

Persistent Rather Than Variable Short Sleep Associates With Cardiovascular Events in Middle-Aged and Older Chinese Adults: A CHARLS Cohort Study

Zehua Wang

Shanghai Chest Hospital, Shanghai Jiao Tong University School of Medicine

Xianxian Fan

Shanghai Tongren Hospital, Shanghai Jiao Tong University School of Medicine

Long Chen

Shanghai Ninth People's Hospital, Shanghai Jiao Tong University School of Medicine

Yiping Shi

Shanghai Chest Hospital, Shanghai Jiao Tong University School of Medicine

Qin Shao

drshaoqin@163.com

Shanghai Chest Hospital, Shanghai Jiao Tong University School of Medicine

Article

Keywords: sleep duration, sleep trajectories, cardiovascular events, prospective cohort study, CHG index, China Health and Retirement Longitudinal Study

Posted Date: October 11th, 2026

DOI: <https://doi.org/10.21203/rs.3.rs-11058097/v1>

License: © ⓘ This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Additional Declarations: No competing interests reported.

Abstract

Background

Short sleep has been linked to cardiometabolic disease, but single-time sleep assessments cannot separate persistent short sleep from recurrent variable short sleep. Whether these sleep-trajectory phenotypes predict incident cardiovascular events in middle-aged and older adults, and whether the cholesterol, high-density lipoprotein, and glucose (CHG) index identifies higher-risk sleep-metabolic profiles, remains uncertain.

Methods

We analysed 11,050 China Health and Retirement Longitudinal Study (CHARLS) participants aged 45 years or older who were free of heart disease and stroke through 2015, had sleep-duration data from at least two of the 2011–2015 survey waves, and had 2018 or 2020 follow-up. Sleep trajectories were classified as persistent optimal, variable short, persistent short, optimal-to-short, or other patterns. Incident cardiovascular events were self-reported physician-diagnosed heart disease or stroke. Multivariable Cox models adjusted for demographic, socioeconomic, lifestyle, clinical, depressive-symptom, and physical-activity covariates; sensitivity, CHG, joint-exposure, and exploratory sex-stratified analyses were performed.

Results

During 51,330 person-years, 1,923 incident cardiovascular events occurred. Compared with persistent optimal sleep, persistent short sleep was associated with higher cardiovascular risk (hazard ratio [HR] 1.22, 95% confidence interval [CI] 1.05–1.42; $p = 0.009$), whereas variable short sleep was not (HR 1.03, 95% CI 0.88–1.21; $p = 0.701$); estimates were similar across sensitivity analyses. CHG was modestly associated with events after adjustment for sleep trajectory (HR per standard deviation 1.06, 95% CI 1.01–1.11; $p = 0.024$). High CHG combined with persistent short sleep identified the highest joint-risk group (HR 1.35, 95% CI 1.08–1.69; $p = 0.008$). In exploratory sex-stratified analyses, persistent versus variable short sleep carried higher risk among women (HR 1.30, 95% CI 1.04–1.64) but not men, with a significant sex-by-CHG interaction ($p = 0.027$).

Conclusions

Persistent short sleep, but not variable short sleep, was associated with incident cardiovascular events after multivariable adjustment in this national cohort of middle-aged and older Chinese adults. The CHG index may help characterise higher-risk sleep-metabolic subgroups, particularly among women in

exploratory analyses. Repeated sleep assessment and routine metabolic markers may support prevention-oriented cardiovascular risk assessment in ageing populations.

Clinical trial number:

Not applicable.

Background

Cardiovascular disease remains the leading cause of morbidity and mortality worldwide, with a particularly large prevention burden in China as population ageing, hypertension, diabetes, and dyslipidemia converge across later life [1, 2]. Sleep has become a core component of cardiovascular health because insufficient, excessive, or poor-quality sleep may cluster with adverse lifestyle behaviors and may contribute to autonomic dysregulation, inflammation, glucose intolerance, hypertension, and unfavorable cardiometabolic profiles [3, 4]. The recommended sleep duration for healthy adults is generally 7 or more hours per night, but older adults often experience shorter, more fragmented, and more heterogeneous sleep patterns [5]. Consistent prospective evidence links short sleep, long sleep, poor sleep quality, and insomnia symptoms with cardiovascular events or cardiometabolic morbidity, although effect sizes vary by population, measurement approach, and outcome definition [6–11]. The addition of sleep duration to the American Heart Association's cardiovascular health construct underscores the clinical relevance of sleep as a modifiable behavior. However, evidence based on a single sleep-duration assessment cannot distinguish sustained sleep habits from changes over time, highlighting the value of repeated measurements [3, 12–18].

The distinction between persistent and changing sleep patterns is important. A person who reports short sleep once may represent transient stress, temporary illness, measurement error, or an emerging chronic sleep deficit. Repeated measurements can separate sustained short sleep from trajectories in which sleep moves from an optimal range into short sleep or fluctuates around the short-sleep threshold. Studies in Western and multiethnic cohorts, including the Multi-Ethnic Study of Atherosclerosis and the Study of Women's Health Across the Nation, have suggested that sleep irregularity and longitudinal sleep patterns may predict cardiovascular events beyond average sleep duration [14–18]. A large prospective analysis of longitudinal habitual sleep duration also reported that changing or persistently unfavorable sleep patterns carried higher risks of cardiovascular events and mortality [15]. Whether the same risk structure applies to middle-aged and older adults in China remains uncertain because sleep habits, cardiometabolic risk profiles, socioeconomic gradients, and stroke burden differ across populations.

CHARLS is a longitudinal study of middle-aged and older adults in China that collected repeated health and sleep information across survey waves [19–21]. Building on prior Chinese cohort work on sleep-duration trajectories and cardiovascular disease [22], the present analysis focused on post-2015 incident cardiovascular events after excluding reported heart disease or stroke through 2015, using 2011–2015 as the sleep-exposure window and 2018/2020 as follow-up endpoints.

Sex-specific evidence on longitudinal sleep patterns, metabolic burden, and cardiovascular risk remains limited in Chinese cohorts, supporting exploratory analyses of whether sleep-metabolic risk patterns differ between women and men [16–18].

We aimed to evaluate whether sleep-duration trajectories are associated with incident cardiovascular events among middle-aged and older Chinese adults. We also examined whether the CHG index derived from actual blood assays was associated with cardiovascular risk and whether it identified higher-risk groups when combined with sleep trajectories. We further conducted exploratory sex-stratified analyses to assess whether sleep-metabolic risk clustering differed between women and men. We hypothesized that repeated short sleep would be associated with higher cardiovascular risk than persistent optimal sleep, but we treated the variable short-sleep phenotype, the CHG index, and the sex-stratified findings as operational or exploratory constructs requiring sensitivity analyses rather than as validated biological phenotypes.

Methods

This prospective cohort study used CHARLS health-status and blood-assay files from 2011, 2013, 2015, 2018, and 2020 that are publicly accessible upon registration and data-use approval, supplemented by H_CHARLS_D_Data.dta, the Harmonized CHARLS file [19–21]. The analytic cohort was anchored at the 2011 wave. Later health waves, blood-assay files, and harmonized baseline covariates were linked to 2011 respondents by harmonized participant identifiers. The exposure window comprised sleep measurements in 2011, 2013, and 2015. Follow-up for incident cardiovascular events began after the 2015 wave and continued through the 2018 or 2020 health follow-up, depending on available outcome information. The CHARLS protocol was approved by the Peking University Biomedical Ethics Review Committee (IRB00001052-11015), and all participants provided informed consent. This study is reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines (Supplementary File 3).

Participants were included if they were enrolled in 2011, were aged 45 years or older at the 2011 baseline, had no reported heart disease or stroke through 2015, had at least two valid night-time sleep-duration measurements during 2011–2015, and had post-2015 follow-up information for heart disease or stroke. Baseline age was taken from Harmonized CHARLS r1agey; when unavailable, 2011 age was approximated as 2020 xrage minus 9 years. This fallback was used only to retain otherwise eligible participants with missing baseline age and is reported in the supplementary missingness table (Supplementary File 2). Participants with missing age after this fallback were excluded from the analytic cohort.

