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Research Article

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Sleep Characteristics and Incident Cardiovascular-Kidney-Metabolic Multimorbidity Among Postmenopausal Women: A Longitudinal Cohort Analysis of CHARLS

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Abstract

Background:

Sleep complaints often accompany the metabolic and vascular changes of menopause. We examined the associations between baseline sleep characteristics and incident cardiovascular-kidney-metabolic (CKM) multimorbidity in Chinese postmenopausal women.

Methods:

This analysis included 5,238 postmenopausal women aged ≥45 years from the China Health and Retirement Longitudinal Study (CHARLS) who were free of CKM multimorbidity at the 2011–2012 baseline. Baseline questionnaires provided information on nighttime sleep duration, daytime napping duration, and sleep quality assessed by restless-sleep frequency. Incident CKM multimorbidity was identified at the 2013, 2015, or 2018 follow-up when reported physician-diagnosed conditions

were present in at least two of the cardiovascular, kidney, and metabolic domains. Cox regression estimated associations; spline terms and stratification examined exposure-response patterns and heterogeneity. Additional analyses used an exploratory matched sample and excluded events first detected in 2013. Three survival models were tuned using fivefold cross-validation in a 70% development set and evaluated in the remaining 30% test set. Shapley additive explanations (SHAP) described their predictor contributions.

Results:

CKM multimorbidity was first identified during follow-up in 216 women. With full covariate adjustment, the hazard ratio (HR) for one additional hour of nightly sleep was 0.89 (95% confidence interval [CI] 0.83–0.95). Short sleepers (<6 h) had an HR of 1.47 (95% CI 1.11–1.95) relative to women sleeping 6 to <9 h; the ≥9 h comparison was nonsignificant. Poor sleep quality carried an HR of 1.86 (95% CI 1.41–2.43) relative to good quality. The nighttime spline supported an overall association, with no detectable nonlinear component. Findings for daytime napping differed between the continuous and categorical analyses and across the sensitivity analyses. Nighttime sleep and sleep quality estimates persisted after removal of the earliest cases. XGBoost had the highest observed test-set concordance index (0.7095); SHAP rankings for the sleep measures differed between algorithms.

Conclusions:

Short nighttime sleep duration and frequent restless sleep were associated with a higher hazard of incident CKM multimorbidity in this postmenopausal cohort.

Evidence for napping was inconsistent. Whether sleep interventions change that hazard requires direct testing.

Keywords: Postmenopausal women; Sleep duration; Daytime napping; Sleep quality; Cardiovascular-kidney-metabolic multimorbidity; CHARLS

1. Introduction

Cardiovascular, kidney, and metabolic disorders share biological pathways and often coexist within the same individual[1,2]. Their combined burden complicates prevention and clinical management[1]. Population studies have operationalized cardiovascular-kidney-metabolic (CKM) multimorbidity using indicators of disease in the cardiovascular system, kidneys and metabolic domain. Its emergence can be traced in longitudinal datasets such as the China Health and Retirement Longitudinal Study (CHARLS) [3].

This clustering of cardiometabolic and renal disorders is particularly relevant in postmenopausal women, who experience marked hormonal and metabolic changes after menopause, including increased visceral adiposity, impaired glucose metabolism, elevated blood pressure, and vascular dysfunction[4–6]. Identifying modifiable factors associated with incident CKM multimorbidity in this population may therefore contribute to early prevention strategies.

Prospective evidence links sleep habits with a broad range of health outcomes, although the direction and shape of associations depend on the endpoint[7].

Cardiovascular cohort syntheses have reported excess risk at both extremes of sleep duration in some populations[8] while shorter sleep has predicted hypertension, especially in women and younger adults[9]. Reviews of metabolic outcomes report associations with metabolic syndrome, diabetes and lipid abnormalities[10–12]. Renal studies also implicate unusually short or long sleep in chronic kidney disease (CKD) and proteinuria[13,14]. These findings motivate examination of sleep alongside disease accumulation across organ systems.

Sleep complaints become common during the transition to menopause[15]. Findings from the Study of Women's Health Across the Nation (SWAN) linked subsequent cardiovascular events to persistent insomnia, including insomnia accompanied by short sleep[4]. Women's Health Initiative (WHI) analyses related insomnia and sleep duration to metabolic syndrome in women after menopause[16]. Evidence from reproductive endocrine disorders further suggests that hormonal status may shape the relationship between sleep and cardiometabolic health[17].

Recent work has addressed sleep and multimorbidity directly. Wang and colleagues examined sleep measures in three cohorts (CHARLS, ELSA and HRS) using a cardiometabolic outcome without a renal component[18]. Wang and Tang investigated longitudinal sleep patterns in relation to cardio-renal-metabolic multimorbidity (CRMM) using Chinese and European cohorts[19]. Xu and colleagues subsequently studied sleep trajectories in postmenopausal CHARLS participants[20]. Our analysis complements this evidence by examining three baseline measures (nighttime sleep duration, daytime napping duration, and restless sleep frequency) in relation to a

CKM endpoint defined across disease domains. We estimated associations with events detected during 2013–2018 and explored how these measures contributed to survival predictions.

2. Methods

2.1 Data source and study population

This study used data from the China Health and Retirement Longitudinal Study (CHARLS), a nationally representative longitudinal cohort of Chinese adults aged 45 years and older and their spouses[21]. We used baseline data collected in 2011–2012 and follow-up data from 2013, 2015, and 2018.

The baseline dataset used for this analysis included 17,705 participants. After excluding 775 participants aged <45 years, 16,930 remained. Eligibility for the postmenopausal sample was based on available age-at-menopause information. This requirement excluded 11,141 participants, leaving 5,789 women. We excluded 114 women with CKM multimorbidity at baseline, leaving 5,675. A further 334 women were excluded because CKM outcome information was missing at all three follow-up waves, and 103 because at least one baseline sleep measure was missing. The final analytic cohort comprised 5,238 women (Fig. 1).

The CHARLS study protocol was approved by the Biomedical Ethics Review Committee of Peking University (IRB00001052-11015), and all participants provided written informed consent. The present study was a secondary analysis of de-identified CHARLS data and involved no new participant recruitment, direct contact with participants, or primary data collection.

2.2 Assessment of sleep characteristics

Sleep assessment drew on three items in the CHARLS baseline questionnaire, documented in the survey's official users' guide[22]. The items concerned sleep at night, naps after lunch and restless sleep.

For nighttime sleep, respondents recalled their average actual hours slept nightly over the previous month. Nighttime sleep duration was analyzed as a continuous variable in hours and in three categories: <6 h, 6 to <9 h, and ≥9 h, with 6 to <9 h as the reference.

The nap item recorded usual post-lunch duration over that same month. Daytime napping duration was analyzed as a continuous variable in minutes and in three categories: 0 min, 0–30 min, and >30 min. Here, 0–30 min denotes a positive duration up to and including 30 min.

Participants reporting no daytime napping (0 min) served as the reference group. A single item on restless sleep during the preceding week was used as a proxy measure of sleep quality, as in earlier CHARLS work[23]. Responses were coded as 1 for rarely or none of the time (<1 day), 2 for some or a little of the time (1–2 days), 3 for occasionally or a moderate amount of the time (3–4 days), and 4 for most or all of the time (5–7 days). Higher scores indicated more frequent restless sleep and poorer sleep quality. For categorical analyses, scores of 1–2 defined good sleep quality, and scores of 3–4 defined poor sleep quality. The eligibility rules in Section 2.1 required all three measurements.

