# Master of Public Health

**Master de Santé Publique**

# Association between behavioural circadian rhythm profiles and incident cardiovascular disease in older adults: results from the UK Biobank accelerometer sub-study.


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## List of acronyms

**BMI**: Body Mass Index
**CI**: Confidence Interval
**CR**: Circadian Rhythm
**CVD**: Cardiovascular Disease
**HR**: Hazard Ratio
**IG**: Intensity Gradient
**IS**: Interdaily stability
**IV**: Intradaily variability
**L5**: Least Active 5-Hour Period
**LIPA**: Light Intensity Physical Activity
**M**: Mean
**M10**: Most Active 10-Hour Period
**MVPA**: Moderate to Vigorous Physical Activity
**PA**: Physical Activity
**PCA**: Principal Component Analysis
**RA:** Relative Amplitude
**RAR**: Rest-Activity Rhythm
**SB**: Sedentary Behaviour
**SD**: Standard Deviation
**TPar,d**: Transition Probability from Activity to Rest during the Day
**TPra,d**: Transition Probability from Rest to Activity during the Day
**TPsw,n**: Transition Probability from Sleep to Wake during the Night
**TPws,n**: Transition Probability from Wake to Sleep during the Night
**UKBB:** UK Biobank
**WASO**: Wake After Sleep Onset

## Abstract

### Background

Evidence suggests that physical activity (PA), sleep, chronotype, and rest-activity rhythm (RAR) play a role in cardiovascular disease (CVD) incidence. These behaviours, regulated over a 24-hour clock, are part of the bio-behavioural expression of circadian rhythm (CR). These four dimensions can be objectively measured using accelerometers. Most studies examining the association between CR and CVD have not considered all CR dimensions simultaneously or accounted for their interdependence. This study aims to examine the association between accelerometer-derived CR profiles accounting for all four dimensions and incident CVD in older adults, and whether these associations vary by sex, age, or BMI.

### Methods

Participants included 48,946 adults older than 60years from the UK Biobank accelerometer sub-study. Nine CR profiles were previously identified using a 2-step approach, comprising principal component analysis following by a clustering method on 36 accelerometer-derived metrics covering all CR dimensions. Cox proportional hazards models estimated the hazard ratios for incident CVD across CR profiles, adjusted for sociodemographic, behavioural, health-related, and cardiometabolic factors. Interaction terms for sex, age, and BMI were added to the models.

### Results

Over a median follow-up of 7.7 years, 4,220 incident CVD cases occurred. Compared to Profile 3 (RAR+/LIPA+/Sleep+), Profile 4 (MVPA++) showed 14% lower CVD risk. In contrast, Profiles 7 (RAR-/PA-/Sleep--), 8 (RAR-/PA+/Restless-Sleep), and 9 (RAR--/PA--/Chronotype-) presented 19%, 20%, and 27% increased CVD risk, respectively. The protective association of Profile 1 (RAR++/PA++) was attenuated after adjusting for cardiometabolic factors. Only Profile 9 (RAR--/PA--/Chronotype-) showed a significant interaction with sex, with a stronger effect in women than in men, although the direction of the association was the same for both sexes.

### Conclusion

These findings highlight the importance of assessing CR holistically to understand CVD risk in ageing populations. An active daytime pattern, particularly involving MVPA, was found to be protective. Differences in RAR, daytime activity and sleep patterns across CR profiles contributed to varying CVD risks. Our results support targeted interventions covering all CR dimensions to promote cardiovascular health in older adults.

### Keywords

Circadian rhythm, cardiovascular disease, older adults, accelerometer.

## Introduction

Cardiovascular diseases (CVD) are the leading cause of death worldwide and significantly contribute to disability and healthcare costs (1). Their prevalence has rapidly increased and is projected to rise considerably due to population ageing (2), generating significant public health challenges to prevent their harmful consequences. Physical Activity (PA) is a well-established protective factor against the development of CVD (3-6). Epidemiological evidence suggests that meeting the current recommendation of 150 minutes of moderate-intensity activity per week (7) is associated with a 17% lower CVD risk (4), and up to a 25% reduction (8).

Furthermore, a growing body of evidence highlights the importance of other health behaviours, such as Rest-activity rhythm (RAR), Sleep patterns, and Chronotype, in relation to CVD risk (9-13). These factors are key dimensions of the sleep-wake cycle, one of the most visible behavioural manifestations of circadian clock, an internal biological process that regulates essential bodily functions and a range of behaviours, following an approximately 24-hour pattern (14, 15).

Emerging epidemiological research suggests that circadian rhythm (CR) plays an important role in maintaining cardiometabolic health and preventing CVD (13, 16). CR disruptions characterised by a misalignment between the internal biological clock and the external environment (17) are particularly prevalent among older adults (18). These disturbances have been linked to an increased risk of CVD (19-21), highlighting the importance of investigating this association in the elderly population, as they are already at a higher risk of developing chronic conditions, such as CVD (22).

However, much of the existing evidence on the association between CR and CVD has primarily relied on self-assessments of CR dimensions (23-25), raising epidemiological concerns due to the increased susceptibility to misclassification bias, specifically recall and response bias (26). The emergence of wearable technologies, such as accelerometers, offers a promising solution. These devices enable the collection of objective activity and sleep data in natural settings (27) over multiple consecutive days, allowing for the assessment of the sleep-wake cycle in large cohort studies (28). These measures provide a scalable, non-invasive and multidimensional estimation of behavioural CR (14, 29, 30), involving several metrics that constitute four dimensions: rest-activity rhythm (RAR), which encompasses the magnitude and regularity of rest-activity patterns (31); daytime activity, referring to multiple movement behaviours during

the day (32); sleep, which includes duration, fragmentation, and overall quality of sleep (33); and chronotype, representing the timing of activity and sleep (25).

Despite this technological progress, most studies using actigraphy-derived metrics that have examined the association of CR with CVD risk have concentrated on individual dimensions of CR (11, 34-37), or have examined limited combinations, such as daytime activity and chronotype (38) or sleep and RAR (11), without fully considering the interdependence and correlation among these four dimensions. When all four CR dimensions have been considered, some relevant metrics were omitted (39, 40), the statistical methods used did not adequately account for the interdependence among these features (19, 41), or the study samples were relatively small (39-41) —factors that collectively limit the generalizability of the findings.

Thus, to address these challenges, this study will use nine distinct CR profiles previously identified in a separate study, currently under review in a journal. These profiles were derived from a large dataset using Principal Component Analysis (PCA) applied to 36 metrics across the four dimensions of CR, followed by a K-means clustering approach. This statistical method allows the natural expression of CR patterns across various profiles in real-world data, ensuring that the correlation and interdependency of dimensions are considered.

The primary objective of this study is to investigate the association between the nine identified CR profiles and incident CVD in older adults, using data from the UK Biobank (UKBB) accelerometer-sub study. As a secondary objective, we aim to determine whether these associations vary by sex, age, and BMI, with different patterns observed across males and females, age groups, and BMI categories. We hypothesise that the CR profiles derived from accelerometers will provide comprehensive and reliable insights into their associations with incident CVD, as they account for the correlation and interdependence among the four CR dimensions and allow their combined expression through real-world data.

This longitudinal study is part of a larger research project aimed at the identification of the CR profiles and their association with health outcomes in older adults. Data are drawn from two prospective cohort population-based studies: the Whitehall II study and the UKBB. As an intern and second-year MPH student, I was responsible for completing all the required steps to successfully carry out the research project focused on the association between CR profiles and incident CVD and mortality in older adults, under the supervision and guidance of the EpiAgeing team.

## Methods

### Study participants

Data for this study were drawn from the UKBB, specifically the accelerometer sub-study. The UKBB study is a large prospective population-based cohort study, initiated between 2006-2010, when baseline characteristics were collected, with over 500,000 participants aged 40-69 years (42). The recruitment strategy aimed to be highly inclusive, inviting every individual within the designated age range who was registered with the National Health Service and residing within approximately 25 miles of one of the 22 assessment centres to participate via letter, with a response rate of around 6% (43).

The accelerometer sub-study was conducted from February 2013 to December 2015, involving 106,053 individuals who provided a valid email address and accepted, through written consent, to participate and wear an accelerometer for seven days (44). As we focus on older adults, participants aged 60 years and older were included in the analyses. Approval was received from the National Information Governance Board for Health and Social Care and the National Health Service North West Centre for Research Ethics Committee (reference number 11/NW/0382). Our study was conducted using the UKB Resource under application number 96856.

### Accelerometer Data

Participants of the sub-study were asked to wear an Axivity AX3 wrist-worn triaxial accelerometer on their dominant wrist over 24 hours for seven consecutive days, starting at 10h on day 1, while they carried on with their normal activities (44). Data were sampled at 100 Hz and processed using GGIR R package version 3.1-2, which differentiates between waking and sleeping periods (45, 46). Raw acceleration was calculated with the metric Euclidean Norm Minus One (ENMO) with negative values rounded to zero. Then these values were corrected for calibration error and non-wear time (45). Data from the sleep onset of the first night until sleep onset on the last night were retained in analyses, including six consecutive full day windows, a full day window comprises a daytime waking period and a following sleep period. Participants were included in the analyses if they had data on at least five valid full day windows (47).

### Exposure

#### *Circadian Rhythm Profiles*

Circadian Rhythm Profiles were identified in a previous study, currently under review in a journal, based on the 36 accelerometer-derived metrics grouped as a function of the circadian rhythm dimensions they represent, as follows:

- *RAR (6 metrics):* from the cosinor function that fit the log of the acceleration signal we have the mesor (average of the function) (48), the amplitude (the peak of the function

minus the mesor) (49), and $R^2$ (goodness of fit) (48). We also use Interdaily Stability (IS) (referring to how constant is the routine of activity over the observation period) (29), Intradaily Variability (IV) (fragmentation of the rhythm) (29), and Relative Amplitude (RA) (based on the mean acceleration of most active10-hour period ($M_{10}$) and least active 5 –hour period ($L_5$)) (49).

- *Daytime activity (15 metrics):* for three intensity categories of activity (Sedentary Behaviour (SB), Light Intensity Physical Activity (LIPA), and Moderate to Vigorous Physical activity (MVPA)) we have the daytime total duration, number of bouts (episodes), and mean duration of bouts (50, 51). In addition, the mean acceleration during waking time and $M_{10}$, the transition probabilities (TPs) to switch from activity to rest and from rest to activity during the waking period ($TP_{ar,d}$ and $TP_{ra,d}$) (29), and two parameters derived from the acceleration distribution (intensity gradient (IG) intercept, and slope) are also taken into account (52).
- *Sleep (10 metrics):* total sleep duration, sleep efficiency, number of sleep bouts, mean duration of sleep bouts, TPs from sleep to wake and wake to sleep during the sleep period, mean acceleration during sleep and $L_5$, duration of wake after sleep onset, and mean duration of wake bouts.
- *Chronotype (5 metrics):* timing of sleep onset, waking time, $M_{10}$ and $L_5$ start, and cosinor acrotime (timing of the peak of the function).