Night-time sleep duration was obtained from da049 in 2011, 2013, and 2015. Values greater than 0 and no more than 14 hours were considered valid to reduce implausible or extreme entries. The 2020 sleep item was not used to define exposure because sleep after the 2015 landmark may lie on the causal pathway or reflect early disease status; additionally, the 2020 health file uses da030 for sleep, whereas

da049 in 2020 refers to smoking-cessation timing. Each valid sleep measurement was classified as short sleep (< 6 hours), optimal sleep (6–8 hours), or long sleep (> 8 hours). Participants were assigned to mutually exclusive trajectory groups. Persistent optimal sleep required all available exposure-window measurements to be within 6–8 hours and a coefficient of variation below 15%. Persistent short sleep required all available exposure-window measurements to be shorter than 6 hours; no additional variability restriction was applied because all available observations already met the short-sleep exposure criterion. The coefficient of variation was calculated across all available 2011–2015 sleep measurements, including non-short values when present. The variable short-sleep category was operationally defined and was assigned only after persistent short sleep had been classified; it required at least two short-sleep measurements and a coefficient of variation of at least 15%. With only two valid exposure-window measurements, two short values were classified as persistent short sleep rather than variable short sleep. Variable short sleep was therefore, in practice, restricted to participants with three valid measurements, two short-sleep values, and one non-short value. Optimal-to-short sleep required the first available category to be optimal and the last available category to be short. All remaining patterns were classified as other, a heterogeneous residual group that could include single-occasion short sleep, long sleep, or mixed sleep-duration patterns. The primary definitions used < 6 hours for short sleep and 6–8 hours for optimal sleep, while guideline-oriented alternatives (< 7 hours for short sleep and 7–8 hours for optimal sleep) were evaluated in sensitivity analyses. Additional sensitivity analyses evaluated complete three-wave sleep data, exclusion of participants with any long-sleep observation, an alternative short-sleep threshold of < 5 hours, and removal of the coefficient-of-variation requirement from the persistent optimal definition.

Incident cardiovascular events were defined as self-reported physician diagnosis of heart disease or stroke after the 2015 exposure window. Disease category 7 represented heart disease or heart problems, and disease category 8 represented stroke. For 2011 through 2018, heart disease and stroke were obtained from da007_7_ and da007_8_. For 2020, the corresponding current diagnosis items were da003_7_ and da003_8_. Participants reporting heart disease or stroke in 2011, 2013, or 2015 were excluded to reduce prevalent-disease contamination during the sleep-exposure window. Event occurrence was observed only at follow-up waves rather than by exact diagnosis date. Wave-based follow-up times were therefore used: 3 years for events first identified in 2018 and 5 years for events first identified in 2020; participants without events were censored at the last available follow-up wave. Cox models were retained as the main comparable time-to-event analysis but were interpreted as wave-based estimates because the data contained only two post-landmark event intervals. To better match the interval-observed outcome structure, a person-period complementary log-log model was fitted as a key complementary analysis. Conventional Schoenfeld residual diagnostics were considered of limited interpretability because exact event dates were unavailable and event times were restricted to two follow-up waves. Component-specific analyses modeled heart disease and stroke separately using the same follow-up framework; the alternate component was not modeled as a competing event. Death during follow-up was not incorporated as a competing event because death information was not available in the analytic dataset, and this limitation is addressed in the Discussion.

Baseline covariates were derived primarily from Harmonized CHARLS [21] and included age, sex, education, rural residence, marital status, household wealth and income, smoking, drinking, body mass index, systolic and diastolic blood pressure, CES-D depressive symptoms [23], physical activity, hypertension, and diabetes. Household wealth and income were summarized descriptively in units of 10000 yuan and transformed using the inverse hyperbolic sine function in regression models. Missing covariates were handled with a pragmatic missing-indicator approach for model stability; detailed missingness is reported in supplementary material (Supplementary File 2), and the absence of multiple imputation is addressed as a limitation.

The cholesterol, high-density lipoprotein, and glucose (CHG) index was calculated from 2011 and 2015 blood assays as $\ln[(TC \times FPG)/(2 \times HDL-C)]$, with all components analysed on the mg/dL scale [24, 25]. Cholesterol measures in mmol/L were multiplied by 38.67 and fasting plasma glucose by 18.0 before applying the formula. The participant-level CHG value was the mean of available wave-specific values and was standardized within the analytic sample. A biomarker-adjusted sensitivity model further adjusted for LDL-C, C-reactive protein, HbA1c, creatinine, and uric acid, and was interpreted cautiously because these markers overlap with or may lie downstream of CHG-related metabolic pathways [26–29].

Baseline characteristics were summarized by sleep-trajectory group, including event proportions, person-years, and incidence rates per 1,000 person-years. Cox proportional hazards models estimated hazard ratios and 95% confidence intervals for incident cardiovascular events with persistent optimal sleep as the reference group. Tied event times were handled using the Efron method. For the sleep-trajectory analysis, the crude model included sleep-trajectory indicators only. The multivariable-adjusted model additionally included age, sex, education, rural residence, marital status, household wealth, household income, smoking, drinking, body mass index, systolic and diastolic blood pressure, depressive symptoms, physical activity, hypertension, and diabetes; this was the main adjustment set for sleep-trajectory inference. This model estimated associations conditional on major baseline demographic, socioeconomic, lifestyle, physical-examination, depressive-symptom, activity, and clinical factors. Because body mass index, blood pressure, hypertension, and diabetes may also partly lie on pathways linking sleep to cardiovascular disease, the model should be interpreted as an adjusted association model rather than as a pure total-effect model. A separate biomarker-adjusted sensitivity model further adjusted for low-density lipoprotein cholesterol, C-reactive protein, glycated hemoglobin, creatinine, and uric acid in complete biomarker cases; because these biomarkers may partly lie downstream of sleep or metabolic dysfunction, this model was interpreted as sensitivity evidence rather than as the main causal-adjustment set.

The person-period complementary log-log model used one record for the 2015–2018 interval and, when applicable, one record for the 2018–2020 interval, with interval indicators included as baseline hazards and robust standard errors. We also decomposed the heterogeneous other-pattern group into long-involved, single-short, repeated short low-variability, and no short/long or missing subgroups. Outcome-specific models were fitted separately for incident heart disease and incident stroke to evaluate whether the composite result was driven by either component.

For CHG analyses, nested Cox models estimated hazard ratios per standard deviation of CHG after demographic/socioeconomic adjustment, after additional lifestyle and clinical adjustment, and after further inclusion of sleep-trajectory indicators. Joint exploratory analyses combined CHG above versus below the median with persistent short sleep and variable short sleep, using low CHG plus persistent optimal sleep as the reference. Two-sided P values below 0.05 were considered statistically significant; subgroup, sensitivity, and interaction analyses were exploratory and were not adjusted for multiplicity.

We conducted exploratory sex-stratified analyses to examine whether sleep-metabolic risk patterns differed between women and men. Descriptive analyses compared the prevalence and event rates of persistent short sleep, high CHG plus persistent short sleep, and high CHG plus persistent short sleep combined with age 60 years or older or hypertension. Within each sex, Cox models estimated the association of CHG per standard-deviation increment and the joint high-CHG plus persistent-short phenotype. Within each sex, a restricted sub-sample analysis among participants classified as either persistent short sleep or variable short sleep estimated the direct contrast of persistent short sleep versus variable short sleep, with the reference group changed from persistent optimal sleep to variable short sleep. This restricted contrast should not be directly compared with the main trajectory models because it used a different analytic subset and reference category. Formal interaction terms were tested for sex with CHG, persistent short sleep, and high CHG plus persistent short sleep. These analyses were considered exploratory; models were adjusted using the same multivariable covariate set except that sex itself was omitted from sex-stratified models.

Results

The cohort construction began with 17,596 CHARLS 2011 health-file respondents. After retaining participants aged 45 years or older at baseline, excluding those with reported heart disease or stroke through 2015, requiring at least two sleep measurements during 2011–2015, and requiring post-2015 follow-up, the final analytic sample included 11,050 participants (Fig. 1). During 51,330 person-years of follow-up, 1,923 incident cardiovascular events occurred, corresponding to an event rate of 17.4%. Among these events, 1,244 were first reported in 2018 and 679 were first reported in 2020. Heart disease was reported by 1,294 participants and stroke by 790 participants, with overlap possible between the two components. Mean follow-up was 4.65 years. CHG based on actual blood assays was available in 9,672 participants. Detailed covariate missingness is summarized in the supplementary tables (Supplementary File 2); missingness was highest for physical activity and household economic variables, with additional missingness for measured examination variables, CHG, and biomarker covariates.

The most common sleep-trajectory pattern was persistent optimal sleep, observed in 3,827 participants (Table 1). Other patterns were observed in 3,556 participants, variable short sleep in 1,208, persistent short sleep in 1,345, and optimal-to-short sleep in 1,114. The persistent optimal group had a mean sleep duration close to 7 hours across all exposure waves. The persistent short-sleep group had mean sleep duration below 4 hours across the exposure window, whereas the variable short-sleep group averaged

5.37 hours in 2011, 4.80 hours in 2013, and 4.96 hours in 2015 (Fig. 2). Incidence rates were 31.94 per 1,000 person-years for persistent optimal sleep, 38.87 for variable short sleep, 46.95 for persistent short sleep, 38.73 for optimal-to-short sleep, and 39.04 for other patterns. The other-pattern group was heterogeneous: 1,447 participants were classified as other single-short patterns, 155 as repeated short low-variability patterns, and 1,954 as long-involved patterns.