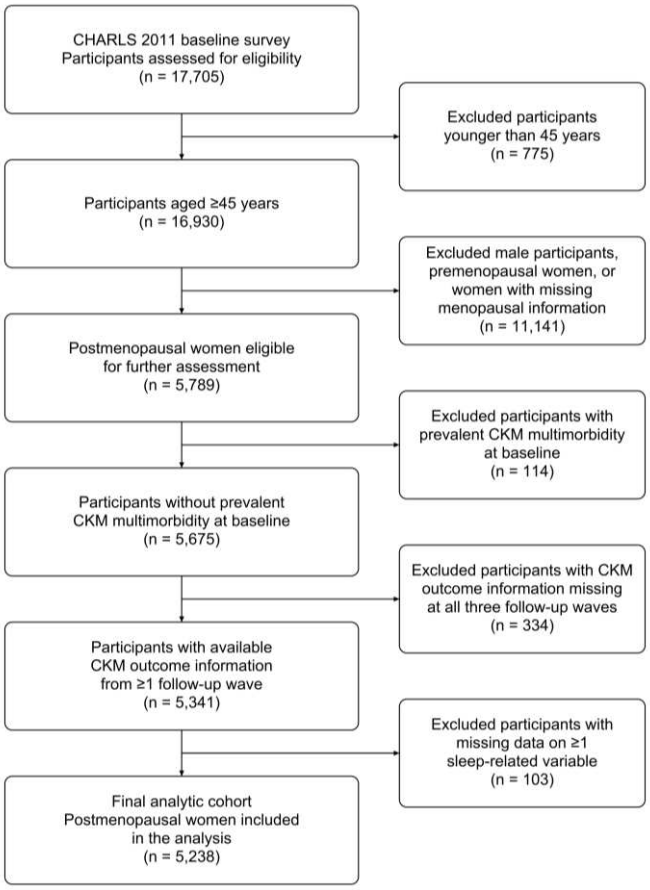


Fig. 1. Participant selection for the analytic cohort. Eligibility for the postmenopausal sample was based on available age-at-menopause information. Women with CKM multimorbidity at baseline, missing CKM outcome information at all three follow-up waves, or missing data on at least one baseline sleep measure were excluded. The final cohort included 5,238 women. CHARLS, China Health and Retirement Longitudinal Study; CKM, cardiovascular-kidney-metabolic.

2.3 Definition of outcomes

2.3.1 CKM multimorbidity definition

CKM multimorbidity was defined as the presence of conditions in at least two of the cardiovascular, kidney, and metabolic domains at a survey assessment, consistent with previous CHARLS operational definitions[1,3]. The component conditions were based on participants' reports of physician diagnoses. The cardiovascular domain included heart disease or stroke, and the kidney domain included kidney disease. The metabolic domain included dyslipidemia, hypertension, or diabetes/high blood

glucose.

2.3.2 Incident CKM multimorbidity

Eligibility required the absence of baseline CKM multimorbidity. Incident status was assigned at the first survey documenting that a woman met the CKM definition. Event time was the elapsed interval between baseline and that survey. If no available record indicated an event, censoring was assigned to 2018, the planned final assessment, including women whose last observed CKM record came from an earlier wave.

2.4 Covariates

Covariate selection reflected relevance to sleep and CKM, together with availability of baseline data. Sociodemographic measures were age (years), residence (rural or urban), annual per-capita household consumption expenditure, education and marital status. Educational attainment was grouped as elementary school or below versus middle school or above. The marital categories distinguished living with a spouse, being married but living apart, and being single, divorced, widowed or separated. Behavioral covariates comprised smoking (never, former, current) and alcohol use (never, less than monthly, at least monthly). Health measures comprised body mass index (BMI) and separate yes/no indicators for antihypertensive, antidiabetic and lipid-lowering medication. BMI was modeled as a continuous variable in the primary Cox analyses and categorized for subgroup analyses. Menopausal-age categories entered the subgroup and exploratory prediction analyses.

2.5 Statistical analysis

R 4.4.0 was used throughout. Eligibility depended on complete sleep measurements

and at least one follow-up record permitting CKM ascertainment, as described in Section 2.1. Missing covariate values were imputed using random forest models within the chained-equations framework implemented in the mice package. Descriptive summaries and Cox-based association analyses used the first completed dataset from this imputation, without pooling estimates. In that workflow, BMI entries above 100 were divided by 100. The threshold for nominal significance was $P<0.05$, using two-sided tests.

2.5.1 Baseline characteristics

Descriptive summaries covered the whole cohort and the two groups defined by follow-up event identification. Continuous measures were expressed with means and standard deviations (SDs), except household consumption expenditure, summarized by its median and interquartile range (IQR). Categorical summaries used frequencies and percentages. Between-group comparisons used t tests for continuous variables other than household consumption expenditure, a Wilcoxon rank-sum test for expenditure, and chi-square tests for categorical variables.

2.5.2 Cox regression analyses

Within each sleep category, we plotted $1 - S(t)$, where $S(t)$ was estimated by Kaplan-Meier analysis. Log-rank testing compared the curves.

Cox proportional hazards regression quantified the sleep associations, expressed as hazard ratios (HRs) with 95% confidence intervals (CIs). The three sleep measures were entered as numeric terms, with HRs reported per 1 h increase in nighttime sleep duration, per 1 min increase in daytime napping duration, and per 1-point increase in

sleep quality score. Separate models used the categories defined in Section 2.2. The crude model was unadjusted. Model 1 included residence, age, annual per-capita household consumption expenditure, marital status and education. Model 2 retained these variables and added BMI, drinking, smoking and the antihypertensive, antidiabetic and lipid-lowering medication indicators.

2.5.3 Restricted cubic spline analyses

We examined the form of the nighttime-sleep and nap associations using restricted cubic splines (RCS), retaining the Model 2 adjustment set. Empirical exposure percentiles determined knot placement. Nighttime knots were 3, 6, 7 and 9 h. The nap distribution placed both its fifth and thirty-fifth percentiles at zero; the resulting distinct knots were 0, 30 and 120 min. Each exposure's median anchored HR=1.00. Tests were performed for the overall association and nonlinearity. RCS was not applied to the four-point ordinal sleep-quality measure.

2.5.4 Subgroup analyses

Separate stratified analyses explored heterogeneity for the nighttime, nap and restless-sleep measures. HRs corresponded to increments of 1 h, 1 min and 1 point, respectively. Stratification used age (<60 or ≥60 years); menopausal age (<40 [premature], 40–44 [early], 45–49, 50–55, or >55 [late] years); drinking, marital and smoking status; BMI category; and each medication indicator. BMI categories were underweight (<18.5 kg/m²), normal weight (18.5 to <24.0 kg/m²), overweight (24.0 to <28.0 kg/m²), and obesity (≥28.0 kg/m²).

For each stratification, adjustment included annual per-capita household consumption

expenditure and all other stratifying variables. The variable defining that stratum was omitted. Interactions were tested by including the corresponding sleep measure-by-subgroup interaction term. Subgroup-specific HRs and 95% CIs were displayed in forest plots. Interaction P values remained uncorrected for multiplicity because these analyses were exploratory.

2.5.5 Exploratory survival machine-learning analysis

The exploratory prediction workflow used a separate exported dataset. The survival outcome comprised CKM multimorbidity event status and follow-up time. Candidate predictors included age, menopausal-age category, residence, education, marital status, drinking status, smoking status, annual per-capita household consumption expenditure, BMI, the three sleep measures, and indicators of antihypertensive, antidiabetic, and lipid-lowering medication use. Identifiers were removed; categorical features retained their numeric codes. In this export, smoking distinguished never-smokers from former or current smokers combined, and BMI retained its original entries. The prediction file contained no missing values when records were randomly allocated to development (70%) and testing (30%), using seed 42.

We fitted random survival forest (RSF), XGBoost using survival:cox, and a gradient boosting machine (GBM) with Cox loss. Tuning used five cross-validation folds drawn from development records: concordance guided RSF and GBM selection, while XGBoost minimized Cox negative log-likelihood. The selected models were refitted in the full development set and evaluated in the test set using the C-index. Shapley additive explanations (SHAP) summarized predictions for the first 200

development observations. SHAP values for RSF and GBM were estimated using 50 Monte Carlo repetitions, whereas XGBoost SHAP values were obtained from its native feature-contribution output. Beeswarm displays and mean absolute SHAP rankings described predictions within each algorithm.