For a better understanding of these metrics, a table summarizing their definitions, descriptions, and observation periods is provided in Supplementary Table S1 (see Appendices).

Initially, a principal component analysis (PCA) was conducted on the 36 metrics to reduce the dimensionality of the data, which returned eight principal components that collectively accounted for 85.4% of the total variance. Subsequently, K-means cluster analysis was conducted on these eight uncorrelated components, leading to the identification of nine clusters or profiles that reflect the natural and optimal expression of behavioural CR in real-world data. The standardized mean and standard deviation (SD) of the 36 metrics for each cluster are presented in Figure 1 to enhance understanding. In addition, the unstandardized mean and SD scores are presented in Supplementary Table S2 (see Appendices).

**Profile 1 (RAR++/PA++)** presented the most efficient RAR and overall active daytime pattern with high values in M10 mean acceleration and acceleration during waking. This active pattern was influenced by both LIPA and MVPA, MVPA being the most significant contributor.

In contrary, **Profile 9 (RAR--/PA--/Chronotype-)** had the most disrupted RAR, the most inactive daytime pattern (characterised by SB duration, number of bouts, and mean duration of bouts nearly 2 SDs above the average in the total population) and a late chronotype.

**Profiles 2 (RAR+/PA+/Sleep-)** and **7 (RAR-/PA-/Sleep--)** both showed inefficient sleep, although they differed in their levels of RAR and daytime activity. The active daytime pattern of profile 2 emerged from the presence of both LIPA and MVPA.

**Profiles 3 (RAR+/LIPA+/Sleep+)** and **6 (RAR-/PA-/Sleep+)** showed efficient sleep but presented varying levels of RAR and daytime activity. In profile 3, LIPA was the driver of the present active pattern.

**Profile 4 (MVPA++)** was characterised by a high-intensity physical activity profile, with higher MVPA duration and mean duration of MVPA bouts, lower IG intercept and higher IG slope metrics values (indicating that less time was spent in SB, and more time in the higher range of intensity).

Finally, **profiles 5 (RAR-/Chronotype--)** and **8 (RAR-/PA+/Restless sleep)** both exhibited a trend towards disrupted RAR, however profile 5 presented a very late chronotype characterized by delayed sleep onset and later activity during the day. In contrast, profile 8 showed a low relative amplitude and high mesor resulting from an active daytime pattern but a restless sleep ($L_5$ mean acceleration and mean acceleration during sleep almost 2 SDs above the mean in the total study population).

## Outcome

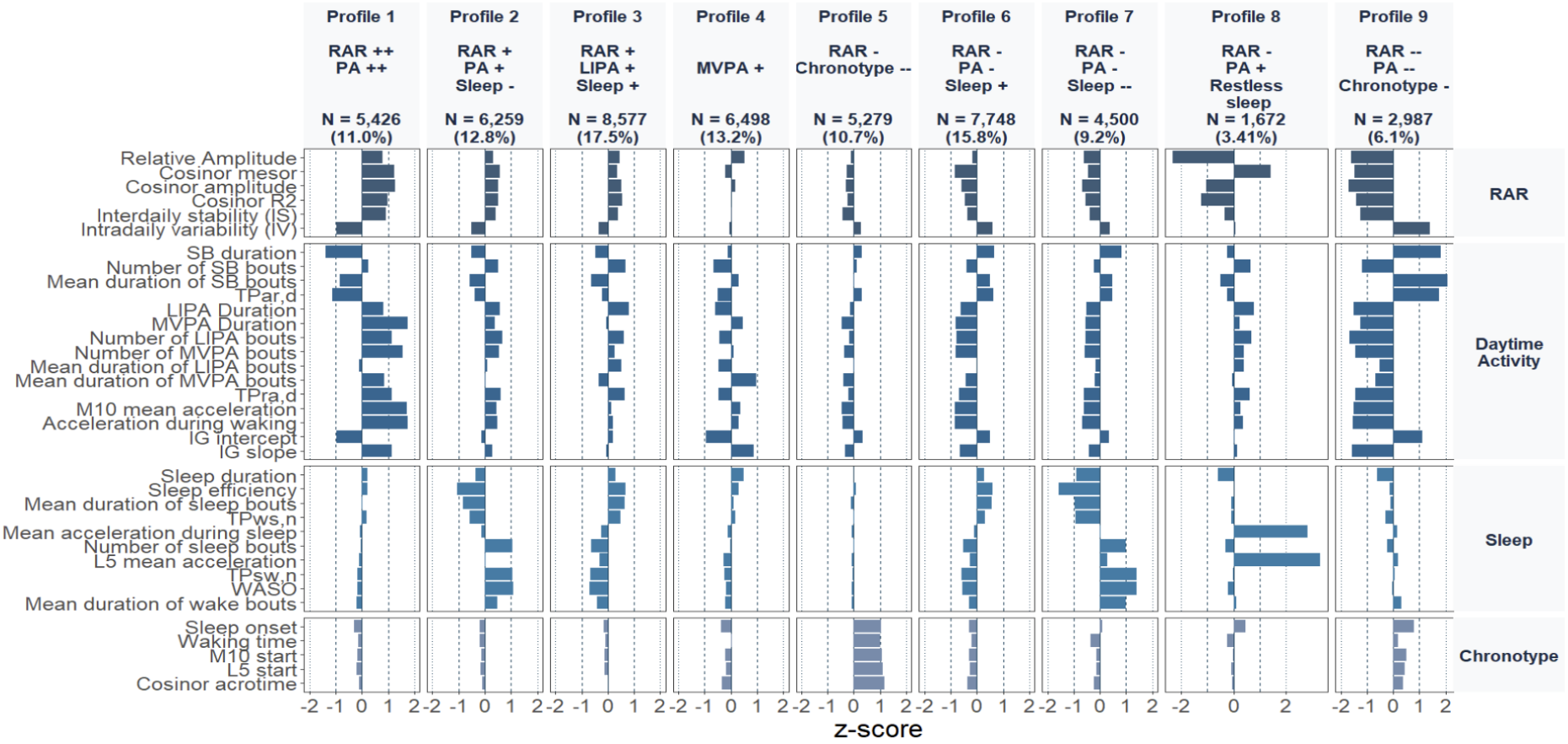
### *Incidence of CVD*

The outcome of this study is the incidence of CVD, which includes fatal and nonfatal coronary heart disease (CHD), stroke, and heart failure. The date of the first event was retained as the date of the event in the analysis.

CVD-related fatal events were obtained from the UK National Mortality Register (NHS) Central Registry (24, 53). Nonfatal CVD events were identified through linkage to electronic health records (EHR) via the Hospital Episode Statistics (HES) database. Events were classified according to relevant ICD codes (International Classification of Disease) as follow:

CHD (ICD-10: I20–I25), stroke (ICD-10: I60–I64), and heart failure (ICD-10: I50).

**Figure 1: Standardized mean scores on 36 metrics as a function of the 9 circadian rhythm profiles in the UKBB study population.**




Abbreviations: IG, intensity gradient; L5, least active 5-hour period; LIPA, light intensity physical activity; M10, most active 10-hour period; MVPA, moderate to vigorous physical activity; PA, physical activity; RAR, rest-activity rhythm; SB, sedentary behaviour; TPar,d, transition probability from activity to rest during the day; TPra,d, transition probability from rest to activity during the day; TPsw,n, transition probability from sleep to wake during the night; TPws,n, transition probability from wake to sleep during the night; WASO, wake after sleep onset.
Results shown in the figure are mean z-scores for each metric in each cluster.

The validity of CVD event ascertainment through linkage to EHR has been supported by previous research. In a validation study conducted within a cohort study in the UK (Whitehall II), the sensitivity and specificity of hospital records for identifying CVD were reported as 71% and 100% for stroke, and 70% and 96% for CHD, respectively (54). Additionally, a systematic review evaluating the validity of acute CVD diagnoses recorded in European EHR, including studies from the UK, reported that, for heart failure, sensitivity was ≤66% in all but one study, while specificity was ≥95% in the three studies that assessed it. For stroke, 73% of studies reported sensitivity estimates ≥70%, and specificity ranged from 99% to 100% across five studies (55). These findings support the reliability of using EHR for CVD ascertainment in research, especially for stroke and CHD.

### Covariates

Individual characteristics were evaluated by either questionnaire, clinical assessment, extracted from the baseline examination (2006-2010) or by linkage to EHR.

Socio-demographic factors included age (at the time of accelerometer wear), sex (female or male), education (lower than secondary school, secondary school, or higher than secondary school), cohabitation status (married/cohabiting or not married/cohabiting) and, professional activity status (employed or not).

Behavioural factors included smoking status (never, ex-, or current smoker), alcohol consumption (0, 1-14, or >14 units/week), and fruit and vegetable consumption (< or ≥ twice daily).

Health-related factors included the use of central nervous system (CNS) medications (antidepressants, antipsychotics, hypnotics, anxiolytics, or Parkinson's medications) and multimorbidity index (0, 1, ≥ 2 diseases), defined as the number of chronic conditions among cancer, arthritis, liver disease, chronic obstructive pulmonary disease, depression, other mental health disorders, and Parkinson's disease. Data on chronic conditions were obtained from HES, clinical measures, and medication records.

Finally, cardiometabolic risk factors included body mass index (BMI) (<25, 25–30, or ≥30 kg/m$^2$), calculated from measured height and weight during the clinical examination; diabetes, defined by fasting glucose ≥7.0 mmol/L at the clinical examination, self-reported doctor-diagnosed diabetes, use of anti-diabetic medications, or a diabetes record in HES; hypertension, defined as systolic/diastolic blood pressure ≥140/90 mmHg or use of

antihypertensive medications; and hyperlipidaemia, defined as LDL cholesterol >4.1 mmol/L or use of lipid-lowering drugs.

### Statistical analysis

Participant characteristics are presented as frequencies and percentages for categorical variables, while continuous variables are summarized as means ± SD. The chi-squared test was used to compare categorical variables between groups. For continuous variables, since the normality assumption was not satisfied, the Wilcoxon test, a non-parametric test, was employed.

