 1.29)
Pivot coordinate: MVPA vs All other behaviours	0.86 (0.84, 0.88)	0.86 (0.82, 0.91)	0.86 (0.83, 0.89)	0.87 (0.84, 0.90)	0.88 (0.83, 0.92)	0.86 (0.83, 0.89)	0.92 (0.87, 0.97)

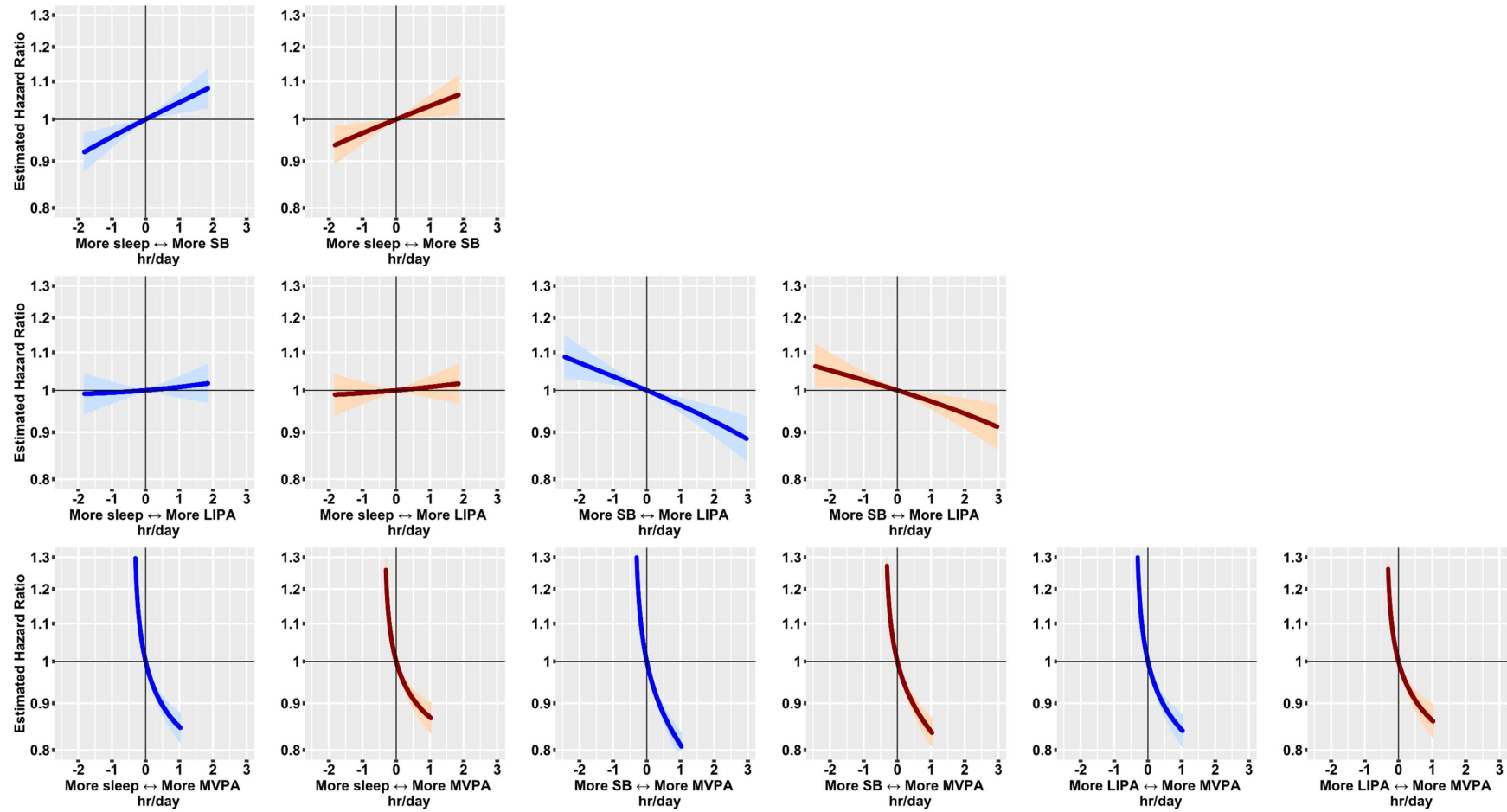
^aSee Methods, Results and Supplementary Figures 3-13 for more details of models. All columns report $\exp(\hat{\beta})$ (95% CI).

Supplementary Figure 3: Hazard Ratios for cardiovascular disease for all behaviour pairs estimated using multivariable-adjusted (blue) and minimally adjusted (red) Cox regression models.^a



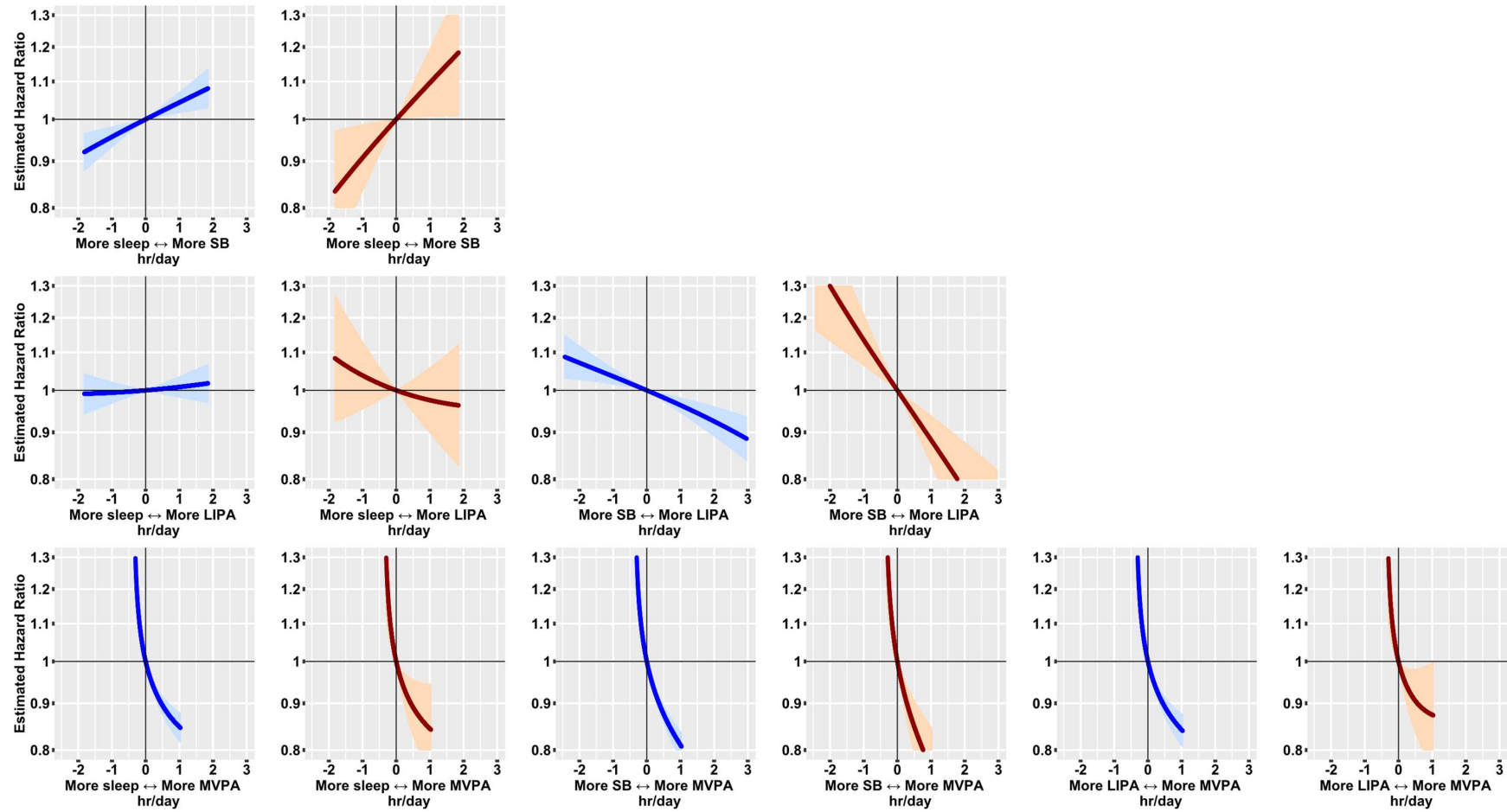
^aModel based on 4,105 events in 87,498 participants. All relative to the mean behaviour composition: 8.8 hours/day sleep, 9.3 hours/day sedentary behaviour, 5.6 hours/day light physical activity behaviours, 0.35 hours/day (21 minutes/day) moderate-to-vigorous physical activity behaviours. Multivariable-adjusted model used age as the timescale, was stratified by sex and was additionally adjusted for ethnicity, smoking status, alcohol consumption, fresh fruit and vegetable consumption, red and processed meat consumption, oily fish consumption, deprivation and education. Minimally-adjusted model used age as the timescale and was stratified by sex.

Supplementary Figure 4: Hazard Ratios for incident cardiovascular disease estimated using a multivariable-adjusted Cox regression model before (blue) and after (red) stratification by BMI.^a



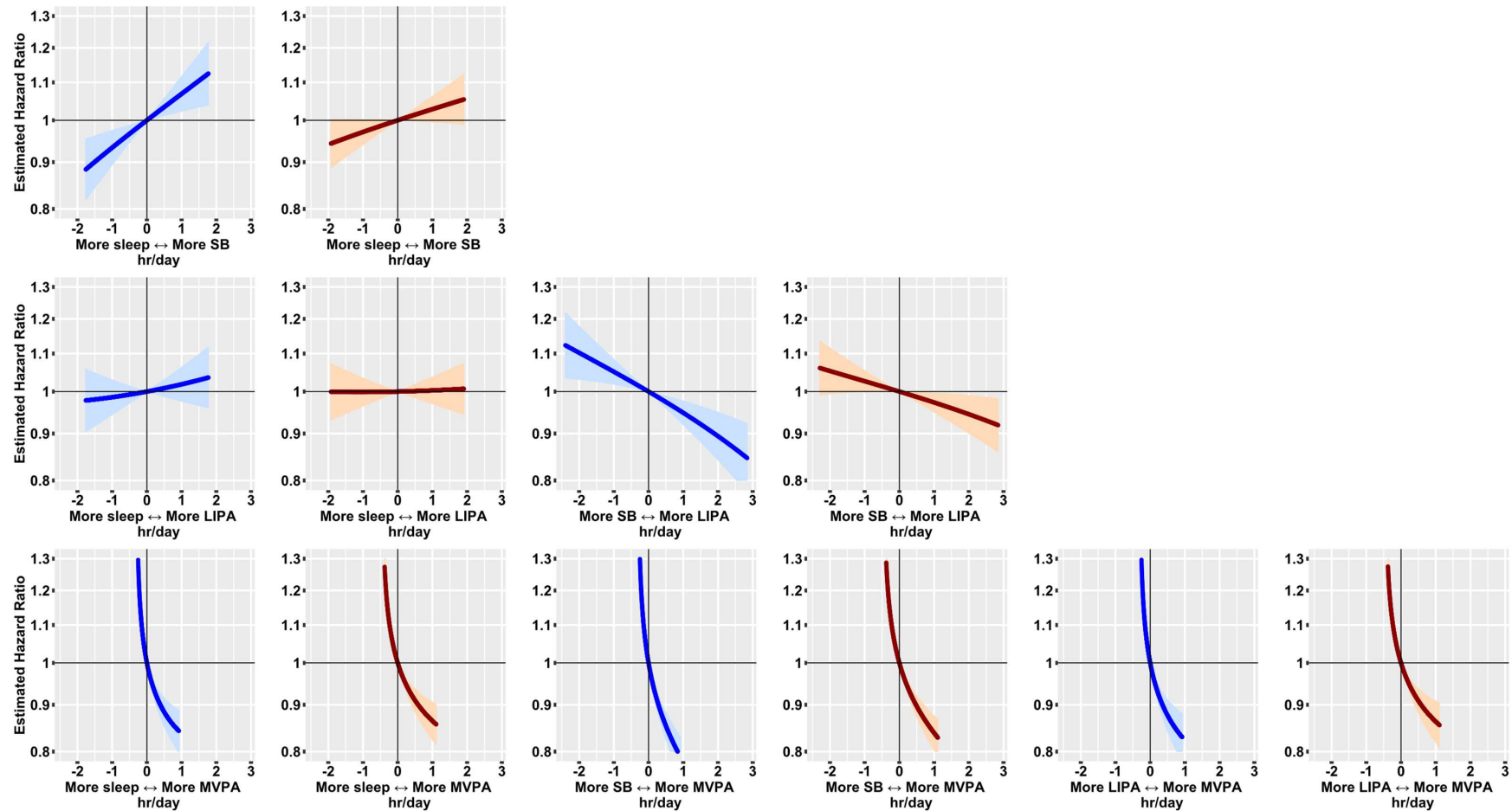
^aModel based on 4,105 events in 87,498 participants. All relative to the mean behaviour composition: 8.8 hours/day sleep, 9.3 hours/day sedentary behaviour, 5.6 hours/day light physical activity behaviours, 0.35 hours/day (21 minutes/day) moderate-to-vigorous physical activity behaviours. Models used age as the timescale, were stratified by sex and were additionally adjusted for ethnicity, smoking status, alcohol consumption, fresh fruit and vegetable consumption, red and processed meat consumption, oily fish consumption, deprivation and education.

Supplementary Figure 5: Hazard Ratios for all (blue) and fatal (red) incident cardiovascular disease for all behaviour pairs estimated using a multivariable-adjusted Cox regression model.^a



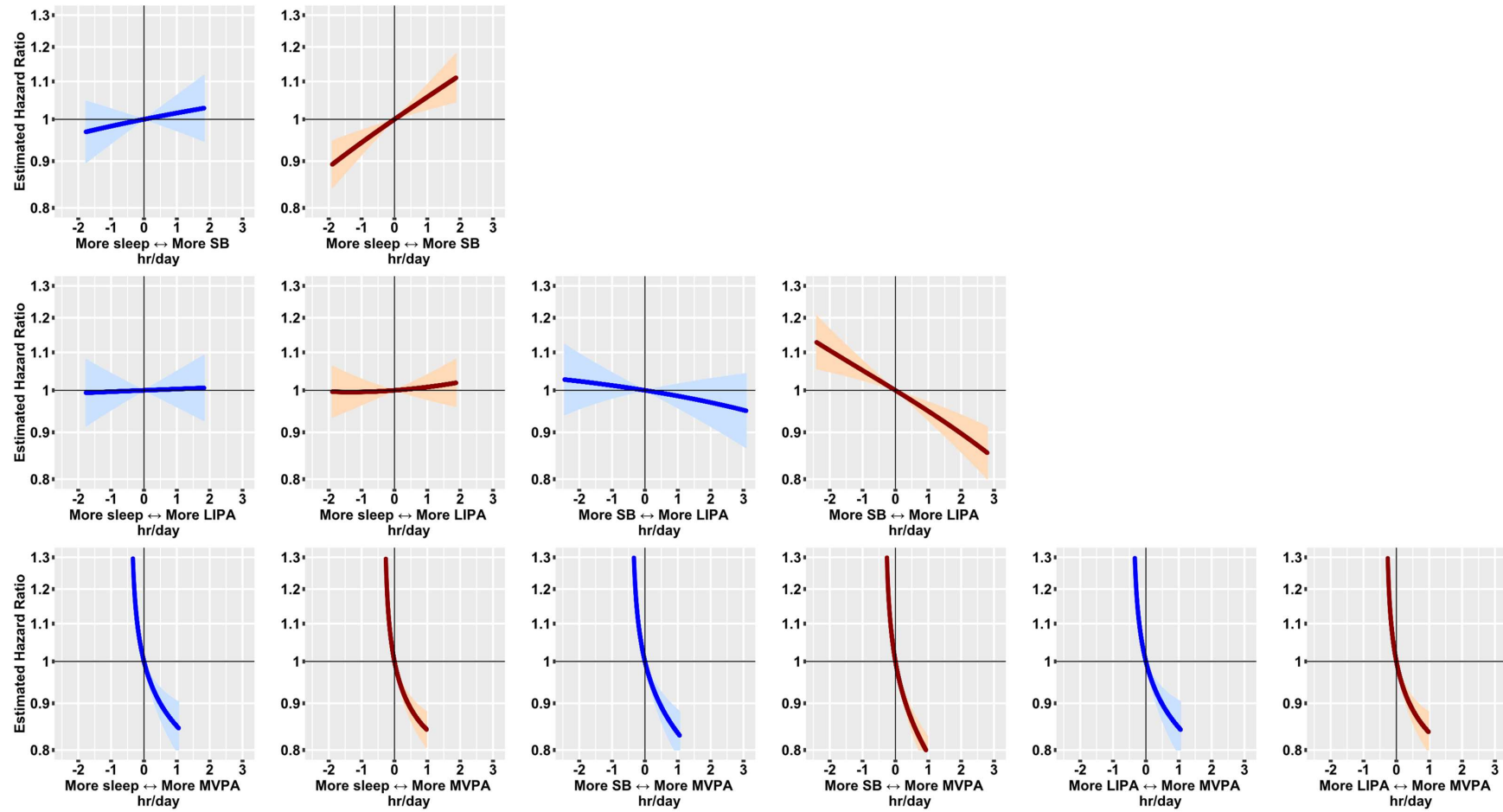
^aModels based on 4,105 events and 348 cardiovascular deaths in 87,498 participants. All relative to the mean behaviour composition: 8.8 hours/day sleep, 9.3 hours/day sedentary behaviour, 5.6 hours/day light physical activity behaviours, 0.35 hours/day (21 minutes/day) moderate-to-vigorous physical activity behaviours. Models used age as the timescale, were stratified by sex and were additionally adjusted for ethnicity, smoking status, alcohol consumption, fresh fruit and vegetable consumption, red and processed meat consumption, oily fish consumption, deprivation and education.

Supplementary Figure 6: Hazard Ratios for incident cardiovascular disease for all behaviour pairs estimated using a multivariable-adjusted Cox regression model for women (blue) and men (red).^a



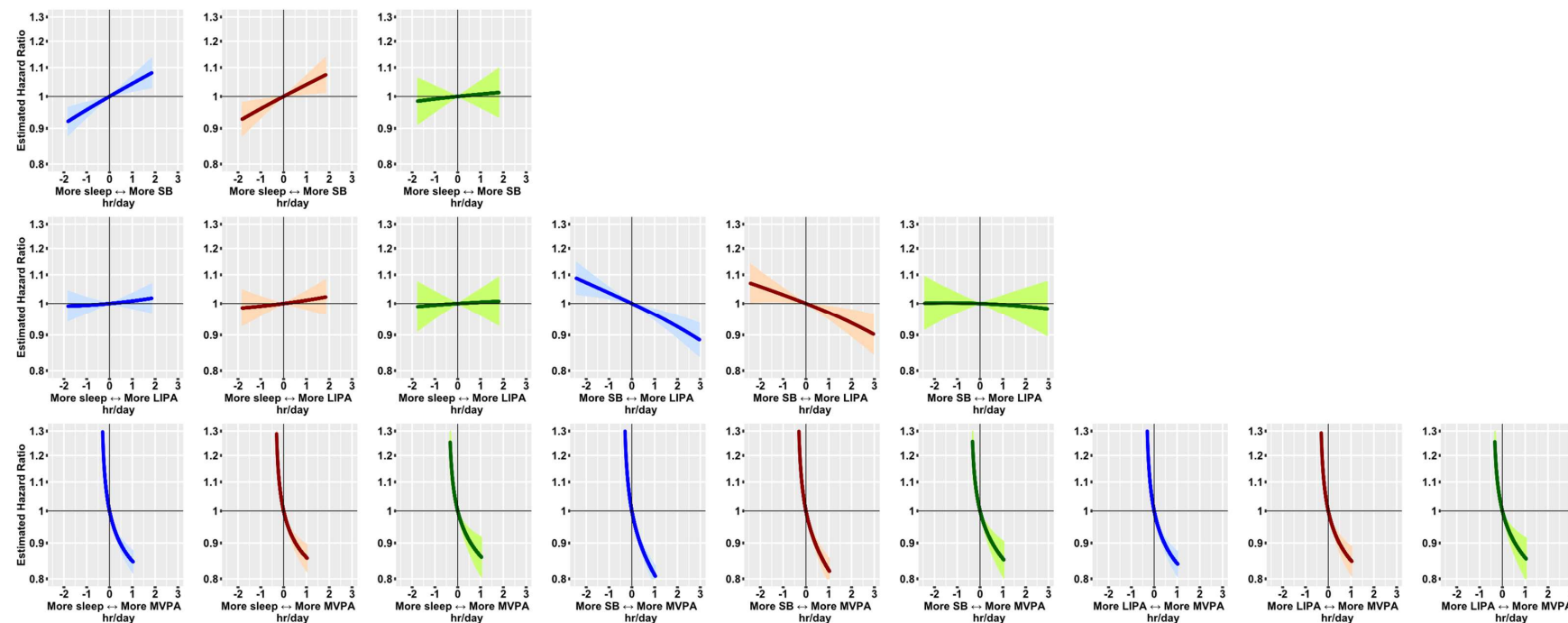
^aModels based on 1,654 events in 50,882 women and 2,451 events in 36,616 men. All relative to the mean behaviour composition in each case (women – 8.9 hours/day sleep, 9.0 hours/day sedentary behaviour, 5.9 hours/day light physical activity behaviours, 0.30 hours/day (18 minutes/day) moderate-to-vigorous physical activity behaviours; men – 8.7 hours/day sleep, 9.7 hours/day sedentary behaviour, 5.1 hours/day light physical activity behaviours, 0.45 hours/day (27 minutes/day) moderate-to-vigorous physical activity behaviours). Models used age as the timescale and were additionally adjusted for ethnicity, smoking status, alcohol consumption, fresh fruit and vegetable consumption, red and processed meat consumption, oily fish consumption, deprivation and education.