Table 1
Baseline characteristics of participants by sleep trajectory pattern.

Characteristics	Overall (N = 11050)	Persistent Optimal (N = 3827)	Variable Short (N = 1208)	Persistent Short (N = 1345)	Optimal- to-Short (N = 1114)	Other (N = 3556)
Demographic characteristics						
Age, years	57.0 [50.0, 63.0]	55.0 [49.0, 61.0]	58.0 [52.0, 64.0]	59.0 [53.0, 65.0]	57.0 [50.0, 63.0]	57.0 [51.0, 64.0]
Male sex	5338 (48.3)	2081 (54.4)	455 (37.7)	552 (41.0)	486 (43.6)	1764 (49.6)
Rural residence	7116 (64.4)	2255 (58.9)	861 (71.3)	885 (65.8)	692 (62.1)	2423 (68.1)
Married or partnered	9948 (90.0)	3561 (93.0)	1076 (89.1)	1144 (85.1)	999 (89.7)	3168 (89.1)
Socioeconomic characteristics						
Education, n (%)						
Less than lower secondary	9814 (88.8)	3197 (83.5)	1139 (94.3)	1250 (92.9)	996 (89.4)	3232 (90.9)
Upper secondary or vocational training	1091 (9.9)	541 (14.1)	64 (5.3)	86 (6.4)	106 (9.5)	294 (8.3)
Tertiary education	145 (1.3)	89 (2.3)	5 (0.4)	9 (0.7)	12 (1.1)	30 (0.8)
Household income, 10,000 yuan	1.20 [0.26, 3.38]	1.56 [0.38, 4.01]	1.05 [0.26, 3.05]	0.88 [0.21, 3.04]	1.10 [0.24, 3.07]	1.04 [0.23, 3.15]
Household wealth, 10,000 yuan	6.09 [1.56, 15.16]	7.53 [2.20, 17.83]	4.68 [1.19, 11.60]	4.19 [0.91, 11.52]	6.12 [1.61, 15.28]	5.87 [1.54, 14.21]
Lifestyle factors						
Current smoking	3361 (30.4)	1247 (32.6)	292 (24.2)	362 (26.9)	316 (28.4)	1144 (32.2)
Current drinking	3853 (34.9)	1499 (39.2)	357 (29.6)	422 (31.4)	389 (34.9)	1186 (33.4)
Physical activity	4116 (37.2)	1455 (38.0)	440 (36.4)	496 (36.9)	404 (36.3)	1321 (37.1)
Note. Values are median [Q1, Q3] or n (%). Percentages were calculated using the column-specific sample size as the denominator. No P values or standardized mean differences are shown.						

Characteristics	Overall (N = 11050)	Persistent Optimal (N = 3827)	Variable Short (N = 1208)	Persistent Short (N = 1345)	Optimal- to-Short (N = 1114)	Other (N = 3556)
Demographic characteristics						
Clinical characteristics						
BMI (kg/m ²)	23.1 [20.9, 25.6]	23.4 [21.2, 25.9]	22.8 [20.7, 25.5]	22.7 [20.6, 25.3]	23.2 [21.0, 25.7]	22.9 [20.6, 25.4]
SBP (mmHg)	125.0 [113.0, 139.5]	125.5 [113.5, 138.5]	124.5 [112.5, 140.1]	126.0 [112.5, 142.0]	125.5 [114.0, 139.0]	125.0 [112.5, 140.0]
DBP (mmHg)	74.0 [66.5, 82.5]	75.0 [67.5, 83.5]	73.5 [66.2, 82.0]	73.0 [66.0, 82.0]	74.5 [67.0, 82.0]	74.0 [66.5, 82.5]
Hypertension	2580 (23.3)	819 (21.4)	302 (25.0)	345 (25.7)	261 (23.4)	853 (24.0)
Diabetes	606 (5.5)	183 (4.8)	72 (6.0)	77 (5.7)	70 (6.3)	204 (5.7)
CES-D score	7.0 [3.0, 12.0]	5.0 [2.0, 9.0]	9.0 [5.0, 15.0]	11.0 [6.0, 16.0]	7.0 [3.0, 11.0]	7.0 [3.0, 11.0]
Biomarkers						
CHG index	5.22 [5.00, 5.46]	5.23 [5.01, 5.47]	5.21 [4.98, 5.45]	5.22 [5.00, 5.43]	5.22 [5.02, 5.48]	5.22 [5.00, 5.47]
LDL-C (mg/dL)	114.0 [93.6, 136.9]	114.0 [93.9, 136.9]	115.6 [93.2, 140.7]	115.6 [94.7, 138.0]	114.0 [94.4, 138.0]	113.7 [92.8, 134.9]
HDL-C (mg/dL)	49.5 [40.6, 59.9]	48.7 [40.6, 59.5]	51.0 [41.4, 60.7]	51.0 [41.2, 61.5]	50.3 [40.4, 59.9]	49.1 [39.8, 59.5]
Total cholesterol (mg/dL)	190.6 [167.4, 214.9]	189.8 [166.9, 214.2]	193.1 [167.4, 220.3]	190.8 [168.9, 218.8]	191.0 [168.4, 214.4]	190.2 [167.0, 214.2]
Fasting plasma glucose (mg/dL)	102.2 [94.1, 112.7]	102.4 [94.5, 112.3]	101.7 [94.0, 112.7]	102.8 [94.5, 112.0]	102.4 [94.7, 112.5]	101.9 [93.8, 113.0]
HbA1c (%)	5.1 [4.9, 5.4]	5.1 [4.9, 5.4]	5.2 [4.9, 5.4]	5.1 [4.9, 5.4]	5.1 [4.9, 5.4]	5.1 [4.9, 5.4]
Note. Values are median [Q1, Q3] or n (%). Percentages were calculated using the column-specific sample size as the denominator. No P values or standardized mean differences are shown.						

Characteristics	Overall (N = 11050)	Persistent Optimal (N = 3827)	Variable Short (N = 1208)	Persistent Short (N = 1345)	Optimal- to-Short (N = 1114)	Other (N = 3556)
Demographic characteristics						
CRP (mg/L)	0.98 [0.53, 2.01]	0.98 [0.53, 1.97]	0.95 [0.53, 2.10]	1.00 [0.55, 2.10]	0.98 [0.53, 1.92]	0.97 [0.52, 2.02]
Creatinine (mg/dL)	0.76 [0.64, 0.87]	0.76 [0.66, 0.88]	0.72 [0.63, 0.85]	0.73 [0.64, 0.86]	0.76 [0.64, 0.88]	0.76 [0.64, 0.88]
Uric acid (mg/dL)	4.28 [3.56, 5.13]	4.35 [3.64, 5.18]	4.12 [3.46, 4.92]	4.12 [3.48, 5.08]	4.26 [3.57, 5.13]	4.31 [3.59, 5.17]
Note. Values are median [Q1, Q3] or n (%). Percentages were calculated using the column-specific sample size as the denominator. No P values or standardized mean differences are shown.						

In crude Cox models, all non-reference sleep-trajectory groups had higher cardiovascular risk than the persistent optimal group. In the multivariable-adjusted model, persistent short sleep was associated with a 22% higher cardiovascular event risk compared with persistent optimal sleep (HR, 1.22; 95% CI, 1.05–1.42; $p = 0.009$) (Fig. 3). The other-pattern group had a modestly higher risk (HR, 1.15; 95% CI, 1.02–1.29; $p = 0.020$). Optimal-to-short sleep was not statistically significant (HR, 1.13; 95% CI, 0.96–1.33; $p = 0.128$), and variable short sleep was not independently associated with incident cardiovascular events after adjustment (HR, 1.03; 95% CI, 0.88–1.21; $p = 0.701$). The biomarker-adjusted sensitivity model included 7,795 participants and 1,414 events; persistent short sleep remained associated with cardiovascular events but with further attenuation (HR, 1.20; 95% CI, 1.00–1.42; $p = 0.046$), whereas variable short sleep remained non-significant (HR, 1.04; 95% CI, 0.86–1.25; $p = 0.685$).

Sensitivity analyses supported the main persistent short-sleep finding while showing that some estimates depended on the operational sleep-rule definition. In the discrete-time complementary log-log model, persistent short sleep had an HR of 1.22 (95% CI, 1.05–1.42; $p = 0.010$), closely matching the primary Cox result. In the complete three-wave sleep subset, persistent short sleep remained associated with cardiovascular events (HR, 1.24; 95% CI, 1.05–1.48; $p = 0.013$), as it did after excluding participants with any long-sleep observation (HR, 1.23; 95% CI, 1.05–1.43; $p = 0.008$). When short sleep was defined more stringently as < 5 hours, persistent short sleep was no longer significant (HR, 1.02; 95% CI, 0.83–1.25; $p = 0.863$), whereas use of a < 7 -hour threshold retained a positive association (HR, 1.19; 95% CI, 1.02–1.40; $p = 0.030$). Removing the coefficient-of-variation requirement from the persistent optimal definition did not materially change the primary estimates.