Cox proportional hazard models were performed, using age as a time-scale, to investigate the associations of the 9 accelerometer-derived CR profiles and CVD incidence, accounting for covariates of interest. The decision to use age as the time-scale was based on its well-established role as a major risk factor for both CR (18) and CVD (1). This approach allows for an accurate control of confounding by age and better captures the age-dependent association between CR and CVD. In contrast to models that rely on time since inclusion and treat age as a covariate, this method aligns participants by their age, allowing for a more precise estimation of the instantaneous risk of CVD at any specific age (56). Profile 3 (RAR+/ LIPA+/Sleep+) was chosen as the reference cluster for subsequent analysis, as it represents the largest group on the population (N=8,577; 17,5%) and it is the cluster in which most of the metrics are closer from the population mean, in the direction of “healthy profile” (efficient RAR, active daytime pattern, efficient sleep, and early chronotype) with metrics between –0.68 and 0.65 SD. The proportionality assumption was examined using Schoenfeld’s test (57).

The follow-up was defined from the date of accelerometer wear until the date of CVD (fatal or non-fatal), non-CVD related death (to account for competing risks), or end of follow-up (30, November 2022), whichever came first. Model 1 was adjusted for socio-demographic variables, model 2 was additionally adjusted for behavioural factors, model 3 was further adjusted for general health-related factors, and finally, model 4 was additionally adjusted for cardio-metabolic risk factors.

### Additional analysis

To enhance the understanding of the results, statistical analyses were repeated using Profiles 1 (RAR++/PA++) and 6 (RAR-/ PA-/Sleep+) as reference groups. This allowed us to explore differences in CVD risk related to daytime activity patterns (e.g., comparing Profile 1 with Profile 4 (characterised by a high-intensity physical activity profile)), and to assess the role of sleep by comparing profiles 6 and 7, which share similar RAR and daytime activity patterns but differ in sleep pattern.

In order to assess whether the associations differ by age (<70, ≥70 years), sex (female, male), and BMI (<25, 25-30, ≥30 kg/m²), interactions terms between the exposure and these variables were included in the models and their significance was tested using the log-likelihood test. If this test was significant, stratified analyses were subsequently performed.

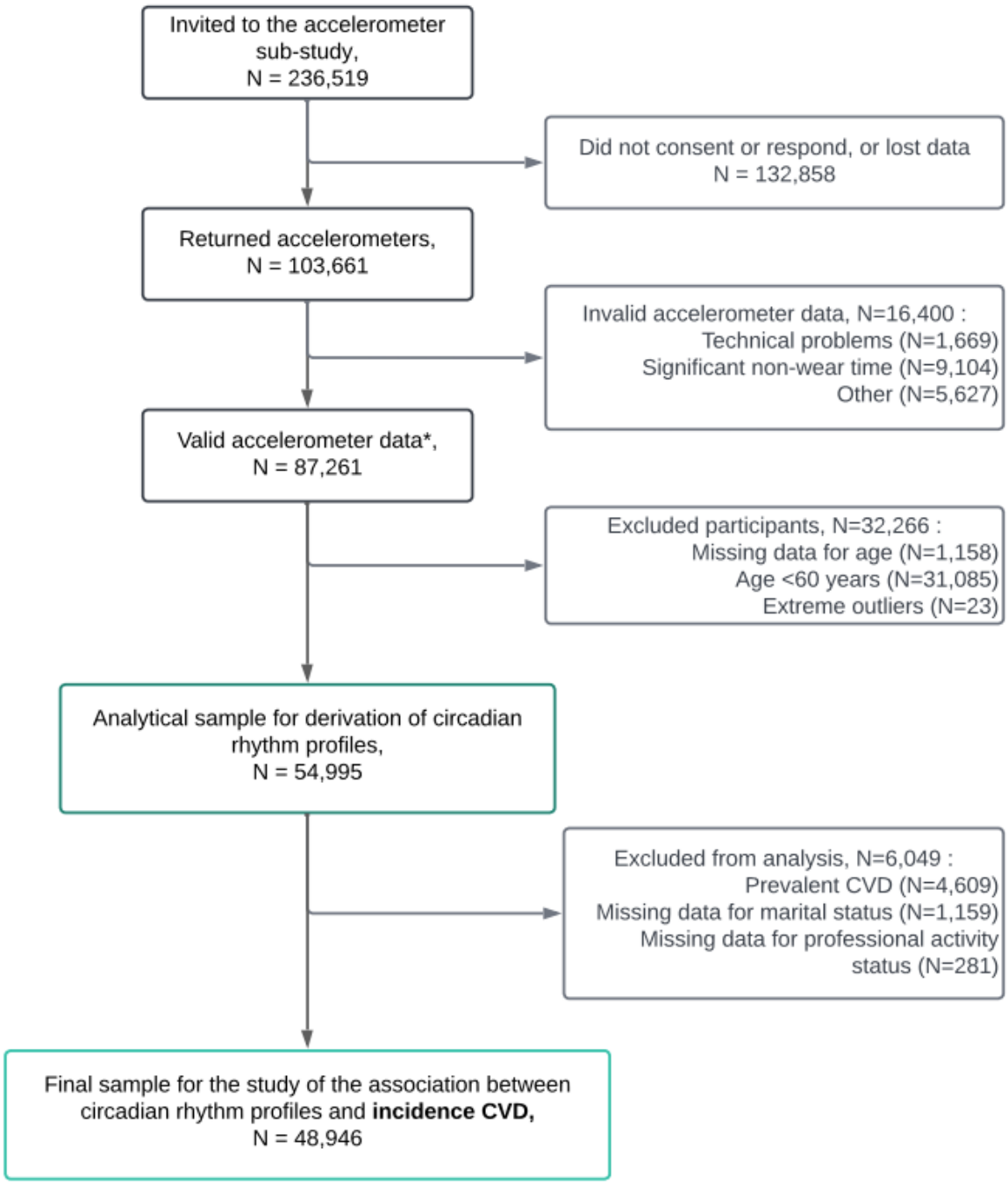
## Results

### Main statistical analysis

Of the 236,519 individuals invited to participate in the accelerometer sub-study, 87,261 submitted valid accelerometer data. After excluding participants aged younger than 60 years (N=31,085), those with missing data for the age variable (N=1,158), and extreme outliers (N=23), the study sample for identifying CR profiles was 54,995. Additionally, 1,440 participants were excluded due to missing data on marital status and professional activity covariates, along with those who had prevalent CVD (N=4,609), which included coronary heart disease (N=3,915), stroke (N=480), and heart failure (N=288). Notably, 1 participant developed both stroke and heart failure, 8 had both stroke and coronary heart disease, and 65 had both heart failure and coronary heart disease as their first CVD event, leading to a final analytical sample of 48,946 (Figure 2).

Compared to participants who did not develop the outcome, those with incident CVD were more likely to be older men, with lower educational levels, not married or cohabiting and non-employed. They were more often ex-smokers, non-drinkers, and reported consuming fewer than two portions of fruits or vegetables per day. Additionally, they more frequently used CNS medications, had two or more concurrent diseases, had a BMI ≥30 kg/m², and a diagnosis of diabetes and hypertension (Table 1). A total of 4,220 CVD incident cases occurred during a median follow-up of 7.7 years.

**Figure 2: Participant flow chart.**




Abbreviations: CVD, cardiovascular disease.

* Corresponds to 5 valid days defined as both wear times during the waking period and the following sleep period ≥2/3 of the respective period.

**Table 1: Characteristics of the UK Biobank study population at baseline by incident CVD.**

| Characteristics | UK Biobank (N=48,946) | | |
|---|---|---|---|
| | Incident CVD | | |
| | No | Yes | P-value |
| N (row %) | 44,726 (91) | 4,220 (9) | |
| **Socio-demographic factors** | | | |
| Age[a] (Years), M (SD) | 67.2 (4.1) | 68.6(4.2) | <0.001*[b] |
| Male | 18,943 (42) | 2,486 (59) | <0.001* |
| Education level | | | <0.001* |
| Lower secondary school or less | 4,686 (10) | 607 (14) | |
| Secondary school | 10,367 (23) | 1,049 (25) | |
| Higher than secondary school | 29,673 (66) | 2,564 (61) | |
| Married or Cohabiting | 36,756 (82) | 3,421 (81) | 0.075 |
| Non-Employed | 23,389 (52) | 2,562 (61) | <0.001* |
| **Behavioural factors** | | | |
| Smoking status | | | <0.001* |
| Never-smoker | 24,908 (56) | 1,996 (47) | |
| Ex-smoker | 17,506 (39) | 1,878 (45) | |
| Current-smoker | 2,312 (5) | 346 (8) | |
| Alcohol consumption | | | 0.003* |
| No consumption | 10,026 (22) | 1,032 (24) | |
| 1-14 units per week | 17,490 (39) | 1,652 (39) | |
| > 14 units of alcohol per week | 17,210 (38) | 1,536 (36) | |
| Daily intake of fruits & vegetables [≥2] | 40,783 (91) | 3,729 (88) | <0.001* |
| **General health-related factors** | | | |
| Intake of CNS medications | 2,706 (6) | 330 (7) | <0.001* |
| Multimorbidity index[c]: | | | <0.001* |
| 0 diseases | 30,083 (67) | 2,475 (59) | |
| 1 disease | 11,369 (25) | 1,288 (31) | |
| ≥ 2 diseases | 3,274 (7) | 457 (11) | |
| **Cardiometabolic risk factors** | | | |
| BMI (Kg/m$^2$) | | | <0.001* |
| < 25 Kg/m$^2$ | 17,523 (39) | 1,246 (30) | |
| ≥ 25 - < 30 Kg/m$^2$ | 19,211 (43) | 1,852 (44) | |
| ≥ 30 Kg/m$^2$ | 7,992 (18) | 1,122 (27) | |
| Diabetes | 1,834 (4) | 397 (9) | <0.001* |
| Hypertension | 25,996 (58) | 3,057 (72) | <0.001* |
| Hyperlipidaemia | 17,413 (39) | 1,590 (38) | 0.11 |

Abbreviations: BMI, Body Mass Index; CVD, Cardiovascular disease; CNS, Central Nervous System.
Values are N (column %) unless otherwise indicated; P-values of Pearson's Chi-squared test unless otherwise indicated ([b]).
[a] Age at the time of accelerometer wear.
[b] P-values of Wilcoxon rank sum test.
[c] Number of chronic conditions: Cancer, arthritis, liver disease, chronic obstructive pulmonary disease, depression, other mental health disorders, and Parkinson disease.

The results of the association between CR profiles and incident CVD are presented in Table 2. The proportional hazard assumption was met in all 4 models. CR profile 5 (RAR-/ Chronotype--) was found to be associated with a higher risk of incident CVD (HR 1.15, CI: 1.02 - 1.30), independently of sociodemographic factors (model 1), compared to profile 3. After adjusting for behavioural factors in model 2, this association lost its significance (HR 1.12, CI: 1.00 - 1.27).