Supplementary Figure 7: Hazard Ratios for incident cardiovascular disease for all behaviour pairs estimated using a multivariable-adjusted Cox regression model for participants aged under 65 (blue) and participants aged over 65 (red).^a



^aModels based on 1,425 events in 51,180 participants aged under 65 and 2,680 events in 36,318 participants aged over 65. All relative to the mean behaviour composition in each case (participants aged under 65 – 8.8 hours/day sleep, 9.3 hours/day sedentary behaviour, 5.5 hours/day light physical activity behaviours, 0.39 hours/day (23 minutes/day) moderate-to-vigorous physical activity behaviours; participants aged over 65 – 8.9 hours/day sleep, 9.2 hours/day sedentary behaviour, 5.6 hours/day light physical activity behaviours, 0.30 hours/day (18 minutes/day) moderate-to-vigorous physical activity behaviours). Models used age as the timescale, were stratified by sex and were additionally adjusted for ethnicity, smoking status, alcohol consumption, fresh fruit and vegetable consumption, red and processed meat consumption, oily fish consumption, deprivation and education.

Supplementary Figure 8: Hazard Ratios for incident cardiovascular disease for all behaviour pairs estimated using a multivariable-adjusted Cox regression model (blue), after removing the first two years of follow-up (red) and after additionally restricting to a healthy subgroup (green).^a



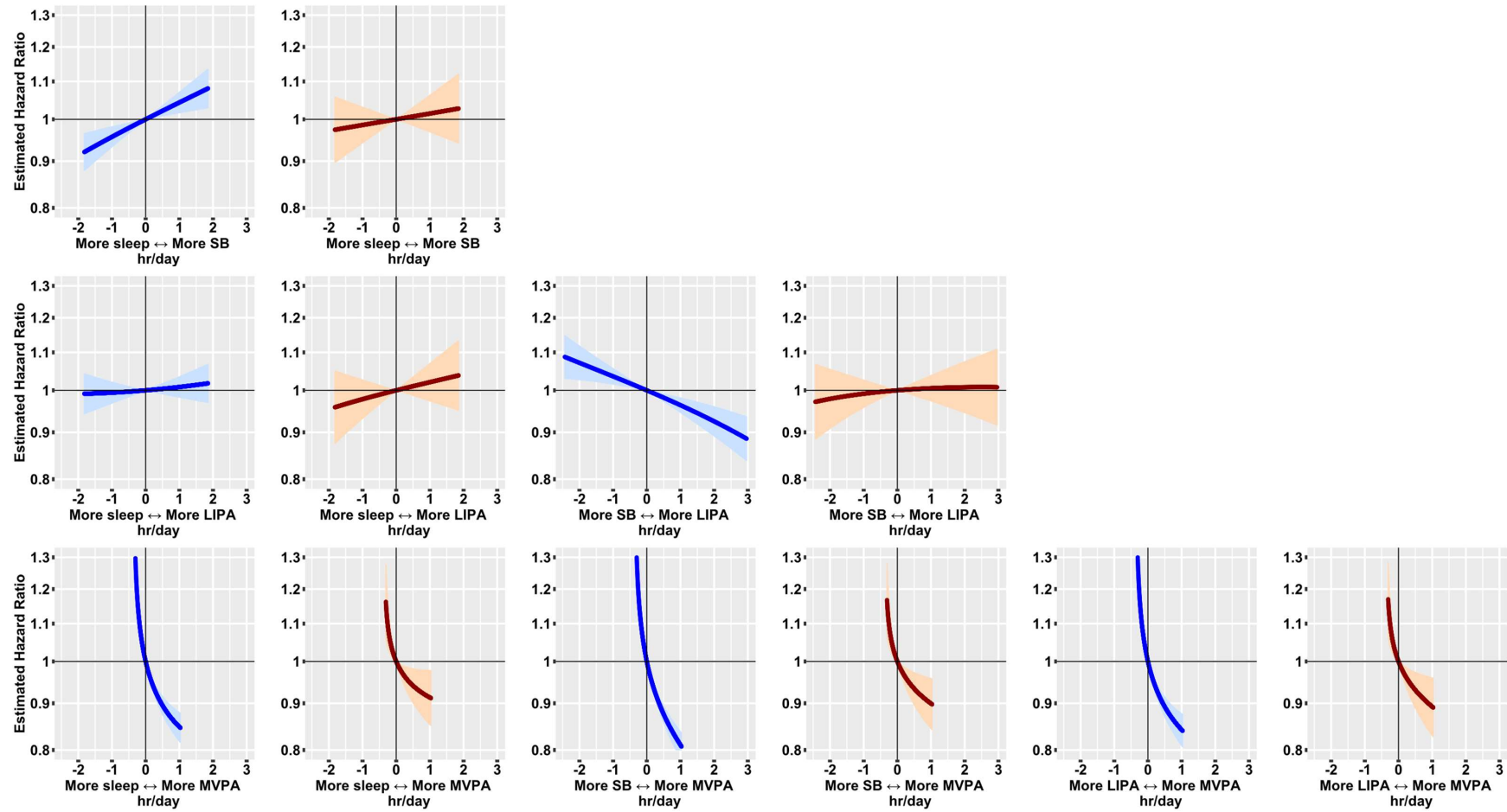
^aMain analysis based on 4,105 events in 87,498 participants. First sensitivity analysis based on 2,947 events in 86,011 participants. Second sensitivity analysis based on 1,597 events in 63,267 participants. Models used age as the timescale, were stratified by sex and were additionally adjusted for ethnicity, smoking status, alcohol consumption, fresh fruit and vegetable consumption, red and processed meat consumption, oily fish consumption, deprivation and education. All values reported relative to the mean behaviour composition in each case:

Main analysis - 8.8 hours/day sleep, 9.3 hours/day sedentary behaviour, 5.6 hours/day light physical activity behaviours, 0.35 hours/day (21 minutes/day) moderate-to-vigorous physical activity behaviours

1st sensitivity - 8.8 hours/day sleep, 9.3 hours/day sedentary behaviour, 5.6 hours/day light physical activity behaviours, 0.35 hours/day (21 minutes/day) moderate-to-vigorous physical activity behaviours

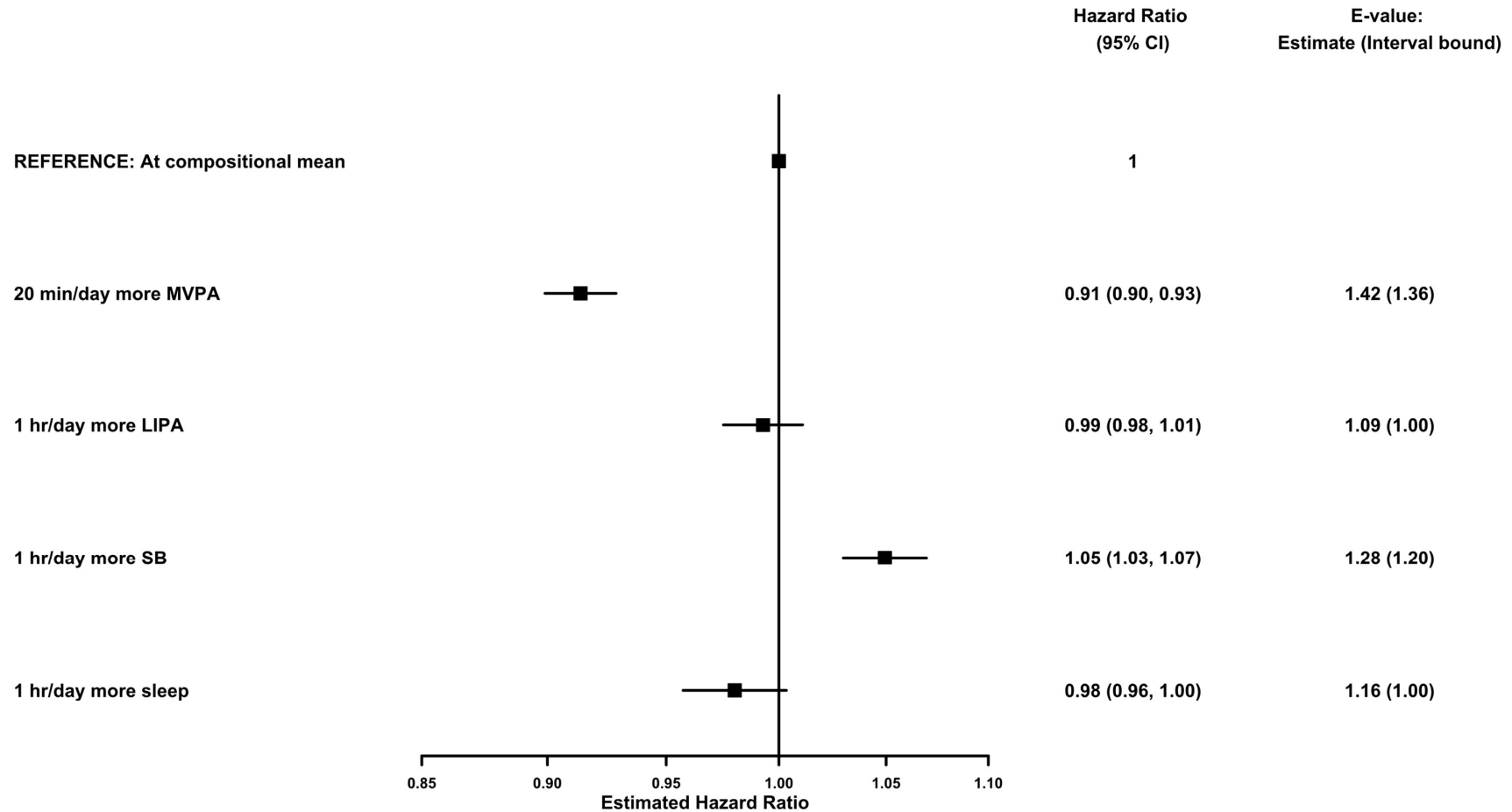
2nd sensitivity - 8.8 hours/day sleep, 9.2 hours/day sedentary behaviour, 5.6 hours/day light physical activity behaviours, 0.39 hours/day (23 minutes/day) moderate-to-vigorous physical activity behaviours.

Supplementary Figure 9: Hazard Ratios for cardiovascular disease (blue) and for non-activity-related accidents (red) for all behaviour pairs estimated using a multivariable-adjusted Cox regression model.^a



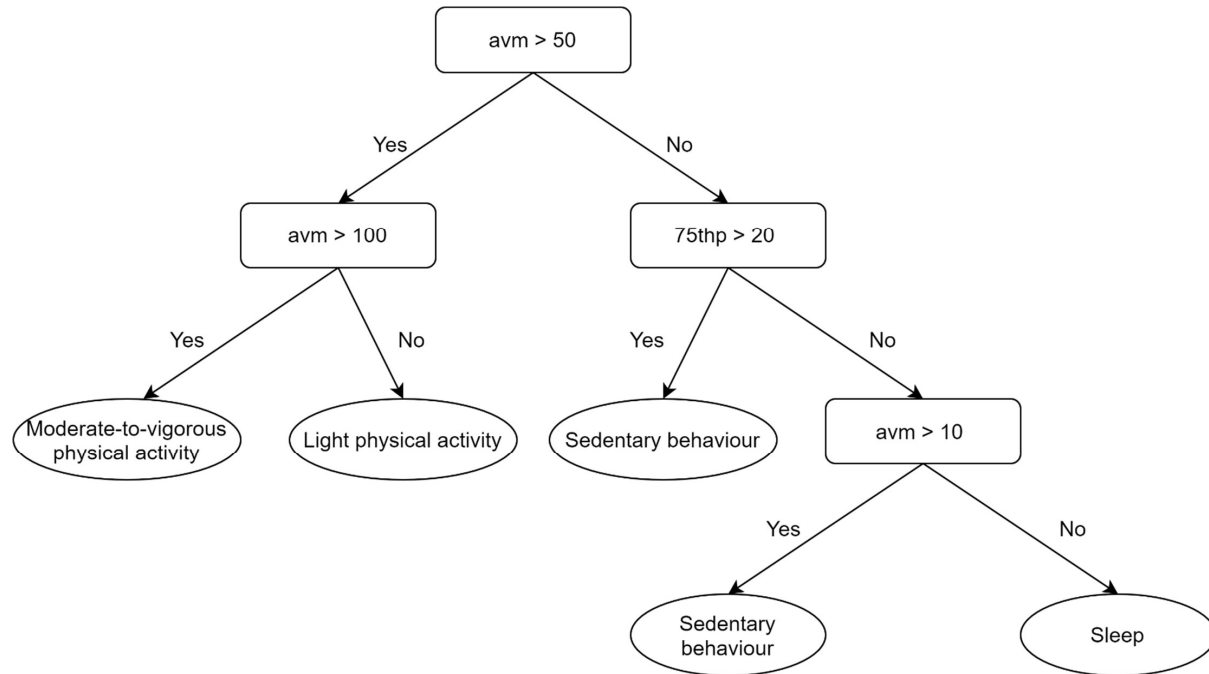
^aMain model based on 4,105 events in 87,498 participants. Negative control model based on 1,393 events in 87,498 participants. All relative to the mean behaviour composition (8.8 hours/day sleep, 9.3 hours/day sedentary behaviour, 5.6 hours/day light physical activity behaviours, 0.35 hours/day (21 minutes/day) moderate-to-vigorous physical activity behaviours). Models used age as the timescale, were stratified by sex and were additionally adjusted for ethnicity, smoking status, alcohol consumption, fresh fruit and vegetable consumption, red and processed meat consumption, oily fish consumption, deprivation and education.

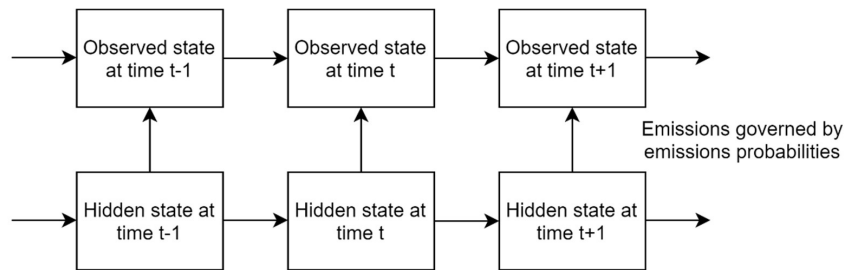
Supplementary Figure 10: Hazard ratios and corresponding E-values for incident cardiovascular disease associated with reallocating time to named behaviour, from all other behaviours proportionally, in 87,498 UK Biobank participants.^a



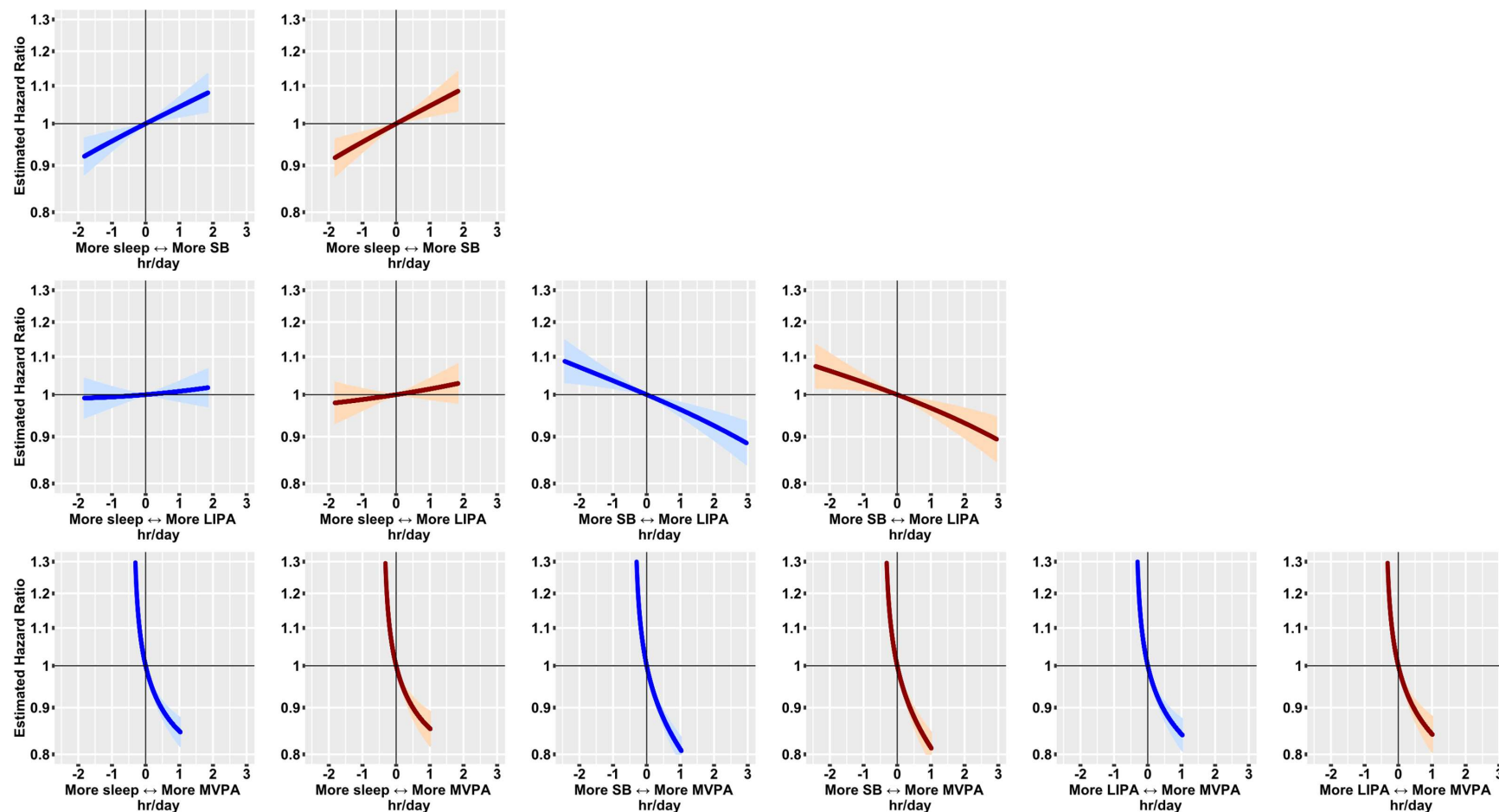
^aModel based on 4,105 events in 87,498 participants. All relative to the mean behaviour composition (8.8 hours/day sleep, 9.3 hours/day sedentary behaviour, 5.6 hours/day light physical activity behaviours, 0.35 hours/day (21 minutes/day) moderate-to-vigorous physical activity behaviours) and more time in named behaviour reallocated from all other behaviours proportionally. Model used age as the timescale, was stratified by sex and was additionally adjusted for ethnicity, smoking status, alcohol consumption, fresh fruit and vegetable consumption, red and processed meat consumption, oily fish consumption, deprivation and education.

Supplementary Figure 11: An example of a decision tree to classify time windows using average acceleration vector magnitude (avm) and the 75th percentile of acceleration vector magnitude (75thp).