Because the residual other-pattern group combined several distinct sleep histories, we separated it into component patterns. Compared with persistent optimal sleep, other single-short patterns were associated with higher cardiovascular risk (HR, 1.20; 95% CI, 1.04–1.39; $p = 0.014$), whereas long-involved patterns (HR, 1.11; 95% CI, 0.97–1.27; $p = 0.132$) and repeated short low-variability patterns (HR,

1.09; 95% CI, 0.74–1.61; $p = 0.661$) were not statistically significant. Outcome-specific models suggested that the composite association was more apparent for stroke than for heart disease. Persistent short sleep was associated with incident stroke (HR, 1.31; 95% CI, 1.04–1.67; $p = 0.024$), whereas the corresponding heart-disease estimate was weaker and not statistically significant (HR, 1.16; 95% CI, 0.97–1.39; $p = 0.106$).

CHG was modestly associated with cardiovascular risk, although the effect size was attenuated after full baseline covariate adjustment. The CHG distribution was approximately centered near the values reported in prior CHG work, with mean 5.26, standard deviation 0.38, median 5.22, and interquartile range 5.00 to 5.46. Among 9,672 participants with CHG data, each standard-deviation increment in CHG was associated with higher event risk after adjustment for demographic and socioeconomic covariates (HR, 1.16; 95% CI, 1.11–1.21; $p < 0.001$). The association persisted after additional adjustment for lifestyle and clinical factors (HR, 1.06; 95% CI, 1.01–1.11; $p = 0.024$) and after further inclusion of sleep-trajectory indicators (HR, 1.06; 95% CI, 1.01–1.11; $p = 0.024$) (Fig. 4). In parallel adjusted models of traditional biomarkers, total cholesterol, fasting plasma glucose, LDL-C, and HbA1c were also positively associated with cardiovascular events, whereas HDL-C and C-reactive protein were not statistically significant. In joint exposure analyses, participants with high CHG and persistent short sleep had the highest cardiovascular risk (HR, 1.35; 95% CI, 1.08–1.69; $p = 0.008$) compared with low CHG and persistent optimal sleep (Fig. 4). By contrast, the corresponding estimate for high CHG plus variable short sleep was close to null (HR, 1.03; 95% CI, 0.81–1.32; $p = 0.786$).

Exploratory sex-stratified analyses suggested that the persistent short-sleep and sleep-metabolic risk signals were more prominent among women (Fig. 5). Persistent short sleep was more common in women than men (13.9% vs 10.3%), as was high CHG plus persistent short sleep (6.8% vs 3.5%). Event rates were also higher in women than men within persistent short sleep (24.0% vs 18.1%), high CHG plus persistent short sleep (27.5% vs 20.1%), and high CHG plus persistent short sleep combined with age 60 years or older or hypertension (32.2% vs 25.2%). Most importantly for distinguishing short-sleep phenotypes, persistent short sleep carried higher risk than variable short sleep within women in a direct comparison among short-sleep participants (HR, 1.30; 95% CI, 1.04–1.64; $p = 0.022$), whereas the corresponding male estimate was not statistically significant (HR, 1.06; 95% CI, 0.79–1.43; $p = 0.677$). CHG per standard-deviation increment was associated with cardiovascular events among women (HR, 1.10; 95% CI, 1.03–1.17; $p = 0.006$) but not among men (HR, 1.01; 95% CI, 0.93–1.09; $p = 0.847$), with a significant sex-by-CHG interaction ($p = 0.027$). Women with high CHG plus persistent short sleep had elevated risk (HR, 1.43; 95% CI, 1.07–1.91; $p = 0.017$). However, formal interaction tests did not support clear sex modification of the persistent-short-sleep effect or of the high-CHG/persistent-short phenotype (p for interaction = 0.926 and 0.678, respectively).

Discussion

In this prospective CHARLS analysis with follow-up through 2020 and expanded baseline covariate adjustment, persistent short sleep was the most robust sleep-trajectory predictor of incident

cardiovascular events. Operationally defined variable short sleep was associated with risk in the crude model, but the estimate was attenuated after demographic and socioeconomic adjustment and remained nonsignificant in the multivariable-adjusted model. In contrast, persistent short sleep remained associated with increased risk in the multivariable-adjusted model, the biomarker-adjusted sensitivity model, the discrete-time complementary log-log sensitivity model, and the complete three-wave sleep subset.

The finding that persistent short sleep carried the clearest risk signal is biologically plausible. Sustained sleep restriction may repeatedly activate sympathetic and hypothalamic-pituitary-adrenal pathways, impair glucose regulation, elevate blood pressure, promote inflammation, and reduce opportunities for nocturnal cardiovascular recovery [4, 11, 26, 30–32]. Objective short sleep in the setting of insomnia has also been associated with cardiometabolic morbidity and incident cardiovascular outcomes, supporting the view that chronic sleep restriction may mark a biologically consequential exposure rather than only a reporting preference [30, 31]. The stronger association for stroke than for heart disease is also compatible with the high stroke burden in older Chinese adults and with pathways involving blood pressure, metabolic dysfunction, and vascular injury, although this component-specific finding should be interpreted cautiously because outcome components were self-reported and not adjudicated.

The results also clarify the interpretation of nonpersistent sleep patterns. The residual other-pattern group contained single-short, long-involved, and repeated short low-variability subgroups, and only the single-short subgroup remained statistically significant after decomposition. Variable short sleep was deliberately narrow and was not independently associated with cardiovascular risk after adjustment. A brief methodological comparison with GBTM suggested that latent classes and the prespecified rule-based categories capture different dimensions of sleep behaviour rather than serving as one-to-one validation.

The CHG findings support a complementary metabolic-risk interpretation. CHG, calculated as $\ln[(TC \times FPG)/(2 \times HDL-C)]$, remained modestly associated with incident cardiovascular events after adjustment for demographic, socioeconomic, lifestyle, and clinical covariates as well as sleep trajectories [24, 25]. This result is consistent with a large body of evidence linking insulin resistance, dyslipidemia, metabolic syndrome, diabetes, and global cardiovascular risk to future vascular events [26–29]. The joint analysis suggested that high CHG and persistent short sleep together identified a subgroup with particularly high risk. This result should be viewed as exploratory risk stratification rather than evidence of biological interaction. The near-null estimate for high CHG plus variable short sleep further supports a cautious interpretation of variable short sleep.

The exploratory sex-stratified findings add a third layer to this interpretation. Within women, persistent short sleep was associated with higher risk than variable short sleep, which directly strengthens the central conclusion that sustained short sleep is the more clinically coherent short-sleep risk phenotype. Women also showed higher prevalence and event-rate enrichment for the high CHG plus persistent short-sleep profile, and CHG had a stronger association with cardiovascular events in women, supported

by a significant sex-by-CHG interaction. These findings suggest that persistent short sleep combined with metabolic burden may be particularly relevant for cardiovascular risk assessment among middle-aged and older women. At the same time, the non-significant sex interactions for persistent short sleep and for the joint high-CHG/persistent-short phenotype argue against claiming definitive sex modification of the sleep-trajectory effect. The female pattern should therefore be interpreted as hypothesis-generating and related to women of postmenopausal age rather than as confirmed menopausal-transition biology.

These results align partly with prior evidence linking short sleep, insomnia, sleep irregularity, and changing sleep patterns to cardiovascular disease, but they also refine the hypothesis for this Chinese aging cohort [6–18, 22]. Prior studies in Western populations have emphasized sleep irregularity or adverse sleep trajectories as risk markers, while Chinese cohort evidence has also suggested that longitudinal sleep-duration patterns may be associated with cardiovascular outcomes [14–16, 22]. Two directly related CHARLS studies should be distinguished from the present analysis: one modeled cumulative exposure and dynamic trajectories of CHG itself in relation to cardiovascular disease, and another examined short sleep among individuals with metabolic syndrome [33, 34]. By contrast, our study treated repeated sleep duration as the primary exposure, used CHG as a measured metabolic context and joint exposure rather than as the trajectory variable, and separated persistent short sleep from variable short sleep. In the present analysis, the CHARLS data pointed more strongly toward sustained short sleep than toward variability among short sleepers.

