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ORIGINAL ARTICLE

Adherence to a healthy sleep pattern and incidence of cardiometabolic multimorbidity among hypertensive patients: a prospective study of UK Biobank

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Abstract

Study Objectives: To investigate whether a healthy sleep pattern would reduce the risk of cardiometabolic multimorbidity (CMM) among hypertensives.

Methods: This is a prospective cohort analysis from the UK Biobank. A total of 69 524 hypertensives without a history of diabetes mellitus, coronary heart disease, or stroke at baseline were enrolled. Five dimensions of healthy sleep at baseline including early chronotype, sleep 7–8 h/d, free of insomnia, no snoring, and no frequent excessive daytime sleepiness were used to generate a healthy sleep score ranging from 0 to 5 (one point was given for each dimension of healthy sleep). A higher score indicated a healthier sleep pattern. We set five groups corresponding to the healthy sleep score of 5, 4, 3, 2, and 0–1, respectively. The primary outcome was the incidence of overall CMM among enrolled hypertensives. We assessed the adjusted hazard ratios (HRs) and 95% confidence intervals (CIs) by Fine-Gray subdistribution hazard models.

Results: We found the full-adjusted HR (95% CI) for overall CMM was 0.93 (0.91–0.95) for a 1-point increase in the healthy sleep score. Compared to hypertensives with a healthy sleep score of 0–1, those with a score of 5 had a 27% lower risk of overall CMM, and 37%, 23%, and 20% lower risks of diabetes mellitus, coronary heart disease, and stroke, respectively, after adjusting for sociodemographic characteristic, lifestyle, and clinical factors.

Conclusions: Our results indicated that a healthy sleep pattern was associated with lower risks of CMM outcomes among hypertensives.

Statement of Significance

As the aging population globally, cardiometabolic multimorbidity (CMM), the cooccurrence of at least two cardiometabolic diseases in one individual, has become a novel and growing medical issue. A healthy sleep pattern combining five dimensions of healthy sleep was demonstrated to be associated with lower risks of cardiovascular diseases, heart failure, cardiac arrhythmias, and mortality in the general population. However, the role of this healthy sleep pattern in the incidence of overall CMM among hypertensives is not clear yet. In this study, we mainly estimated the risk of overall CMM among 69 524 hypertensives and found a significant inverse association between the healthy sleep score and the incidence of overall CMM. These results showed this healthy sleep pattern might be regarded as one of the healthy lifestyles for individuals with hypertension to lower the risk of CMM.

Key words: healthy sleep score; healthy sleep pattern; hypertensives; cardiometabolic multimorbidity; UK Biobank

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Introduction

With the aging of the global population, the prevalence of multimorbidity, especially cardiometabolic multimorbidity (CMM), which refers to the cooccurrence of at least two cardiometabolic diseases (CMDs) (including hypertension, diabetes mellitus [DM], coronary heart disease [CHD] and stroke in our study) in an individual, has been increasing rapidly [1, 2]. Studies on the global, United Kingdom, and Chinese populations showed that CMM cumulatively increased the risk of all-cause mortality and reduced life expectancy [3–5]. Considering its high prevalence and poor prognosis, CMM has been rising as a global issue of public health, which needs our concern. In addition, hypertension, the most prevalent chronic disease, contributes to common comorbidities worldwide [6]. In the UK Biobank (UKB), the most pervasive comorbidities include hypertension and chronic kidney disease (70%), and hypertension and DM (64%) [7]. Furthermore, a previous study showed an increased risk of all-cause mortality among hypertensives significantly elevated from 7% to 30% and 136% after cooccurrences with DM and cardiovascular diseases (CVD), respectively [5]. Therefore, it is urgent to explore practical strategies to reduce the risk of progression from hypertension to CMM. A few existing studies indicated the critical role of socioeconomic class, some behavioral factors, and clinical profiles in the progress of CMM [8, 9]. However, the potential effects of other lifestyle behaviors which have been demonstrated to be associated with lower risks of CMDs, on the trajectory from hypertension to CMM are unclear yet.