2.5.6 Sensitivity analyses

Two supplementary analyses examined stability of the primary estimates. For the exploratory matched analysis, participants were grouped according to whether CKM multimorbidity was identified during follow-up. Covariate-balancing propensity scores (CBPS) were estimated from residence, age, annual per-capita household consumption expenditure, marital status and education. Greedy nearest-neighbor matching selected up to five women without an identified event per case, without replacement. The caliper setting was 0.2, with its scaling left at the MatchIt default. The average treatment effect on the treated (ATT) setting designated cases as the focal group; it did not confer a causal interpretation on this outcome-based comparison. Balance was summarized by absolute standardized mean differences (SMDs) before matching and afterward, using <0.10 as the criterion. The crude, Model 1, and Model 2 Cox models were refitted in the matched sample using the same numeric and categorical forms of the sleep measures as in the primary analyses.

The other analysis removed women whose CKM event was first detected in 2013 to examine the possible influence of reverse causation. We re-estimated the primary Cox specifications in the remaining sample.

3. Results

3.1 Baseline characteristics

There were 5,238 postmenopausal women in the analysis. CKM multimorbidity was first identified during follow-up in 216 women; no event was identified in the available follow-up records for the remaining 5,022. At study entry, age averaged 60.8 years and BMI averaged 23.8 kg/m² (Table 1).

Urban residence accounted for 47.2% of the incident group and 39.2% of the group with no identified event (P=0.022). Median per-capita household consumption expenditure was 5,312.0 and 4,667.8, respectively (P=0.014), while mean BMI was 24.9 and 23.8 kg/m² (P<0.001). Use of antidiabetic therapy occurred in 9.7% versus 3.8% (P < 0.001). The corresponding proportions were 9.7% versus 4.9% for lipid-lowering therapy (P=0.002) and 40.3% versus 21.1% for antihypertensive therapy (P<0.001).

There were no statistically significant between-group differences in smoking status, education, age, drinking status, or marital status. Mean nighttime sleep was 5.7 h in women with an incident event and 6.1 h in the comparison group (P=0.002). Mean sleep quality scores were 2.7 in women with incident CKM multimorbidity and 2.2 in those without an identified event (P<0.001).

Table 1. Baseline characteristics according to incident CKM multimorbidity status.

Characteristics	Category	Overall	No identified incident CKM multimorbidity	Incident CKM multimorbidity	P value
Total, n		5238	5022	216	-
Residence, n (%)	Rural	3167 (60.5)	3053 (60.8)	114 (52.8)	0.022
	Urban	2071 (39.5)	1969 (39.2)	102 (47.2)	
Marital status, n (%)	Married and living with a spouse	4090 (78.1)	3919 (78.0)	171 (79.2)	0.915

Characteristics	Category	Overall	No identified incident CKM multimorbidity	Incident CKM multimorbidity	P value
	Married but not living with a spouse	240 (4.6)	231 (4.6)	9 (4.2)	
	Single, divorced, widowed, or separated	908 (17.3)	872 (17.4)	36 (16.7)	
Education level, n (%)	Elementary school or below	4228 (80.7)	4058 (80.8)	170 (78.7)	0.498
	Middle school or above	1010 (19.3)	964 (19.2)	46 (21.3)	
Drinking status, n (%)	Never	4752 (90.7)	4549 (90.6)	203 (94.0)	0.236
	Less than once a month	244 (4.7)	237 (4.7)	7 (3.2)	
	At least once a month	242 (4.6)	236 (4.7)	6 (2.8)	
Smoking status, n (%)	Non-smoker	4788 (91.4)	4597 (91.5)	191 (88.4)	0.066
	Ex-smoker	107 (2.0)	98 (2.0)	9 (4.2)	
	Current smoker	343 (6.5)	327 (6.5)	16 (7.4)	
Antidiabetic medication use, n (%)	No	5026 (96.0)	4831 (96.2)	195 (90.3)	<0.001
	Yes	212 (4.0)	191 (3.8)	21 (9.7)	
Lipid-lowering medication use, n (%)	No	4973 (94.9)	4778 (95.1)	195 (90.3)	0.002
	Yes	265 (5.1)	244 (4.9)	21 (9.7)	
Antihypertensive medication use, n (%)	No	4092 (78.1)	3963 (78.9)	129 (59.7)	<0.001
	Yes	1146 (21.9)	1059 (21.1)	87 (40.3)	
Nighttime sleep duration, h, mean (SD)		6.1 (2.0)	6.1 (2.0)	5.7 (1.9)	0.002
Daytime napping duration, min, mean (SD)		27.3 (40.2)	27.5 (40.4)	23.8 (36.5)	0.194
Sleep quality score, mean (SD)		2.3 (1.2)	2.2 (1.2)	2.7 (1.2)	<0.001
Age, years, mean (SD)		60.8 (8.5)	60.8 (8.6)	61.4 (7.5)	0.337
BMI, kg/m^2, mean (SD)		23.8 (4.1)	23.8 (4.1)	24.9 (4.4)	<0.001
Household per capita consumption expenditure, median [IQR]		4695.0 [2701.7, 8446.7]	4667.8 [2691.2, 8440.0]	5312.0 [3104.4, 9222.5]	0.014

Note. Categorical entries give n (%). Continuous entries give mean (SD), except consumption expenditure, shown as median [IQR]. Comparisons applied chi-square testing to categories, a Wilcoxon rank-sum test to expenditure, and t tests to the other continuous measures. Sleep quality was scored from restless-sleep frequency; larger numbers indicate more frequent disturbance. CKM, cardiovascular-kidney-metabolic; BMI, body mass index; SD, standard deviation; IQR, interquartile range.

3.2 Cumulative incidence of CKM multimorbidity

Fig. 2 displays the unadjusted event curves for each sleep measure.

Cumulative-incidence curves differed across nighttime sleep categories (log-rank P=0.019), with the highest curve observed in the <6 h group (Fig. 2A). For daytime napping, the log-rank result did not provide evidence of a difference among groups

(P=0.42; Fig. 2B). Curves for the two sleep-quality categories differed, with greater cumulative incidence in the poor-quality group (P<0.0001; Fig. 2C).

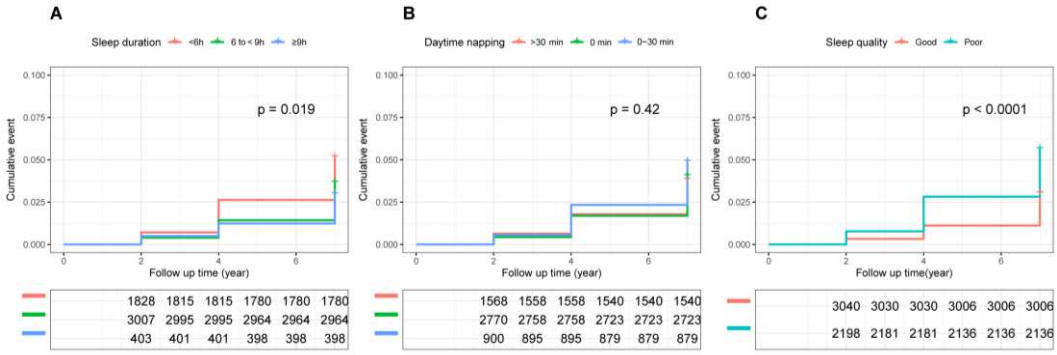


Fig. 2. Cumulative incidence of CKM multimorbidity according to baseline sleep characteristics. (A) Nighttime sleep duration (<6 h, 6 to <9 h, and ≥9 h); (B) daytime napping duration (0 min, 0-30 min, and >30 min); and (C) sleep quality (good, scores 1-2; poor, scores 3-4). The 0-30 min napping category includes durations >0 and ≤30 min. Curves show 1 − S(t), where S(t) was estimated using the Kaplan-Meier method. P values were obtained from log-rank tests comparing the groups within each panel. Numbers at risk are shown below each panel; CKM, cardiovascular-kidney-metabolic.