The study has several strengths. It used repeated sleep measurements across a four-year exposure window rather than a single baseline sleep report. It separated the exposure window from post-2015 follow-up and excluded participants with reported heart disease or stroke through 2015. It harmonized disease-category coding for heart disease and stroke and accounted for the different 2020 health-file variable structure. It incorporated covariates derived primarily from Harmonized CHARLS, including sex, education, residence, marital status, household economic status, measured body mass index, blood pressure, depressive symptoms, and physical activity, reducing confounding by major demographic, socioeconomic, lifestyle, and clinical factors. It also used actual blood assays to construct CHG rather than proxy imputation based on hypertension or diabetes, and added sensitivity analyses addressing interval-based follow-up, sleep-rule definitions, other-pattern heterogeneity, and component outcomes.

Several limitations remain. Sleep duration and cardiovascular events were self-reported rather than objectively measured [35], exact event dates were unavailable, and Cox models used wave-based event times; however, a complementary discrete-time model gave similar estimates. The variable short-sleep phenotype was operationally narrow and should not be interpreted as a comprehensive measure of sleep variability. Residual confounding and reverse causation cannot be fully excluded, particularly from subclinical disease or unmeasured sleep-disordered breathing, which shows well-documented sex differences in prevalence and clinical presentation [36]. Some adjusted covariates, including body mass index, blood pressure, hypertension, and diabetes, may partly lie on causal pathways, so estimates should be read as conditional associations rather than pure total effects. Menopausal status, hormone

therapy, survey weights, multiple imputation, competing-risk methods for death, clustered standard errors, and adjudicated outcomes were unavailable or not implemented. CHG dichotomization and sex-stratified analyses were exploratory and require external validation.

Conclusions

In this prospective CHARLS cohort with follow-up through 2020, persistent short sleep during 2011–2015, but not variable short sleep, was associated with incident cardiovascular events after multivariable adjustment. CHG was modestly associated with risk and identified higher-risk subgroups when combined with persistent short sleep, with particularly notable exploratory enrichment among women. These findings support focusing on sustained short sleep and cardiometabolic burden in prevention-oriented risk assessment.

Abbreviations

BMI

Body mass index

CES-D

Center for Epidemiologic Studies Depression Scale

CHARLS

China Health and Retirement Longitudinal Study

CHG

Cholesterol, high-density lipoprotein, and glucose index

CI

Confidence interval

CV

Coefficient of variation

FPG

Fasting plasma glucose

GBTM

Group-based trajectory modelling

HbA1c

Glycated haemoglobin

HDL-C

High-density lipoprotein cholesterol

HR

Hazard ratio

LDL-C

Low-density lipoprotein cholesterol

STROBE

Strengthening the Reporting of Observational Studies in Epidemiology

TC

Total cholesterol

Declarations

Ethics approval and consent to participate

The CHARLS protocol was approved by the Peking University Biomedical Ethics Review Committee (IRB00001052-11015), and all participants provided informed consent. The present study was a secondary analysis of de-identified CHARLS data.

Consent for publication

Not applicable.

Availability of data and materials

The CHARLS datasets analysed during the current study are available from the CHARLS project website (<https://charls.pku.edu.cn>) subject to registration and data-use requirements. The analysis and figure-generation code and aggregate output tables are provided in the supplementary files (Supplementary Files 1 and 2); participant-level CHARLS data are not redistributed.

Competing interests

The authors declare that they have no competing interests.

Funding

This work was supported by the Shanghai 2024 "Science and Technology Innovation Action Plan" Natural Science Foundation Project (Grant No. 24ZR1464500) and the Shanghai Xuhui District Health Commission Joint Research Program on Major Diseases (Grant No. XHLHGG202108). The funders had no role in study design, data analysis, or manuscript preparation.

Authors' contributions

ZW and XF contributed equally to this work. ZW and QS conceived and designed the study. ZW performed data management, statistical analysis, and figure preparation. XF contributed to methodology, interpretation of findings, and manuscript drafting. LC and YS contributed to clinical interpretation and

critical revision of the manuscript. QS supervised the study and critically revised the manuscript for important intellectual content. All authors read and approved the final manuscript.

Acknowledgements

The authors thank the CHARLS research team and participants for making the data available for scientific research.

References

1. Roth, G. A. et al. Global burden of cardiovascular diseases and risk factors, 1990–2019: update from the GBD 2019 Study. *J. Am. Coll. Cardiol.* **76**, 2982–3021. 10.1016/j.jacc.2020.11.010 (2020).
2. Zhao, D., Liu, J., Wang, M., Zhang, X. & Zhou, M. Epidemiology of cardiovascular disease in China: current features and implications. *Nat. Rev. Cardiol.* **16**, 203–212. 10.1038/s41569-018-0119-4 (2019).
3. Lloyd-Jones, D. M. et al. Life's Essential 8: updating and enhancing the American Heart Association's construct of cardiovascular health. *Circulation* **146**, e18–e43. 10.1161/CIR.0000000000001078 (2022).
4. St-Onge, M. P. et al. American Heart Association Obesity, Behavior Change, Diabetes, and Nutrition Committees of the Council on Lifestyle and Cardiometabolic Health. Sleep duration and quality: impact on lifestyle behaviors and cardiometabolic health: a scientific statement from the American Heart Association. *Circulation* **134**, e367–e386. 10.1161/CIR.0000000000000444 (2016).
5. Watson, N. F. et al. Recommended amount of sleep for a healthy adult: a joint consensus statement of the American Academy of Sleep Medicine and Sleep Research Society. *Sleep* **38**, 843–844. 10.5665/sleep.4716 (2015).
6. Cappuccio, F. P., Cooper, D., D'Elia, L., Strazzullo, P. & Miller, M. A. Sleep duration predicts cardiovascular outcomes: a systematic review and meta-analysis of prospective studies. *Eur. Heart J.* **32**, 1484–1492. 10.1093/eurheartj/ehr007 (2011).
7. Kwok, C. S. et al. Self-reported sleep duration and quality and cardiovascular disease and mortality: a dose-response meta-analysis. *J. Am. Heart Assoc.* **7**, e008552. 10.1161/JAHA.118.008552 (2018).
8. Krittanawong, C. et al. Association between short and long sleep durations and cardiovascular outcomes: a systematic review and meta-analysis. *Eur. Heart J. Acute Cardiovasc. Care.* **8**, 762–770. 10.1177/2048872617741733 (2019).
9. Dean, Y. E. et al. Association between insomnia and the incidence of myocardial infarction: a systematic review and meta-analysis. *Clin. Cardiol.* **46**, 376–385. 10.1002/clc.23984 (2023).
10. Wu, T. T. et al. Insomnia and multiple health outcomes: umbrella review of meta-analyses of prospective cohort studies. *Public. Health.* **215**, 66–74. 10.1016/j.puhe.2022.11.021 (2023).

11. Hall, M. H., Brindle, R. C. & Buysse, D. J. Sleep and cardiovascular disease: emerging opportunities for psychology. *Am. Psychol.* **73**, 994–1006. 10.1037/amp0000362 (2018).
12. Buysse, D. J. Sleep health: can we define it? Does it matter? *Sleep* **37**, 9–17. 10.5665/sleep.3298 (2014).
13. Li, J., Vitiello, M. V. & Gooneratne, N. S. Sleep in normal aging. *Sleep. Med. Clin.* **17**, 161–171. 10.1016/j.jsmc.2022.02.007 (2022).
14. Huang, T., Mariani, S. & Redline, S. Sleep irregularity and risk of cardiovascular events: the Multi-Ethnic Study of Atherosclerosis. *J. Am. Coll. Cardiol.* **75**, 991–999. 10.1016/j.jacc.2019.12.054 (2020).
15. Wang, Y. H. et al. Association of longitudinal patterns of habitual sleep duration with risk of cardiovascular events and all-cause mortality. *JAMA Netw. Open.* **3**, e205246. 10.1001/jamanetworkopen.2020.5246 (2020).
16. Thurston, R. C. et al. Trajectories of sleep over midlife and incident cardiovascular disease events in the Study of Women's Health Across the Nation. *Circulation* **149**, 545–555. 10.1161/CIRCULATIONAHA.123.066491 (2024).
17. Kravitz, H. M. et al. Sleep trajectories before and after the final menstrual period in the Study of Women's Health Across the Nation (SWAN). *Curr. Sleep. Med. Rep.* **3**, 235–250. 10.1007/s40675-017-0084-1 (2017).
18. Kline, C. E. et al. Associations between longitudinal trajectories of insomnia symptoms and sleep duration with objective physical function in postmenopausal women: the Study of Women's Health Across the Nation. *Sleep* **44**, zsab059. 10.1093/sleep/zsab059 (2021).
19. Zhao, Y., Hu, Y., Smith, J. P., Strauss, J. & Yang, G. Cohort profile: the China Health and Retirement Longitudinal Study. *Int. J. Epidemiol.* **43**, 61–68. 10.1093/ije/dys203 (2014).
20. Strauss, J. et al. Health outcomes and socio-economic status among the elderly in China: evidence from the CHARLS pilot. *J. Popul. Ageing.* **3**, 111–142. 10.1007/s12062-011-9033-9 (2010).
21. Gateway to Global Aging Data, Harmonized, C. H. A. R. L. S. & Documentation, V. D. Los Angeles: Center for Economic and Social Research, University of Southern California; (2023).
22. Liu, H. et al. Subsequent hypertension's mediation of the association between sleep duration trajectories and new-onset cardiovascular disease: population-based cohort study. *JMIR Aging.* **9**, e78914. 10.2196/78914 (2026).
23. Radloff, L. S. The CES-D scale: a self-report depression scale for research in the general population. *Appl. Psychol. Meas.* **1**, 385–401. 10.1177/014662167700100306 (1977).
24. Mansoori, A. et al. A novel index for diagnosis of type 2 diabetes mellitus: cholesterol, high density lipoprotein, and glucose (CHG) index. *J. Diabetes Investig.* **16**, 309–314. 10.1111/jdi.14343 (2025).
25. Mo, D., Zhang, P., Zhang, M., Dai, H. & Guan, J. Cholesterol, high-density lipoprotein, and glucose index versus triglyceride-glucose index in predicting cardiovascular disease risk: a cohort study. *Cardiovasc. Diabetol.* **24**, 116. 10.1186/s12933-025-02675-y (2025).