Sleep is increasingly recognized as one of the essential factors in our health. Previous studies have found that some common dimensions of unhealthy sleep, including long or short sleep duration [10, 11], insomnia [12, 13], snoring [14, 15], daytime sleepiness [16, 17], and late chronotype [18, 19], were related to increased risks of CMDs and mortality in the general population. Additionally, short sleep duration and insomnia were also found to be associated with a higher risk of CVD among hypertensives [20–22]. However, sleep is a multidimensional concept, and the sleep pattern combining various dimensions of sleep collectively would be closer to the real world [23]. Recently, Lu et al. generated a healthy sleep pattern combining five dimensions of sleep health, including early chronotype, proper sleep duration, free of insomnia, no snoring, and no frequent daytime sleepiness, and demonstrated associations of this healthy sleep pattern with lower risks of CVD, heart failure, cardiac arrhythmias, and mortality in the general population [24–27]. Moreover, a recent study showed that this healthy sleep pattern was associated with a lower risk of DM in hypertensives [28]. Nevertheless, the role of this compositive healthy sleep pattern in the incidence of overall CMM, which was defined as occurrences of at least one disease of DM, CHD, and stroke among hypertensives, needs to be further investigated.

Thus, we conducted this study by utilizing the data from the UKB [29], a prospective cohort of over half a million middle-aged and elderly individuals, to examine the associations between the healthy sleep pattern and CMM outcomes in hypertensives.

Methods

Data and study population

The data used in this study were derived from the UKB (application number: 76118), which has previously been described in detail [29]. Briefly, the UKB is a large-scale prospective cohort study that recruited over 500 000 general population aged 40–69 years in 2006–2010 at 22 assessment centers throughout the United Kingdom. With written informed consents, the information of each participant about demography, lifestyles, anthropometry, and other clinical-related measurements were collected, after that, linked to their medical records and presented by the corresponding filed ID [30]. The UKB was approved by the UKB Research Ethics Committee.

In this study, we enrolled 149 148 patients with hypertension, excluded 40 514 patients with DM, CHD, or stroke at baseline, and excluded 39 110 patients with missing data on five dimensions of sleep and involved covariates, leaving 69 524 patients with validated information for the principal analysis. The participants' flow chart is presented in Supplementary Figure S1.

Assessment of sleep behaviors

In the UKB, self-reported dimensions of sleep, including chronotype, sleep duration, sleeplessness/insomnia, snoring, and daytime sleepiness, were recorded by touchscreen questionnaires. For chronotype, participants were asked, "Do you consider yourself to be: (1) definitely a 'morning' person; (2) more a 'morning' person than 'evening' person; (3) more an 'evening' person than a 'morning' person; or (4) definitely an 'evening' person." For sleep duration, participants were asked "About how many hours sleep including naps do you get in every 24 hours?." For sleeplessness/insomnia, participants were asked "Do you have trouble falling asleep at night or do you wake up in the middle of the night?," and with several choices provided: (1) never/rarely; (2) sometimes, or (3) usually. For snoring, participants were asked, "Does your partner or a close relative or friend complain about your snoring?" and with responses provided: (1) yes; or (2) no. For daytime sleepiness, participants were asked, "How likely are you to doze off or fall asleep during the daytime when you don't mean to? (e.g. when working, reading, or driving)," and with multiple choices provided: (1) never/rarely; (2) sometimes; (3) often, or (4) all of the time.

Assessment of healthy sleep score

The definitions of the five dimensions of healthy sleep and the healthy sleep score have been described in detail in the previous study [24]. Five dimensions of healthy sleep included early chronotype (definitely a "morning" person or "morning" than "evening" person); sleep 7 to 8 h/d; reported free of insomnia ("never/rarely"); no snoring; and no frequent excessive daytime sleepiness ("never/rarely" or "sometimes"). These dimensions of healthy sleep were used to generate a healthy sleep score ranging from 0 to 5 (one point was given for each dimension of healthy sleep). A higher score indicated a healthier sleep pattern. This study set five groups corresponding to the healthy sleep score of 5, 4, 3, 2, 0–1, respectively.

Assessment of CMDs and the main outcome

The information presented by the filed ID recording disease status or medications was used to define CMDs including hypertension, DM, CHD, and stroke. In brief, the screening of these four CMDs was conducted according to self-reported information (including medical history, physician diagnoses obtained from the verbal interview, and surgery history) and digital

medical records (including diagnoses derived from the code of the International Classification of Diseases, 9th revision [ICD-9], [ICD-10], and the Office of Population Censuses and Surveys Classification of Interventions and Procedures, version 4 [OPCS-4]). The detailed definitions of specific CMDs are summarized in Supplementary Table S1 [31]. For example, a participant who met at least one of the following conditions would be defined as a patient with hypertension in our study: (1) reported hypertension through oral interview; (2) replied with "high blood pressure" to the touchscreen question "Has a doctor ever told you that you have had a heart attack, angina, high blood pressure, or stroke?"; (3) answered the touchscreen question "Do you regularly take cholesterol-lowering medication, blood pressure medication, or insulin?" with "blood pressure medication"; (4) his or her diagnosis information of hypertension was recorded in the hospital admission data (including ICD-9 and ICD-10). For a specific CMD, if the diagnosis was confirmed after recruitment, the disease would be considered to occur during follow-up, otherwise exist at baseline.