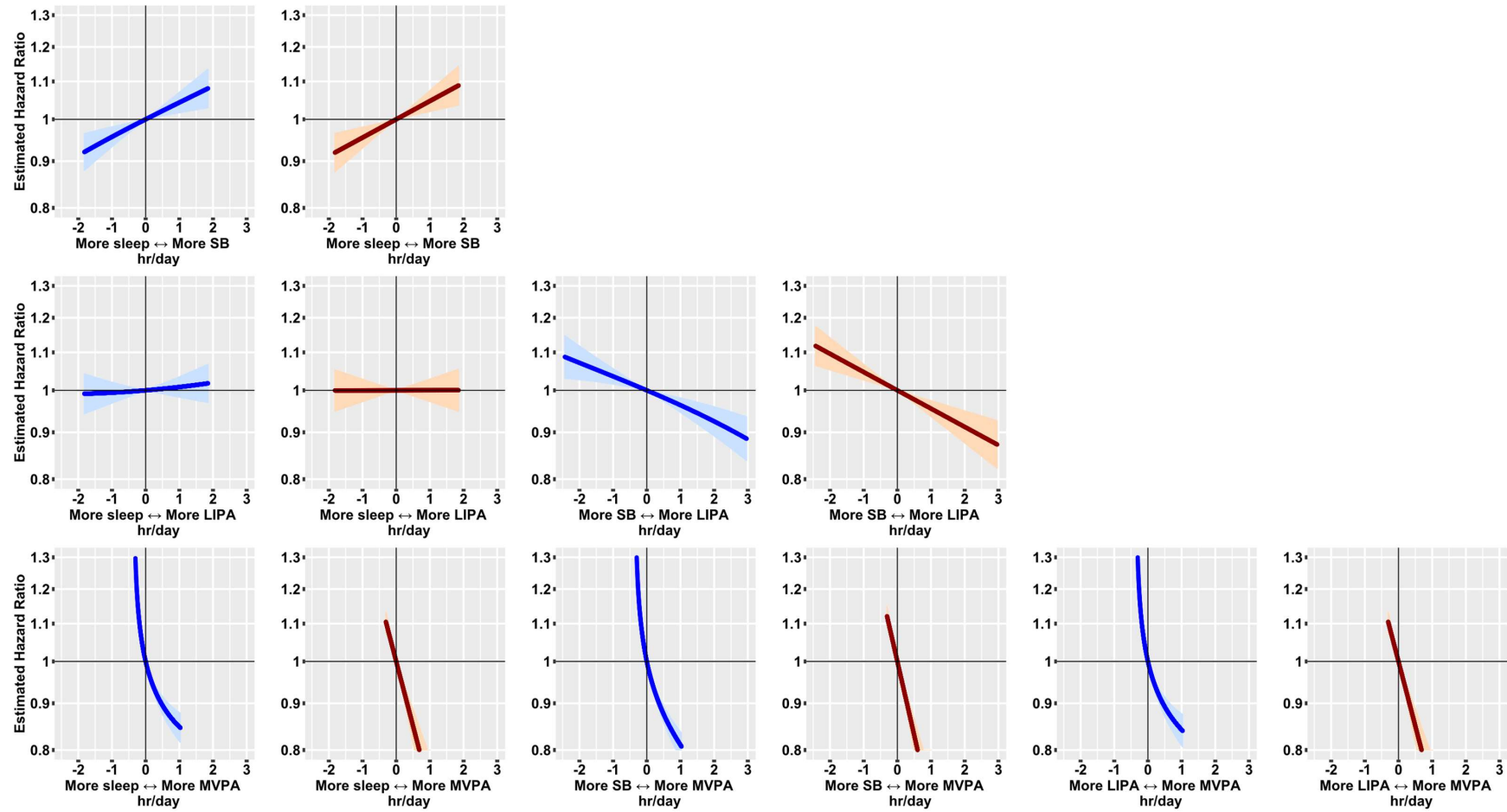
Supplementary Figure 12: The structure of a Hidden Markov Model.

Supplementary Figure 13: Hazard Ratios for incident cardiovascular disease for all behaviour pairs estimated using a multivariable-adjusted Cox regression model for all participants (blue) and in a sensitivity analysis excluding individuals with a zero value in any behaviour (red).^a



^aMain model based on 4,105 events in 87,498 participants. Model excluding individuals with zero values based on 4,017 events in 86,696 participants. All relative to the mean behaviour composition in each case (main analysis – 8.8 hours/day sleep, 9.3 hours/day sedentary behaviour, 5.6 hours/day light physical activity behaviours, 0.35 hours/day (21 minutes/day) moderate-to-vigorous physical activity behaviours; analysis excluding individuals with zero values – 8.8 hours/day sleep, 9.3 hours/day sedentary behaviour, 5.6 hours/day light physical activity behaviours, 0.37 hours/day (22 minutes/day) moderate-to-vigorous physical activity behaviours). Models used age as the timescale, were stratified by sex and were additionally adjusted for ethnicity, smoking status, alcohol consumption, fresh fruit and vegetable consumption, red and processed meat consumption, oily fish consumption, deprivation and education.

Supplementary Figure 14: Hazard Ratios for incident cardiovascular disease estimated using a multivariable-adjusted Compositional Data Analysis Cox regression model (blue) and using a multivariable-adjusted linear isotemporal substitution Cox regression model (red).^a



^aModel based on 4,105 events in 87,498 participants. All relative to the mean behaviour composition: 8.8 hours/day sleep, 9.3 hours/day sedentary behaviour, 5.6 hours/day light physical activity behaviours, 0.35 hours/day (21 minutes/day) moderate-to-vigorous physical activity behaviours. Models used age as the timescale, were stratified by sex and were additionally adjusted for ethnicity, smoking status, alcohol consumption, fresh fruit and vegetable consumption, red and processed meat consumption, oily fish consumption, deprivation and education.

STROBE Statement—Checklist of items that should be included in reports of cohort studies

	Item No	Recommendation	Included
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	Yes
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	Yes
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	Yes
Objectives	3	State specific objectives, including any prespecified hypotheses	Yes, No pre-specified hypotheses
Methods			
Study design	4	Present key elements of study design early in the paper	Yes
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Yes
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	Yes
		(b) For matched studies, give matching criteria and number of exposed and unexposed	NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	Yes
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	Yes
Bias	9	Describe any efforts to address potential sources of bias	Yes
Study size	10	Explain how the study size was arrived at	Yes
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Yes
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	Yes
		(b) Describe any methods used to examine subgroups and interactions	Yes
		(c) Explain how missing data were addressed	Yes
		(d) If applicable, explain how loss to follow-up was addressed	Yes
		(e) Describe any sensitivity analyses	Yes
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Yes
		(b) Give reasons for non-participation at each stage	Yes
		(c) Consider use of a flow diagram	Yes
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Yes
		(b) Indicate number of participants with missing data for each variable of interest	Yes
		(c) Summarise follow-up time (eg, average and total amount)	Yes
Outcome data	15*	Report numbers of outcome events or summary measures over time	Yes
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Yes: confounder-adjusted estimates and estimates adjusted for only age and sex given.
		(b) Report category boundaries when continuous variables were categorized	Yes.
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Not included.
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Yes.
Discussion			
Key results	18	Summarise key results with reference to study objectives	Yes.
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	Yes.
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Yes.
Generalisability	21	Discuss the generalisability (external validity) of the study results	Yes.
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	Yes.

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at <http://www.strobe-statement.org>.

Supplementary Material

Supplementary material for **Reallocation of time between device-measured movement behaviours and risk of incident cardiovascular disease**

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Contents

Supplementary Methods	4
‘Ground truth’ labelling of movement behaviours in image data	4
Machine-learning methods	5
Machine-learning methods: Features	5
Machine-learning methods: Random Forest models	5
Machine-learning methods: Hidden Markov models	5
Machine-learning methods: Evaluation	5
Machine-learning methods: model in participants aged 38 years or older	6
A Compositional Data Analysis approach to movement behaviour data	7
Log-ratio transformation	7
Interpreting isometric log-ratio pivot coordinates	7
Zero values	8
Software	9
Sensitivity analyses: further details on E-values	10
Sensitivity analyses: linear isotemporal substitution	11
References	12
Supplementary Tables and Figures	14
Supplementary Table 1: Assignment of fine-grained camera image annotations from the Compendium of Physical Activities to broad movement behaviour classes.	14
Supplementary Table 2: Features of accelerometry signal used for behaviour classification.	22
Supplementary Table 3: Definition of variables from UK Biobank data included in statistical models.	24
Supplementary Table 4: Characteristics of CAPTURE-24 participants.	28
Supplementary Figure 1: Participant-wise mean (a) precision and (b) recall for classification of behaviours from accelerometer data calculated in Leave-One-Participant-Out Cross-Validation (with 95% confidence interval for the mean). The x-axis gives the minimum required recorded annotator-labelled time in the behaviour for inclusion in the calculation. For precision, participants with no model-labelled time in the behaviour were also excluded as precision is undefined in this case.	29
Supplementary Figure 2: Probability of being in sleep, sedentary behaviour (SB), light physical activity behaviours (LIPA) and moderate-to-vigorous physical activity behaviours (MVPA) among 87,498 UK Biobank participants according to machine-learned behaviour classification by hour of the day.	30
Supplementary Table 5: Coefficient of first isometric log-ratio pivot coordinate ^a for each movement behaviour estimated using a multivariable-adjusted Compositional Data Analysis Cox regression model.	31
Supplementary Table 6: Coefficient of first isometric log-ratio pivot coordinate for each movement behaviour estimated using all Compositional Data Analysis Cox regression models. ^a	32
Supplementary Figure 3: Hazard Ratios for cardiovascular disease for all behaviour pairs estimated using multivariable-adjusted (blue) and minimally adjusted (red) Cox regression models. ^a	33
Supplementary Figure 4: Hazard Ratios for incident cardiovascular disease estimated using a multivariable-adjusted Cox regression model before (blue) and after (red) stratification by BMI. ^a	34
Supplementary Figure 5: Hazard Ratios for all (blue) and fatal (red) incident cardiovascular disease for all behaviour pairs estimated using a multivariable-adjusted Cox regression model. ^a	35
Supplementary Figure 6: Hazard Ratios for incident cardiovascular disease for all behaviour pairs estimated using a multivariable-adjusted Cox regression model for women (blue) and men (red). ^a	36
Supplementary Figure 7: Hazard Ratios for incident cardiovascular disease for all behaviour pairs estimated using a multivariable-adjusted Cox regression model for participants aged under 65 (blue) and participants aged over 65 (red). ^a	37

Supplementary Figure 8: Hazard Ratios for incident cardiovascular disease for all behaviour pairs estimated using a multivariable-adjusted Cox regression model (blue), after removing the first two years of follow-up (red) and after additionally restricting to a healthy subgroup (green). ^a	38
Supplementary Figure 9: Hazard Ratios for cardiovascular disease (blue) and for non-activity-related accidents (red) for all behaviour pairs estimated using a multivariable-adjusted Cox regression model. ^a	39
Supplementary Figure 10: Hazard ratios and corresponding E-values for incident cardiovascular disease associated with reallocating time to named behaviour, from all other behaviours proportionally, in 87,498 UK Biobank participants. ^a	40
Supplementary Figure 11: An example of a decision tree to classify time windows using average acceleration vector magnitude (avm) and the 75 th percentile of acceleration vector magnitude (75thp).	41
Supplementary Figure 12: The structure of a Hidden Markov Model.....	42
Supplementary Figure 13: Hazard Ratios for incident cardiovascular disease for all behaviour pairs estimated using a multivariable-adjusted Cox regression model for all participants (blue) and in a sensitivity analysis excluding individuals with a zero value in any behaviour (red). ^a	43
Supplementary Figure 14: Hazard Ratios for incident cardiovascular disease estimated using a multivariable-adjusted Compositional Data Analysis Cox regression model (blue) and using a multivariable-adjusted linear isotemporal substitution Cox regression model (red). ^a	44
STROBE Statement—Checklist of items that should be included in reports of cohort studies.....	45

Supplementary Methods

'Ground truth' labelling of movement behaviours in image data

As described in the main text, to provide the 'ground truth' labels for machine-learning based behaviour classification, fine-grained behaviour annotations of image data were mapped to sleep, sedentary behaviour, light physical activity behaviours and moderate-to-vigorous physical activity behaviours based on the definition in the main text. In practice, this involved the following steps (the final mapping is given in **Supplementary Table 1**):

1. The fine-grained annotation for sleeping was assigned to sleep.
2. Behaviours at 3 or more METs (Metabolic Equivalent of Task, where 1 MET is energy expenditure in quiet sitting), as described in Compendium of Physical Activities [1], were assigned to moderate-to-vigorous physical activity behaviours.
3. For waking behaviours at <3 METs, if the fine-grained annotation indicated a sitting, lying or reclining posture, the behaviour was assigned to sedentary behaviour.
4. Waking behaviours at <3 METs not assigned to sedentary behaviour were assigned to light physical activity behaviours.
5. All labels were reviewed by two reviewers. Where reviewers agreed the fine-grained annotation was typically used by annotators for behaviours in a different category to the label given, the fine-grained annotation was recoded. This review was performed prior to model training, and no changes were made after results were obtained.

Machine-learning methods

As described in the main text, a Random Forest (RF) with 100 decision trees was developed to classify 30-second time windows as sleep, sedentary behaviour, light physical activity behaviours or moderate-to-vigorous physical activity behaviours using the time and frequency domain features outlined in **Supplementary Table 2**. A Hidden Markov model (HMM) was then employed to use time sequence information to improve on the RF-assigned label sequence. As described in the main text, models were trained using labelled data from the CAPTURE-24 study, in which participants wore wearable cameras and kept time use diaries alongside wearing an accelerometer.

Machine-learning methods: Features

Time windows of acceleration were classified using a list of features (variables) based on features used in the study of Willetts et al (this included time and frequency domain features e.g. mean and kurtosis of the acceleration vector magnitude, and power at different frequencies from the Fast Fourier Transform of acceleration vector magnitude) [2]. In the present study, only rotation-invariant features were used (see **Supplementary Table 2**). This addressed concerns about risk of overfitting and possible time trends in the data driven by sensitivity to device orientation within the wrist strap (orientation became more standardised over 2013-2015).

Machine-learning methods: Random Forest models

Random Forests are based on decision trees. Decision trees assign class labels based on splits of the data using feature value thresholds (as shown in the example in **Supplementary Figure 11**). They can be trained using the Classification and Regression Tree (CART) algorithm [3].

In a RF, many decision trees are used. When training the trees (using the CART algorithm), randomness is introduced by (i) training each tree on a set of data points picked randomly (with replacement) and (ii) at each split node, restricting the choice of splitting feature to a randomly picked subset of features.

To classify a data point using an RF, it is classified by each decision tree. Because they are trained on different subsets of data and use different features, different trees in the RF may classify data points differently. The overall classification given by the RF is the class that is assigned to the data point by the largest number of trees. This approach, whereby multiple randomly-differing instances are used in order to reduce variance on the output, is the technique of bootstrap-aggregating or ‘bagging’ [4].

For this application, a balanced RF was used. The fact some behaviours are much more common than others in the labelled data (e.g. sleep is much more common than moderate-to-vigorous physical activity behaviours) can cause a standard RF, which is trained by picking N examples at random with replacement, to favour assigning common labels at the expense of less common behaviours [2]. Using the balanced RF, if there were n_{rare} examples of the rarest behaviour, n_{rare} examples of each behaviour were picked with replacement to train each tree.

Machine-learning methods: Hidden Markov models

In an HMM, there is a sequence of unobserved hidden states, which is assumed to have the Markov property (i.e. future states only depend on past states through present states). This sequence is governed by transition probabilities, which determine the probability of transitioning between each pair of states. There is a sequence of observed states, which depend probabilistically on the sequence of hidden states (described as ‘emissions’ from the sequence of hidden states; **Supplementary Figure 12**).

Here, the hidden states were the true behaviours, and the emissions were the RF-assigned labels. The Viterbi algorithm, the standard approach to this problem, was used to estimate the most likely true behaviour sequence given the observed sequence of RF-assigned labels [5]. Applying the Viterbi algorithm required estimates of:

1. **Transition probabilities between hidden states:** Transition probabilities between behaviour pairs were estimated using the proportions of transitions that occurred between each behaviour pair in the labelled data.
2. **Emission probabilities of observed states from hidden states:** To estimate emission probabilities, time windows were first classified using out-of-bag predictions from the RF i.e. trees were used to classify data points on which they were not trained. This mimics use on unseen data, without requiring additional data. Emission probabilities were then estimated using the proportions of different pairs of true behaviour and RF out-of-bag estimate.

By using this HMM to estimate the most likely true behaviour sequence given the RF-assigned labels, a more plausible sequence of states was obtained. The HMM re-labelled behaviours which formed unrealistic sequences and were likely to be attributable to misclassification (e.g. short periods of moderate-to-vigorous physical activity behaviours during sleep time). Therefore, compared to the unadjusted RF-assigned labels, the labels after using the HMM gave improved measures of the behaviours of interest for subsequent epidemiological analyses.

Machine-learning methods: Evaluation

All metrics were calculated in Leave-One-Participant-Out Cross-Validation.

Leave-One-Participant-Out Cross-Validation involves, for each participant, a model trained on all other participants’ data (i.e. with this participant’s data left-out). The trained model is then used to label the left-out participant’s data and evaluation metrics are calculated. This is repeated for all participants, and metrics are aggregated or calculated across all participants.

Leave-One-Participant-Out Cross-Validation allows evaluation of the performance of the models on data not used in training, while retaining the maximal amount of data for use in training these models. Moreover, all of the data can then be used to train the final model used for classification.

For model performance, the following evaluation metrics were used:

1. We reported mean per-participant accuracy across all behaviours. This is a simple, intuitive metric of model performance, describing the proportion of 30-second time windows that were correctly classified. Using mean per-participant accuracy, rather than aggregate accuracy over all data, prevents the result being dominated by performance on a few participants with larger amounts of data (important as there may be inter-individual differences in classification performance).
2. We reported mean per-participant Cohen's kappa across all behaviours. This is a metric of interrater reliability. It evaluates how much higher the agreement between two raters (here, annotator-assigned 'ground truth' label and model-assigned label) is than that which would be achieved by chance, given the proportions in each class. It is preferable to accuracy, as it takes into account the proportions in each class (in particular, in data where some classes are dominant, a classifier assigning solely to the dominant classes can achieve high accuracy but not high Cohen's kappa).
3. We reported mean per-participant precision and recall for each behaviour. Precision for a given behaviour is the proportion of examples labelled by the model as that behaviour which are 'true' examples of that behaviour. Recall for a given behaviour is the proportion of 'true' examples of that behaviour labelled as that behaviour. Again, taking the mean across participants prevents performance being dominated by performance on participants with larger amounts of data. However, it also upweights the contribution of individuals with very small amounts of data for a given behaviour. Therefore, precision and recall were additionally calculated after excluding participants with up to 20 minutes in the behaviour.

Taken together, these metrics help to understand the validity of the model as a method to derive measures of movement behaviours for subsequent epidemiological analyses. After applying the model to derive measures of movement behaviours for UK Biobank participants, face validity was assessed by plotting behaviour profiles over the day.

Machine-learning methods: model in participants aged 38 years or older

We also carried out the above steps using only data from participants aged 38 years or older i.e. nearer to the age group represented in the UK Biobank sample. The age group 38+ years was used as this corresponds to the information available in a release version of this dataset.

In Leave-One-Participant-Out analysis, the mean per-participant accuracy was 86% (84, 88) and the mean per-participant Cohen's kappa was 0.79 (0.76, 0.81).

Given the results reported in the main text, showing that the model trained on all participants performed well when restricted to the age group of interest, we used the model trained on all participants for the main classification.

A Compositional Data Analysis approach to movement behaviour data

Log-ratio transformation

A Compositional Data Analysis approach is a set of methods for working with compositional data, based on the use of log-transformed ratios to describe the data [6–8]. Ratios between behaviours are used to describe compositional data as they capture the relative values of the different behaviours. Log-transforming ratios ensures the relationships and distances between different compositions are well-described: using log-transformed ratios is equivalent to working with compositional data in a ‘natural’ space for it, with operations which map compositions to genuine compositions and an appropriate distance metric [9,10]. For statistical purposes, log-transformed ratios are also typically more conveniently distributed than ratios [11].