26. Reaven, G. M. Banting lecture 1988. Role of insulin resistance in human disease. *Diabetes* **37**, 1595–1607. 10.2337/diab.37.12.1595 (1988).
27. Grundy, S. M. et al. American Heart Association; National Heart, Lung, and Blood Institute. Diagnosis and management of the metabolic syndrome: an American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement. *Circulation* **112**, 2735–2752. 10.1161/CIRCULATIONAHA.105.169404 (2005).
28. Collaboration, E. R. F. et al. Diabetes mellitus, fasting blood glucose concentration, and risk of vascular disease: a collaborative meta-analysis of 102 prospective studies. *Lancet* **375**, 2215–2222. 10.1016/S0140-6736(10)60484-9 (2010).
29. Goff, D. C. Jr et al. 2013 ACC/AHA guideline on the assessment of cardiovascular risk. *Circulation* **129**, S49–S73. 10.1161/01.cir.0000437741.48606.98 (2014).
30. Johnson, K. A. et al. The association of insomnia disorder characterised by objective short sleep duration with hypertension, diabetes and body mass index: a systematic review and meta-analysis. *Sleep. Med. Rev.* **59**, 101456. 10.1016/j.smr.2021.101456 (2021).
31. Bertisch, S. M. et al. Insomnia with objective short sleep duration and risk of incident cardiovascular disease and all-cause mortality: Sleep Heart Health Study. *Sleep* **41**, zsy047. 10.1093/sleep/zsy047 (2018).
32. Medic, G., Wille, M. & Hemels, M. E. H. Short- and long-term health consequences of sleep disruption. *Nat. Sci. Sleep.* **9**, 151–161. 10.2147/NSS.S134864 (2017).
33. Zhang, Y. et al. Associations of cumulative exposure and dynamic trajectories of cholesterol-HDL-glucose (CHG) index with cardiovascular disease in middle-aged and older Chinese adults: a longitudinal analysis. *Cardiovasc. Diabetol.* **25**, 88. 10.1186/s12933-026-03137-9 (2026).
34. Sun, J., Chen, Y., Sun, Y., Yang, B. & Zhou, J. Short sleep duration associated with increased risk for new-onset cardiovascular diseases in individuals with metabolic syndromes: evidence from the China Health and Retirement Longitudinal Study. *Front. Cardiovasc. Med.* **9**, 1010941. 10.3389/fcvm.2022.1010941 (2022).
35. Lehrer, M. et al. Comparing polysomnography, actigraphy, and sleep diary in the home environment: the Study of Women's Health Across the Nation Sleep Study. *Sleep. Adv.* **3**, zpac001. 10.1093/sleepadvances/zpac001 (2022).
36. Bonsignore, M. R., Saareanta, T. & Riha, R. L. Sex differences in obstructive sleep apnoea. *Eur. Respir Rev.* **28**, 190030. 10.1183/16000617.0030-2019 (2019).

Figures

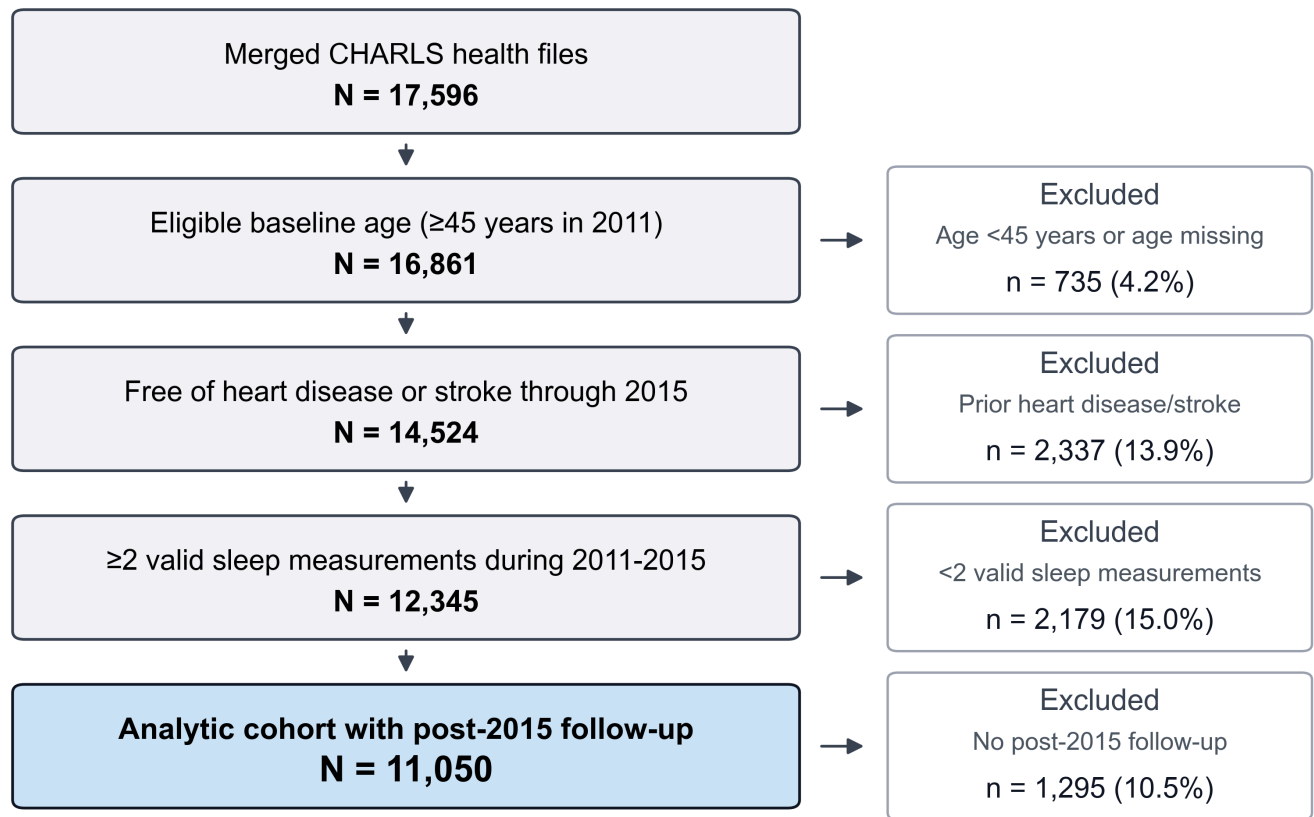


Figure 1

Study flow diagram. The analytic cohort was anchored at the 2011 CHARLS health-status file. Participants were excluded if they were younger than 45 years when age was observed, had reported heart disease or stroke through 2015, had fewer than two valid sleep measurements during 2011-2015, or lacked post-2015 follow-up.