In this study, the primary outcome was the incidence of overall CMM, which was defined as occurrences of at least one disease of DM, CHD, and stroke among enrolled hypertensives during the follow-up.

Assessment of covariates

In our analysis, other covariates of participants including demographic variables, lifestyle factors, and clinical characteristics were documented through touchscreen questionnaires, verbal interview records, and physical measures at baseline. Sociodemographic variables included age, gender (male/female), ethnicity (white/nonwhite), and Townsend Deprivation Index (TDI), an area-based proxy measure for socioeconomic status provided in the UKB directly [32]. Lifestyle factors included smoking status (current/past or never), alcohol consumption (never or occasionally drinking/usually drinking), physical activity, and diet. In terms of physical activity, participants were dichotomized according to whether they met the 2019 UK Physical Activity Guidelines (150 minutes of walking or moderate activity per week or 75 minutes of vigorous activity) [33]. The American Heart Association Guidelines were used to assess each participant's diet condition at baseline [34], and more details were recorded in Supplementary Table S2. A healthy diet was considered if ≥ 2 healthy food items were fulfilled. Clinical characteristics included body mass index (BMI), the use of antihypertensives, cholesterol-lowering drugs, aspirin, and mental/sleep medication. BMI (kg/m^2) was calculated as the body weight (kg) divided by the square of height (m). Detailed information on mental/sleep medication use was provided in Supplementary Table S3.

Statistical analysis

Baseline characteristics of 69 524 participants were expressed as mean (*SD*) or number (percentage) in each category of the healthy sleep score. Using the group of participants who had a healthy sleep score ≤ 1 as the reference group, we estimate the hazard ratio (HR) and 95% confidence interval (CI) with the Fine-Gray sub-distribution hazard model, accounting for competing risk of mortality and set follow-up duration as the time scale. The dose-dependent association of the healthy sleep score with the incidence of overall CMM was analyzed by setting the healthy sleep score as a continuous variable. In the present analyses, we developed three models. Model 1 was adjusted for age and gender. Model 2 was additionally adjusted for ethnicity, TDI, smoking status, alcohol consumption, diet, and physical activity. Model 3 (the full-adjusted model) contained all covariates in Model 2 and clinical profiles including BMI and the use of aspirin, cholesterol-lowering, and antihypertensive drugs. After the Spearman rank correlation coefficients (Rs) among five components of the healthy sleep pattern were demonstrated to be below 0.10 (Supplementary Table S4), we also set three models above and further adjusted for the other four components when analyzing the association between a single dimension of the healthy sleep pattern and the risk of overall CMM. In addition, we used the same strategy to assess the associations of the healthy sleep score and its components with the incidence of DM, CHD, and stroke, respectively.

To confirm the robustness of our results, we conducted several sensitivity analyses. In sensitivity analysis 1, we excluded 4251 newly diagnosed (<1 year) hypertensives. In sensitivity analysis 2, we excluded 376 participants who died within the first 2 years of follow-up. In sensitivity analysis 3, we adjusted the calculation of physical activity to partly offset the exclusion of participants with missing data in physical activity questionnaires. For those who answered their weekly frequency of walking/moderate/vigorous physical activity 10 + minutes but did not record detailed duration, we conservatively substituted the corresponding duration with 10 minutes and reperformed the analysis. In sensitivity analysis 4, we additionally adjusted for the use of mental/sleeping medicine [35]. In sensitivity analysis 5, we modified the definition of DM by excluding self-reported information. In sensitivity analysis 6, we constructed a weighted healthy sleep score ranging from 0 to 5 points. This weighted score based on five dimensions of healthy sleep was calculated by using the following equation: weighted healthy sleep score = (β1 × dimension 1 + β2 × dimension 2 + β3 × dimension 3 + β4 × dimension 4 + β5 × dimension 5) × 5/ (sum of the β coefficients) [24].

Furthermore, to assess whether the association between the healthy sleep score and the incidence of overall CMM was consistent among different subgroups, the primary analysis was stratified by gender (male or female), age (<60 or ≥ 60 years), healthy diet (yes or no), BMI (≥30 or < 30 kg/m2), and the use of antihypertensives (yes or no).