While many different sets of log-transformed ratios can be used, isometric log-ratio pivot coordinates are widely used in movement behaviour research [12] and were used in this study. They were calculated as follows:

$$coordinate_1 = \sqrt{\frac{3}{4}} \ln \left(\frac{\text{sleep}}{\sqrt[3]{\text{SB} \times \text{LIPA} \times \text{MVPA}}} \right) = \sqrt{\frac{1}{12}} \ln \left(\frac{\text{sleep}}{\text{SB}} \right) + \sqrt{\frac{1}{12}} \ln \left(\frac{\text{sleep}}{\text{LIPA}} \right) + \sqrt{\frac{1}{12}} \ln \left(\frac{\text{sleep}}{\text{MVPA}} \right)$$

$$coordinate_2 = \sqrt{\frac{2}{3}} \ln \left(\frac{\text{SB}}{\sqrt[3]{\text{LIPA} \times \text{MVPA}}} \right) = \sqrt{\frac{1}{6}} \ln \left(\frac{\text{SB}}{\text{LIPA}} \right) + \sqrt{\frac{1}{6}} \ln \left(\frac{\text{SB}}{\text{MVPA}} \right)$$

$$coordinate_3 = \sqrt{\frac{1}{2}} \ln \left(\frac{\text{LIPA}}{\text{MVPA}} \right)$$

Interpreting isometric log-ratio pivot coordinates

As the coefficients in the model relate to the isometric log-ratio pivot coordinates, rather than the raw behaviour variables, interpreting them is not straightforward.

The first coordinate describes the balance between sleep and all other behaviours. Therefore, the coefficient of the first coordinate can be interpreted as the effect of reallocating time to sleep from all other behaviours proportionally i.e. if the coefficient of the first coordinate is greater than 0 (its exponent is greater than 1) reallocating time to sleep from all other behaviours proportionally is associated with higher risk of cardiovascular disease. However, the second and third coordinates are harder to interpret analogously. Therefore, to interpret individually the effect of reallocating time to each behaviour from all others proportionally, and following standard methods in movement behaviour research, one model per behaviour was produced (with different first coordinate). This approach was used to present the model parameters in **Supplementary Table 5** and **Supplementary Table 6** (note that, in consequence, they do not parametrise a single model).

However, even using this approach, the magnitudes of the coefficients are hard to interpret. Therefore, as described in the main text, and following established methods, model estimates of the hazard ratio at different compositions relative to the mean behaviour composition were reported e.g. using pairwise time reallocation plots.

In detail, suppose we have a Cox regression model in the isometric log-ratio pivot coordinates laid out above:

$$\ln \frac{h(t)}{h_0(t)} = \beta_1(\text{coordinate}_1) + \beta_2(\text{coordinate}_2) + \beta_3(\text{coordinate}_3) + \sum_{i=1}^k \gamma_i(\text{covariate}_i)$$

and that the value of the coordinates at the mean behaviour composition is $(m_coordinate_1, m_coordinate_2, m_coordinate_3)$. [This notation is not misleading: the value of the coordinates at the compositional mean behaviour composition is also the mean of the coordinate values.].

Then, we consider a new behaviour composition, which corresponds to isometric log-ratio pivot coordinate values $(coordinate_1, coordinate_2, coordinate_3)$. In particular, when considering a pairwise time reallocation plot we use would use a new composition where time in two behaviours remained at its value in the mean behaviour composition, a value was subtracted from time in one of the remaining behaviours, and that value added to the time in the other behaviour. The log hazard ratio, now relative to the mean behaviour composition, is then calculated as:

$$\ln(HR) = \beta_1(\text{coordinate}_1 - m_coordinate_1) + \beta_2(\text{coordinate}_2 - m_coordinate_2) + \beta_3(\text{coordinate}_3 - m_coordinate_3)$$

The standard error on this can be calculated using the variance-covariance matrix of the coefficients $\boldsymbol{\beta} = (\beta_1, \beta_2, \beta_3)$, denoted V . Writing $\mathbf{x} = (\text{coordinate}_1 - m_coordinate_1, \text{coordinate}_2 - m_coordinate_2, \text{coordinate}_3 - m_coordinate_3)^T$, then

$$SE = \sqrt{\mathbf{x}^T V \mathbf{x}}$$

This can be used to calculate the HR and an (approximate) 95% CI as:

$$\exp(\ln(HR)) (\exp(\ln(HR) - 1.96SE), \exp(\ln(HR) + 1.96SE)).$$

While here we follow an exposition similar to that of Dumuid et al in the context of linear regression [13] and Chastin et al [14], the approach is mathematically equivalent to that of McGregor et al.[15]

To ensure results were plotted within the range supported by the data, times plotted were truncated at the 5th and 95th centile for the behaviour in the pair for which this range was narrower.

Zero values

All participants recorded time in sleep, sedentary behaviour and light physical activity behaviours, but 1% of participants recorded no time in moderate-to-vigorous physical activity behaviours. As zero values cannot be incorporated directly into the coordinates above, different approaches to work with them have been developed. The appropriate method depends on the source of the zero values:

1. ‘Rounded’ zeroes relate to measurement precision: even where no time in a given behaviour was observed, had the wear time been long enough, or the time resolution of the measurement short enough, some time in the behaviour would be expected. If data contains rounded zeroes, they can be imputed as small positive values [16].
2. ‘True’ zeroes occur where no matter the precision of the measurement, no time in that behaviour would be observed. For example, this may occur in movement behaviour research if someone is physically unable to take part in certain behaviours. If data contains true zeroes, participants with a true zero in a particular behaviour should be excluded from the main analysis and analysed separately.

We followed established methods in movement behaviour research by considering zero values to be ‘rounded’ and imputing them using the log-ratio expectation maximization algorithm from the ‘zCompositions’ R package [8,15–17]. We used the smallest observed value in the data as the detection limit (0.0001 on the unitless scale, corresponding to 0.14 min/day). Sensitivity of results to the method of treating zero values (imputation or exclusion) under the Compositional Data Analysis approach was examined by performing an analysis restricted to participants with non-zero values in all behaviour variables. This did not materially impact the results (**Supplementary Figure 13**).

Software

Development of the machine-learning models and processing of accelerometer data used Python 3.6.6, with the ‘biobankAccelerometerAnalysis’ tool[2,18,19] for preparing accelerometer data and training machine-learning models.

Data preparation was performed in Python 3.6.6 and R 4.0.5, and used the ‘ukb_download_and_prep_template’ tool [20] for preparing covariate and outcome data.

Statistical analysis was performed in R 4.0.5[21] with ‘zCompositions’, ‘survival’, ‘forestplot’, ‘EValue’, ‘plyr’, ‘data.table’, ‘rlist’, ‘ggtern’, ‘ggplot2’, and ‘gtools’[16,22–32]. The R package ‘epicoda’ was developed for this analysis[33].

Code is available at github.com/activityMonitoring/manuscript_ml_behaviours_cvd_2021. For further directions, please contact Aiden Doherty.

Sensitivity analyses: further details on E-values

As described in the main text, E-values were reported alongside hazard ratios. The E-value for the estimate quantifies the minimum strength of association that an unmeasured confounder would need with both exposure and outcome to explain away the observed association. The E-value for the 95% confidence interval quantifies the minimum strength of association an unmeasured confounder would need with both exposure and outcome to reduce the interval to overlap the null [27,28]. As the exposure is continuous, in both cases the risk ratio would apply to hypothetical groups with either the specified behaviour composition or the reference (the mean behaviour composition) [28].

Sensitivity analyses: linear isotemporal substitution

For comparability with previous literature, a sensitivity analysis using a linear isotemporal substitution approach was conducted.

Under a linear isotemporal substitution approach, all but one of the movement behaviours are included in the model (so the included variables are not perfectly multicollinear). [In this study, as non-wear time was imputed all subjects had the same wear time. Therefore, a total time variable was not included, meaning the approach may be more properly called 'leave-one-out regression' than true linear isotemporal substitution [8].] Associations are modelled as linear (rather than linear in the log-ratios, as under a Compositional Data Analysis approach). The coefficient of each behaviour can be interpreted in terms of replacing time in the left-out behaviour with time in that behaviour. Linear isotemporal substitution has been widely used in movement behaviour epidemiology [34], but has been criticised for not addressing the fact movement behaviour data only conveys relative information [8].

While there were some differences in shape of the associations observed (due to the different assumptions), results using this approach were broadly similar to the results of the main analysis using Compositional Data Analysis (**Supplementary Figure 14**).

References

- 1 Ainsworth BE, Haskell WL, Herrmann SD, *et al.* 2011 compendium of physical activities: A second update of codes and MET values. *Med Sci Sports Exerc* 2011;**43**:1575–81. doi:10.1249/MSS.0b013e31821ece12
- 2 Willetts M, Hollowell S, Aslett L, *et al.* Statistical machine learning of sleep and physical activity phenotypes from sensor data in 96,220 UK Biobank participants. *Sci Rep* 2018;**8**:0–10. doi:10.1038/s41598-018-26174-1
- 3 Breiman L, Friedman JH, Olshen RA, *et al.* *Classification and regression trees*. 1984. doi:10.1201/9781315139470
- 4 Breiman L. Bagging predictors. *Mach Learn* 1996;**24**:123–40. doi:10.1007/bf00058655
- 5 Forney GD. The Viterbi Algorithm. *Proc IEEE* 1973;**61**:268–78. doi:10.1109/PROC.1973.9030
- 6 Pawlowsky-Glahn V, Egozcue JJ, Tolosana-Delgado R. Lecture notes on Compositional Data Analysis. 2011;:1–100. doi:10.13140/RG.2.1.1296.2728
- 7 Filzmoser P, Hron K, Templ M. *Applied Compositional Data Analysis*. 2018. doi:10.1007/978-3-319-96422-5
- 8 Dumuid D, Pedišić Ž, Palarea-Albaladejo J, *et al.* Compositional Data Analysis in Time-Use Epidemiology : What , Why , How. *Int J Environ Res Public Health* 2020;**17**:2220. doi:10.3390/ijerph17072220
- 9 Aitchison J, Egozcue JJ. Compositional data analysis: Where are we and where should we be heading? *Math Geol* Published Online First: 2005. doi:10.1007/s11004-005-7383-7
- 10 Egozcue JJ, Pawlowsky-Glahn V, Mateu-Figueras G, *et al.* Isometric Logratio Transformations for Compositional Data Analysis. *Math Geol* 2003;**35**:279–300. doi:10.1023/A:1023818214614
- 11 Aitchison J. The statistical analysis of compositional data. *Stat Anal Compos Data* 1982;**44**:139–77. doi:10.1007/978-94-009-4109-0
- 12 Dumuid D, Stanford TE, Martín-Fernández J-AA, *et al.* Compositional data analysis for physical activity, sedentary time and sleep research. *Stat Methods Med Res* 2017;**27**:096228021771083. doi:10.1177/0962280217710835
- 13 Dumuid D, Pedišić Ž, Stanford TE, *et al.* The compositional isotemporal substitution model: A method for estimating changes in a health outcome for reallocation of time between sleep, physical activity and sedentary behaviour. *Stat Methods Med Res* 2017;**28**:846–57. doi:10.1177/0962280217737805
- 14 Chastin S, McGregor D, Palarea-Albaladejo J, *et al.* Joint association between accelerometry-measured daily combination of time spent in physical activity, sedentary behaviour and sleep and all-cause mortality: a pooled analysis of six prospective cohorts using compositional analysis. *Br J Sports Med* 2021;:bjssports-2020-102345. doi:10.1136/bjssports-2020-102345
- 15 McGregor DE, Palarea-Albaladejo J, Dall PMP, *et al.* Cox regression survival analysis with compositional covariates: Application to modelling mortality risk from 24-h physical activity patterns. *Stat Methods Med Res* 2019;**29**:1447–65. doi:10.1177/0962280219864125
- 16 Palarea-Albaladejo J, Martín-Fernández JA. ZCompositions - R package for multivariate imputation of left-censored data under a compositional approach. *Chemom. Intell. Lab. Syst.* 2015;**143**:85–96. doi:10.1016/j.chemolab.2015.02.019
- 17 Rasmussen CL, Palarea-Albaladejo J, Johansson MS, *et al.* Zero problems with compositional data of physical behaviors: a comparison of three zero replacement methods. *Int J Behav Nutr Phys Act* 2020.
- 18 Doherty A, Jackson D, Hammerla N, *et al.* Large scale population assessment of physical activity using wrist worn accelerometers: The UK biobank study. *PLoS One* 2017;**12**:1–14. doi:10.1371/journal.pone.0169649
- 19 Doherty A, Smith-Byrne K, Ferreira T, *et al.* GWAS identifies 14 loci for device-measured physical activity and sleep duration. *Nat Commun* 2018;**9**. doi:10.1093/acrefore/9780190236557.013.204
- 20 Walmsley R, Chan S, Doherty A. `ukb_download_and_prep_template`. 2020.https://github.com/activityMonitoring/ukb_download_and_prep_template
- 21 R Core Team. R: A Language and Environment for Statistical Computing. *Vienna, Austria* Published Online First: 2019.<https://www.r-project.org/>
- 22 Therneau TM. A Package for Survival Analysis in R. 2021.<https://cran.r-project.org/package=survival>
- 23 Wickham H. *ggplot2: Elegant Graphics for Data Analysis*. New York: : Springer-Verlag 2016. <https://ggplot2.tidyverse.org>
- 24 Warnes GR, Bolker B, Lumley T. `gtools`: Various R Programming Tools. *R Packag version 381* 2018.
- 25 Terry M, Therneau, Patricia M. Grambsch. *Modeling Survival Data: Extending the Cox Model*. New York: : Springer 2000.
- 26 Max Gordon and Thomas Lumley. `forestplot`: Advanced Forest Plot Using ‘grid’ Graphics. R package version 1.9. 2019.<https://cran.r-project.org/package=forestplot>
- 27 Van Der Wee TJ, Ding P. Sensitivity analysis in observational research: Introducing the E-Value. *Ann Intern Med* 2017;**167**:268–74. doi:10.7326/M16-2607

- 28 Mathur MB, Ding P, Riddell CA, *et al.* Web Site and R Package for Computing E-values. *Epidemiology* 2018;**29**:e45. doi:10.1097/EDE.0000000000000864
- 29 Wickham H. The Split-Apply-Combine Strategy for Data Analysis. *J Stat Softw* 2011;**40**:1–29. <http://www.jstatsoft.org/v40/i01/>
- 30 Dowle M, Srinivasan A. data.table: Extension of `data.frame`. 2021. <https://cran.r-project.org/package=data.table>
- 31 Ren K. rlist: A Toolbox for Non-Tabular Data Manipulation. 2016. <https://cran.r-project.org/package=rlist>
- 32 Hamilton NE, Ferry M. Ggtern: Ternary diagrams using ggplot2. *J Stat Softw* 2018;**87**:1–17. doi:10.18637/jss.v087.c03
- 33 Walmsley R. epicoda. 2020. github.com/activityMonitoring/epicoda
- 34 Mekary RA, Ding EL. Isotemporal substitution as the gold standard model for physical activity epidemiology: Why it is the most appropriate for activity time research. *Int J Environ Res Public Health* 2019;**16**:11–3. doi:10.3390/ijerph16050797

Supplementary Tables and Figures

Supplementary Table 1: Assignment of fine-grained camera image annotations from the Compendium of Physical Activities to broad movement behaviour classes.

<p><u>Sleep</u></p> <p>7030 sleeping</p>
<p><u>Sedentary behaviour</u></p> <p>occupation;office and administrative support;11580 office/computer work general</p> <p>occupation;office and administrative support;11580 office wok/computer work general</p> <p>home activity;miscellaneous;sitting;9060 sitting/lying reading or without observable/identifiable activities</p> <p>leisure;miscellaneous;sitting;0010 sitting / lying dialysis</p> <p>transportation;private transportation;16010 driving automobile or light truck (not a semi)</p> <p>home activity;miscellaneous;sitting;7010 sitting/lying and watching television with TV on as the primary activity</p> <p>home activity;miscellaneous;sitting;11580 office/computer work general</p> <p>home activity;miscellaneous;sitting;9055 sitting/lying talking in person/using a mobile phone/smartphone/tablet or talking on the phone/computer (skype chatting)</p> <p>home activity;miscellaneous;sitting;11580 office work such as writing and typing (with or without eating at the same time)</p> <p>home activity;eating;13030 eating sitting alone or with someone</p> <p>home activity;miscellaneous;sitting;9030 sitting desk entertainment/hobby (with or without eating at the same time)</p> <p>home activity;miscellaneous;sitting;5080 sitting non-desk work (with or without eating at the same time)</p> <p>occupation;interruption;sitting;11585 sitting meeting/talking to colleagues with or without eating</p> <p>leisure;miscellaneous;sitting;9060 (generic) sitting/lying reading or without observable/identifiable activities</p> <p>occupation;interruption;11585 sitting meeting/talking to colleages with or without eating</p> <p>home activity;leisure;activities for maintenance of a household;miscellaneous;9100 retreat/family reunion activities involving sitting eating relaxing talking with more than one person</p> <p>home activity;miscellaneous;sitting;9060 sitting/lying reading or without observable activities</p> <p>leisure;eating;social;13030 eating sitting indoor/outdoor</p> <p>home activity;leisure;activities for maintenance of a household;miscellaneous;9100 retreat/family reunion activities involving sitting eating relaxing talking with more than one person</p> <p>occupation;public admin/education/health;education;9065 students/attending seminars or talks</p> <p>home activity;miscellaneous;sitting;9030 sitting desk work (with or without eating at the same time)</p> <p>occupation;interruption;sitting;9060 sitting without observable/identifiable activities</p>

leisure;miscellaneous;sitting;9055 sitting talking to person/using the phone
transportation;private transportation;16015 riding in a car or truck
leisure;eating;13030 eating sitting indoor/outdoor
occupation;interruption;13030 eating sitting
home activity;miscellaneous;sitting;9045 sitting playing traditional video game computer game
home activity;miscellaneous;sitting;9030 sitting desk work (with or without eating at the same time)
occupation;interruption;sitting;13030 eating sitting
home activity;leisure;individual activities;9075 sitting arts and crafts carving/wood weaving/spinning wool
home activity;household chores;washing/ironing/mending clothes;5080 knitting sewing sitting
occupation;interruption;sitting;9055 sitting using a mobile phone/smartphone/tablet or talking on the phone/computer (skype meeting etc.)
leisure;miscellaneous;sitting;21000 sitting meeting
leisure;miscellaneous;sitting;21005 (generic) sitting light office writing typing work
occupation;office and administrative support;11580 office work/computer work general
home activity;miscellaneous;sitting;7010 lying and watching television with TV on as the primary activity
leisure;miscellaneous;sitting;9060 (generic) sitting/lying reading or without observable activities
transportation;waiting;7021 sitting
occupation;interruption;11585 sitting meeting/talking to colleagues with or without eating
leisure;religious activities;20000 sitting in church in service attending a ceremony sitting quietly
transportation;private transportation;16030 motor scooter motorcycle
occupation;interruption;9055 sitting using a mobile phone/smartphone/tablet or talking on the phone/computer (skype meeting etc.)
leisure;miscellaneous;21005 (generic) sitting light office writing typing work
home activity;miscellaneous;sitting;7021 sitting without observable activities
home activity;leisure;activities for maintenance of a household;with children;5170 sitting playing with child(ren)
home activity;leisure;activities for maintenance of a household;with children;5170 sitting playing with child(ren)
occupation;interruption;9060 (generic) sitting without observable activities
home activity;child/elderly/pet care;child care;5185 child care sitting/kneeling
home activity;miscellaneous;sitting;21010 sitting non-desk work (with or without eating at the same time)
leisure;eating;not-social;13030 eating sitting indoor/outdoor
leisure;miscellaneous;sitting;5080 sitting non-desk work (with or without eating at the same time)
home activity;leisure;activities for maintenance of a household;9100 retreat/family reunion activities involving sitting eating relaxing talking with more than one person

leisure;miscellaneous;sitting;21016 sitting child care only active periods
 home activity;leisure;activities for maintenance of a household;5170 sitting playing with child(ren)
 home activity;lawn and garden;gardening service;8055 driving tractor
 occupation;interruption;9060 (generic) sitting without observable/identifiable activities
 home activity;self care;13036 taking medication
 leisure;miscellaneous;21000 sitting meeting or talking with others
 home activity;self care;13046 having hair or nails done by someone else sitting
 home activity;household chores;washing/ironing/mending clothes;5080 knitting sewing wrapping presents sitting
 home activity;miscellaneous;sitting;9060 sitting reading or using a mobile phone/smartphone/tablet or talking on the phone/computer (skype chatting)
 leisure;miscellaneous;21010 sitting non-desk work (with or without eating at the same time)
 occupation;interruption;9060 sitting using a mobile phone/smartphone/tablet or talking on the phone/computer (skype meeting etc.)
 leisure;religious activities;20005 sitting in church talking or singing attending a ceremony sitting active
 home activity;child/elderly/pet care;child care;5185 child care sitting/kneeling occasional lifting
 leisure;miscellaneous;21016 sitting child care only active periods
 home activity;miscellaneous;sitting;7021 sitting without observable activities
 home activity;leisure;activities for maintenance of a household;with animals;5190 sitting playing with animals active periods
 transportation;public transportation;16016 riding in a bus or train
 leisure;sports;water activities;18012 boating power passenger