3.3 Associations between sleep characteristics and incident CKM multimorbidity

Adjusted Cox estimates appear in Table 2. Model 2 yielded an HR of 0.89 for every additional hour of nighttime sleep (95% CI, 0.83-0.95; P<0.001). With 6 to <9 h as the reference, the hazard was elevated for <6 h (HR, 1.47; 95% CI, 1.11–1.95; P=0.007). The estimate for the ≥9 h group was imprecise and nonsignificant (HR, 0.88; 95% CI, 0.48–1.60; P=0.666).

For nap length as a continuous measure, Model 2 produced an HR of 0.997 per minute (95% CI, 0.993-1.000; P=0.066). Relative to no napping, estimates were 1.08 for 0-30 min (95% CI, 0.76-1.53; P=0.676) and 0.84 for >30 min (95% CI, 0.61-1.15; P=0.284).

Each one-point increment in the restless-sleep score corresponded to an HR of 1.33 (95% CI, 1.19–1.49; P<0.001). Categorically, poor sleep quality versus good quality

gave an HR of 1.86 (95% CI, 1.41-2.43; P<0.001).

Table 2. Associations between baseline sleep characteristics and incident CKM multimorbidity.

Exposure	Category	Crude	P value	Model 1	P value	Model 2	P value
Nighttime sleep duration	Per 1 h increase	0.90 (0.84–0.96)	0.002	0.90 (0.84–0.96)	0.001	0.89 (0.83–0.95)	<0.001
	6 to <9 h	1.00 (Reference)	–	1.00 (Reference)	–	1.00 (Reference)	–
	<6 h	1.42 (1.08–1.87)	0.012	1.46 (1.10–1.93)	0.008	1.47 (1.11–1.95)	0.007
	≥9 h	0.81 (0.45–1.47)	0.493	0.85 (0.47–1.55)	0.604	0.88 (0.48–1.60)	0.666
Daytime napping duration	Per 1 min increase	0.998 (0.994–1.001)	0.197	0.997 (0.994–1.001)	0.157	0.997 (0.993–1.000)	0.066
	0 min	1.00 (Reference)	–	1.00 (Reference)	–	1.00 (Reference)	–
	0–30 min	1.22 (0.86–1.72)	0.272	1.17 (0.82–1.65)	0.393	1.08 (0.76–1.53)	0.676
	>30 min	0.95 (0.69–1.30)	0.732	0.92 (0.67–1.26)	0.620	0.84 (0.61–1.15)	0.284
Sleep quality score	Per 1-point increase	1.34 (1.20–1.50)	<0.001	1.35 (1.21–1.51)	<0.001	1.33 (1.19–1.49)	<0.001
Sleep quality	Good sleep quality	1.00 (Reference)	–	1.00 (Reference)	–	1.00 (Reference)	–
	Poor sleep quality	1.89 (1.45–2.48)	<0.001	1.91 (1.46–2.51)	<0.001	1.86 (1.41–2.43)	<0.001

Note. Values are HRs with 95% CIs from Cox regression models. The crude model was unadjusted. Model 1 was adjusted for age, education, residence, marital status, and annual per-capita household consumption expenditure. Model 2 additionally included BMI, smoking status, drinking status, and antihypertensive, antidiabetic, and lipid-lowering medication use. The 0–30 min napping category includes durations >0 and ≤30 min. Sleep quality scores ranged from 1 to 4, with scores of 1–2 classified as good and 3-4 as poor sleep quality. Higher scores indicate more frequent restless sleep. HRs and CIs for continuous napping duration are displayed to three decimal places. BMI, body mass index; CI, confidence interval; CKM, cardiovascular-kidney-metabolic; HR, hazard ratio.

3.4 Restricted cubic spline analyses

Nighttime sleep duration showed an overall association with incident CKM multimorbidity (P for overall association=0.003), with no evidence of nonlinearity (P for nonlinearity=0.180; Fig. 3A).

The daytime-nap spline yielded P = 0.185 for the overall test and P=0.789 for nonlinearity (Fig. 3B); neither met the prespecified significance threshold.

3.5 Subgroup analyses

Supplementary Figures S1-S3 report the stratum-specific estimates for nighttime sleep, napping, and the restless-sleep score.

Several strata produced significant HRs below 1.00 for the continuous nighttime measure; interaction testing gave no evidence that these estimates differed across subgroup levels (Supplementary Fig. S1). Nap-duration HRs generally clustered around 1.00. Heterogeneity by BMI was the exception; Supplementary Fig. S2 reports an interaction P value of 0.012. For the restless-sleep score, significant HRs above 1.00 appeared in several strata, yet all interaction P values were nonsignificant (Supplementary Fig. S3).

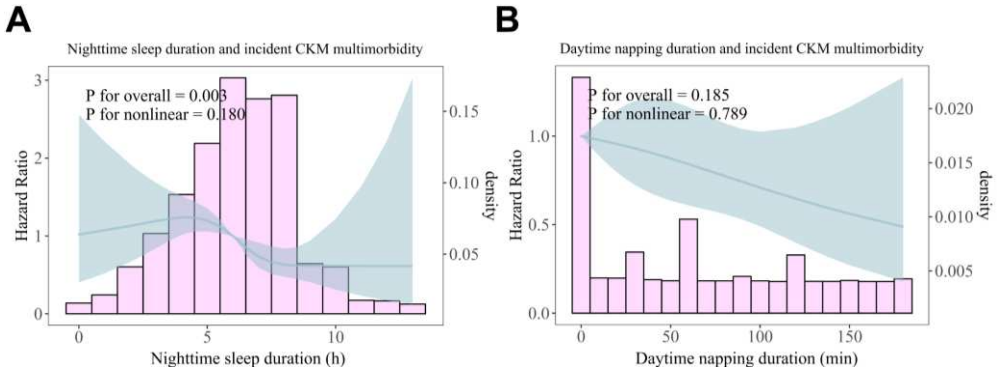


Fig. 3. Restricted cubic spline associations of nighttime sleep and daytime napping with incident CKM multimorbidity. (A) Nighttime sleep duration, with knots at 3, 6, 7, and 9 h; (B) daytime napping duration, with knots at 0, 30, and 120 min. Curves and shaded areas represent adjusted HRs and 95% CIs, respectively. Histograms show the exposure distributions. The median of each exposure was used as the reference (HR = 1.00). Models were adjusted for age, education, residence, marital status, annual per-capita household consumption expenditure, BMI, smoking status, drinking status, and antihypertensive, antidiabetic, and lipid-lowering medication use. P values for the overall association and nonlinearity are shown in each panel. BMI, body mass index; CI, confidence interval; CKM, cardiovascular-kidney-metabolic; HR, hazard ratio.

3.6 Machine-learning analyses

Among the three observed test-set C-indices, XGBoost had the largest value (0.7095);

the values were 0.6991 for random survival forest and 0.6378 for gradient boosting machine (Fig. 4A). No inferential comparison between models was performed.

The same subset of 200 training observations underpinned each SHAP display. Sleep quality score ranked first by mean absolute SHAP value in the XGBoost model. Larger scores appeared mainly on the positive side of the prediction scale, whereas longer nighttime sleep tended toward negative contributions (Fig. 4B).

In the random survival forest model, BMI, sleep quality score, and per-capita annual household consumption expenditure had the highest mean absolute SHAP values. Nighttime sleep duration ranked higher than daytime napping duration (Fig. 4C). The gradient boosting machine placed BMI, per-capita annual household consumption expenditure, and age first through third. Sleep quality score and nighttime sleep duration both ranked above daytime napping duration by mean absolute SHAP value in the gradient boosting machine model (Fig. 4D). SHAP magnitude was evaluated within each algorithm only because the model-specific scales differ.