All analyses were performed using R, version 4.1.1. All *p* values for the tests were two-sided, and the *p* value < 0.05 was considered statistically significant.

Results

The baseline characteristics of 69 524 enrolled hypertensives are expressed in Table 1. Of the 69 524 participants, the mean age (*SD*) was 59.33 (7.23) years, and 34 731 (50.00%) were male. 5.15%, 22.13%, 39.30%, 27.97%, and 5.45% had a healthy sleep score of 5, 4, 3, 2, and ≤ 1, respectively. Participants with higher healthy sleep scores were less probably to be current smokers and cholesterol-lowering drug users. They tended to have a healthy diet, proper physical activity, and lower measurements of BMI. Furthermore, participants with no frequent daytime sleepiness

contributed the most significant proportion in each group (Table 1).

During a median of 11.92 years of follow-up, 13 539 CMM cases were recorded, including 7 418 CHD, 4 765 DM, and 3 492 stroke cases. The cumulative incidence of overall CMM among five groups during follow-up is presented in Supplementary Figure S2, indicating a lower cumulative incidence of overall CMM in the patients with a higher healthy sleep score.

Table 2 shows the association of the healthy sleep score and its components with the risk of overall CMM in three models, respectively. The healthy sleep score was inversely associated with the incidence of overall CMM (p for trend < 0.001 for three models). After adjusting for age, gender, ethnicity, TDI, and lifestyle factors, the HR (95% CI) for overall CMM was 0.90 (0.89–0.92) for a 1-point increase in the healthy sleep score. The association was slightly attenuated but remained significant after further adjusting for BMI and the use of aspirin, cholesterol-lowering drugs, and antihypertensives. Compared to participants with a healthy sleep score of 0 to 1, the fully adjusted HR (95% CI) for overall CMM was 0.73 (0.66–0.81) among patients with a healthy sleep score of 5. For each binary (low risk vs. high risk) component of the healthy sleep pattern, early chronotype, sleep 7–8 h/d, no frequent daytime sleepiness, and free of insomnia were independently associated with a decreased risk of overall CMM by 4%, 9%, 22%, and 10%, respectively. No snoring was related to a lower risk of overall CMM after adjustment for demographic variables and lifestyle factors. However, the association was eliminated in the full-adjusted model (HR = 0.98; 95% CI 0.94–1.01) (Table 2).

We also found inverse associations between the healthy sleep score and the risks of CHD, DM, and stroke, respectively (Figure 1). In the full-adjusted model, each unit increase in the healthy sleep score was associated with an HR (95% CI) of 0.89 (0.87–0.92) for DM, 0.93 (0.91–0.96) for CHD, and 0.96 (0.93–1.00) for stroke (Figure 1). Compared to the reference group, the fully adjusted HRs (95% CI) of participants with a healthy sleep score of 5 were 0.77 (0.67–0.89) for CHD, 0.63 (0.53–0.74) for DM, and 0.80 (0.66–0.98) for stroke, respectively (Figure 1). The associations of different components of the healthy sleep pattern with risks of CHD, DM, and stroke appeared varied. Sleep 7–8 h/d and no frequent daytime sleepiness was independently associated with a decreased risk of DM, CHD, and stroke; free of insomnia was related to a decreased risk of DM and CHD, respectively; while early chronotype was only associated with a lower risk of stroke; and no snoring was only related to a decreased risk of DM (Supplementary Table S5).

The relationship between the healthier sleep pattern and the lower risk of overall CMM remained consistent in the first five sensitivity analyses. Additionally, the results were not substantially changed for the weighted healthy sleep score in sensitivity analysis 6 (Supplementary Figure S3). The inverse association was not modified in the different subgroups of the population (p for interaction >0.05) (Figure 2).

Conclusion and Discussion

In this large-scale prospective study enrolling 69 524 hypertensives at baseline from the UKB, we found inverse associations of the healthy sleep score with CMM outcomes. After fully adjusting for covariables, participants with a healthy sleep score of 5 had a 27% lower risk of overall CMM than those with a healthy sleep score of 0–1. The association between a higher healthy sleep score and a lower risk of overall CMM among hypertensives remained consistent in a series of sensitivity analyses. It was not modified by age, gender, BMI, diet, and use of antihypertensives.