CR profile 1 (RAR++/PA++) was significantly associated with lower CVD risk after adjusting for sociodemographic, behavioural, and general health-related factors, in model 3, (HR 0.85, CI: 0.75 - 0.98) compared to profile 3. Profile 6 (RAR-/PA-/Sleep+) was associated with a higher risk of incident CVD in the same model, (HR 1.14, CI: 1.02 – 1.27). Both associations were no longer significant after adjusting for cardiometabolic risk factors in model 4. When adjusting individually for each cardiometabolic risk factor, these profiles lost their significance after adjustment for BMI. Adjustments for the other cardiometabolic risk factors did not impact the significance found in model 3.

After controlling for sociodemographic, behavioural, general health-related, and cardiometabolic risk factors, CR profile 4 (MVPA++) was associated with a reduced risk of incident CVD (HR 0.86, CI: 0.76 – 0.97) compared to profile 3. Conversely, CR profiles 7 (RAR-/ PA -/ Sleep --), 8 (RAR -/ PA +/ Restless Sleep), and 9 (RAR --/ PA --/ Chronotype -) were associated with an increased hazard of incident CVD compared to profile 3, with hazard ratios of (HR 1.19, CI: 1.06 – 1.34), (HR 1.20, CI: 1.01 – 1.43), and (HR 1.27, CI: 1.11 – 1.44), respectively.

## Table 2. Cox Proportional Hazards Models for the association of CR profiles with incident CVD in the UKBB study population

| CR Profiles | N CVD cases/ N | UK Biobank (N=48,946) | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Model 1[a] | | Model 2[b] | | Model 3[c] | | Model 4[d] | |
| | | HR (95% CI) | P value | HR (95% CI) | P value | HR (95% CI) | P value | HR (95% CI) | P value |
| 1. RAR ++ / PA ++ | 330/5,426 | **0.84 (0.74 - 0.96)** | **0.01*** | **0.85 (0.74 - 0.97)** | **0.02*** | **0.85 (0.75 - 0.98)** | **0.02*** | 0.90 (0.78 - 1.03) | 0.13 |
| 2. RAR +/ PA +/ Sleep - | 479/6,259 | 0.94 (0.83 - 1.06) | 0.34 | 0.94 (0.83 - 1.06) | 0.31 | 0.93 (0.83 - 1.05) | 0.28 | 0.93 (0.83 - 1.05) | 0.28 |
| 3. RAR+, LIPA+, Sleep+ [Ref] | 624/8,577 | 1.00 | | 1.00 | | 1.00 | | 1.00 | |
| 4. MVPA ++ | 439/6,498 | **0.84 (0.74 - 0.95)** | **<0.01*** | **0.85 (0.75 - 0.96)** | **0.01*** | **0.85 (0.75 - 0.97)** | **0.01*** | **0.86 (0.76 - 0.97)** | **0.02*** |
| 5. RAR -/ Chronotype -- | 464/5,279 | **1.15 (1.02 - 1.30)** | **0.01*** | 1.12 (1.00 - 1.27) | 0.05 | 1.09 (0.97 - 1.24) | 0.12 | 1.04 (0.92 - 1.27) | 0.50 |
| 6. RAR -/ PA -/ Sleep + | 743/7,748 | **1.16 (1.04 - 1.29)** | **<0.01*** | **1.15 (1.04 - 1.28)** | **<0.01*** | **1.14 (1.02 - 1.27)** | **0.01*** | 1.06 (0.95 - 1.18) | 0.25 |
| 7. RAR -/ PA - / Sleep -- | 548/4,500 | **1.35 (1.20 - 1.52)** | **<0.001*** | **1.32 (1.18 - 1.49)** | **<0.001*** | **1.30 (1.15 - 1.46)** | **<0.001*** | **1.19 (1.06 - 1.34)** | **<0.01*** |
| 8. RAR -/ PA +/ Restless sleep | 159/1,672 | **1.26 (1.06 - 1.51)** | **<0.01*** | **1.25 (1.05 - 1.49)** | **0.01*** | **1.23 (1.03 - 1.47)** | **0.01*** | **1.20 (1.01 - 1.43)** | **0.03*** |
| 9. RAR --/ PA -- / Chronotype - | 434/2,987 | **1.60 (1.44 - 1.85)** | **<0.001*** | **1.56 (1.37 - 1.76)** | **<0.001*** | **1.49 (1.31 - 1.69)** | **<0.001*** | **1.27 (1.11 - 1.44)** | **<0.001*** |

Abbreviations: BMI body mass index; CI confidence interval; CR Circadian Rhythm; CVD cardiovascular disease; HR hazard ratio; LIPA light intensity physical activity; M mean; MVPA moderate-to-vigorous physical activity; N number; PA Physical activity; RAR Rest-Activity Rhythm; SB sedentary behaviour.

* indicates statistically significance at $p < 0.05$

[a] **Model 1 is adjusted for sociodemographic factors:** Sex, education, marital status, occupational position and age (age considered as a time-scale).

[b] **Model 2 is additionally adjusted for behavioural factors:** Smoking status, alcohol consumption and daily intake of fruit and vegetables.

[c] **Model 3 is additionally adjusted for general health-related factors: I**ntake of CNS medication and multimorbidity index (number of chronic conditions: Cancer, arthritis, liver disease, chronic obstructive pulmonary disease, depression, other mental health disorders, and Parkinson disease).

[d] **Model 4 is additionally adjusted for cardiometabolic factors**: BMI, hyperlipidaemia, diabetes and hypertension .

## Additional analysis

Table 3 shows the HR for incident CVD, using alternatively profile 1 (RAR++/PA++) and profile 6 (RAR-/PA-/Sleep+) as the reference group. When profile 1 (RAR++/PA++) was the reference, profile 3 (RAR+/LIPA+/Sleep+) demonstrated an increased risk of incident CVD (HR 1.16, CI: 1.01 – 1.33), independent of sociodemographic, behavioural and general health-related factors. This association was attenuated and lost statistical significance when additionally controlling for cardiometabolic risk factors (HR 1.10, CI: 0.96 – 1.26). CR profiles 5 (RAR - / Chronotype --), 6 (RAR-/PA-/Sleep+), 7 (RAR -/PA -/Sleep --), 8 (RAR -/PA +/Restless Sleep), and 9 (RAR --/PA --/Chronotype -) were all associated with an elevated hazard of incident CVD compared to profile 1, with hazard ratios of (HR 1.15, CI: 1.01 – 1.33), (HR 1.18, CI: 1.03 – 1.34), (HR 1.32, CI: 1.14 – 1.52), (HR 1.33, CI: 1.10 – 1.61), (HR 1.40, CI: 1.21 – 1.63), respectively, in the fully adjusted model. While the adjustment for cardiometabolic factors in the fully adjusted model did attenuate the risk coefficients, all remained statistically significant.

When profile 6 (RAR-/PA-/Sleep+) was used as the reference, profiles 1 (RAR++/PA++), 2 (RAR+/PA+/Sleep-), 3 (RAR+/LIPA+/Sleep+) and 4 (MVPA++), showed a lower hazard of CVD by 25%, 19%; 13% and 25%, respectively, after adjusting for sociodemographic, behavioural and general health-related factors. However, these associations were attenuated when further adjusted for cardiometabolic factors in model 4, (HR 0.84, CI: 0.74 – 0.96), (HR 0.88, CI: 0.78 – 0.98), (HR 0.93, CI: 0.84 – 1.04), (HR 0.81, CI: 0.72 – 0.91), respectively. It is important to note that the relationship between profile 3 (RAR+/LIPA+/Sleep+) and incident CVD lost its significance in this adjusted model.

Profiles 7 (RAR -/ PA -/ Sleep --) and 9 (RAR --/ PA --/ Chronotype-) were associated with an increased risk of incident CVD compared to profile 6, in the fully adjusted model with HR of (HR 1.12, CI: 1.01 – 1.25), (HR 1.19, CI: 1.05 – 1.34), respectively. Notably, for profile 9, the risk coefficient was stronger prior to the adjustment for cardiometabolic factors.

**Table 3 Cox Proportional Hazards Models for the association of CR profiles with Incident CVD in the UK Biobank study population, using profiles 1 (RAR ++ / PA ++) and 6 (RAR - / PA - / Sleep +) as reference.**

| CR Profiles | UK Biobank (N=48,946) | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Model 3[a] | | Model 4[b] | | Model 3[a] | | Model 4[b] | |
| | **HR (95% CI)** | **P value** | **HR (95% CI)** | **P value** | **HR (95% CI)** | **P value** | **HR (95% CI)** | **P value** |
| 1. RAR ++ / PA ++ | 1.00 [Ref] | | 1.00 [Ref] | | **0.75 (0.65 - 0.85)** | **<0.001*** | **0.84 (0.74 - 0.96)** | **0.01*** |
| 2. RAR +/ PA +/ Sleep - | 1.09 (0.94 - 1.25) | 0.22 | 1.03 (0.90 - 1.19) | 0.59 | **0.81 (0.73 - 0.91)** | **0.01*** | **0.88 (0.78 - 0.98)** | **0.03*** |
| 3. RAR+, LIPA+, Sleep+ | **1.16 (1.01 - 1.33)** | **0.025*** | 1.10 (0.96 - 1.26) | 0.13 | **0.87 (0.78 - 0.97)** | **0.01*** | 0.93 (0.84 - 1.04) | 0.25 |
| 4. MVPA ++ | 0.99 (0.86 - 1.15) | 0.98 | 0.95 (0.83 - 1.10) | 0.56 | **0.75 (0.66 - 0.84)** | **<0.001*** | **0.81 (0.72 - 0.91)** | **<0.001*** |
| 5. RAR -/ Chronotype -- | **1.28 (1.11 - 1.47)** | **<0.001*** | **1.15 (1.01 - 1.33)** | **0.04*** | 0.96 (0.85 - 1.08) | 0.51 | 0.97 (0.87 - 1.10) | 0.72 |
| 6. RAR -/ PA -/ Sleep + | **1.33 (1.16 - 1.51)** | **<0.001*** | **1.18 (1.03 - 1.34)** | **0.01*** | 1.00 [Ref] | | 1.00 [Ref] | |
| 7. RAR -/ PA - / Sleep -- | **1.51 (1.31 - 1.73)** | **<0.001*** | **1.32 (1.14 - 1.52)** | **<0.001*** | **1.13 (1.01 - 1.27)** | **0.02*** | **1.12 (1.01 - 1.25)** | **0.04*** |
| 8. RAR -/ PA +/ Restless sleep | **1.44 (1.19 - 1.74)** | **<0.001*** | **1.33 (1.10 - 1.61)** | **<0.01*** | 1.08 (0.91 - 1.28) | 0.36 | 1.12 (0.95 - 1.34) | 0.16 |
| 9. RAR --/ PA -- / Chronotype - | **1.74 (1.50 - 2.01)** | **<0.001*** | **1.40 (1.21 - 1.63)** | **<0.001*** | **1.30 (1.116 - 1.47)** | **<0.001*** | **1.19 (1.05 - 1.34)** | **<0.01*** |

Abbreviations: CI confidence interval; CR Circadian Rhythm; HR hazard ratio; LIPA light intensity physical activity; MVPA moderate-to-vigorous physical activity; PA Physical activity; RAR Rest-Activity Rhythm; SB sedentary behaviour.