3.7 Sensitivity analyses

CBPS matching formed a dataset of 1,292 women: 216 with an incident CKM event and 1,076 matched women for whom no event was identified. Each of the five matching covariates had an absolute postmatch SMD below 0.10 (Supplementary Table S1).

In the matched sample, shorter nighttime sleep duration and higher sleep quality scores remained associated with incident CKM multimorbidity. Nap results depended on parameterization: the Model 2 per-minute estimate was inverse (HR, 0.9953; 95%

CI, 0.9916-0.9991; P=0.014), while both category contrasts with non-nappers were nonsignificant. Supplementary Table S2 contains the complete crude and adjusted estimates.

Excluding the 27 women whose CKM multimorbidity was first identified in 2013 left 5,211 participants, including 189 incident cases. Associations involving nighttime sleep and sleep quality persisted. The Model 2 nap HR per minute was 0.9957 (95% CI, 0.9917-0.9996; P=0.033); neither category contrast reached significance (Supplementary Table S3).

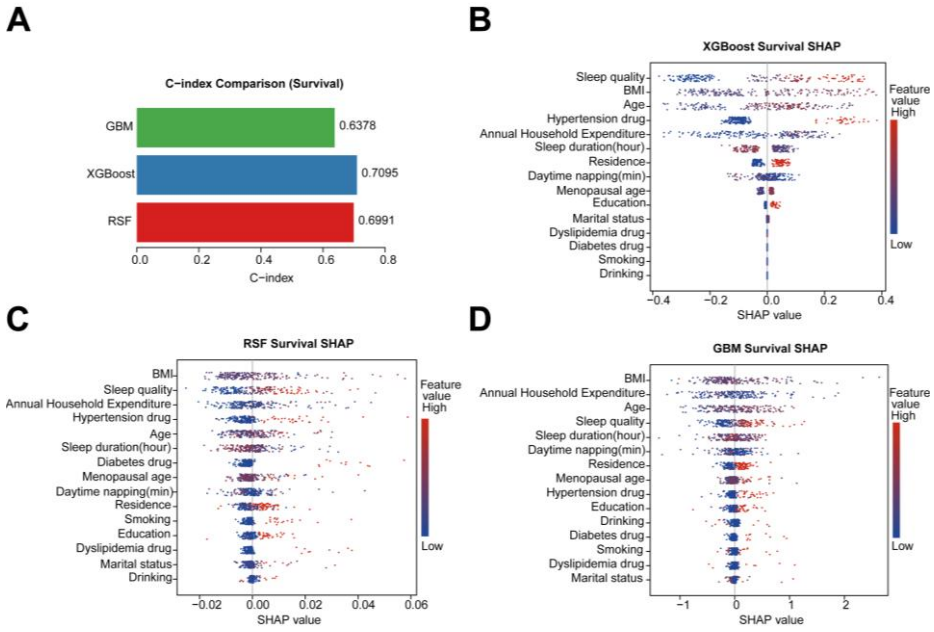


Fig. 4. Test-set C-indices and SHAP summaries for exploratory survival models. (A) C-indices for gradient boosting machine (GBM), XGBoost, and random survival forest (RSF); (B–D) SHAP summaries for XGBoost, RSF, and GBM, respectively. SHAP values were calculated for the same first 200 participants in the development set. Each point represents a participant's SHAP value for a given predictor. Blue and red indicate lower and higher predictor values, respectively. Predictors are ordered by decreasing mean absolute SHAP value within each panel. Positive and negative SHAP values indicate upward and downward contributions to the model output. In the plots, "Annual Household Expenditure" denotes annual per-capita household consumption expenditure; "Menopausal age" denotes menopausal-age category; "Sleep quality" denotes the restless-sleep score, with higher scores indicating more frequent restless sleep and poorer sleep quality; and "Sleep duration (hour)" denotes nighttime sleep

duration in hours. BMI, body mass index; C-index, concordance index; SHAP, Shapley additive explanations.

4. Discussion

4.1 Principal findings

The CHARLS sample comprised 5,238 women after menopause. Women reporting less than 6 h of nightly sleep at baseline subsequently had a greater adjusted CKM hazard relative to the reference interval (6 to <9 h); no statistical evidence of a difference emerged for at least 9 h. Higher sleep quality scores were associated with a higher hazard of incident CKM multimorbidity. The comparison of poor versus good sleep quality showed a similar association. Comparable patterns appeared in the exploratory matched analysis and after removal of cases first recorded in 2013. Findings for post-lunch naps were not uniform. Category-based contrasts failed to reach significance, whereas an inverse estimate per minute appeared only in sensitivity analyses. The spline analysis showed an overall association between nighttime sleep duration and incident CKM multimorbidity, with no evidence of nonlinearity. Exploratory survival models assigned predictive contributions to both the restless-sleep score and nighttime duration, with rankings that varied by algorithm.

4.2 Comparison with previous studies

Research increasingly considers composite disease outcomes rather than single disorders. In UK Biobank, a favorable multicomponent sleep profile corresponded to less progression from an initial cardiorenal or metabolic condition to multiple such conditions[2]. Wang and Tang analyzed 5,782 CHARLS adults together with 12,677

SHARE participants; repeated sleep reports were summarized as duration trajectories and latent quality classes[19]. They defined CRMM by any two of cardiovascular disease, CKD and type 2 diabetes. Their population included both sexes, and naps were outside the analysis.

Two further reports provide especially close context. Xu and colleagues selected 2,859 CHARLS women who were postmenopausal, grouped four reports of nocturnal sleep from 2011 through 2018 into trajectories, and used logistic models for CRMM arising in the 2018–2020 interval[20]. Wang and colleagues examined sleep quality alongside nighttime duration in three cohorts: HRS, CHARLS and ELSA[18]. Their CHARLS analysis additionally considered naps, and the study also used interpretable prediction models. Its cardiometabolic multimorbidity (CMM) endpoint counted at least two among hypertension, type 2 diabetes, stroke and coronary disease, with no renal condition. Differences in exposure windows, populations and disease composition limit direct comparison with our estimates.

Other longitudinal cohorts connect insufficient or disturbed sleep with the accumulation of chronic conditions[24,25]. Separate syntheses have reported relations with hypertension[9], type 2 diabetes[12], CKD[13], and metabolic syndrome[10]. Evidence specific to women includes SWAN, where persistent insomnia, including insomnia accompanied by short sleep, preceded cardiovascular events[4], and WHI findings relating insomnia and sleep length to metabolic syndrome and its component traits[16].

Our study contributes a complementary baseline perspective. Three baseline self-

reported measures (nighttime sleep duration, daytime napping duration, and restless sleep frequency) were related to CKM events first identified during 2013–2018. The population comprised women after menopause, and the endpoint combined disease indicators across cardiovascular, renal and metabolic domains. The analysis examined baseline sleep characteristics rather than changes in sleep over time and included a kidney disease domain in the outcome. It complements the recent reports without replicating their exposure windows or endpoint definitions[18–20].

4.3 Possible mechanisms

During menopause, vasomotor symptoms, nocturnal awakening, and insomnia commonly contribute to sleep disturbance[26]. Several mechanisms could connect such disturbance or curtailed night sleep to CKM accumulation. Increased sympathetic activity and changes in hypothalamic-pituitary-adrenal regulation may affect glucose handling and vascular function, promote inflammation, or increase oxidative stress. These processes were not examined here.

Concomitant endocrine change may make women after menopause more susceptible. Declining estrogen is linked to redistribution of adiposity, lipid and glycaemic abnormalities, higher arterial pressure, and impaired vascular function[27]. In a controlled experiment involving postmenopausal participants, restricted sleep affected energy metabolism as well as insulin sensitivity[28]. These observations suggest ways in which short sleep could compound menopause-related metabolic vulnerability, but they do not demonstrate such interaction in our cohort.