Light physical activity behaviours

home activity;household chores;preparing meals/cooking/washing dishes;5035 kitchen activity general cooking/washing/dishes/cleaning up
 home activity;miscellaneous;walking;17150 walking household without observable loads
 home activity;miscellaneous;walking;5165 (generic) walking non-cleaning task such as closing windows lock door putting away items
 leisure;miscellaneous;walking;21070 (generic) walking and occasional standing (no more than two consecutive images)
 transportation;walking;17161 walking not as the single means of transports e.g.from house to transports or vice versa/from car to places or vice versa/between transports
 leisure;miscellaneous;walking;5060 shopping miscellaneous
 occupation;interruption;11791 walking on job in office or lab area
 home activity;miscellaneous;standing;9050 standing talking in person/on the phone/computer (skype chatting) or using a mobile phone/smartphone/tablet
 home activity;household chores;washing/ironing/mending clothes;5090 folding or hanging clothes/put clothes in or out of washer or dryer/packing suitcase limited walking

home activity;miscellaneous;standing;9070 standing reading or without observable/identifiable activities
occupation;interruption;walking;11791 walking on job in office or lab area
occupation;manufacturing;11115 chef
home activity;self care;13040 (generic) self care such as grooming/washing hands/shaving/brushing teeth/putting on make-up not eliminating and bathing (not necessary in the toilet)
occupation;office and administrative support;11600 (generic) standing tasks such as store clerk/librarian/packing boxes/repair heavy parts
leisure;miscellaneous;5060 shopping miscellaneous
home activity;household chores;washing/ironing/mending clothes;5070 ironing
leisure;miscellaneous;standing;9050 standing talking in person/using a phone/smartphone/tablet
home activity;miscellaneous;walking;5147 walking moving away light items (pens/papers/keys not included)
occupation;miscellaneous;11475 (generic) manual labour
occupation;interruption;standing;9050 standing talking in person/using a phone/smartphone/tablet
occupation;personal services;11413 kitchen maid
home activity;household chores;grocery shopping;5060 shopping
home activity;home repair;indoor;6126 home repair miscellaneous
leisure;miscellaneous;standing;9070 standing reading or without observable/identifiable activities
transportation;waiting;7040 standing in a line
home activity;child/elderly/pet care;child care;5185 child care sitting/kneeling occasional lifting
home activity;miscellaneous;standing;9071 (generic) standing miscellaneous
leisure;miscellaneous;standing;9071 (generic) standing miscellaneous
occupation;interruption;standing;9070 standing reading or without observable/identifiable activities
home activity;miscellaneous;standing;9020 standing writing/drawing/painting
home activity;leisure;individual activities;10074 playing musical instruments
occupation;interruption;5041 kitchen activity in the working place
home activity;miscellaneous;walking;17140 using crutches or frame
occupation;interruption;9050 standing talking in person/using a phone/smartphone/tablet
home activity;leisure;individual activities;9085 standing arts and crafts/sand painting/carving weaving
home activity;miscellaneous;5025 (generic) multiple household tasks all at once including standing/lifting/sitting
home activity;miscellaneous;standing;9070 standing reading or without obvious activities
home activity;household chores;washing/ironing/mending clothes;5095 putting away /gathering clothes involving walking
home activity;lawn and garden;lawn care service;8135 planting potting transplanting seedlings or plants

occupation;interruption;standing;9071 (generic) standing miscellaneous
transportation;walking;9050 standing miscellaneous (talking to others etc.)
occupation;interruption;miscellaneous;5041 kitchen activity in the working place
home activity;household chores;house cleaning;miscellaneous;5100 making bed/changing linens
occupation;interruption;standing;9015 standing scanning documents
home activity;household chores;house cleaning;furniture;5032 dusting or polishing furniture
home activity;eating;13035 eating standing alone or with others
occupation;miscellaneous;11870 working in scene shop theatre actor backstage employee
occupation;office and administrative support;11600 (generic) standing tasks such as store clerk/librarian/packing boxes/repair heavy parts
home activity;miscellaneous;standing;9050 standing talking in person on the phone/computer (skype chatting) or using a mobile phone/smartphone/tablet
home activity;household chores;house cleaning;floors;5010 cleaning sweeping carpet or floors
leisure;sports;ball games;15090 bowling
home activity;self care;13020 dressing/undressing
occupation;interruption;9070 standing reading or without observable/identifiable activities
leisure;music playing;10074 playing musical instruments
home activity;home repair;indoor;6205 sharpening tools
home activity;home repair;indoor;6124 hammering nails
home activity;child/elderly/pet care;child care;5186 child care standing occasional lifting
occupation;interruption;13035 eating standing
home activity;child/elderly/pet care;pet care;5197 household animal care aside from feeding
leisure;recreation;outdoor;5171 standing playing with child(ren)
occupation;interruption;miscellaneous;13009 toilet break
home activity;household chores;house cleaning;miscellaneous;5148 watering plants
occupation;miscellaneous;11475 (generic) manual or unskilled labour
occupation;interruption;standing;9020 standing writing/drawing/painting
leisure;eating;social;13035 eating standing indoor/outdoor
home activity;household chores;house cleaning;floors;5131 scrubbing floors on hands and knees scrubbing bathroom bathtub
occupation;public admin/education/health;education;09071 teaching standing
home activity;household chores;preparing meals/cooking/washing dishes;5051 serving food/setting table implied walking and standing
home activity;household chores;preparing meals/cooking/washing dishes;5035 cleaning up table after meal implied walking (e.g. leaving from eating table to the kitchen)

leisure;eating;not-social;5060 buying foods or drinks as a takeaway
leisure;miscellaneous;21070 (generic) walking/standing combination indoor
home activity;self care;13009 toilet eliminating or squatting
home activity;self care;13045 hairstyling standing
home activity;lawn and garden;gardening service;8230 watering garden
occupation;interruption;13009 toilet break
leisure;miscellaneous;standing;9070 standing reading or without obvious activities
home activity;leisure;activities for maintenance of a household;miscellaneous;9101 retreat/family reunion activities playing games with more than one person
occupation;interruption;9015 standing scanning documents
home activity;child/elderly/pet care;child care;5183 standing holding child
occupation;interruption;9070 standing reading or without obvious activities
leisure;miscellaneous;standing;9020 standing writing/drawing/painting
leisure;religious activities;20039 walking/standing combination for religious purposes usher
leisure;recreation;indoor;9020 drawing writing painting standing
leisure;miscellaneous;21017 standing child care only active periods
home activity;child/elderly/pet care;pet care;5053 feeding household animals
leisure;eating;13035 eating standing indoor/outdoor
leisure;miscellaneous;9071 (generic) standing miscellaneous indoor or outdoor
leisure;sports;conditioning;2115 upper body exercise arm ergometer
occupation;interruption;standing;9050 standing talking in person/using a phone/smartphone/tablet
home activity;self care;13000 getting ready for bed standing
leisure;eating;social;5060 buying foods or drinks as a takeaway
home activity;home repair;indoor;5160 standing light effort tasks
transportation;walking;9071 standing miscellaneous (talking to others etc.)
occupation;interruption;standing;13035 eating standing
occupation;interruption;9020 standing writing/drawing/painting
home activity;lawn and garden;gardening service;8220 walking applying fertilizer or seeding a lawn push applicator
leisure;eating;5060 buying foods or drinks as a takeaway
leisure;religious activities;20030 standing talking in church
leisure;eating;not-social;13035 eating standing indoor/outdoor

occupation;public admin/education/health;education;9071 teaching standing
home activity;household chores;washing/ironing/mending clothes;5082 sewing with a machine

Moderate-to-vigorous physical activity behaviours

transportation;private transportation;1010 bicycling
transportation;walking;17165 walking the dog
occupation;interruption;17133 walking upstairs
leisure;miscellaneous;walking;17031 loading /unloading a car implied walking
home activity;child/elderly/pet care;child care;5181 walking and carrying child
home activity;lawn and garden;gardening service;8050 digging spading filling garden compositing
leisure;sports;miscellaneous;17082 hiking or walking at a normal pace through fields and hillsides
home activity;lawn and garden;tree and shrub service;8025 clearing light brush thinning garden
home activity;lawn and garden;lawn care service;8165 raking lawn
occupation;interruption;walking;11795 walking on job and carrying light objects such as boxes or pushing trolleys
leisure;sports;water activities;18070 canoeing/rowing
home activity;lawn and garden;lawn care service;8080 laying crushed rock
leisure;sports;gymnasium and athletics;athletics;12150 running
leisure;sports;ball games;15235 football or baseball playing catch
home activity;miscellaneous;standing;5146 standing packing/unpacking household items occasional lifting
home activity;lawn and garden;gardening service;8245 gardening/picking up fruits vegetables flowers
leisure;miscellaneous;walking;17105 pushing a wheelchair non-occupational
leisure;sports;ball games;15680 tennis doubles
home activity;lawn and garden;gardening service;8192 shovelling dirt or mud
leisure;sports;miscellaneous;17082 hiking or walking at a normal pace through fields and hillsides
leisure;dancing;3010 ballet modern or jazz general rehearsal or class
leisure;sports;conditioning;2060 health club exercise
leisure;sports;ball games;15690 tennis singles
home activity;lawn and garden;lawn care service;8095 mowing lawn
occupation;public admin/education/health;health;11615 nursing patient care

occupation;miscellaneous;11615 (generic) standing lifting items continuously with limited walking
leisure;miscellaneous;17031 loading /unloading a car implied walking
leisure;sports;conditioning;2019 bicycling stationary RPM/Spin bike class
home activity;leisure;activities for maintenance of a household;with animals;5192 walking/running playing with animals active periods
home activity;lawn and garden;gardening service;8192 shoveling dirt or mud
home activity;household chores;house cleaning;furniture;5020 cleaning heavy such as car/windows/garage
leisure;sports;conditioning;2048 elliptical trainer
occupation;interruption;11795 walking on job and carrying light objects such as boxes or pushing trolleys
leisure;sports;conditioning;2050 resistance training
leisure;sports;conditioning;2070 rowing stationary ergometer
leisure;recreation;outdoor;5175 walking/running playing with child(ren)
leisure;sports;conditioning;2010 bicycling stationary
leisure;sports;conditioning;2120 water aerobics water calisthenics water exercise
home activity;home repair;outdoor;6020 automobile body work
occupation;agriculture/forestry/fishing;11192 taking care of animals
leisure;miscellaneous;standing;21017 standing child care only active periods
leisure;sports;conditioning;2065 stair-treadmill ergometer general
home activity;household chores;washing/ironing/mending clothes;5092 washing clothes by hand (with or without hanging wash)
leisure;miscellaneous;walking;17133 walking upstairs
transportation;walking;12150 running
occupation;interruption;walking;17070 walking downstairs
home activity;household chores;house cleaning;floors;5140 sweeping garage sidewalk or outside of house
occupation;interruption;walking;17133 walking upstairs
occupation;agriculture/forestry/fishing;11540 shovelling digging ditches
occupation;construction;11050 carrying heavy loads
transportation;walking;17250 walking as the single means to a destination not to work or class
leisure;miscellaneous;walking;17070 descending stairs
home activity;miscellaneous;walking;5121 walking with moving and lifting loads such as bikes and furniture
transportation;walking;17270 walking as the single means to work or class (not from)

Supplementary Table 2: Features of accelerometry signal used for behaviour classification.

Feature	Description
enmoTrunc	Euclidean Norm Minus One truncated below at 0
mean	Mean
sd	Standard Deviation
coefvariation	Coefficient of Variation
median	Median
min	Minimum
max	Maximum
25thp	25 th percentile
75thp	75 th percentile
autocorr	Autocorrelation
fmax	Frequency of signal with highest power
pmax	Maximal power of signal
fmaxband	Frequency of signal with highest power between 0.3 and 3 Hz
pmaxband	Maximal power of signal between 0.3 and 3 Hz
entropy	Entropy
fft1	Power at 1Hz
fft2	Power at 2Hz
fft3	Power at 3Hz
fft4	Power at 4Hz
fft5	Power at 5Hz
fft6	Power at 6Hz
fft7	Power at 7Hz
fft8	Power at 8Hz
fft9	Power at 9Hz
fft10	Power at 10Hz
fft11	Power at 11Hz
fft12	Power at 12Hz

Feature	Description
MAD	Mean Amplitude Deviation
MPD	Mean Power Deviation
skew	Skew
kurt	Kurtosis
f1	Frequency of signal with highest power between 0.3 and 15 Hz
p1	Maximal power of signal between 0.3 and 15 Hz
f2	Frequency of signal with second highest power between 0.3 and 15 Hz
p2	Second highest power of signal between 0.3 and 15 Hz
f625	Frequency of signal with highest power between 0.6 and 2.5 Hz
p625	Maximal power of signal between 0.6 and 2.5 Hz
totalPower	Total power for frequencies between 0.3 and 15 Hz
vmfft1	Power at 1/30 Hz
vmfft2	Power at 2/30 Hz
vmfft3	Power at 3/30 Hz
vmfft4	Power at 4/30 Hz
vmfft5	Power at 5/30 Hz
vmfft6	Power at 6/30 Hz
vmfft7	Power at 7/30 Hz
vmfft8	Power at 8/30 Hz
vmfft9	Power at 9/30 Hz
vmfft10	Power at 10/30 Hz
vmfft11	Power at 11/30 Hz
vmfft12	Power at 12/30 Hz

Supplementary Table 3: Definition of variables from UK Biobank data included in statistical models.

Characteristic	Source	Notes	UK Biobank field	Coding
OUTCOME				
Age at first cardiovascular disease event	Death Registry, HES.	First appearance of ICD-10 codes I20-25 (ischaemic heart disease) or I60-69 (cerebrovascular disease) in either HES or death register data.	Derived from Category 100093, Category 2000.	
Age at loss-to-follow-up	Death Registry.	Earliest of: date of latest study data available and date of non-cardiovascular disease death.	Derived from Category 100093.	
EXPOSURE				
Sleep	Accelerometry.	Derived using machine-learning methods described in main text.	Derived from 90001.	
Sedentary behaviour	Accelerometry.	Derived using machine-learning methods described in main text.	Derived from 90001.	
Light physical activity behaviours	Accelerometry.	Derived using machine-learning methods described in main text.	Derived from 90001.	
Moderate-to-vigorous physical activity behaviours	Accelerometry.	Derived using machine-learning methods described in main text.	Derived from 90001.	
EXCLUSION VARIABLES – MAIN ANALYSIS				
Prior HES-recorded cardiovascular disease	HES.	Appearance of ICD-10 codes I20-25 (ischaemic heart disease) or I60-69 (cerebrovascular disease) or ICD-9 codes 410 – 414 or 430 – 438 in HES data prior to accelerometer wear.	Derived from Category 2000.	

Characteristic	Source	Notes	UK Biobank field	Coding
Prior self-reported cardiovascular disease	Baseline.	Self-reported heart attack or stroke.	Derived from 6150.	
ADJUSTMENT VARIABLES – MAIN ANALYSIS				
Age	Baseline.	Age used as the timescale in Cox regression analysis; participants entered study at the end of accelerometer wear.	Derived from 90011, 34, 52.	
Sex	Baseline.	Used to stratify analysis.	31	Female, Male.
Ethnicity	Baseline.		Derived from 21000.	Asian, Black, Other, White. (Categorised as in Resource 100336; Other includes Mixed, Chinese and Other due to small numbers).
Smoking status	Baseline.		20116	Never smoker, Ex-smoker, Current smoker.
Frequency of alcohol consumption	Baseline.		Derived from 1558.	Never, <3 times/week, 3+ times/week.
Education	Baseline.		Derived from 6138.	School leaver, Further education (education beyond O-Levels/CSEs, excluding college/ university degree) and Higher education (college/university degree).
Townsend Deprivation Index	Baseline.	Townsend Deprivation Index of address at time of UKB baseline assessment.	Derived from 189.	Divided by quartile in the study population.
Daily servings of fresh fruit and vegetables.	Baseline.		Derived from 1289, 1299, 1309.	Less than one coded as 0·5, then sum of 1289, 1299, 1309. Categorised as < 3, 3-4·9, 5-7·9, 8+ servings/ day.

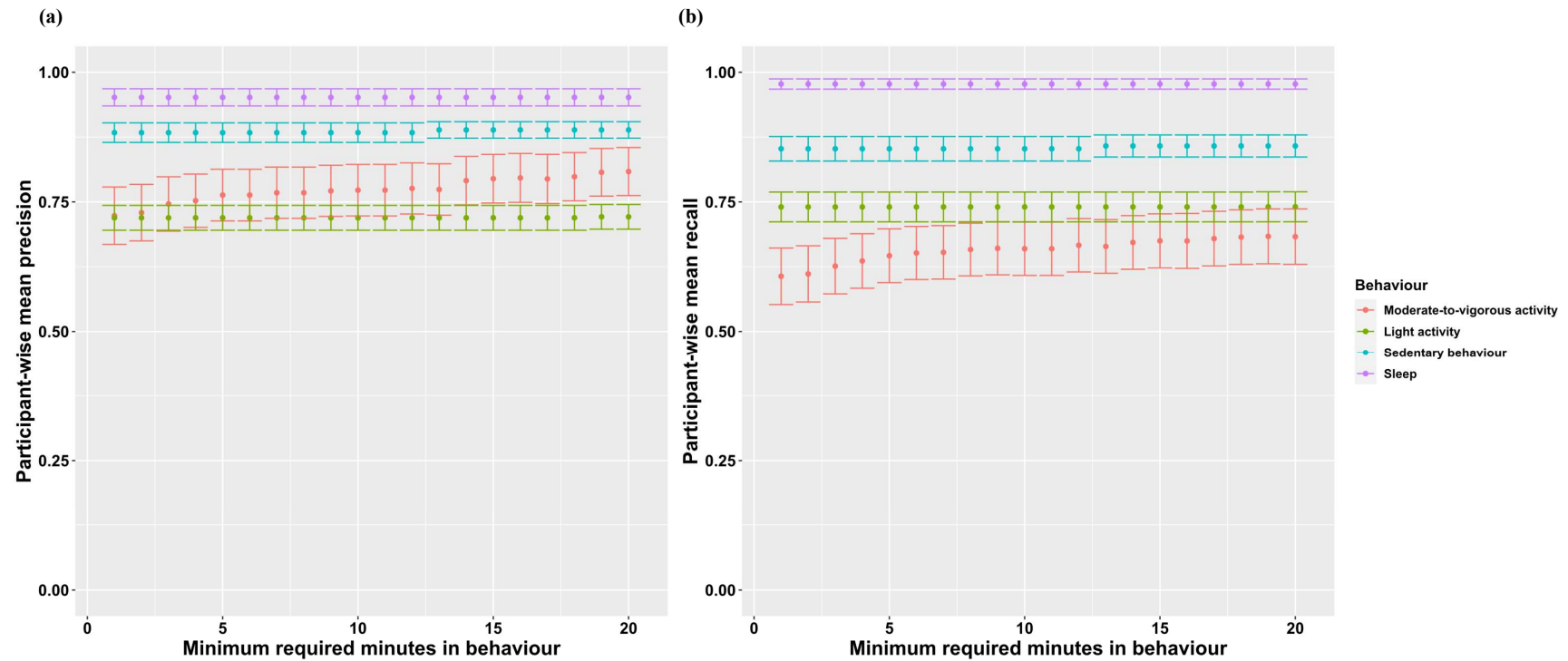
Characteristic	Source	Notes	UK Biobank field	Coding
Frequency of red and processed meat consumption.	Baseline.		Derived from 1369, 1379, 1389, 1349.	Less than one coded as 0·5, then sum of 1369, 1379, 1389. Categorised as <1, 1-2·9, 3-4·9, 5+ times/ week.
Frequency of oily fish consumption.	Baseline.		Derived from 1329.	< 1, 1, 2-4, >4 times/week.
ADJUSTMENT VARIABLES – ADDITIONAL				
BMI	Baseline.		Derived from 21001.	For descriptive analyses: Underweight (<18·5kgm ⁻²), Normal weight (18·5 -24·9 kgm ⁻²), Overweight (25 -29·9 kgm ⁻²), Obese (30+ kgm ⁻²). For BMI-stratified analysis, Underweight and Normal weight categories combined.
EXCLUSION VARIABLES – SENSITIVITY ANALYSIS FOR REVERSE CAUSALITY				
Medication for diabetes, cholesterol or blood pressure	Baseline.		Derived from 6177, 6153.	
Self-reported overall health rating	Baseline.		2178	
Prior primary admission for disease of the circulatory system.	HES.	Hospital admission with primary diagnosis of I00-I99 before accelerometer wear.	Derived from Category 2000.	
NEGATIVE CONTROL OUTCOME – SENSITIVITY ANALYSIS FOR RESIDUAL CONFOUNDING				
Age at first accident unrelated to movement behaviour.	Death Registry, HES.	First appearance of ICD-10 codes V00-09, V20-99, W20-W99, X00-X59.	Derived from Category 100093, Category 2000.	
Age at loss-to-follow-up	Death Registry.	Earliest of: date of latest study data available and date of death.	Derived from Category 100093.	