* indicates statistically significance at $p < 0.05$

[a]Model 3 is adjusted for sociodemographic, behavioural and general health-related factors: Sex, education, marital status, occupational position and age (age considered as a time-scale), smoking status, alcohol consumption and daily intake of fruit and vegetables, intake of CNS medication and multimorbidity index (number of chronic conditions: Cancer, arthritis, liver disease, chronic obstructive pulmonary disease, depression, other mental health disorders, and Parkinson disease).

[b]Model 4 is additionally adjusted for cardiometabolic factors: BMI, hyperlipidaemia, diabetes and hypertension.

There was no evidence of effect modification by age or BMI, as the global p-values for interaction, using the log-likelihood ratio test, were greater than 0.05 in all cases. However, a significant effect modification by sex was observed, with a global P value of 0.02 independently of sociodemographic, behavioural, and general health-related factors. In the fully adjusted model, additionally controlling for cardiometabolic factors, the global interaction term was borderline (P value 0.06).

When adding the interaction term between CR profiles and sex to the models, only Profile 9 (RAR--/PA--/Chronotype-) was found to have a significant interaction by sex (P value for interaction < 0.01), after adjusting for sociodemographic, behavioural, and general health-related factors, in model 3. This interaction was still significant, in model 4, additionally controlling for cardiometabolic factors (P value for interaction 0.01).

Table 4 shows the results of the stratified analyses conducted for men and women. Profile 9 (RAR--/PA--/Chronotype-) was significantly associated with an increased risk of incident CVD in both men (HR 1.32, CI: 1.12 – 1.57) and women (HR 1.77, CI: 1.46 – 2.15), independent of sociodemographic, behavioural, and general health-related factors (model 3) compared to model 3. After additional adjustment for cardiometabolic factors (model 4), the association remained significant in women (HR 1.43, CI: 1.18 – 1.75), but was attenuated and no longer significant in men (HR 1.16, CI: 0.98 – 1.38).

**Table 4 Cox Proportional Hazards Models for the association of CR profiles with Incident CVD in the UK Biobank study population, stratified by sex.**

| Variables | UK Biobank (N=48,946) | | | |
|---|---|---|---|---|
| | Men (N=21,429) | | Women (N=27,517) | |
| | Model 3[a] | Model 4[b] | Model 3[a] | Model 4[b] |
| | HR (95% CI) | HR (95% CI) | HR (95% CI) | HR (95% CI) |
| 1. RAR ++ / PA ++ | **0.75 (0.62 - 0.92)** | **0.80 (0.66 - 0.97)** | 0.96 (0.80 - 1.16) | 1.01 (0.83 - 1.21) |
| 2. RAR +/ PA +/ Sleep - | 0.87 (0.74 - 1.03) | 0.88 (0.75 - 1.04) | 0.97 (0.81 - 1.17) | 0.97 (0.80 - 1.17) |
| 3. RAR+, LIPA+, Sleep+ [Ref] | 1.00 | 1.00 | 1.00 | 1.00 |
| 4. MVPA ++ | 0.86 (0.73 - 1.01) | 0.88 (0.74 - 1.03) | **0.77 (0.63 - 0.94)** | **0.78 (0.64 - 0.95)** |
| 5. RAR -/ Chronotype -- | 1.00 (0.84 - 1.19) | 0.96 (0.81 - 1.15) | **1.18 (1.01 - 1.40)** | 1.10 (0.93 - 1.31) |
| 6. RAR -/ PA -/ Sleep + | 1.03 (0.89 - 1.21) | 0.98 (0.84 - 1.14) | **1.23 (1.05 - 1.42)** | 1.12 (0.97 - 1.31) |
| 7. RAR -/ PA - / Sleep -- | **1.22 (1.05 - 1.42)** | 1.14 (0.97 - 1.33) | **1.36 (1.11 - 1.66)** | **1.23 (1.01 - 1.51)** |
| 8. RAR -/ PA +/ Restless sleep | 1.22 (0.97 - 1.54) | 1.19 (0.94 - 1.50) | 1.18 (0.90 - 1.56) | 1.16 (0.85 - 1.53) |
| 9. RAR --/ PA -- / Chronotype - | **1.32 (1.12 - 1.57)** | 1.16 (0.98 - 1.38) | **1.77 (1.46 - 2.15)** | **1.43 (1.18 - 1.75)** |

Abbreviations: CI confidence interval; HR hazard ratio; LIPA light intensity physical activity; MVPA moderate-to-vigorous physical activity; N number; PA Physical activity; RAR Rest-Activity Rhythm; SB sedentary behaviour.

* indicates statistical significance at $p < 0.05$

[a] Model 3 is additionally adjusted for general health-related factors: Intake of CNS medication and multimorbidity index (number of chronic conditions: Cancer, arthritis, liver disease, chronic obstructive pulmonary disease, depression, other mental health disorders, and Parkinson disease).

[b]Model 4 is additionally adjusted for cardiometabolic factors: BMI, hyperlipidaemia, diabetes and hypertension.

## Discussion

This longitudinal study, based on a large population-based cohort of 48,946 older adults, confirms the protective role of active daytime patterns, particularly in those CR profiles characterised by MVPA, on incident CVD among older adults. Importantly, our findings highlight the need for a holistic assessment of CR by demonstrating that its fourth dimensions collectively influence CVD risk. We observed a potential dose–response relationship for RAR, with participants exhibiting more efficient RAR profiles showing lower CVD risk, particularly when combined with active daytime patterns. However, profiles sharing similar levels of daytime activity and RAR showed differential CVD risk when sleep varied, suggesting that the individual or partial assessment of CR dimensions may lead to misclassification or biased risk estimates. Notably, sleep emerged as a contributor to CVD risk, with distinct real-world sleep patterns reinforcing the value of assessing integrated CR profiles. The role of chronotype in these associations warrants further investigation. Altogether, our findings highlight the significance of CR for cardiovascular health in older adults.

We found that participants with the most active (1 RAR ++ / PA ++) and most inactive (9 RAR-- / PA -- / Chronotype -) profiles exhibited the lowest and highest risks of incident CVD, respectively, independent of socio-demographic, behavioural, and health-related factors, with these profiles also characterised by the most efficient and most disrupted RAR. These findings align with previous evidence. For example, a large prospective cohort study involving over 130,000 participants from 17 low-, middle-, and high-income countries found that individuals not meeting the MVPA WHO-recommendation had a significantly higher risk of CVD (58). Additionally, a systematic review and meta-analysis of 36 longitudinal studies, reported that individuals in 18 studies with high levels of SB had a significantly increased risk of CVD (pooled HR: 1.34, CI: 1.26 – 1.43), while 21 studies demonstrated that long-term engagement in PA was associated with a reduced risk of CVD (pooled HR: 0.71, CI: 0.66 – 0.77), reporting in addition that sustained PA also improves key cardiovascular risk indicators (59). Notably, after adjusting for cardiometabolic risk factors, the association between these CR profiles and CVD was attenuated, losing significance for Profile 1. This suggests that these factors, particularly BMI, may significantly influence the observed associations. However, due to the lack of temporal alignment between the exposure and covariates measurements in our study, definitive conclusions regarding the underlying pathways cannot be established. Although a longitudinal study using UK Biobank data from baseline and two follow-up waves reported stability for most of these variables (70), further research, ensuring temporal alignment of the measurements, is needed to determine, through

for example mediation analysis, whether cardiometabolic factors lie on the causal pathway between CR and incident CVD in older adults.

Moreover, our results highlight the critical role of MVPA in mitigating CVD risk. The protective association was observed in profiles characterised by engagement in MVPA, either alone or in combination with LIPA. This pattern became particularly evident when profiles 3 (RAR+/LIPA+/Sleep+) and 1 (RAR++/PA++) were used as the reference group. We cannot draw definitive conclusions about the role of LIPA in this association, as our study population did not exhibit a profile primarily characterised by LIPA, as was the case with MVPA in profile 4. Consequently, the specific contribution of LIPA remains inconclusive and warrants further investigation, especially given the contradictory findings reported in the literature (32, 60, 61). Nonetheless, our findings underscore the importance of maintaining an active lifestyle in older populations, particularly through regular MVPA, as inactive profiles were consistently associated with an elevated risk of CVD.

In addition, we observed a likely dose–response relationship related to RAR patterns and CVD. Participants with more efficient RAR profiles showed a lower CVD risk, while those with disrupted RAR patterns faced an elevated risk, even after adjusting for socio-demographic, behavioural, and general health-related factors. This is consistent with findings from a cross-sectional study of 4,521 U.S. adults, that reported a linear dose-response association between objectively measured RAR metrics, specifically IS, IV and RA, and CVD risk (13), and a longitudinal study among 10,143 individuals with metabolic dysfunction-associated steatotic liver disease (62) that indicates a linear association between RAR (cosinor amplitude and mesor) and CVD mortality. Previous studies have shown a correlation between RAR and daytime activity metrics (39, 40). We advance the existing evidence by adopting a holistic approach that accounts for the correlation and interdependence among all CR dimensions. This approach enabled us to identify 1,672 participants with inefficient RAR despite maintaining an active daytime pattern (Profile 8), emphasising the limitations of assessing CR dimensions in isolation, as relying solely on daytime activity patterns could lead to misclassification, mistakenly categorising these individuals as having a healthy lifestyle while overlooking a potential higher CVD risk due to disrupted RAR pattern.

Our findings demonstrate that in free-living conditions, older adults can exhibit varying combinations of RAR and daytime activity patterns, which may contribute to differential CVD risk. For instance, compared to individuals in Profile 3 (RAR+, LIPA+, Sleep+) the hazard of CVD was 19% higher in Profile 7 (RAR– / PA– / Sleep–), 20% higher in Profile 8 (RAR– / PA+ / Restless Sleep), and 27% higher in Profile 9 (RAR— / PA— / Chronotype–) in the fully

adjusted model. This association was not significant in profile 6 (RAR– / PA– / Sleep+) after additionally adjusting for cardiometabolic factors (HR 1.06, CI: 0.95 – 1.18).