Psychological distress is another candidate route. Sleep disruption and menopausal

symptoms can adversely affect mood; persistent stress may in turn amplify endocrine and immune activation. Because the analysis did not test mediators, these ideas remain explanatory hypotheses. Future work pairing serial sleep assessment with hormone assays and metabolic or inflammatory biomarkers could examine them directly.

4.4 Interpretation of daytime napping findings

Daytime napping duration showed no statistically significant association in the categorical analyses; an inverse association per minute was observed only in the sensitivity analyses. The CHARLS component of a recent multicohort study also reported nonsignificant adjusted CMM estimates for nap categories, although its cut points and nonrenal outcome differ from ours[18]. Earlier CHARLS reports linked naps bidirectionally with metabolic syndrome[29], described heterogeneity by sex and age[30], and observed fewer CKD cases among short sleepers who napped[31]. A post-lunch nap may serve as recovery from curtailed night sleep, yet it can also accompany illness, inactivity, fatigue, or fragmented sleep. These contexts were not distinguished in our analysis and may have obscured an overall pattern.

4.5 Clinical implications

Brief questions about nocturnal sleep and restlessness could provide context during CKM risk assessment in women after menopause. They are adjuncts to, not substitutes for, established renal, metabolic, and cardiovascular evaluation. Within Life's Essential 8, the American Heart Association counts sleep duration among its eight health metrics[32]. Our data, however, supply neither a validated screening

threshold nor evidence that changing sleep prevents CKM multimorbidity. Intervention studies with serial, preferably objective, measurements would be needed before preventive recommendations are made.

4.6 Strengths and limitations

Methodological strengths include use of 5,238 CHARLS participants, three scheduled outcome assessments, and restriction to a clinically relevant group of women after menopause. The same cohort supplied baseline information on nocturnal sleep, post-lunch naps, and restlessness. Spline and subgroup results accompanied the main Cox estimates. Two sensitivity analyses examined stability, while survival algorithms explored prediction patterns.

Available CHARLS fields set important limits. Objective recordings, such as actigraphy or polysomnography, were unavailable in the data used here; exposure classification therefore relied on participant reports and is vulnerable to recall or reporting error. Our analyses used baseline sleep responses only, so within-person change could not be evaluated. One question about restless sleep served as the quality indicator and cannot represent every facet of sleep quality.

Outcome ascertainment depended on participant reports that a physician had diagnosed each component, leaving scope for classification error, especially for kidney conditions. Individuals with no recorded CKM event contributed time until study close in 2018, including some whose outcome information was absent in later waves. This approach may have missed events after the last observed assessment and overestimated event-free follow-up time. Residual confounding remains possible.

Physical activity was omitted because of substantial missingness, and information on diet, menopausal symptoms, hormone therapy, sleep apnea, and sleep medication use was unavailable or incomplete. Only one completed imputed dataset was analyzed, so between-imputation uncertainty was not incorporated.

The CBPS sensitivity exercise formed groups from later CKM status; its role was to re-examine associations after balancing selected covariates, not to estimate a causal treatment effect. For the prediction export, we could not verify whether data-dependent preprocessing had been restricted to training observations. Numeric category codes and extreme BMI inputs may also have influenced the exploratory predictions. Discrimination was evaluated using a single internal train-test split without external validation. SHAP values describe contributions to predictions within each fitted model; they do not estimate independent associations or causal effects.

5. Conclusion

Within the CHARLS cohort of postmenopausal women, subsequent CKM hazards were greater among those reporting less than 6 h of nighttime sleep and among those assigned to the poor-quality category using restless-sleep frequency. Nap estimates were not stable across continuous and categorical parameterizations. These observations warrant further investigation with repeated, objective sleep measurements. Whether modifying sleep can prevent CKM multimorbidity requires evidence from intervention studies.

Abbreviations

ATT, average treatment effect on the treated;

BMI, body mass index;

CBPS, covariate-balancing propensity score;

CHARLS, China Health and Retirement Longitudinal Study;

CI, confidence interval;

C-index, concordance index;

CKD, chronic kidney disease;

CKM, cardiovascular-kidney-metabolic;

CMM, cardiometabolic multimorbidity;

CRMM, cardio-renal-metabolic multimorbidity;

ELSA, English Longitudinal Study of Ageing;

GBM, gradient boosting machine;

HR, hazard ratio;

HRS, Health and Retirement Study;

IQR, interquartile range;

RCS, restricted cubic spline;

RSF, random survival forest;

SD, standard deviation;

SHAP, Shapley additive explanations;

SHARE, Survey of Health, Ageing and Retirement in Europe;

SMD, standardized mean difference;

SWAN, Study of Women's Health Across the Nation;

WHI, Women's Health Initiative;

XGBoost, extreme gradient boosting.

Declarations

Ethics approval and consent to participate

This study was a secondary analysis of de-identified data from the China Health and Retirement Longitudinal Study (CHARLS). The original CHARLS study was approved by the Biomedical Ethics Review Committee of Peking University (approval no. IRB00001052-11015), and all participants provided written informed consent. The author accessed and analysed the data in accordance with the CHARLS data-use agreement. No new participants were recruited or contacted, and no new participant data were collected for this study. The present study was conducted in accordance with the ethical principles of the Declaration of Helsinki.

Consent for publication

Not applicable. This manuscript reports only aggregate findings derived from de-identified data and contains no identifiable individual information, images, or videos.

Availability of data and materials

The de-identified datasets analysed during the current study comprised the 2011–2012 CHARLS baseline survey and follow-up waves conducted in 2013, 2015, and 2018. The datasets are available through the official CHARLS website (https://charls.pku.edu.cn/en/), subject to registration, acceptance of the data-use agreement, and approval of access to the relevant datasets. The original participant-level data are held and distributed by CHARLS and cannot be redistributed by the author.

Competing interests

The author declares no competing interests.

Funding

This study received no specific funding.

Authors' contributions

TJ conceived and designed the study, prepared the analytic dataset, conducted the statistical analyses, interpreted the findings, prepared the figures and tables, drafted and revised the manuscript, and read and approved the final manuscript.