Characteristic	Source	Notes	UK Biobank field	Coding
Prior HES-recorded accident unrelated to movement behaviour.	HES.	First appearance of ICD-10 codes V00-09, V20-99, W20-W99, X00-X59.	Derived from Category 2000.	

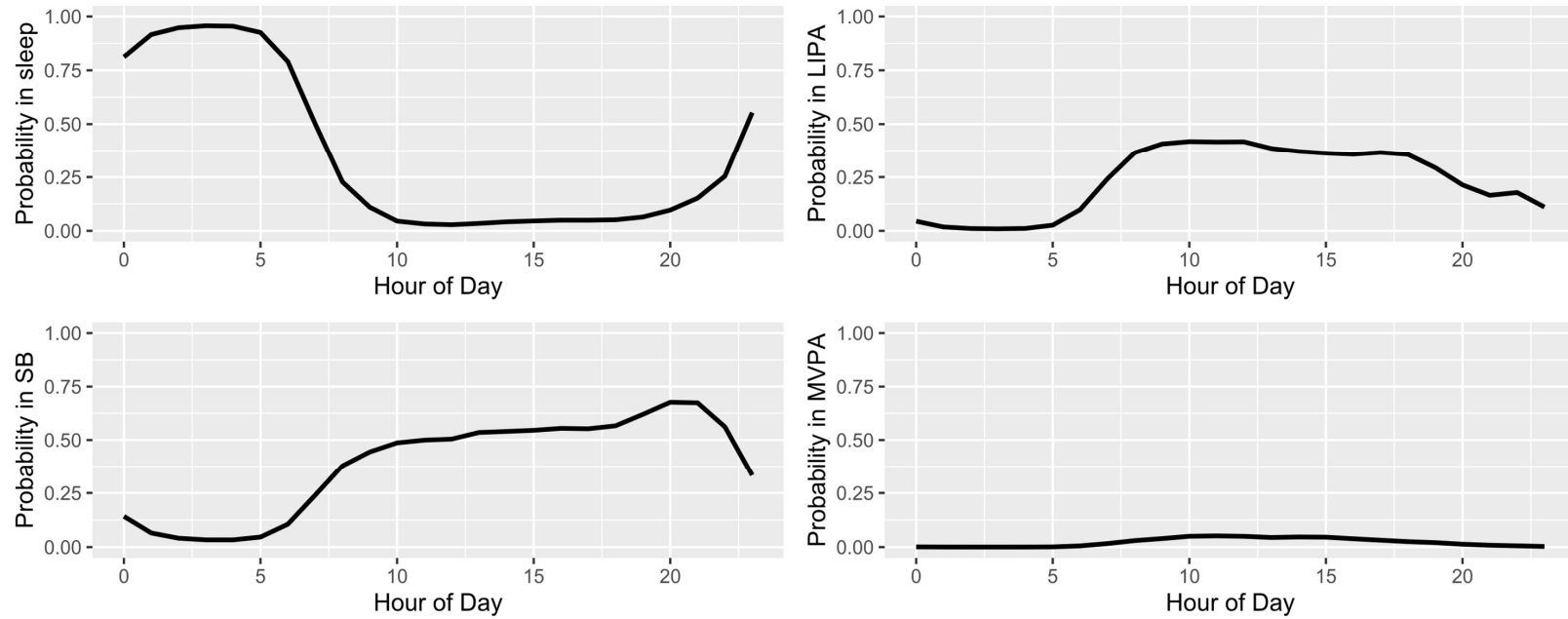
Supplementary Table 4: Characteristics of CAPTURE-24 participants.

	n (%)
Overall	152
Age, years	
18-29	39 (26)
30-39	41 (27)
40-49	24 (16)
50-59	21 (14)
60-69	17 (11)
70-79	7 (5)
80-91	2 (1)
Not recorded	1 (1)
Sex	
Female	99 (65)
Male	53 (35)

Supplementary Figure 1: Participant-wise mean (a) precision and (b) recall for classification of behaviours from accelerometer data calculated in Leave-One-Participant-Out Cross-Validation (with 95% confidence interval for the mean). The x-axis gives the minimum required recorded annotator-labelled time in the behaviour for inclusion in the calculation. For precision, participants with no model-labelled time in the behaviour were also excluded as precision is undefined in this case.



Supplementary Figure 2: Probability of being in sleep, sedentary behaviour (SB), light physical activity behaviours (LIPA) and moderate-to-vigorous physical activity behaviours (MVPA) among 87,498 UK Biobank participants according to machine-learned behaviour classification by hour of the day.



Supplementary Table 5: Coefficient of first isometric log-ratio pivot coordinate^a for each movement behaviour estimated using a multivariable-adjusted Compositional Data Analysis Cox regression model.

Movement behaviour variable	$exp(\hat{\beta})$ (95% CI)
Pivot coordinate: Sleep vs All other behaviours	0.88 (0.75, 1.02)
Pivot coordinate: SB vs All other behaviours	1.38 (1.22, 1.57)
Pivot coordinate: LIPA vs All other behaviours	0.96 (0.88, 1.06)
Pivot coordinate: MVPA vs All other behaviours	0.86 (0.84, 0.88)

^aSee **Supplementary Methods**. Model based on 4,105 events in 87,498 participants. Model used age as the timescale, was stratified by sex and was additionally adjusted for ethnicity, smoking status, alcohol consumption, fresh fruit and vegetable consumption, red and processed meat consumption, oily fish consumption, deprivation and education.

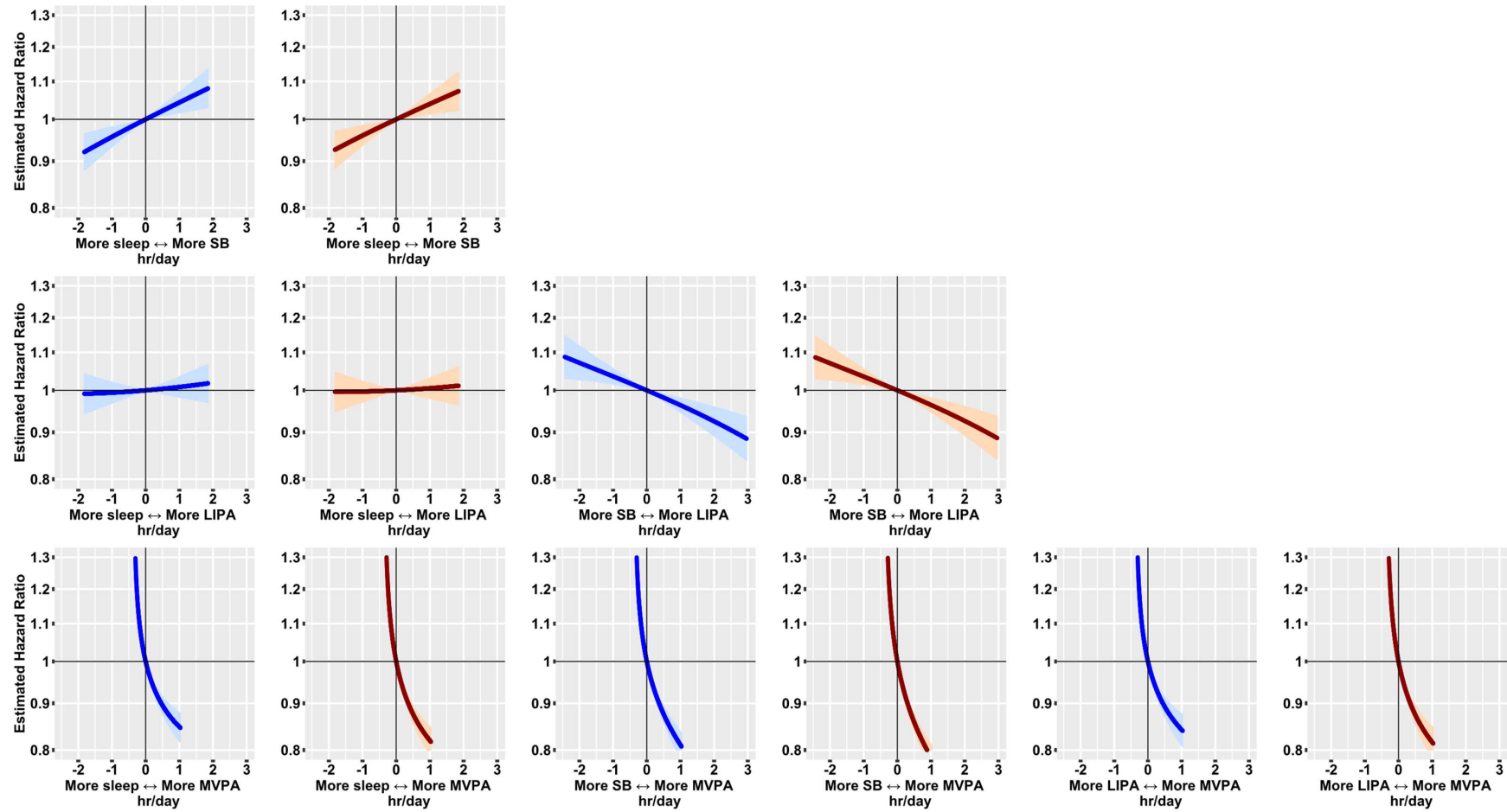
Supplementary Table 6: Coefficient of first isometric log-ratio pivot coordinate for each movement behaviour estimated using all Compositional Data Analysis Cox regression models.^a

Movement behaviour variable	Main analysis	Minimally adjusted	Additionally stratified by BMI	Fatal events	Women only	Men only
Pivot coordinate: sleep vs All other behaviours	0.88 (0.75, 1.02)	0.90 (0.77, 1.05)	0.90 (0.77, 1.05)	0.79 (0.48, 1.29)	0.78 (0.60, 1.02)	0.93 (0.77, 1.13)
Pivot coordinate: SB vs All other behaviours	1.38 (1.22, 1.57)	1.37 (1.21, 1.56)	1.29 (1.13, 1.46)	2.13 (1.40, 3.22)	1.57 (1.28, 1.94)	1.28 (1.09, 1.50)
Pivot coordinate: LIPA vs All other behaviours	0.96 (0.88, 1.06)	0.96 (0.88, 1.06)	0.98 (0.89, 1.08)	0.71 (0.52, 0.95)	0.95 (0.81, 1.11)	0.97 (0.86, 1.09)
Pivot coordinate: MVPA vs All other behaviours	0.86 (0.84, 0.88)	0.84 (0.81, 0.86)	0.88 (0.85, 0.90)	0.85 (0.78, 0.92)	0.85 (0.82, 0.89)	0.86 (0.83, 0.90)

Movement behaviour variable	Main analysis	Under 65s only	Over 65s only	First 2 years of follow-up removed	Follow-up removed + healthy subgroup	Excluding zero values	Negative control: accidents
Pivot coordinate: sleep vs All other behaviours	0.88 (0.75, 1.02)	0.98 (0.75, 1.28)	0.83 (0.69, 1.00)	0.88 (0.73, 1.06)	1.01 (0.77, 1.31)	0.86 (0.73, 1.01)	0.91 (0.69, 1.20)
Pivot coordinate: SB vs All other behaviours	1.38 (1.22, 1.57)	1.17 (0.95, 1.45)	1.52 (1.30, 1.77)	1.33 (1.15, 1.55)	1.09 (0.89, 1.35)	1.38 (1.21, 1.57)	1.09 (0.87, 1.36)
Pivot coordinate: LIPA vs All other behaviours	0.96 (0.88, 1.06)	1.01 (0.86, 1.18)	0.93 (0.82, 1.04)	0.98 (0.88, 1.10)	1.04 (0.88, 1.21)	0.99 (0.89, 1.09)	1.10 (0.93, 1.30)
Pivot coordinate: MVPA vs All other behaviours	0.86 (0.84, 0.88)	0.86 (0.82, 0.91)	0.86 (0.83, 0.89)	0.87 (0.84, 0.90)	0.88 (0.83, 0.92)	0.86 (0.83, 0.89)	0.92 (0.87, 0.97)

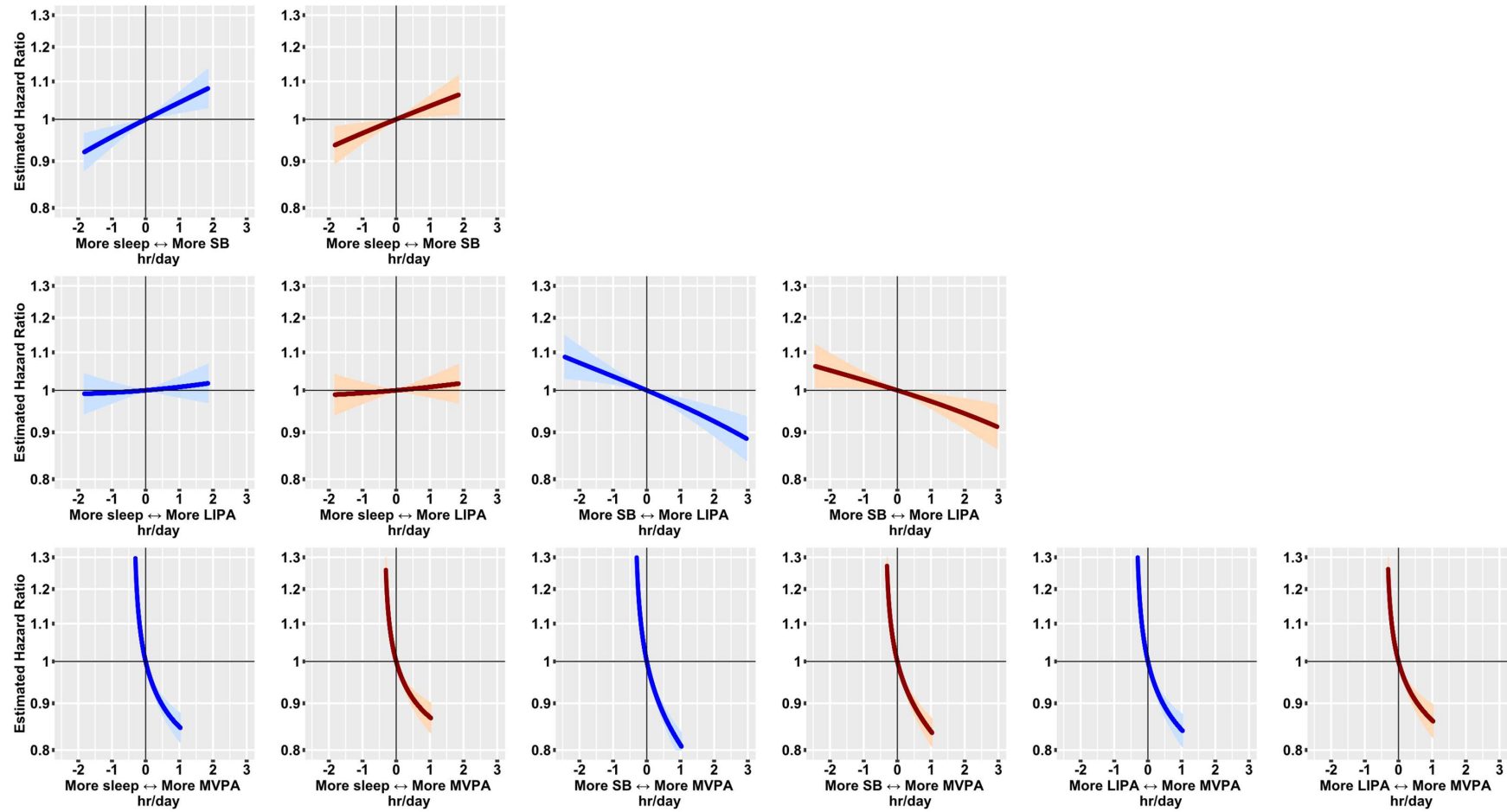
^aSee Methods, Results and Supplementary Figures 3-13 for more details of models. All columns report $\exp(\hat{\beta})$ (95% CI).

Supplementary Figure 3: Hazard Ratios for cardiovascular disease for all behaviour pairs estimated using multivariable-adjusted (blue) and minimally adjusted (red) Cox regression models.^a



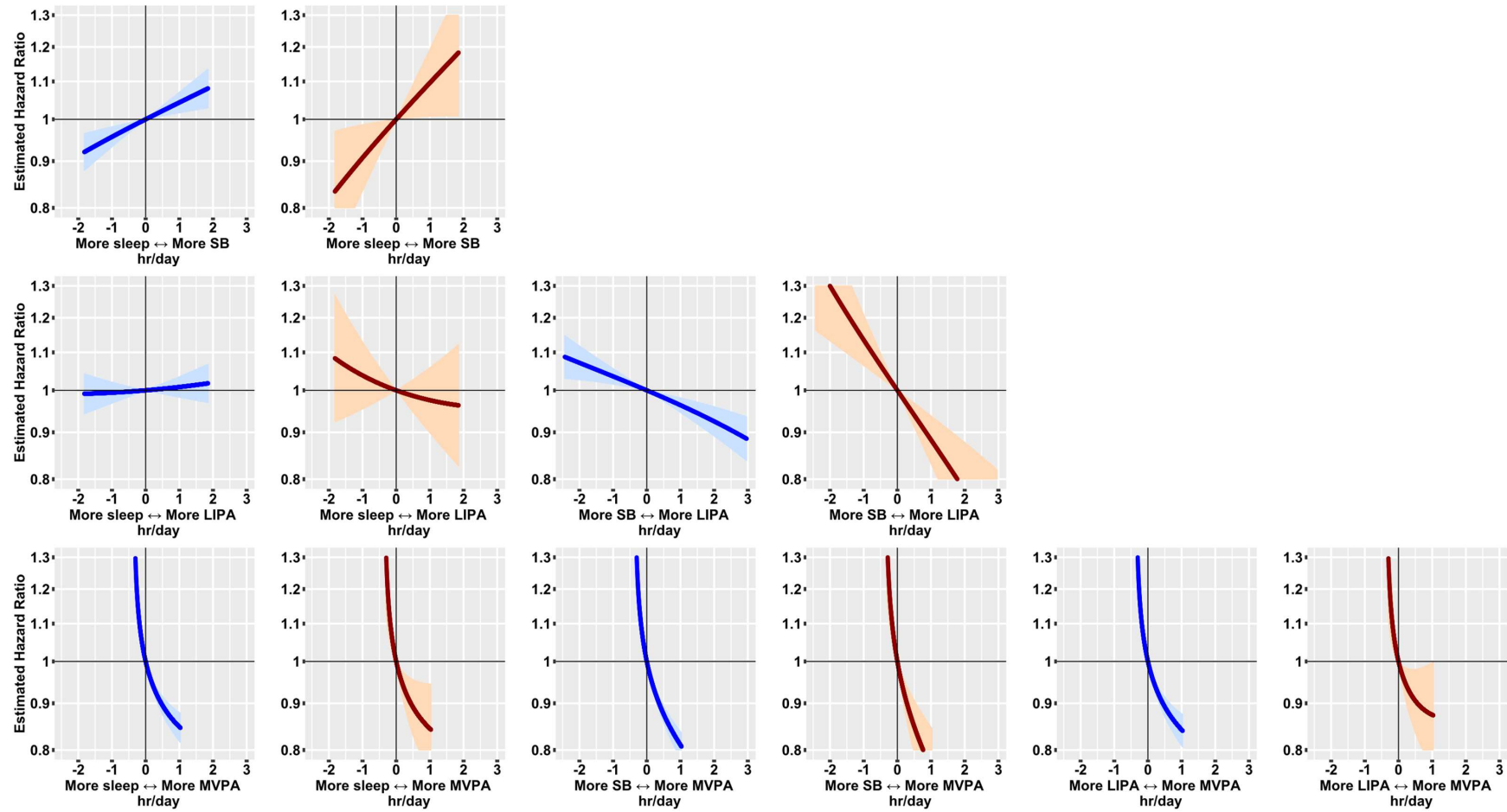
^aModel based on 4,105 events in 87,498 participants. All relative to the mean behaviour composition: 8.8 hours/day sleep, 9.3 hours/day sedentary behaviour, 5.6 hours/day light physical activity behaviours, 0.35 hours/day (21 minutes/day) moderate-to-vigorous physical activity behaviours. Multivariable-adjusted model used age as the timescale, was stratified by sex and was additionally adjusted for ethnicity, smoking status, alcohol consumption, fresh fruit and vegetable consumption, red and processed meat consumption, oily fish consumption, deprivation and education. Minimally-adjusted model used age as the timescale and was stratified by sex.