Furthermore, the differences in these effect estimates suggest that RAR and daytime activity alone do not fully account for the observed associations with CVD risk; other CR dimensions, particularly sleep, also appear to play a critical role. This is evidenced by the comparison between participants in Profiles 6 and 7, who shared similar RAR and daytime activity patterns but differed in sleep patterns. Those in Profile 7, characterised by a very inefficient sleep, exhibited a 12% higher risk of CVD compared to Profile 6, highlighting the contribution of sleep disturbances to CVD risk. These findings align with a previous cross-sectional study that employed objective sleep assessments and similarly identified an elevated risk of CVD associated with inefficient sleep (13). While much of the epidemiological research has traditionally focused on isolated metrics such as sleep duration (63-66), our study underscores the value of considering a broader range of sleep parameters. This approach enables the identification not only of distinct sleep characteristics but also of real-world sleep patterns. For example, Profile 8 was characterised by a restless sleep, driven primarily by high values for mean acceleration during sleep and during $L_5$, with most other sleep metrics remaining near the mean. In contrast, Profile 7 reflected a very inefficient sleep, characterized by a lower duration, more fragmentation, but not more acceleration. Notably, the risk of incident CVD varied across these profiles, which also presented different patterns of RAR, daytime activity, and chronotype.

Consistently, we found a differential CVD risk among profiles with a trend towards late chronotype. Compared to individuals in Profile 3 (RAR+, LIPA+, Sleep+), those characterised by a late chronotype, inefficient RAR, and inactive daytime pattern (Profile 9) presented a persistent association with increased CVD risk across all models. Conversely, those with a very late chronotype combined with an inefficient RAR (Profile 5) did not exhibit an association with CVD after controlling for sociodemographic and behavioural factors. These findings limit our ability to conclude regarding the influence of chronotype on these associations. Previous epidemiological studies have linked subjectively assessed chronotype preference with cardiovascular outcomes, showing that individuals with a definite evening chronotype have an increased CVD risk (67) , and those with evening chronotype have an increased cardiometabolic burden (25). Additionally, a prospective study using objective chronotype assessments reported a U-shaped relationship between chronotype metrics, specifically sleep onset time, and CVD, suggesting that both extreme morning and evening chronotypes are associated with higher CVD risk (68). In our study, only two of the nine identified profiles were characterised by a late chronotype, while the majority exhibited chronotype metric values close to the population mean. This limited variation further restricted our ability to explore the role of

chronotype, along with the different RAR, daytime activity, and sleep patterns, in relation to CVD risk in older adults.

To our knowledge, this is the first prospective study to investigate the association between CR and incident CVD using 9 distinct profiles that allow the expression of CR patterns in the real world, an approach never adopted in previous research. This study has several notable strengths. It used data from a large, population-based cohort study, with over 48,000 participants. Its prospective design, including a mean follow-up of more than 7.5 years, ensures temporality in the observed associations. We utilised actigraphy-derived metrics from wrist-worn accelerometers in free-living settings to assess CR, which helps to avoid common limitations of self-reported measures, such as recall and misclassification bias. To minimise confounding, our models were adjusted for a broad range of variables. Additionally, the ascertainment of incident CVD events relied on multiple sources, including the link to EHR and clinical data, with previously validated measures of sensitivity and specificity for event detection.

However, this study is not without limitations. First, the UKBB has a relatively low response rate, and its participants tend to be healthier and from higher socioeconomic backgrounds compared to the general population (69). This "healthy volunteer bias" may limit the generalizability of our findings. Second, there is a concern regarding potential misclassification bias, particularly for heart failure, due to previously reported low sensitivity in EHR. Third, key covariates, including sociodemographic, behavioural, health-related and cardiometabolic risk factors, were measured between 3-9 years before the CR assessment, probably introducing bias, as covariates might not accurately reflect participants' status at the time of behavioural CR measurement. Finally, a sleep diary was not incorporated into the accelerometer measurements, which could result in misclassification of sleep and waking times due to inaccuracies in estimating sedentary behaviour, sleep, and chronotype metrics, especially if participants were inactive before sleep. However, the algorithm used in this research has previously demonstrated its ability to accurately determine the sleep period time window in the UKBB, without a sleep diary(46).

## Conclusions

Our findings emphasise the critical role of CR for cardiovascular health in older adults, particularly highlighting the protective effects of CR profiles characterised by efficient RAR, active daytime patterns that include MVPA, and efficient sleep patterns. While the impact of chronotype and LIPA warrants further exploration, the overall evidence supports the implementation of targeted public health interventions that address all dimensions of CR

simultaneously. Such strategies should consider the distinct health and personal challenges encountered by older adults to promote regularity across rest-activity patterns, engagement in PA, good sleep hygiene, and consistent sleep patterns. It is equally important to tackle the environmental, social, and health-related barriers that may impede the adoption of healthy behaviours. This includes improving access to safe spaces for practising PA, minimising nighttime noise and light pollution, and enhancing healthcare support for sleep-related issues. These public health strategies aim to support healthier CR and lower the risk of CVD in older populations.

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## List of Appendices

Table S1: Definition and description of the 36 metrics that compose the circadian rhythm dimensions. *This table has been adapted with permission from a manuscript submitted to a journal [2025], Vidil S, Danilevicz IM, Dugravot A, Fayosse A, Landré B, et al. Accelerometer-based measures of rest-activity rhythm, chronotype, daytime activity, and sleep to characterize clusters of behavioural circadian rhythm.*

| Metrics | Name in GGIR | Description | Period of observation |
|---|---|---|---|
| **Dimension: Rest-activity rhythm (RAR)** | | | |
| Relative amplitude | (m10value - l5value) / (m10value + l5value) | Calculated as $\frac{M_{10}-L_5}{M_{10}+L_5}$ with $M_{10}$ corresponding to the mean acceleration of the most active 10-hour period and $L_5$ the mean acceleration of the least active 5-hour period. Higher values indicate larger amplitude in the rhythm.(49) | Calculated for each full day (waking and sleeping periods) and averaged over valid days. |
| Cosinor mesor | cosinor_mes | The mean value of the cosinor function fitted to the log transformed acceleration signal (ENMO time series). Higher values indicate more activity.(70) | Calculated using the full observation period (including day and night periods), non-wear periods were omitted. |
| Cosinor amplitude | cosinor_amp | The amplitude of the cosinor function fitted to the log transformed acceleration signal, corresponding to the peak of the function minus the mesor. Higher values indicate larger amplitude in the rhythm.(70) | |
| Cosinor $R^2$ | cosinor_r2 | Measure of goodness of fit of the cosinor function to the log transformed acceleration signal. Higher values indicate better goodness of fit.(70) | |
| Interdaily stability (IS) | is | Calculated as $IS = \frac{P\sum_{h=1}^{H}(\bar{x}_h-\bar{x})^2}{H\sum_{p=1}^{P}(x_p-\bar{x})^2}$, where *H* is the number of hours per day, *P* the total number of hours over the observation period, $x_p$ is the $p^{th}$ element of a vector of P hourly proportions of activity , $\bar{x}_h$ is the $h^{th}$ element of a vector of *H* hourly proportions of being active (defined as mean acceleration >40 m*g*), and $\bar{x}$ is the overall mean hourly proportion of being active over the entire period.<br>IS measures how constant is the routine of activity over several days and ranges from 0 to 1, values close to 1 indicate more constant routine.(71) | |
| Intradaily variability (IV) | iv | Calculated as $IV = \frac{P\sum_{p=2}^{P}(x_p-x_{p-1})^2}{(P-1)\sum_{p=1}^{P}(x_p-\bar{x})^2}$<br>See notations in the row above. It measures the variability in activity hour by hour throughout the days. It ranges from 0 to +∞, value close to 2 indicates more fragmented rhythm, and >2 indicates ultradian rhythm (very uncommon).(71) | |

*Table S1. Continued*

| Metrics | Name in GGIR | Description | Period of observation |
|---|---|---|---|
| **Dimension: Daytime activity** | | | |
| SB, LIPA, and MVPA durations | SB: dur_day_total_in_min_pla<br>LIPA: dur_day_total_lig_min_pla<br>MVPA: dur_day_total_mod_min_pla + dur_day_total_vig_min_pla | Total daily time during waking period spent in 60s-epoch acceleration<40 m*g* for SB (in hours), 40-99 m*g* for LIPA (in hours), ≥100 m*g* for MVPA (in minutes)(50, 51) | Calculated for each waking period and averaged over valid days. Non-wear periods of valid days were imputed using the average of the signal at the same time of the day on other valid days. |
| Number of SB, LIPA, and MVPA bouts | SB: frag_nfrag_in_day_pla<br>LIPA: frag_nfrag_lipa_day_pla<br>MVPA: frag_nfrag_mvpa_day_pla | Number of bouts spent in SB, LIPA, and MVPA per day. Higher numbers denote more fragmented episodes in the activity level. | |
| Mean duration of SB, LIPA, and MVPA bouts | SB: dur_day_total_in_min_pla / data_acc2$frag_nfrag_in_day_pla<br>LIPA: dur_day_total_lig_min_pla / frag_nfrag_lipa_day_pla<br>MVPA: (dur_day_total_mod_min_pla + dur_day_total_vig_min_pla) / frag_nfrag_mvpa_day_pla | Average duration of bouts (in minutes) in SB, LIPA, and MVPA, computed as the total daily duration during waking period divided by daily number of bouts. Longer mean durations in an activity level represent less fragmented activity. | |
| Intensity gradient intercept and slope | ig_day_intercept_pla<br>ig_day_gradient_pla | Intensity gradient (IG) relies on the acceleration distribution during the waking period per day defined as the time spent (ordinate) in each acceleration (abscissa) over the day. IG intercept and slope are extracted from the linear regression between log transformed abscissa and log transformed ordinate.(52)<br>Examples: Higher intercept and steeper gradient (i.e. more negative gradient) represent more time in SB and little time spent in midrange and higher intensity. Lower intercept and shallow gradient correspond to more time spread across the range of intensities. | |
| Acceleration during waking | acc_day_mg_pla | Mean acceleration during waking period (in m*g*). Higher values represent higher activity level over the day. | |
| $M_{10}$ mean acceleration | m10value | Mean acceleration during the most active 10-hour period (in m*g*) of the entire day. Higher values represent higher activity level over the most active hours. | Calculated for each full day window. Non-wear periods of valid days were imputed using the average of the signal at the same time of the day on other valid days. |
| Transition probability from activity to rest during the day ($TP_{ar,d}$) | frag_tp_pa2in_day | Calculated as $\mathrm{TP}_{\mathrm{ar,d}} = \frac{n_{a,d}+\delta}{T_{a,d}+\delta}$, where $n_{a,d}$ is the number of bouts of activity during the day (waking period), $T_{a,d}$ is the total time of activity during the day (waking period), and $\delta$ is a small number, $10^{-6}$, to avoid potential division by zero.<br>It corresponds to the probability of transitioning from a physically active (LIPA or MVPA) to sedentary state and ranges from 0 to 1, values close to 1 indicate frequent switching from one state to the other. | Calculated using the full observation period (including only valid day periods), sleep and non-wear periods were omitted. |
| Transition probability rest to activity during the day ($TP_{ra,d}$) | frag_tp_in2pa_day | Calculated as $\mathrm{TP}_{\mathrm{ra,d}} = \frac{n_{r,d}+\delta}{T_{r,d}+\delta}$, where $\delta$ is $10^{-6}$, $n_{r,d}$ the number of bouts of rest during the day (waking period), and $T_{r,d}$ the total time of rest during the day (waking period).<br>It corresponds to the probability of transitioning from a sedentary to physically active (LIPA or MVPA) state and ranges from 0 to 1. | |