There were no existing studies investigating the role of this sleep pattern in the progression from hypertension to overall CMM. Only one recent cohort study explored the implication of the healthy sleep pattern in the passage from hypertension to

Table 1. Baseline characteristic of 69 524 hypertensives according to healthy sleep score

	Healthy sleep score				
Baseline characteristics	0-1	2	3	4	5
No. (%) of participants	3579 (5.15)	15385 (22.13)	27327 (39.30)	19445 (27.97)	3788 (5.45)
Age, mean (*SD*), year	58.11 (7.42)	58.82 (7.28)	59.48 (7.11)	59.79 (7.18)	59.15 (7.66)
Male, No. (%)	1905 (53.2)	8193 (53.3)	13432 (49.2)	9175 (47.2)	2026 (53.5)
White, No. (%)	3358 (93.8)	14629 (95.1)	26158 (95.7)	18651 (95.9)	3562 (94.0)
Townsend Deprivation Index, mean (*SD*)	−0.92 (3.29)	−1.28 (3.11)	−1.48 (2.99)	−1.59 (2.93)	−1.54 (2.98)
Current smoker, No. (%)	493 (13.8)	1768 (11.5)	2246 (8.2)	1323 (6.8)	236 (6.2)
Alcohol consumption, No. (%)	—	—	—	—	—
Never drinking or drinking occasionally	1891 (52.8)	7923 (51.5)	14169 (51.8)	10546 (53.5)	2160 (56.2)
Drinking usually	1688 (47.2)	7462 (48.5)	13158 (48.2)	9061 (46.6)	1661 (43.8)
Healthy diet, No. (%)	1750 (48.9)	8102 (52.7)	15658 (57.3)	12017 (61.8)	2479 (65.4)
Proper physicalactivity, No. (%)	2586 (72.3)	12009 (78.1)	22101 (80.9)	16307 (83.9)	3252 (85.9)
BMI, mean (*SD*)	30.50 (5.47)	29.61 (5.19)	28.76 (4.80)	28.04 (4.62)	27.71 (4.59)
Aspirin, No. (%)	574 (16.0)	2620 (17.0)	4716 (17.3)	3282 (16.9)	631 (16.7)
Cholesterol-lowering drugs, No. (%)	989 (27.6)	4104 (26.7)	7235 (26.5)	5023 (25.8)	908 (24.0)
Antihypertensive drugs, No. (%)	2234 (62.4)	9719 (63.2)	17429 (63.8)	12571 (64.6)	2387 (63.0)
Healthy sleep factors, No. (%)	—	—	—	—	—
Early chronotype	278 (7.8)	5507 (35.8)	17976 (65.8)	17366 (89.3)	3788 (100.0)
Sleep 7–8h/d	143 (4.0)	5721 (37.2)	18156 (66.4)	18293 (94.1)	3788 (100.0)
No frequent daytime sleepiness	2771 (77.4)	14627 (95.1)	26923 (98.5)	19390 (99.7)	3788 (100.0)
Free of insomnia	41 (1.1)	757 (4.9)	3927 (14.4)	6591 (33.9)	3788 (100.0)
No snoring	157 (4.4)	4158 (27.0)	14999 (54.9)	16140 (83.0)	3788 (100.0)

Table 2. HRs (95% CIs) for overall CMM by healthy sleep score and its components

		Model 1*		Model 2†		Model 3‡	
	Number of cases (%)	HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P
Healthy sleep score		0.89 (0.87–0.90)	<0.001	0.90 (0.89–0.92)	<0.001	0.93 (0.91–0.95)	<0.001
0–1	887 (24.78)	Reference	…	Reference	…	Reference	…
2	3269 (21.25)	0.82 (0.76–0.88)	<0.001	0.85 (0.79–0.91)	<0.001	0.88 (0.81–0.94)	<0.001
3	5308 (19.42)	0.73 (0.68–0.79)	<0.001	0.77 (0.72–0.83)	<0.001	0.82 (0.77–0.89)	<0.001
4	3438 (17.68)	0.65 (0.61–0.71)	<0.001	0.70 (0.65–0.75)	<0.001	0.77 (0.71–0.83)	<0.001
5	637 (16.82)	0.62 (0.56–0.68)	<0.001	0.66 (0.59–0.73)	<0.001	0.73 (0.66–0.81)	<0.001
Components§							
Early chronotype	8661 (19.28)	0.93 (0.90–0.96)	<0.001	0.95 (0.92–0.99)	0.008	0.96 (0.93–1.00)	0.028
Sleep 7-8h/d	8545 (18.54)	0.86 (0.83–0.89)	<0.001	0.89 (0.86–0.92)	<0.001	0.91 (0.88–0.94)	<0.001
No frequent daytime sleepiness	12974 (19.22)	0.70 (0.64–0.76)	<0.001	0.75 (0.69–0.82)	<0.001	0.78 (0.72–0.85)	<0.001
Free of insomnia	2809 (18.60)	0.90 (0.86–0.94)	<0.001	0.90 (0.86–0.94)	<0.001	0.90 (0.87–0.94)	<0.001
No snoring	7231 (18.43)	0.91 (0.88–0.94)	<0.001	0.90 (0.87–0.94)	<0.001	0.98 (0.94–1.01)	0.190