Supplementary Figure 4: Hazard Ratios for incident cardiovascular disease estimated using a multivariable-adjusted Cox regression model before (blue) and after (red) stratification by BMI.^a



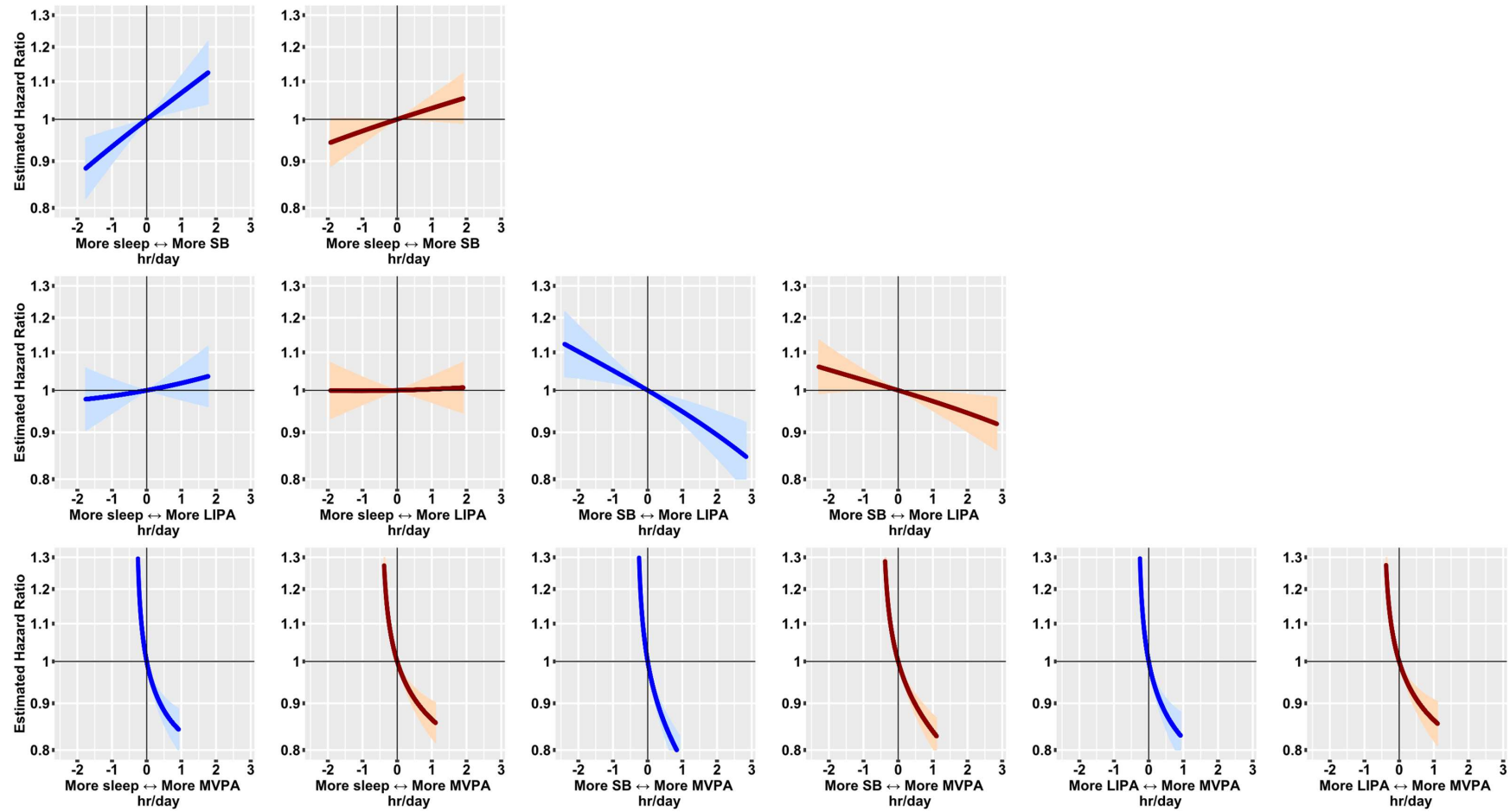
^aModel based on 4,105 events in 87,498 participants. All relative to the mean behaviour composition: 8.8 hours/day sleep, 9.3 hours/day sedentary behaviour, 5.6 hours/day light physical activity behaviours, 0.35 hours/day (21 minutes/day) moderate-to-vigorous physical activity behaviours. Models used age as the timescale, were stratified by sex and were additionally adjusted for ethnicity, smoking status, alcohol consumption, fresh fruit and vegetable consumption, red and processed meat consumption, oily fish consumption, deprivation and education.

Supplementary Figure 5: Hazard Ratios for all (blue) and fatal (red) incident cardiovascular disease for all behaviour pairs estimated using a multivariable-adjusted Cox regression model.^a



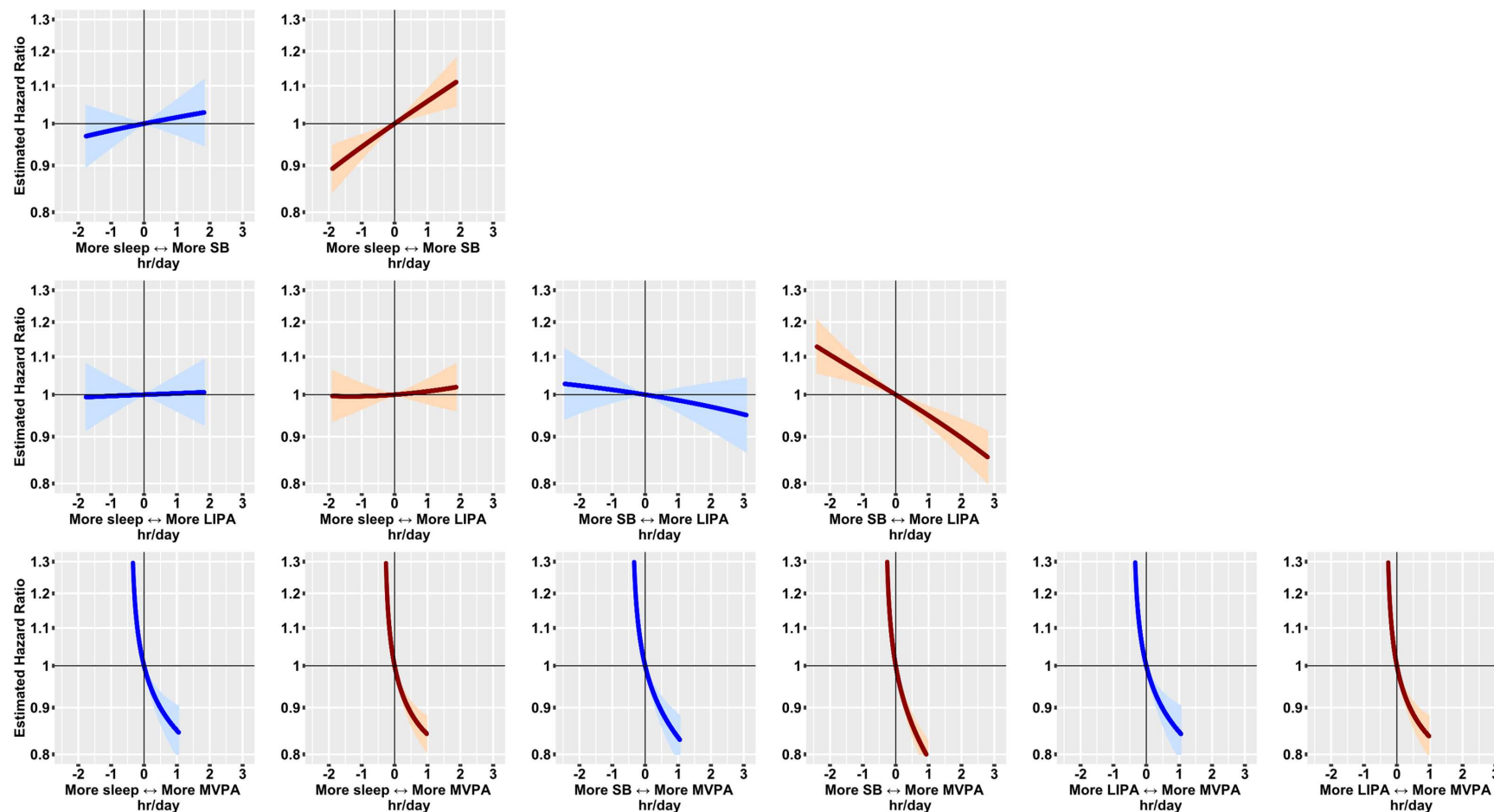
^aModels based on 4,105 events and 348 cardiovascular deaths in 87,498 participants. All relative to the mean behaviour composition: 8.8 hours/day sleep, 9.3 hours/day sedentary behaviour, 5.6 hours/day light physical activity behaviours, 0.35 hours/day (21 minutes/day) moderate-to-vigorous physical activity behaviours. Models used age as the timescale, were stratified by sex and were additionally adjusted for ethnicity, smoking status, alcohol consumption, fresh fruit and vegetable consumption, red and processed meat consumption, oily fish consumption, deprivation and education.

Supplementary Figure 6: Hazard Ratios for incident cardiovascular disease for all behaviour pairs estimated using a multivariable-adjusted Cox regression model for women (blue) and men (red).^a



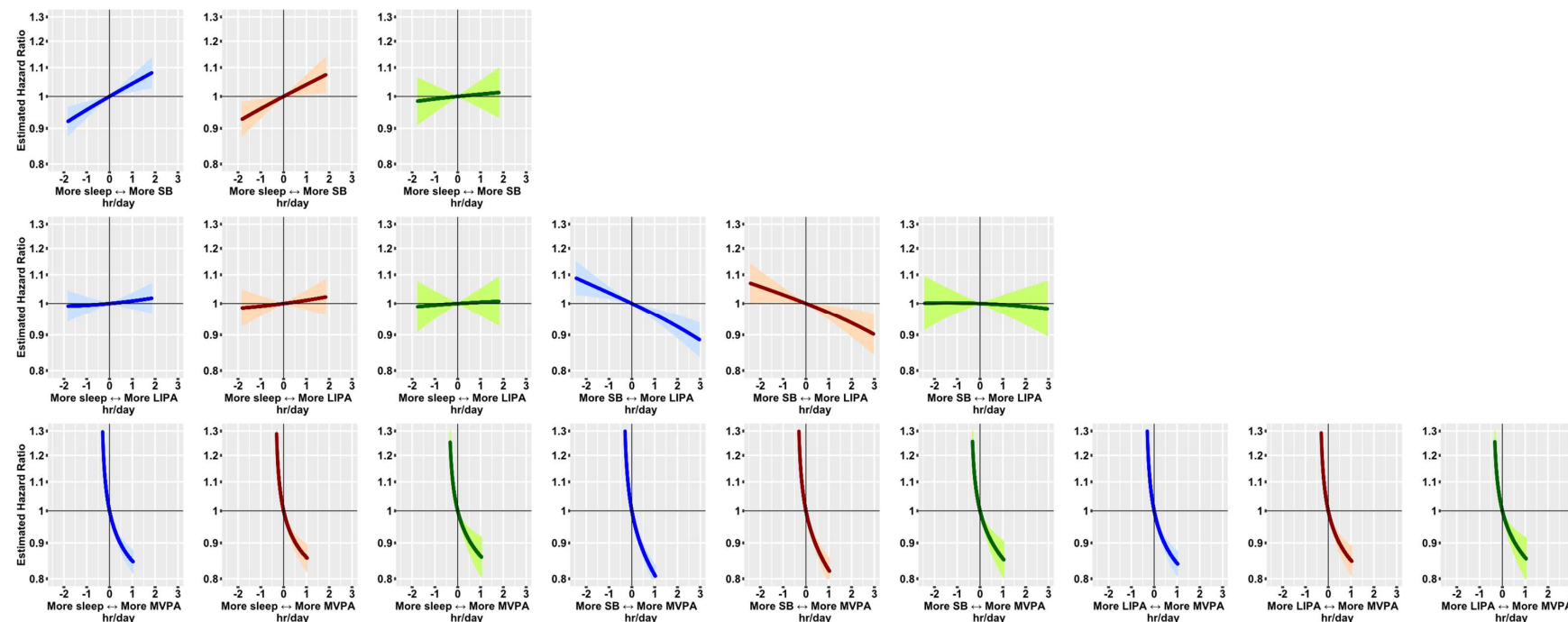
^aModels based on 1,654 events in 50,882 women and 2,451 events in 36,616 men. All relative to the mean behaviour composition in each case (women – 8.9 hours/day sleep, 9.0 hours/day sedentary behaviour, 5.9 hours/day light physical activity behaviours, 0.30 hours/day (18 minutes/day) moderate-to-vigorous physical activity behaviours; men – 8.7 hours/day sleep, 9.7 hours/day sedentary behaviour, 5.1 hours/day light physical activity behaviours, 0.45 hours/day (27 minutes/day) moderate-to-vigorous physical activity behaviours). Models used age as the timescale and were additionally adjusted for ethnicity, smoking status, alcohol consumption, fresh fruit and vegetable consumption, red and processed meat consumption, oily fish consumption, deprivation and education.

Supplementary Figure 7: Hazard Ratios for incident cardiovascular disease for all behaviour pairs estimated using a multivariable-adjusted Cox regression model for participants aged under 65 (blue) and participants aged over 65 (red).^a



^aModels based on 1,425 events in 51,180 participants aged under 65 and 2,680 events in 36,318 participants aged over 65. All relative to the mean behaviour composition in each case (participants aged under 65 – 8.8 hours/day sleep, 9.3 hours/day sedentary behaviour, 5.5 hours/day light physical activity behaviours, 0.39 hours/day (23 minutes/day) moderate-to-vigorous physical activity behaviours; participants aged over 65 – 8.9 hours/day sleep, 9.2 hours/day sedentary behaviour, 5.6 hours/day light physical activity behaviours, 0.30 hours/day (18 minutes/day) moderate-to-vigorous physical activity behaviours). Models used age as the timescale, were stratified by sex and were additionally adjusted for ethnicity, smoking status, alcohol consumption, fresh fruit and vegetable consumption, red and processed meat consumption, oily fish consumption, deprivation and education.

Supplementary Figure 8: Hazard Ratios for incident cardiovascular disease for all behaviour pairs estimated using a multivariable-adjusted Cox regression model (blue), after removing the first two years of follow-up (red) and after additionally restricting to a healthy subgroup (green).^a



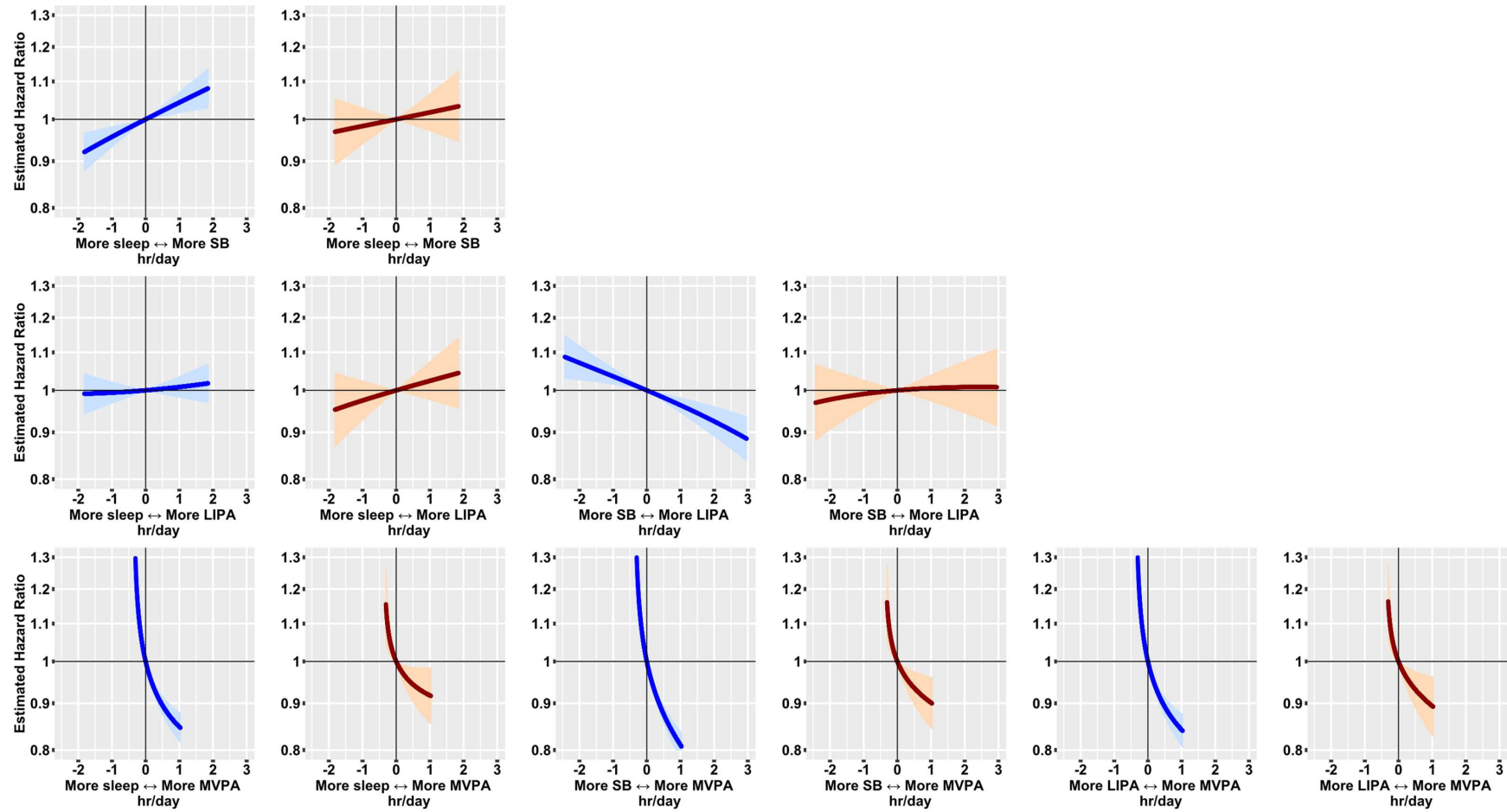
^aMain analysis based on 4,105 events in 87,498 participants. First sensitivity analysis based on 2,947 events in 86,011 participants. Second sensitivity analysis based on 1,597 events in 63,267 participants. Models used age as the timescale, were stratified by sex and were additionally adjusted for ethnicity, smoking status, alcohol consumption, fresh fruit and vegetable consumption, red and processed meat consumption, oily fish consumption, deprivation and education. All values reported relative to the mean behaviour composition in each case:

Main analysis - 8.8 hours/day sleep, 9.3 hours/day sedentary behaviour, 5.6 hours/day light physical activity behaviours, 0.35 hours/day (21 minutes/day) moderate-to-vigorous physical activity behaviours

1st sensitivity - 8.8 hours/day sleep, 9.3 hours/day sedentary behaviour, 5.6 hours/day light physical activity behaviours, 0.35 hours/day (21 minutes/day) moderate-to-vigorous physical activity behaviours