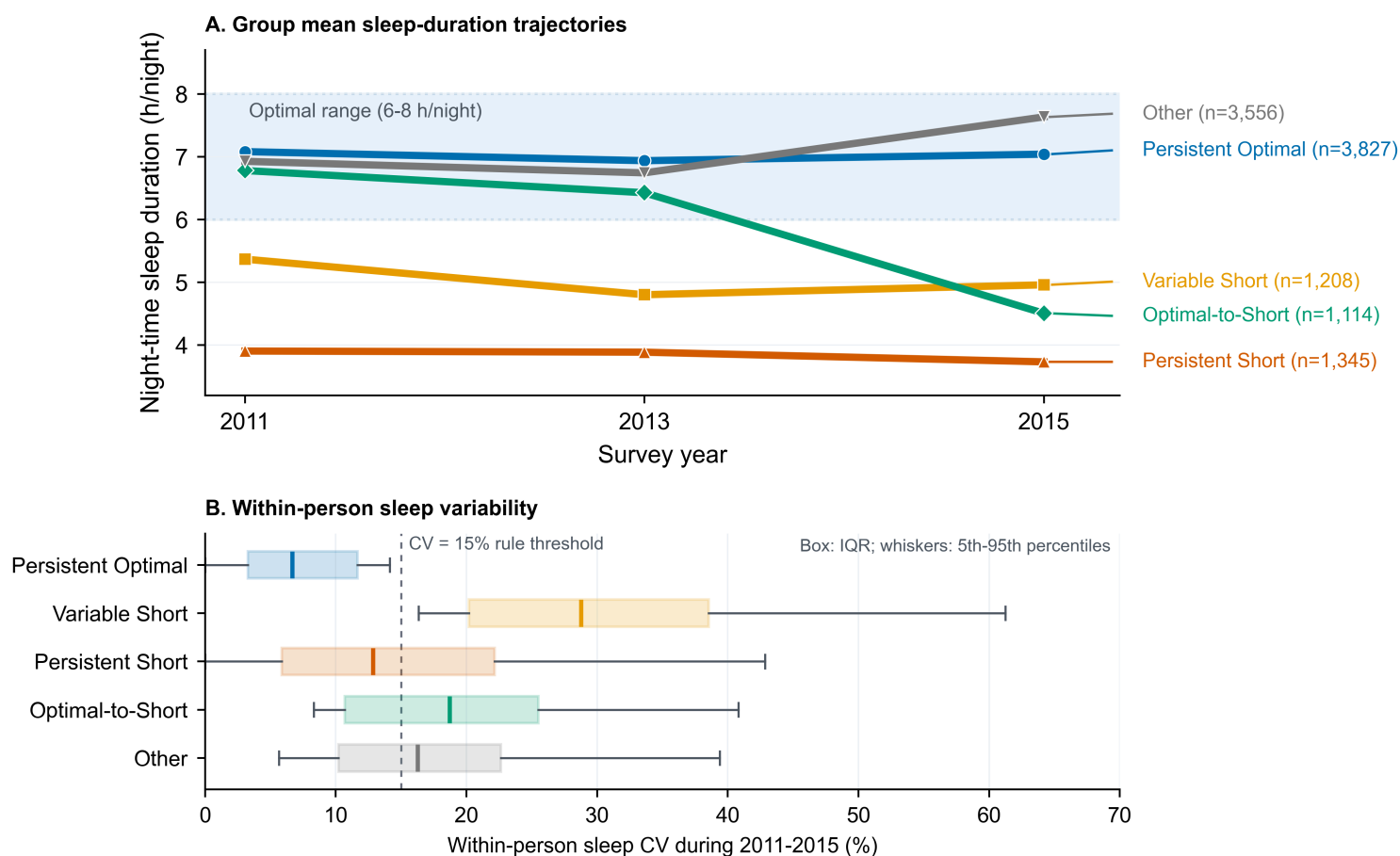


Figure 2

Sleep-duration trajectory profiles and within-person variability. Panel A shows group-specific mean night-time sleep duration. The shaded region indicates the prespecified optimal sleep-duration range of 6-8 hours per night. Panel B shows the distribution of within-person sleep coefficient of variation (CV, %) calculated across available 2011-2015 sleep measurements using the same formula as the trajectory-classification rule. Because group-mean curves can mask individual-level fluctuation, within-person variability is shown separately in Panel B.

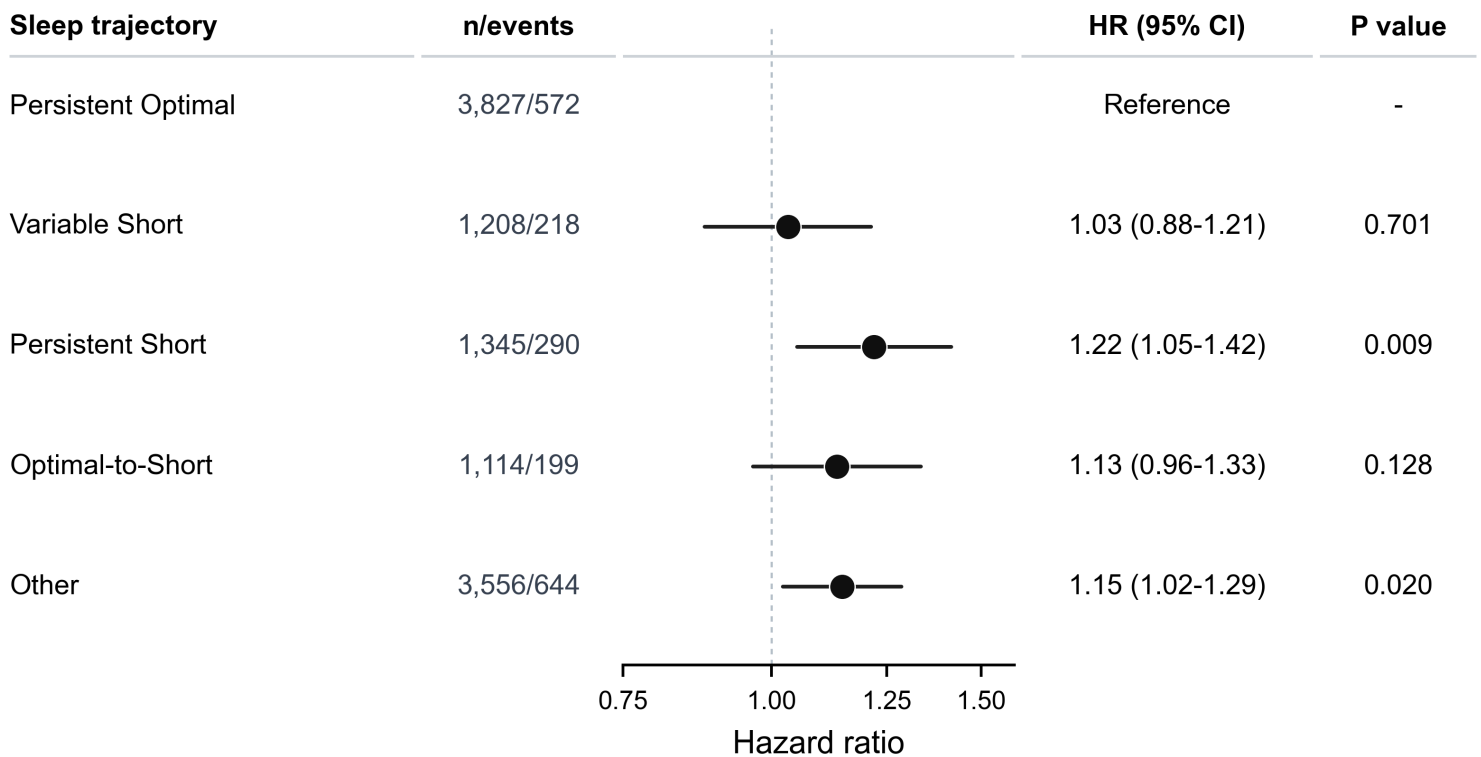
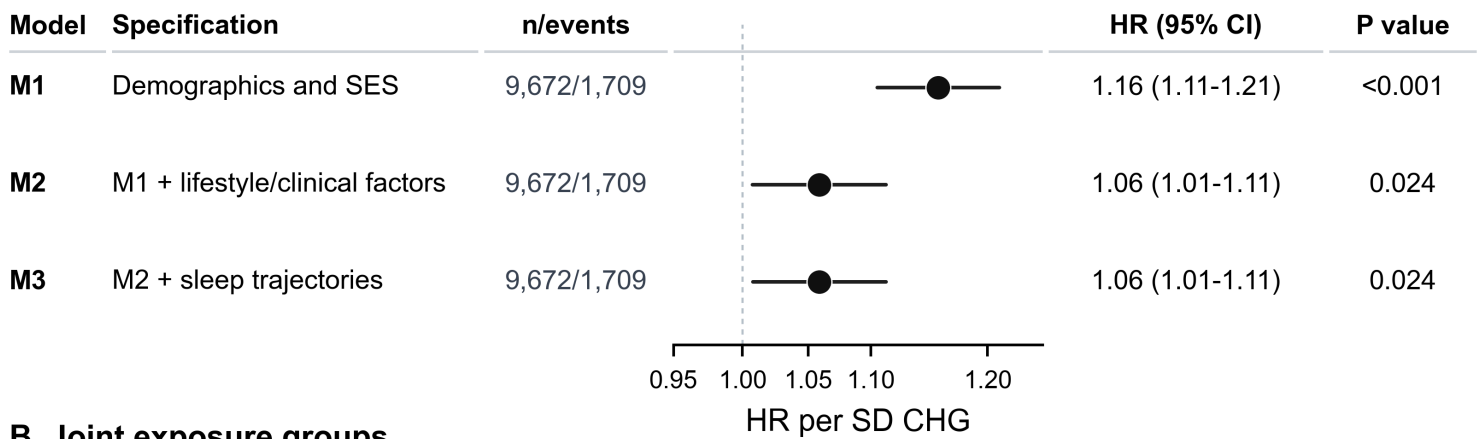


Figure 3

Adjusted associations between sleep trajectories and incident cardiovascular events. Hazard ratios were estimated from the multivariable-adjusted Cox model adjusted for baseline age, sex, education, rural residence, marital status, household wealth and income, smoking, drinking, body mass index, systolic and diastolic blood pressure, depressive symptoms, physical activity, hypertension, and diabetes. Persistent optimal sleep was the reference group.