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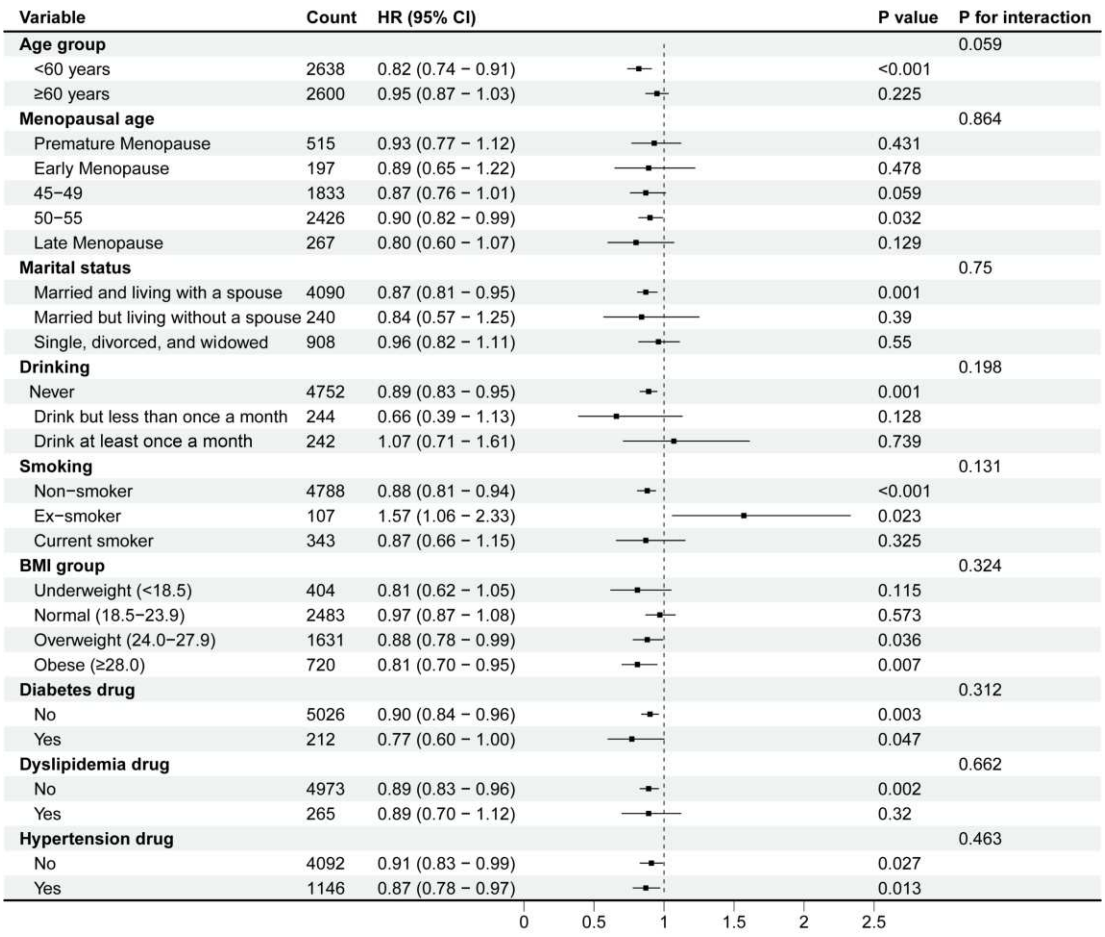
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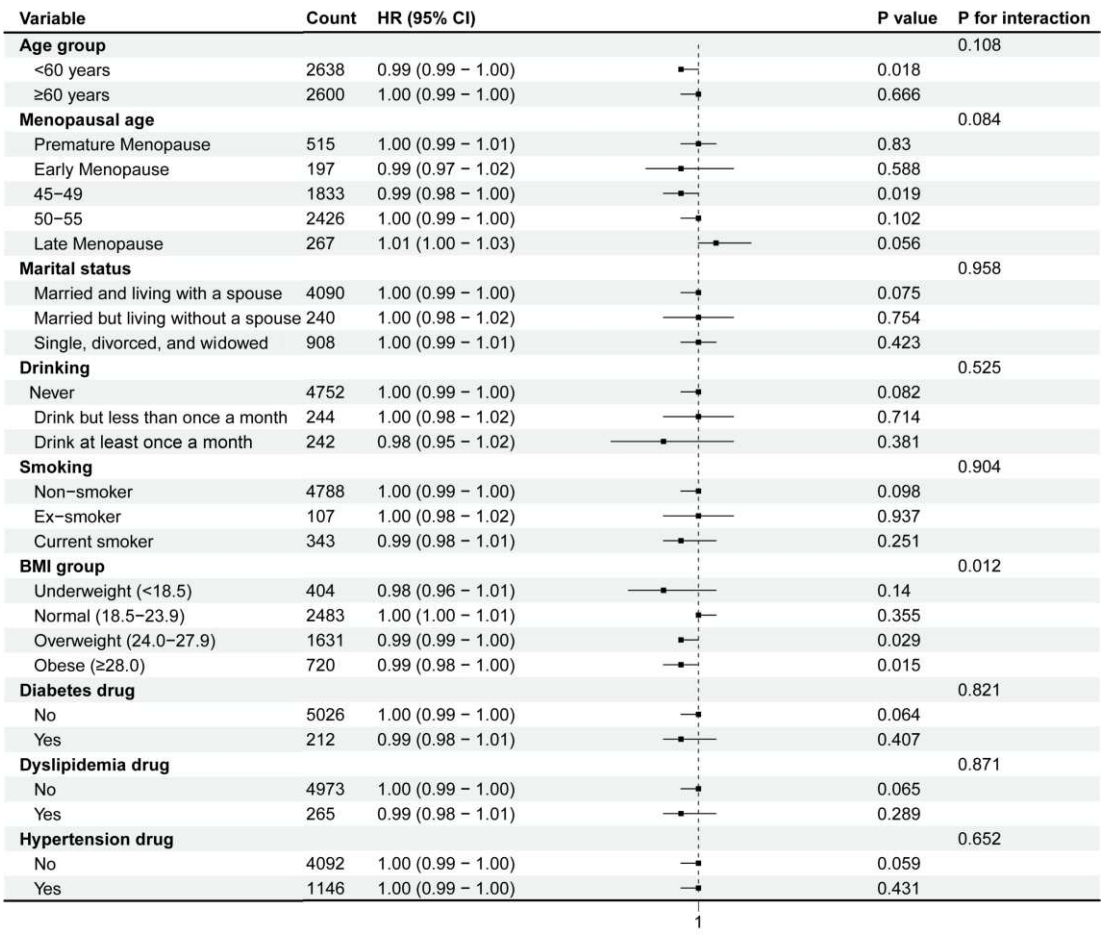
Supplementary Information

Supplementary Fig. S1. Nighttime-sleep HRs within prespecified participant strata.



Note. Cox models express the exposure contrast as 1 additional hour of sleep per night and display HRs with 95% CIs. Stratification covered age, age at menopause, marital status, smoking, drinking, BMI class, and separate indicators for antihypertensive, antidiabetic, and lipid-lowering therapy. For a given stratum, adjustment retained the other stratification variables plus per-capita annual household consumption expenditure; the defining factor was left out. Interaction P values were obtained from models including an interaction term between nighttime sleep duration and the subgroup variable. BMI, body mass index; HR, hazard ratio; CKM, cardiovascular-kidney-metabolic; CI, confidence interval.

Supplementary Fig. S2. Daytime-nap HRs within prespecified participant strata.



Note. The plotted HRs and 95% CIs correspond to a 1 min increase in daytime napping duration. Strata represent age, age at menopause, marital status, smoking, drinking, BMI class, and separate indicators for antihypertensive, antidiabetic, and lipid-lowering therapy. A stratum-specific model retains all other stratification variables together with per-capita annual household consumption expenditure and excludes its defining factor. Interaction P values were obtained from models including an interaction term between daytime napping duration and the subgroup variable. HRs and CIs are rounded to two decimal places; confidence limits displayed as 1.00 may differ from 1 before rounding. BMI, body mass index; HR, hazard ratio; CKM, cardiovascular-kidney-metabolic; CI, confidence interval.

Supplementary Fig. S3. Subgroup analyses of the association between sleep quality

score and incident CKM multimorbidity.

Variable	Count	HR (95% CI)	P value	P for interaction
Age group				0.126
<60 years	2638	1.48 (1.25 − 1.74)	<0.001	
≥60 years	2600	1.22 (1.05 − 1.41)	0.009	
Menopausal age				0.947
Premature Menopause	515	1.37 (0.99 − 1.89)	0.055	
Early Menopause	197	1.92 (0.92 − 4.02)	0.084	
45−49	1833	1.31 (1.05 − 1.62)	0.016	
50−55	2426	1.33 (1.14 − 1.55)	<0.001	
Late Menopause	267	1.18 (0.70 − 2.00)	0.527	
Marital status				0.284
Married and living with a spouse	4090	1.35 (1.20 − 1.53)	<0.001	
Married but living without a spouse	240	2.51 (1.09 − 5.80)	0.031	
Single, divorced, and widowed	908	1.12 (0.85 − 1.48)	0.404	
Drinking				0.463
Never	4752	1.35 (1.20 − 1.51)	<0.001	
Drink but less than once a month	244	1.02 (0.46 − 2.26)	0.969	
Drink at least once a month	242	0.95 (0.45 − 2.04)	0.902	
Smoking				0.36
Non−smoker	4788	1.34 (1.19 − 1.51)	<0.001	
Ex−smoker	107	0.83 (0.48 − 1.45)	0.516	
Current smoker	343	1.59 (1.01 − 2.51)	0.046	
BMI group				0.919
Underweight (<18.5)	404	1.22 (0.79 − 1.88)	0.372	
Normal (18.5−23.9)	2483	1.27 (1.05 − 1.52)	0.011	
Overweight (24.0−27.9)	1631	1.38 (1.14 − 1.67)	0.001	
Obese (≥28.0)	720	1.41 (1.11 − 1.78)	0.005	
Diabetes drug				0.068
No	5026	1.28 (1.14 − 1.44)	<0.001	
Yes	212	2.23 (1.41 − 3.53)	0.001	
Dyslipidemia drug				0.871
No	4973	1.34 (1.19 − 1.50)	<0.001	
Yes	265	1.29 (0.89 − 1.88)	0.184	
Hypertension drug				0.583
No	4092	1.37 (1.18 − 1.57)	<0.001	
Yes	1146	1.28 (1.08 − 1.53)	0.005	