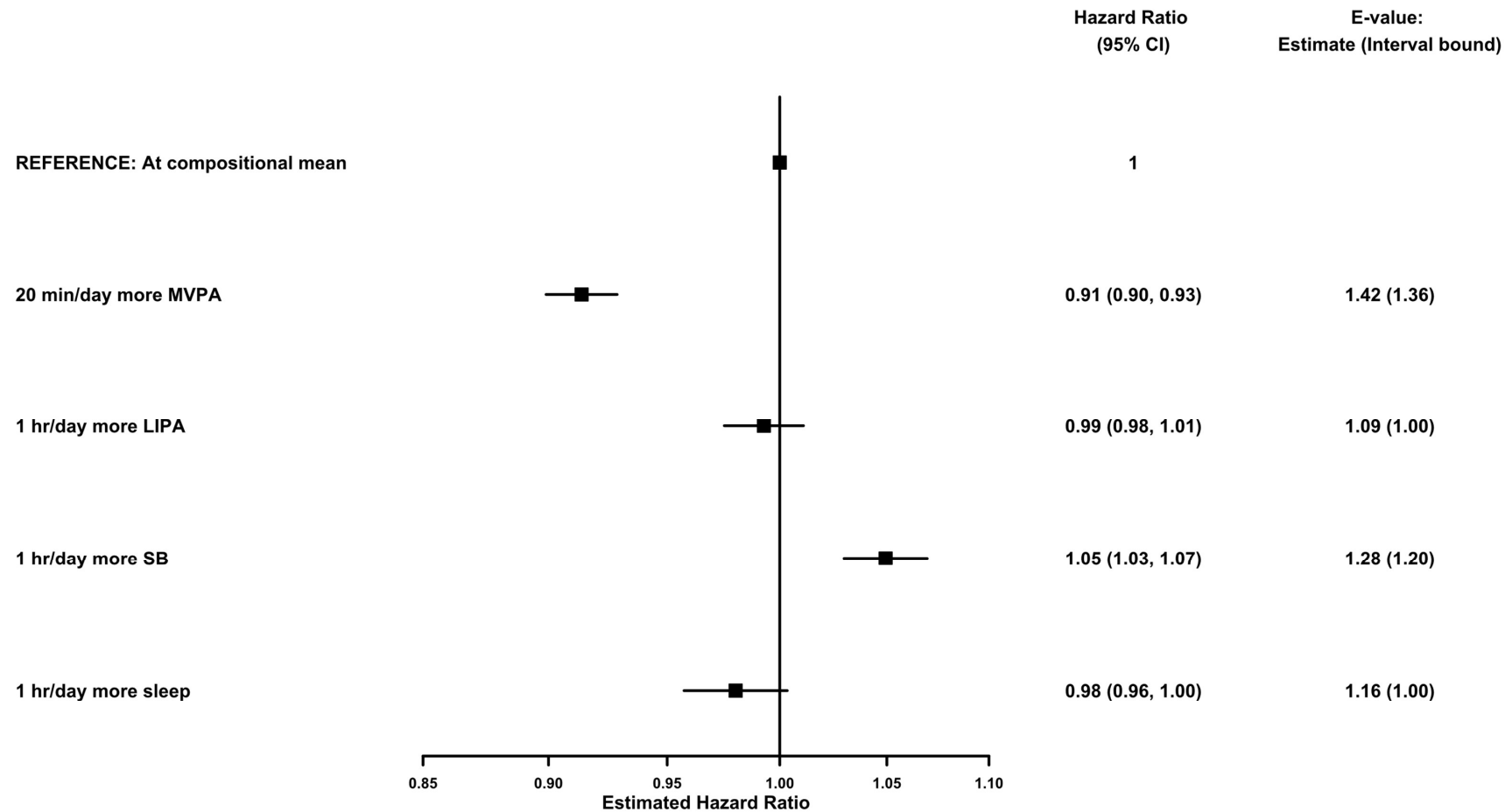
2nd sensitivity - 8.8 hours/day sleep, 9.2 hours/day sedentary behaviour, 5.6 hours/day light physical activity behaviours, 0.39 hours/day (23 minutes/day) moderate-to-vigorous physical activity behaviours.

Supplementary Figure 9: Hazard Ratios for cardiovascular disease (blue) and for non-activity-related accidents (red) for all behaviour pairs estimated using a multivariable-adjusted Cox regression model.^a



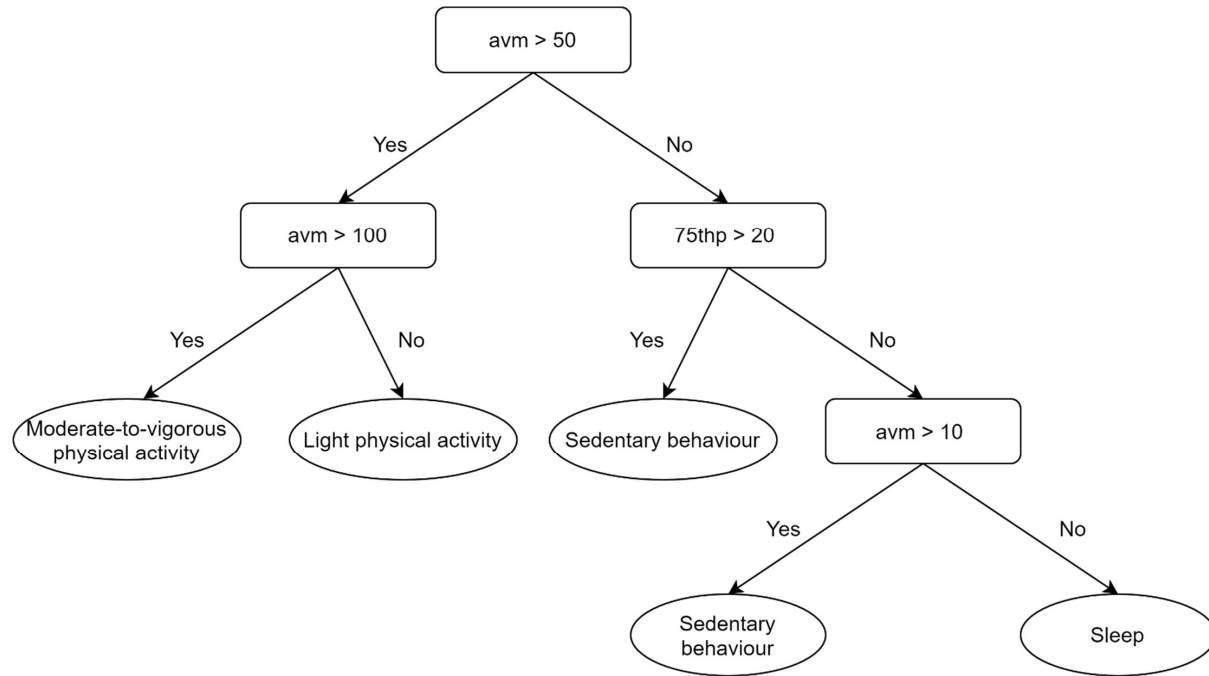
^aMain model based on 4,105 events in 87,498 participants. Negative control model based on 1,375 events in 84,552 participants (participants with prior accident additionally excluded). All relative to the mean behaviour composition in each case (both 8.8 hours/day sleep, 9.3 hours/day sedentary behaviour, 5.6 hours/day light physical activity behaviours, 0.35 hours/day (21 minutes/day) moderate-to-vigorous physical activity behaviours). Models used age as the timescale, were stratified by sex and were additionally adjusted for ethnicity, smoking status, alcohol consumption, fresh fruit and vegetable consumption, red and processed meat consumption, oily fish consumption, deprivation and education.

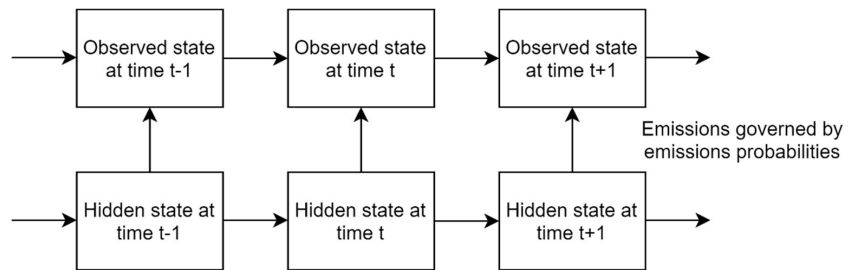
Supplementary Figure 10: Hazard ratios and corresponding E-values for incident cardiovascular disease associated with reallocating time to named behaviour, from all other behaviours proportionally, in 87,498 UK Biobank participants.^a



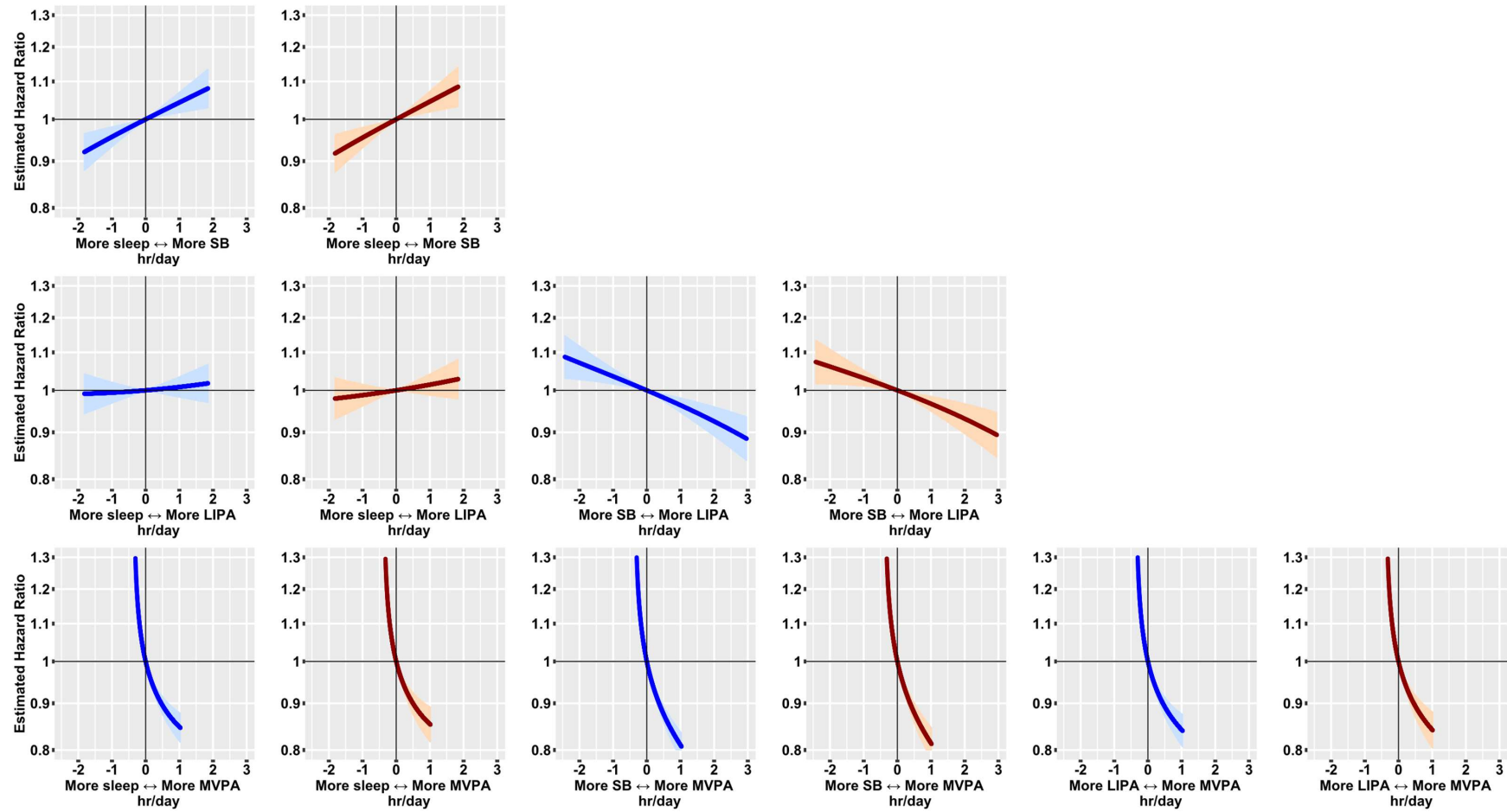
^aModel based on 4,105 events in 87,498 participants. All relative to the mean behaviour composition (8.8 hours/day sleep, 9.3 hours/day sedentary behaviour, 5.6 hours/day light physical activity behaviours, 0.35 hours/day (21 minutes/day) moderate-to-vigorous physical activity behaviours) and more time in named behaviour reallocated from all other behaviours proportionally. Model used age as the timescale, was stratified by sex and was additionally adjusted for ethnicity, smoking status, alcohol consumption, fresh fruit and vegetable consumption, red and processed meat consumption, oily fish consumption, deprivation and education.

Supplementary Figure 11: An example of a decision tree to classify time windows using average acceleration vector magnitude (avm) and the 75th percentile of acceleration vector magnitude (75thp).



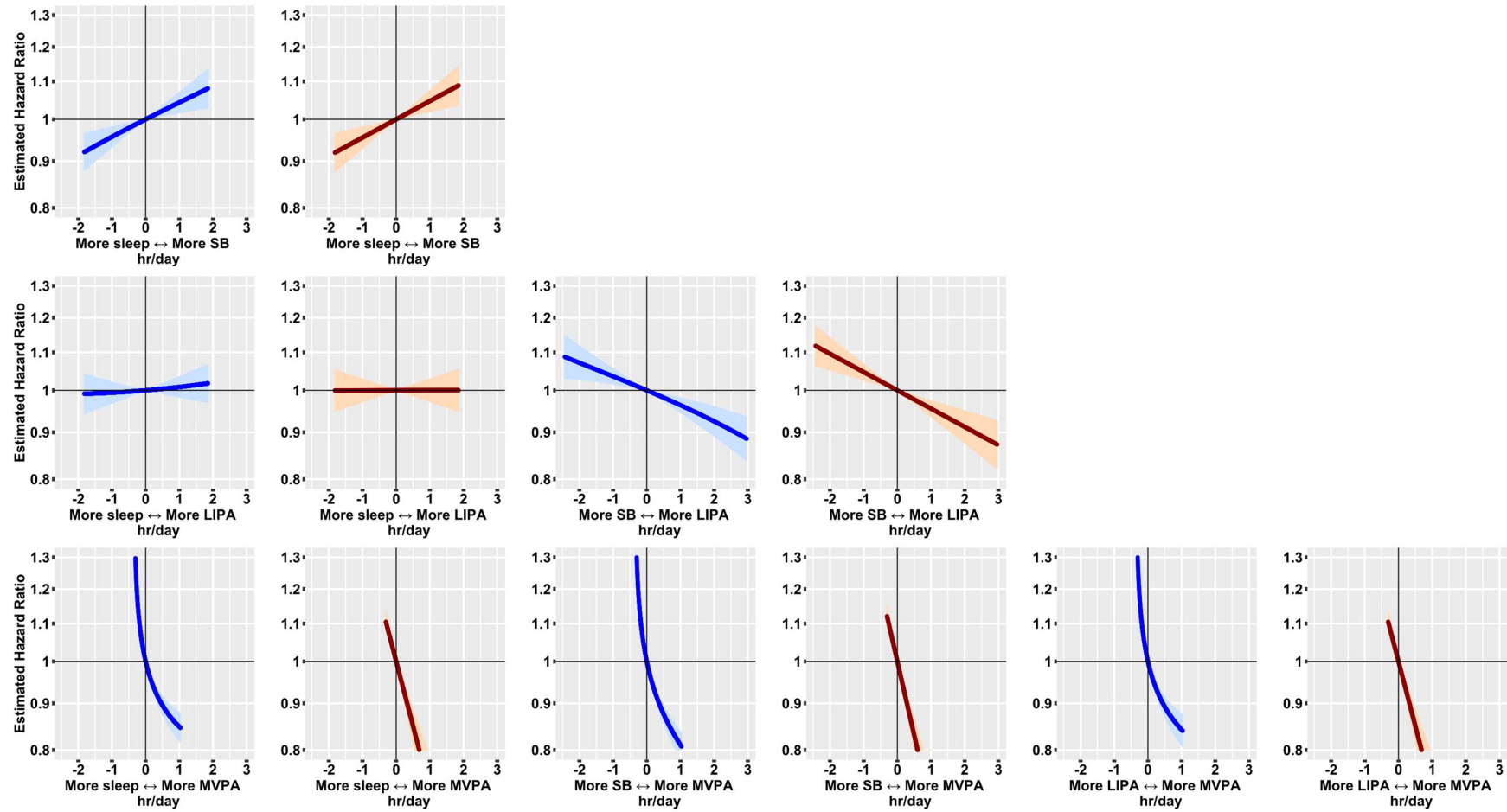
Supplementary Figure 12: The structure of a Hidden Markov Model.

Supplementary Figure 13: Hazard Ratios for incident cardiovascular disease for all behaviour pairs estimated using a multivariable-adjusted Cox regression model for all participants (blue) and in a sensitivity analysis excluding individuals with a zero value in any behaviour (red).^a



^aMain model based on 4,105 events in 87,498 participants. Model excluding individuals with zero values based on 4,017 events in 86,696 participants. All relative to the mean behaviour composition in each case (main analysis – 8.8 hours/day sleep, 9.3 hours/day sedentary behaviour, 5.6 hours/day light physical activity behaviours, 0.35 hours/day (21 minutes/day) moderate-to-vigorous physical activity behaviours; analysis excluding individuals with zero values – 8.8 hours/day sleep, 9.3 hours/day sedentary behaviour, 5.6 hours/day light physical activity behaviours, 0.37 hours/day (22 minutes/day) moderate-to-vigorous physical activity behaviours). Models used age as the timescale, were stratified by sex and were additionally adjusted for ethnicity, smoking status, alcohol consumption, fresh fruit and vegetable consumption, red and processed meat consumption, oily fish consumption, deprivation and education.

Supplementary Figure 14: Hazard Ratios for incident cardiovascular disease estimated using a multivariable-adjusted Compositional Data Analysis Cox regression model (blue) and using a multivariable-adjusted linear isotemporal substitution Cox regression model (red).^a



^aModel based on 4,105 events in 87,498 participants. All relative to the mean behaviour composition: 8.8 hours/day sleep, 9.3 hours/day sedentary behaviour, 5.6 hours/day light physical activity behaviours, 0.35 hours/day (21 minutes/day) moderate-to-vigorous physical activity behaviours. Models used age as the timescale, were stratified by sex and were additionally adjusted for ethnicity, smoking status, alcohol consumption, fresh fruit and vegetable consumption, red and processed meat consumption, oily fish consumption, deprivation and education.

STROBE Statement—Checklist of items that should be included in reports of cohort studies

	Item No	Recommendation	Included
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	Yes
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	Yes
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	Yes
Objectives	3	State specific objectives, including any prespecified hypotheses	Yes, No pre-specified hypotheses
Methods			
Study design	4	Present key elements of study design early in the paper	Yes
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Yes
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	Yes
		(b) For matched studies, give matching criteria and number of exposed and unexposed	NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	Yes
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	Yes
Bias	9	Describe any efforts to address potential sources of bias	Yes
Study size	10	Explain how the study size was arrived at	Yes
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Yes
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	Yes
		(b) Describe any methods used to examine subgroups and interactions	Yes
		(c) Explain how missing data were addressed	Yes
		(d) If applicable, explain how loss to follow-up was addressed	Yes
		(e) Describe any sensitivity analyses	Yes

Results

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Yes
		(b) Give reasons for non-participation at each stage	Yes
		(c) Consider use of a flow diagram	Yes
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Yes
		(b) Indicate number of participants with missing data for each variable of interest	Yes
		(c) Summarise follow-up time (eg, average and total amount)	Yes
Outcome data	15*	Report numbers of outcome events or summary measures over time	Yes
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Yes: confounder-adjusted estimates and estimates adjusted for only age and sex given.
		(b) Report category boundaries when continuous variables were categorized	Yes.
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Not included.
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Yes.
Discussion			
Key results	18	Summarise key results with reference to study objectives	Yes.
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	Yes.
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Yes.
Generalisability	21	Discuss the generalisability (external validity) of the study results	Yes.
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	Yes.

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at <http://www.strobe-statement.org>.