*Table S1. continued*

| Metrics | Name in GGIR | Description | Period of observation |
|---|---|---|---|
| **Dimension: Sleep** | | | |
| Sleep duration | dur_spt_sleep_min_pla | Duration (in hours) of time spent sleeping during the sleep period. | Calculated for each sleep period and averaged over valid days. Non-wear periods of valid days were imputed using the average of the signal at the same time of the day on other valid days. |
| Sleep efficiency | sleep_efficiency_pla | Percent of time spent sleeping during the sleep period. Higher values denote a better sleep quality. | |
| Mean duration of sleep bouts | dur_spt_sleep_min_pla / nblocks_spt_sleep_pla | Mean duration (in minutes) of sleep bouts during the sleep period. Longer mean duration denotes longer sleep bouts. | |
| Number of sleep bouts | nblocks_spt_sleep_pla | Number of sleep bouts during the sleep period. More sleep bouts denote more fragmented sleep. | |
| Mean acceleration during sleep period | acc_spt_sleep_mg_pla | Mean acceleration during sleep period (in m*g*). For cluster calculation, this variable was log transformed to reduce its skewness. Higher values denote more movements during the sleep period. | |
| Duration of wake after sleep onset (WASO) | dur_spt_min_pla - dur_spt_sleep_min_pla | Time spent awake (in minutes) during the sleep period. Higher values indicate more fragmented sleep. | |
| Mean duration of wake bouts | (dur_spt_min_pla - dur_spt_sleep_min_pla) / (nblocks_spt_sleep_pla - 1) | Mean duration of bouts spent awake during sleep period (in minutes). Longer duration denotes more difficulties falling asleep when awake. | |
| $L_5$ mean acceleration | l5value | Mean acceleration during the 5 least active hours (in m*g*). Higher values indicate more activity during the 5 least active hours (commonly during the sleep period). | Calculated for each full day window. Non-wear periods of valid days were imputed using the average of the signal at the same time of the day on other valid days. |
| Transition probabilities from wake to sleep during the night ($TP_{ws,n}$) | frag_tp_wake2sleep_spt | Calculated as $\mathrm{TP}_{\mathrm{ws,n}} = \frac{n_{w,n}+\delta}{T_{w,n}+\delta}$, where $\delta$ is $10^{-6}$, $n_{w,n}$ the number of bouts of wake during the night, and $T_{w,n}$ the total waking time during the night. It corresponds to the probability of transitioning from wake to sleep state during the sleep period and range from 0 to 1, value close to 1 indicates frequent changes between wake to sleep states. | Calculated using the full observation period (including only sleep periods), waking and non-wear periods were omitted. |
| TP from sleep to wake during sleep period ($TP_{sw,n}$) | frag_tp_sleep2wake_spt | Probability of transitioning from sleep to wake state during the sleep period Range from 0 to 1. Value close to 1 indicates frequent changes from sleep to wake states. | |
| **Dimension: Chronotype** | | | |
| Sleep onset | sleeponset_pla | Timing of the sleep onset (in hours of the day) | Calculated for each sleep period and averaged over valid days. |
| Waking time | wakeup_pla - 24 | Timing of the waking up to start the day (in hours of the day) | |
| $M_{10}$ start | m10time_num | Timing of the start of $M_{10}$ (in hours of the day) | Calculated for each entire day (waking and sleeping periods) and averaged over valid days. |
| $L_5$ start | l5time_num | Timing of the start of $L_5$ (in hours of the day) | |
| Cosinor acrotime | cosinor_acrotime | Time at which the cosinor function fitted to the log transformed acceleration signal reaches its maximum | Calculated using the full observation period (including day and night periods), non-wear periods were omitted. |

Abbreviations: IG, intensity gradient; $L_5$, least 5 active hours; LIPA, light intensity physical activity; $M_{10}$, most active 10-hour period; MVPA, moderate to vigorous physical activity; SB, sedentary behaviour; $TP_{ar,d}$, transition probability from activity to rest during the day; $TP_{ra,d}$, transition probability from rest to activity during the day; $TP_{sw,n}$, transition probability from sleep to wake during the night; $TP_{ws,n}$, transition probability from wake to sleep during the night; WASO, wake after sleep onset.
Definitions: A *bout* corresponds to an uninterrupted episode spent in a given range of state; *Sleep period* is from sleep onset to waking time to start the day.

Table S2: Unstandardized mean (standard deviation) scores of each metric across the circadian rhythm profiles in the UK Biobank accelerometer sub-study

| Characteristic | Total study population | Profile 1 | Profile 2 | Profile 3 | Profile 4 | Profile 5 | Profile 6 | Profile 7 | Profile 8 | Profile 9 |
|---|---|---|---|---|---|---|---|---|---|---|
| ***N (%)*** | 48,946 | 5,426(11) | 6,259(12.8) | 8,577(17.5) | 6,498(13.2) | 5,279(10.7) | 7,748(15.8) | 4,500(9.2) | 1,672(3.41) | 2,987(6.1) |
| ***Rest-activity rhythm*** | | | | | | | | | | |
| *Relative amplitude* | 0.85 (0.07) | 0.91 (0.03) | 0.87 (0.04) | 0.88 (0.04) | 0.89 (0.03) | 0.84 (0.05) | 0.84 (0.05) | 0.80 (0.06) | 0.68 (0.10) | 0.73 (0.08) |
| *Cosinor mesor* | 2.44 (0.23) | 2.73 (0.15) | 2.57 (0.14) | 2.53 (0.14) | 2.39 (0.14) | 2.38 (0.15) | 2.25 (0.15) | 2.34 (0.16) | 2.77 (0.24) | 2.10 (0.18) |
| *Cosinor amplitude* | 1.13 (0.24) | 1.43 (0.16) | 1.25 (0.14) | 1.25 (0.15) | 1.17 (0.16) | 1.06 (0.16) | 0.99 (0.15) | 0.97 (0.15) | 0.87 (0.22) | 0.72 (0.17) |
| *Cosinor $R^2$* | 0.33 (0.10) | 0.43 (0.08) | 0.38 (0.07) | 0.38 (0.07) | 0.33 (0.08) | 0.31 (0.08) | 0.28 (0.08) | 0.27 (0.08) | 0.21 (0.08) | 0.19 (0.08) |
| *Intradaily Stability (IS)* | 0.58 (0.12) | 0.68 (0.09) | 0.62 (0.09) | 0.62 (0.09) | 0.58 (0.10) | 0.52 (0.10) | 0.53 (0.10) | 0.53 (0.10) | 0.53 (0.13) | 0.43 (0.11) |
| *Interdaily Variability (IV)* | 0.90 (0.23) | 0.67 (0.15) | 0.78 (0.16) | 0.82 (0.16) | 0.89 (0.19) | 0.96 (0.19) | 1.03 (0.20) | 0.99 (0.21) | 0.92 (0.24) | 1.22 (0.24) |
| ***Daytime activity*** | | | | | | | | | | |
| *SB duration (hours)* | 11.2 (1.9) | 8.6 (1.1) | 10.3(1.1) | 10.3 (1) | 11.0(1.0) | 11.8(1.1) | 12.5 (1.02) | 12.7(1.3) | 10.8 (1.9) | 14.6 (1.4) |
| *Number of SB bouts* | 68 (13) | 71 (12) | 75 (12) | 77 (11) | 59 (9) | 69 (12) | 63 (11) | 65 (11) | 77 (14) | 52 (12) |
| *Mean Duration of SB bouts (min)* | 10.4 (3.6) | 7.5 (1.5) | 8.4 (1.5) | 8.2 (1.4) | 11.5 (2.2) | 10.5 (2.1) | 12.3 (2.4) | 12.2 (2.6) | 8.7 (2.2) | 17.9 (6.0) |
| *TPar,d (%)* | 22 (6) | 16 (3) | 20 (4) | 21 (4) | 19 (4) | 24 (4) | 26 (5) | 25 (5) | 21 (5) | 33 (8) |
| *LIPA Duration (hours)* | 3.9 (1.1) | 4.8 (0.9) | 4.6 (0.8) | 4.8 (0.7) | 3.3 (0.6) | 3.8 (0.7) | 3.3 (0.6) | 3.4 (0.7) | 4.8 (1.2) | 2.3 (0.6) |
| *MVPA Duration (min)* | 93 (52) | 184 (46) | 113 (35) | 91 (29) | 118 (31) | 69 (27) | 52 (21) | 64 (27) | 106 (49) | 29 (18) |
| *Number of LIPA Bouts* | 94 (20) | 116 (15) | 107 (13) | 106 (12) | 85 (11) | 91 (13) | 79 (11) | 83 (13) | 108 (18) | 60 (13) |
| *Number of MVPA Bouts* | 37 (16) | 61 (12) | 45 (11) | 41 (10) | 38 (10) | 31 (9) | 24 (8) | 27 (9) | 43 (15) | 14 (7) |
| *Mean Duration of LIPA Bouts (min)* | 2.5 (0.4) | 2.5 (0.4) | 2.6 (0.4) | 2.7 (0.4) | 2.4 (0.3) | 2.5 (0.4) | 2.5 (0.4) | 2.4 (0.4) | 2.7 (0.6) | 2.3 (0.4) |
| *Mean Duration of MVPA Bouts (min)* | 2.5 (0.7) | 3.1 (0.7) | 2.5 (0.5) | 2.2 (0.4) | 3.1 (0.8) | 2.2 (0.5) | 2.2 (0.5) | 2.3 (0.6) | 2.4 (0.6) | 2.0 (0.7) |