CMM: cardiometabolic multimorbidity; HR: hazard ratio; CI: confidence interval.
*Model 1: adjusted for age and gender, while additionally adjusted for the other four components when analyzing the association between components of the healthy sleep pattern and the incidence of overall CMM.
†Model 2: adjusted for variables in model 1, Townsend deprivation index, ethnicity, smoking status, alcohol consumption, diet, and physical activity.
‡Model 3: adjusted for variables in model 2, BMI and the use of aspirin, cholesterol-lowering, and antihypertensive drugs.
§Each component of the healthy sleep pattern was modeled as a binary variable: met or did not meet the healthy criterion.

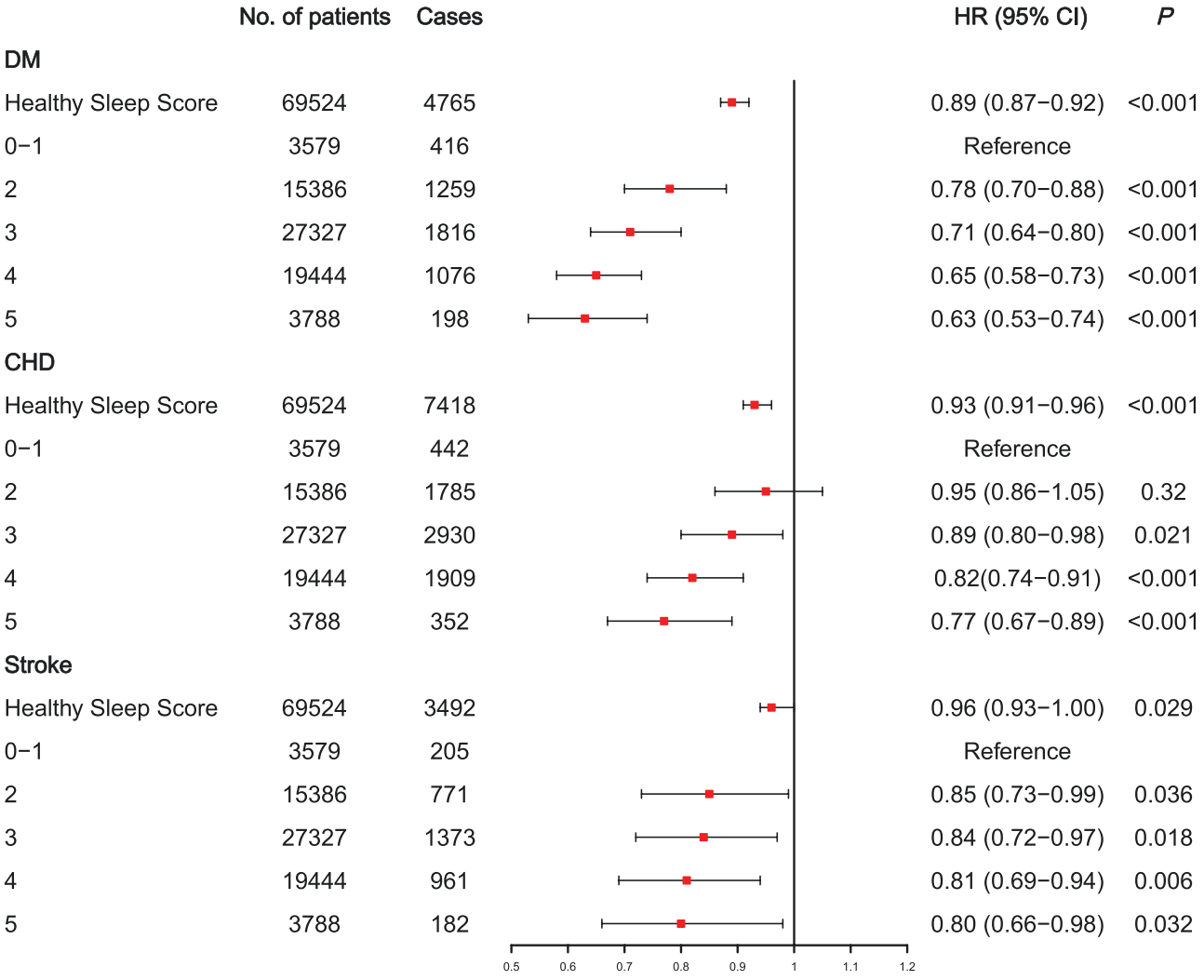

Figure 1. The association between the healthy sleep score with the incidence of CHD, DM, and stroke in the full-adjusted model The full-adjusted model was adjusted for age, sex, Townsend Deprivation Index, ethnicity, physical activity, diet, smoking status, alcohol consumption, BMI, and the use of aspirin, cholesterol-lowering drugs, and antihypertensives. CHD: coronary heart disease; DM: diabetes mellitus; HR: hazard ratio; CI: confidence interval.

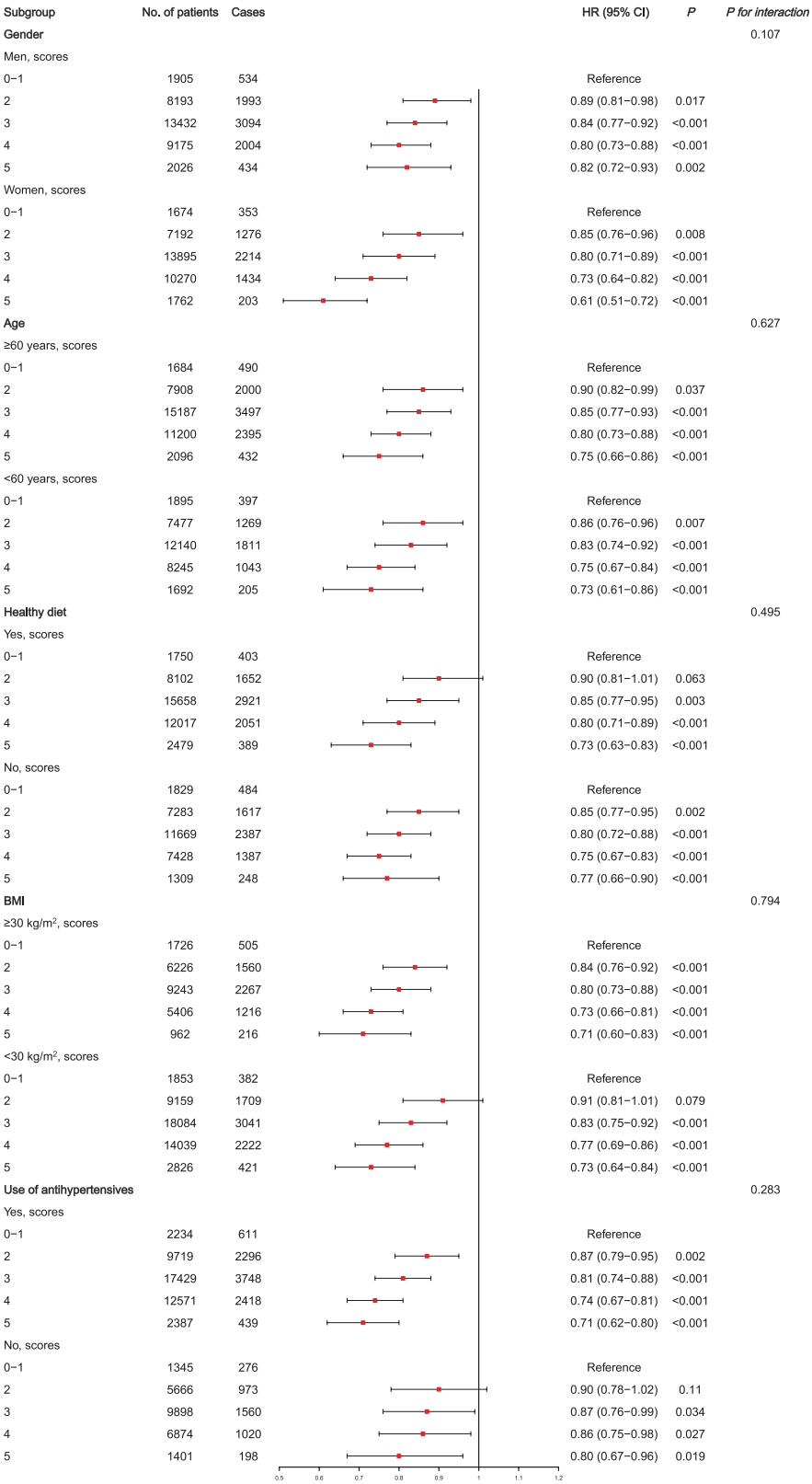

Figure 2. The association of healthy sleep score with the incidence of cardiometabolic multimorbidity in several subgroups. HR: hazard ratio; CI: confidence interval.