Note. Plotted Cox estimates with 95% CIs refer to a 1-point score increment. Larger scores mean that restless sleep occurred more often and therefore indicate poorer quality. Strata represent age, age at menopause, marital status, smoking, drinking, BMI class, and separate indicators for antihypertensive, antidiabetic, and lipid-lowering therapy. Each analysis retains the other stratification variables and per-capita annual household consumption expenditure but excludes the factor defining that stratum. Interaction P values were obtained from models including an interaction term between sleep quality score and the subgroup variable. BMI, body mass index; HR, hazard ratio; CKM, cardiovascular-kidney-metabolic; CI, confidence interval.

Supplementary Table S1. Covariate balance before and after CBPS matching.

Covariate	SMD before matching	SMD after matching
Age	0.071	0.005
Residence	0.162	0.004
Marital status	0.030	0.019
Education level	0.052	<0.001
Annual household per capita consumption expenditure	0.086	0.091

Note. Incident-event status served as the grouping variable for distance estimation. Predictors were age, education, residence, marital status, and per-capita annual household consumption expenditure. Matching proceeded by nearest neighbors without replacement and allowed as many as five women with no identified event per incident case. Its caliper parameter was 0.2; scaling followed the MatchIt default. The ATT option designated the incident-event group as focal and does not imply estimation of a causal treatment effect. Balance was considered adequate when the absolute SMD was below 0.10. Counts changed from 216 incident cases and 5,022 women with no event identified before matching to 216 and 1,076 afterward. CBPS, covariate-balancing propensity score; CKM, cardiovascular-kidney-metabolic; SMD, standardized mean difference.

Supplementary Table S2. Cox estimates obtained from the CBPS-matched data.

Exposure or contrast	Crude HR (95% CI)	P value	Model 1 HR (95% CI)	P value	Model 2 HR (95% CI)	P value
Nighttime sleep duration, per 1 h increase	0.89 (0.83–0.96)	0.001	0.89 (0.83–0.95)	0.001	0.89 (0.83–0.95)	<0.001
6 to <9 h	1.00 (Reference)	–	1.00 (Reference)	–	1.00 (Reference)	–
<6 h	1.43 (1.08–1.88)	0.011	1.44 (1.08–1.90)	0.012	1.40 (1.06–1.85)	0.019
≥9 h	0.81 (0.45–1.47)	0.486	0.83 (0.45–1.50)	0.532	0.85 (0.47–1.56)	0.606
Daytime napping duration, per 1 min increase	0.9968 (0.9932–1.0004)	0.083	0.9968 (0.9932–1.0004)	0.079	0.9953 (0.9916–0.9991)	0.014
0 min	1.00 (Reference)	–	1.00 (Reference)	–	1.00 (Reference)	–
0–30 min	1.17 (0.82–1.65)	0.388	1.17 (0.82–1.66)	0.380	1.01 (0.70–1.44)	0.968
>30 min	0.87 (0.64–1.19)	0.389	0.86 (0.63–1.18)	0.365	0.76 (0.55–1.04)	0.086
Sleep quality score, per 1-point increase	1.35 (1.21–1.50)	<0.001	1.35 (1.21–1.50)	<0.001	1.33 (1.19–1.48)	<0.001
Good sleep quality	1.00 (Reference)	–	1.00 (Reference)	–	1.00 (Reference)	–
Poor sleep quality	1.89 (1.45–2.48)	<0.001	1.91 (1.45–2.50)	<0.001	1.84 (1.40–2.42)	<0.001

Note. CBPS matching by incident CKM multimorbidity status yielded 1,292 women, including 216 incident cases. Values are HRs with 95% CIs from Cox regression models. The crude model was unadjusted. Model 1 was adjusted for age, education, residence, marital status, and annual per-capita household consumption expenditure. Model 2 additionally included BMI, smoking status, drinking status, and antihypertensive, antidiabetic, and lipid-lowering medication use. The 0–30 min napping category includes durations >0 and ≤30 min. Sleep quality scores ranged from 1 to 4, with scores of 1–2 classified as good and 3–4 as poor sleep quality. Higher scores indicate more frequent restless sleep. HRs and CIs for continuous napping duration are displayed to four decimal places. BMI, body mass index; CBPS, covariate-balancing propensity score; CI, confidence interval; CKM, cardiovascular-kidney-metabolic; HR, hazard ratio.

Supplementary Table S3. Cox regression results after excluding participants whose

CKM multimorbidity was first identified in 2013.

Exposure or contrast	Crude HR (95% CI)	P value	Model 1 HR (95% CI)	P value	Model 2 HR (95% CI)	P value
Nighttime sleep duration, per 1 h increase	0.91 (0.85–0.98)	0.012	0.91 (0.85–0.98)	0.011	0.90 (0.84–0.97)	0.006
6 to <9 h	1.00 (Reference)	–	1.00 (Reference)	–	1.00 (Reference)	–
<6 h	1.38 (1.02–1.85)	0.034	1.40 (1.04–1.89)	0.026	1.42 (1.05–1.91)	0.021
≥9 h	0.76 (0.40–1.46)	0.406	0.79 (0.41–1.52)	0.486	0.81 (0.42–1.56)	0.530
Daytime napping duration, per 1 min increase	0.9968 (0.9929–1.0007)	0.108	0.9966 (0.9926–1.0005)	0.086	0.9957 (0.9917–0.9996)	0.033
0 min	1.00 (Reference)	–	1.00 (Reference)	–	1.00 (Reference)	–
0–30 min	1.21 (0.83–1.75)	0.317	1.16 (0.80–1.68)	0.433	1.07 (0.74–1.56)	0.719
>30 min	0.88 (0.63–1.24)	0.474	0.86 (0.61–1.21)	0.393	0.78 (0.56–1.10)	0.159
Sleep quality score, per 1-point increase	1.32 (1.18–1.49)	<0.001	1.33 (1.18–1.49)	<0.001	1.31 (1.17–1.47)	<0.001
Good sleep quality	1.00 (Reference)	–	1.00 (Reference)	–	1.00 (Reference)	–
Poor sleep quality	1.84 (1.38–2.45)	<0.001	1.85 (1.39–2.47)	<0.001	1.79 (1.34–2.40)	<0.001

Note. Excluding 27 women whose CKM multimorbidity was first identified in 2013 left 5,211 women, including 189 incident cases. Values are HRs with 95% CIs from Cox regression models. The crude model was unadjusted. Model 1 was adjusted for age, education, residence, marital status, and annual per-capita household consumption expenditure. Model 2 additionally included BMI, smoking status, drinking status, and antihypertensive, antidiabetic, and lipid-lowering medication use. The 0–30 min napping category includes durations >0 and ≤30 min. Sleep quality scores ranged from 1 to 4, with scores of 1–2 classified as good and 3–4 as poor sleep quality. Higher scores indicate more frequent restless sleep. HRs and CIs for continuous napping duration are displayed to four decimal places. BMI, body mass index; CI, confidence interval; CKM, cardiovascular-kidney-metabolic; HR, hazard ratio.