A. CHG across nested models



B. Joint exposure groups

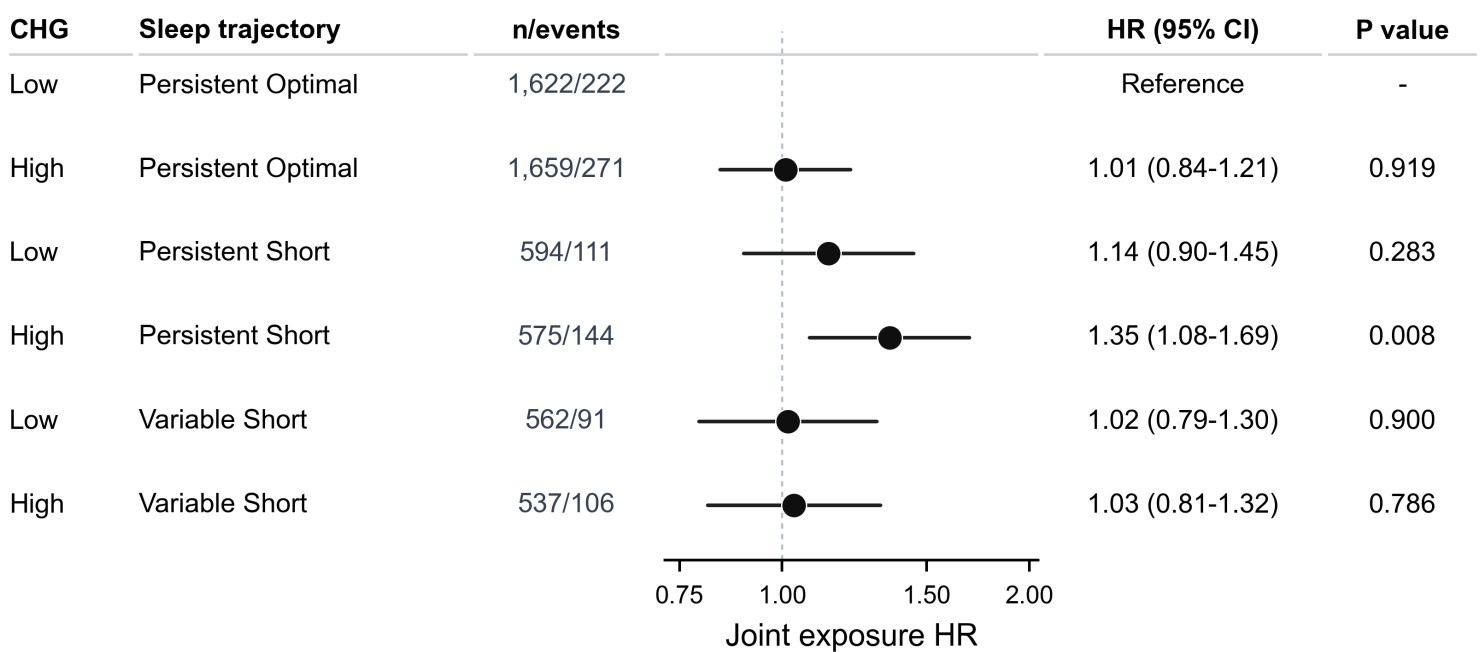


Figure 4

CHG and joint sleep-metabolic risk. The figure shows hazard ratios per standard-deviation increment in CHG across nested models together with joint risk groups defined by CHG above or below the median and persistent short sleep or variable short sleep, using low CHG plus persistent optimal sleep as the reference.

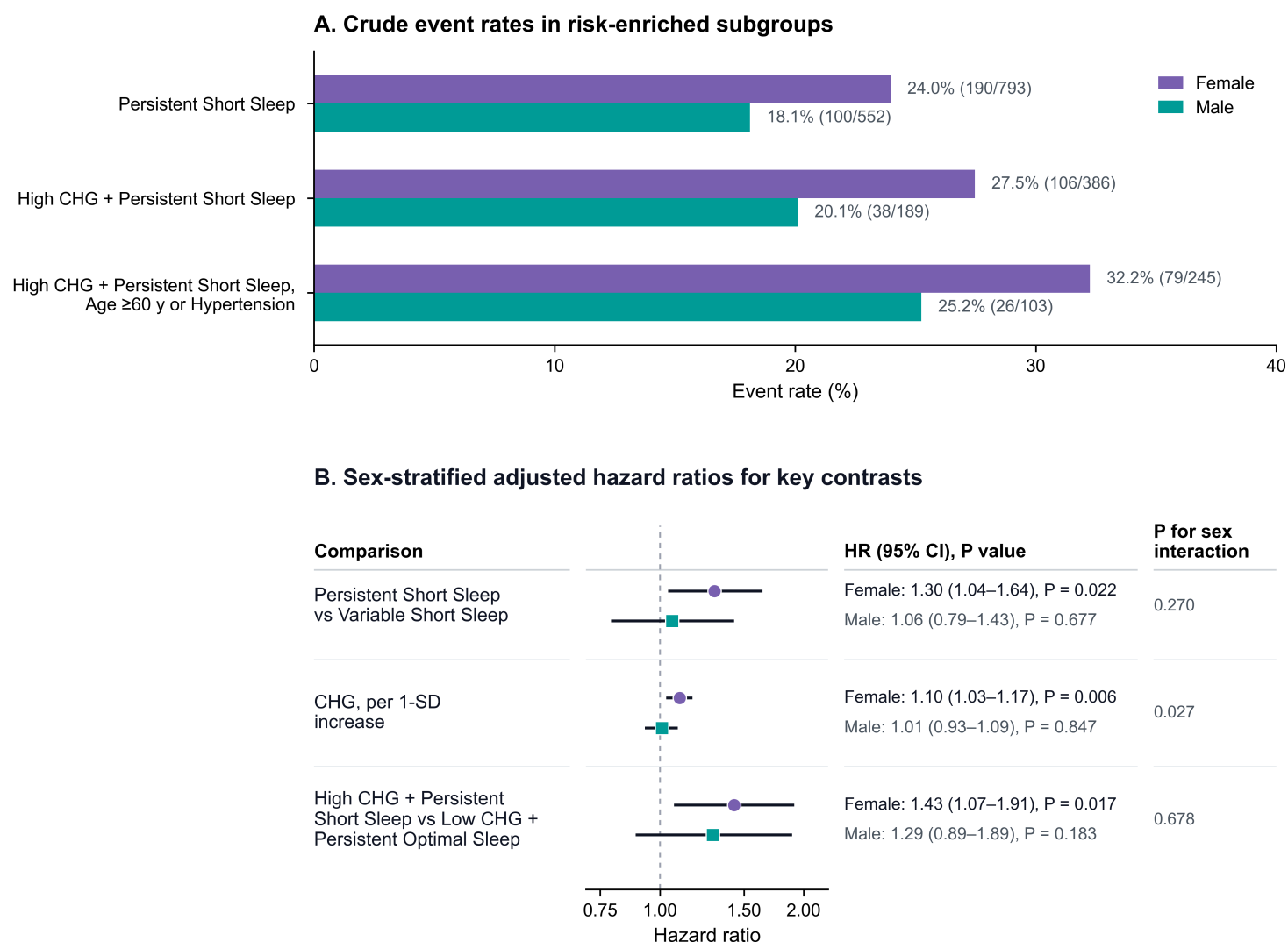


Figure 5

Exploratory sex-stratified sleep-metabolic risk analyses. Panel A shows crude post-2015 event rates in risk-enriched subgroups, stratified by sex. Panel B shows sex-stratified adjusted hazard ratios from Cox proportional hazards models for key contrasts. Purple markers and bars indicate female participants; teal markers and bars indicate male participants. The joint exposure reference group was low CHG plus persistent optimal sleep. For the persistent-short versus variable-short contrast, the sex-interaction P value was estimated in the restricted short-sleep subset with variable short sleep as the reference. The sex-stratified analyses were exploratory, and menopausal status was not directly measured.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [SupplementaryFile2Tables.xlsx](#)