*Table S2. Continued*

| Characteristic | Total study population | Profile 1 | Profile 2 | Profile 3 | Profile 4 | Profile 5 | Profile 6 | Profile 7 | Profile 8 | Profile 9 |
|---|---|---|---|---|---|---|---|---|---|---|
| ***N (%)*** | 48,946 | 5,426(11) | 6,259(12.8) | 8,577(17.5) | 6,498(13.2) | 5,279(10.7) | 7,748(15.8) | 4,500(9.2) | 1,672(3.41) | 2,987(6.1) |
| *TPra,d (%)* | 11 (3) | 14 (3) | 13 (2) | 13 (2) | 9 (2) | 10 (2) | 9 (2) | 9 (2) | 13 (4) | 6 (1) |
| *M10 mean acceleration (mg)* | 50 (15) | 76 (15) | 57 (9) | 52 (6) | 55 (10) | 43 (6) | 37 (5) | 41 (7) | 54 (12) | 27 (5) |
| *Acceleration during waking (mg)* | 39 (11) | 59 (10) | 44 (6) | 41 (5) | 43 (7) | 34 (5) | 29 (4) | 31 (5) | 43 (9) | 21 (4) |
| *IG Intercept* | 12.2 (0.6) | 11.6 (0.6) | 12.1 (0.4) | 12.3 (0.4) | 11.6 (0.5) | 12.4 (0.4) | 12.5 (0.4) | 12.4 (0.5) | 12.2 (0.5) | 12.9 (0.6) |
| *IG Slope* | -2.0 (0.2) | -1.8 (0.1) | -1.9 (0.1) | -1.9 (0.1) | -1.8 (0.1) | -2.0 (0.1) | -2.1 (0.1) | -2.1 (0.1) | -2.0 (0.2) | -2.3 (0.2) |
| ***Sleep*** | | | | | | | | | | |
| *Sleep duration (hours)* | 6.6 (1.1) | 6.8 (0.8) | 6.2 (0.9) | 6.9 (0.8) | 7.1 (0.8) | 6.5 (0.9) | 6.8 (0.9) | 5.6 (1.1) | 5.9 (1.2) | 5.9 (1.3) |
| *Sleep efficiency (%)* | 90 (5) | 91 (3) | 85 (4) | 93 (2) | 91 (3) | 90 (3) | 93 (2) | 82 (5) | 90 (4) | 89 (4) |
| *Mean duration sleep bouts (min)* | 52 (18) | 53 (15) | 37 (6) | 63 (18) | 54 (15) | 50 (13) | 62 (19) | 35 (7) | 51 (16) | 50 (16) |
| *TPws,n (%)* | 20 (5) | 21 (4) | 17 (3) | 22 (5) | 21 (4) | 20 (4) | 21 (5) | 15 (3) | 20 (5) | 18 (5) |
| *Mean acceleration during sleep (mg)* | 3.3 (1.4) | 3.3 (1.1) | 3.2 (1.0) | 3.1 (0.9) | 3.2 (1.0) | 3.2 (1.0) | 3.2 (1.0) | 3.4 (1.27) | 8.9 (5.8) | 3.6 (1.3) |
| *Number of sleep bouts* | 9.2 (2.8) | 9.1 (2.3) | 12.1 (2.3) | 7.4 (1.9) | 9.1 (2.3) | 9.2 (2.2) | 7.7 (2.1) | 11.9 (2.8) | 8.3 (2.4) | 8.5 (2.6) |
| *L5 mean acceleration (mg)* | 3.8 (2.0) | 3.6 (1.5) | 3.9 (1.3) | 3.2 (1.1) | 3.3 (1.1) | 3.7 (1.3) | 3.3 (1.1) | 4.4 (1.6) | 10.3 (4.4) | 4.2 (1.6) |
| *TPsw,n (%)* | 2.1 (0.8) | 2.0 (0.6) | 3.0 (0.7) | 1.6 (0.5) | 1.9 (0.6) | 2.1 (0.6) | 1.6 (0.5) | 3.3 (0.8) | 2.1 (0.8) | 2.2 (0.8) |
| *WASO (min)* | 44 (21) | 41 (15) | 66 (18) | 30 (10) | 41 (14) | 42 (13) | 32 (12) | 73 (22) | 39 (16) | 43 (17) |
| *Mean duration of wake bouts (min)* | 5.3 (1.5) | 5.0 (1.1) | 6.1 (1.3) | 4.7 (1.2) | 5.0 (1.1) | 5.2 (1.3) | 5.0 (1.3) | 6.8 (1.9) | 5.5 (1.8) | 5.8 (1.8) |

*Table S2. Continued*

| Characteristic | Total study population | Profile 1 | Profile 2 | Profile 3 | Profile 4 | Profile 5 | Profile 6 | Profile 7 | Profile 8 | Profile 9 |
|---|---|---|---|---|---|---|---|---|---|---|
| ***N (%)*** | 48,946 | 5,426(11) | 6,259(12.8) | 8,577(17.5) | 6,498(13.2) | 5,279(10.7) | 7,748(15.8) | 4,500(9.2) | 1,672(3.41) | 2,987(6.1) |
| ***Chronotype*** | | | | | | | | | | |
| *Sleep onset (hours of the day)* | 23.9 (1.1) | 23.6 (0.9) | 23.7 (1.0) | 23.7 (0.8) | 23.5 (0.8) | 1.0 (1.0) | 23.6 (0.8) | 0.0 (1.1) | 0.4 (1.3) | 0.7 (1.4) |
| *Sleep offset (hours of the day)* | 7.1 (1.1) | 7.0 (0.1) | 7.0 (1.0) | 7.1 (0.9) | 7.2 (0.9) | 8.2 (0.9) | 6.9 (1.0) | 6.8 (1.1) | 6.9 (1.2) | 7.3 (1.4) |
| *M10 start (hours of the day)* | 8.6 (1.1) | 8.4 (1.0) | 8.5 (0.9) | 8.5 (0.9) | 8.4 (0.9) | 9.7 (1.0) | 8.3 (0.9) | 8.4 (1.0) | 8.6 (1.2) | 9.1 (1.3) |
| *L5 start (hours of the day)* | 1.0 (1.1) | 0.8 (0.9) | 0.9(0.9) | 0.9 (0.8) | 0.8 (0.9) | 2.1 (0.9) | 0.7 (0.9) | 0.9 (1.1) | 0.9 (1.5) | 1.5 (1.4) |
| *Cosinor acrotime (hours of the day)* | 14.5 (1.0) | 14.4 (0.9) | 14.4 (0.9) | 14.5 (0.8) | 14.1 (0.8) | 15.6 (0.9) | 14.1 (0.9) | 14.2 (0.9) | 14.4 (1.4) | 14.9 (1.3) |

Abbreviations: IG, intensity gradient; $L_5$, least active 5-hour period; LIPA, light intensity physical activity; $M_{10}$, most active 10-hour period; m*g*, milligravity; min, minute; MVPA, moderate to vigorous physical activity; PA, physical activity; RAR, rest-activity rhythm; SB, sedentary behaviour; $TP_{ar,d}$, transition probability from activity to rest during the day; $TP_{ra,d}$, transition probability from rest to activity during the day; $TP_{sw,n}$, transition probability from sleep to wake during the night; $TP_{ws,n}$, transition probability from wake to sleep during the night; WASO, wake after sleep onset.

## Abstract in French

### Contexte

Des données suggèrent que l'activité physique (AP), le sommeil, le chronotype et le rythme repos-activité (RAR) jouent un rôle dans l'incidence des maladies cardiovasculaires (MCV). Ces comportements, régulés sur une horloge de 24 heures, font partie de l'expression biocomportementale du rythme circadien (RC). Ces quatre dimensions peuvent être mesurées objectivement à l'aide d'accéléromètres. La plupart des études examinant l'association entre le RC et les MCV n'ont pas considéré toutes les dimensions du RC simultanément ni tenu compte de leur interdépendance. Cette étude vise à examiner l'association entre des profils du RC dérivés des accéléromètres tenant compte des quatre dimensions et l'incidence des MCV chez les personnes âgées, et si ces associations varient selon le sexe, l'âge ou l'IMC.

### Méthodes

L'étude inclut 48 946 adultes de plus de 60 ans issus de la sous-étude accélérométrique de la UK Biobank. Neuf profils du RC ont été identifiés précédemment à l'aide d'une approche en deux étapes, combinant une analyse en composantes principales suivie d'un regroupement sur 36 indicateurs dérivés de l'accéléromètre couvrant toutes les dimensions du RC. Des modèles de régression de Cox ont permis d'estimer les rapports de risque (HR) d'incidence des MCV selon les profils du RC, ajustés pour les facteurs sociodémographiques, comportementaux, liés à la santé et cardiométaboliques. Des termes d'interaction pour le sexe, l'âge et l'IMC ont également été ajoutés.

### Résultats

Au cours d'un suivi médian de 7,7 ans, 4 220 cas incidents de MCV ont été recensés. Comparé au Profil 3 (RAR+/LIPA+/Sommeil+), le Profil 4 (MVPA++) était associé à un risque de MCV réduit de 14 %. En revanche, les Profils 7 (RAR-/AP-/Sommeil--), 8 (RAR-/AP+/Sommeil agité) et 9 (RAR--/AP--/Chronotype-) présentaient respectivement une augmentation du risque de 19 %, 20 % et 27 %. L'association protectrice du Profil 1 (RAR++/AP++) était atténuée après ajustement sur les facteurs cardiométaboliques. Seul le Profil 9 (RAR--/AP--/Chronotype-) a montré une interaction significative avec le sexe, avec un effet plus marqué chez les femmes que chez les hommes, bien que la direction de l'association soit restée la même pour les deux sexes.

### Conclusion

Ces résultats soulignent l'importance d'une évaluation holistique du RC pour mieux comprendre le risque cardiovasculaire chez les personnes âgées. Un schéma d'activité diurne actif, incluant notamment de l'AP modérée à vigoureuse, s'est révélé protecteur. Les différences de RAR, d'activité diurne et de sommeil selon les profils du RC contribuent aux variations du risque de MCV. Nos résultats soutiennent le développement d'interventions

ciblées intégrant l'ensemble des dimensions du RC afin de promouvoir la santé cardiovasculaire chez les personnes âgées.

Mots-clés

Rythme circadien, maladies cardiovasculaires, personnes âgées, accéléromètre.

**Titre :** Association entre les profils comportementaux du rythme circadien et l'incidence de la maladie cardiovasculaire chez les personnes âgées : résultats de la sous-étude accéléromètre de la UK Biobank.