DM [28]. An inverse association was observed between a healthy sleep score and DM outcome among hypertensives (HR = 0.78; 95% CI 0.75–0.81), similar to our results (HR = 0.89; 95% CI 0.87–0.92). A few researchers pointed out that poor sleep quality assessed by specific sleep patterns was related to several risk factors of CVD among hypertensives [36,37]. Additionally, the relationship between a single dimension of sleep and the prognosis of hypertension, such as CVD complications, has been

assessed previously [20,21]. Based on the intimate association of hypertension with sleep and other CMDs including DM, CHD, and stroke [38–40], we first explored the implication of a healthy sleep pattern combining five common dimensions of sleep health on the progression from hypertension to overall CMM and found this healthy sleep pattern was related to lower risks of CMM outcomes among hypertensives.

Our results appeared in line with the previous studies which explored the association between other particular sleep patterns and CMDs outcomes in the general population [41–43]. A recent study based on the Midlife in the United States study showed that the sleep health score, which was calculated by empirically derived cut-off values for six dimensions of sleep (daytime alertness and sleep quality, timing, regularity, efficiency, and duration), was associated with about a 10% lower risk of total cardiometabolic morbidity [44]. In another observational study, researchers found the poor sleep quality assessed by the Pittsburgh sleep quality index was related to a 2.6-fold higher risk of DM [42]. A similar result was observed in our study that each unit increase in the healthy sleep score was associated with a 7% lower risk of overall CMM among patients with hypertension. In addition, a large-scale cohort study demonstrated that general participants with a healthy sleep score of 5 had a 35%, 34%, and 34% decreased risk of CVD, CHD, and stroke, respectively, compared to those with a sleep score of 0–1 [24]. In the current study, we also observed 23% and 20% decreased risks of CHD and stroke among hypertensives with the highest healthy sleep score, which was slightly weaker than that in CVD prevention in the general population [24]. It indicated that the compositive healthy sleep pattern which played an essential role in the primary prevention of CMDs in the general population might play a similar role in the secondary prevention among patients with hypertension.

To determine which individual component of the healthy sleep pattern contributed to the incidence of CMM, we further explored the relationships between the five dimensions and risks of CMM outcomes. We found that no frequent daytime sleepiness, free of insomnia, sleep 7–8 h/day, and early chronotype was independently associated with a 22%, 10%, 9%, and 4% lower risk of overall CMM in the fully adjusted model. Our results were parallel to those of previous studies reporting that late chronotype [19], short or long sleep duration [45–47], daytime sleepiness [48, 49], and insomnia [13, 50] increased the risk of CMDs in the general population. However, for no snoring, its association with a lower risk of overall CMM was eliminated after further adjusting for BMI and the use of aspirin, cholesterol-lowering drugs, and antihypertensives, which was observed in several previous studies [24, 48].

No current study has explored how the combination of sleep dimensions might affect CMM risk. However, these different dimensions of unhealthy sleep may individually act through several mechanisms that could operate synergistically to increase the risk of CMM, such as inflammatory responses, oxidative stress, endothelial dysfunction, atherosclerosis, insulin resistance, prothrombotic state, and disrupted circadian rhythm [51–53].

Strengths and limitations

The main strength of our study is the enormous and detailed data from the UKB. Thus, we could account for potential confounding factors and conduct a series of sensitivity analyses and stratification analyses to verify our results. Another strength of the current study is that we used the healthy sleep pattern combining five common and essential dimensions of sleep health to assess its association with the incidence of CMM.

However, our study has several limitations. First, the associations between the healthy sleep pattern and lower risks of CMM outcomes cannot be interpreted as causal relations in this observational study. Second, the sleep behaviors at baseline only reflected the sleep condition of participants in the last 4 weeks. Whether they changed their sleep habits in the follow-up was not acquired. Thus, future cohort studies with repeated measurements are needed to ensure sleep behaviors consistence. Third, as discussed in the previous study [24], this healthy sleep pattern combining five dimensions of sleep health could not reflect the holistic sleep condition. Other dimensions of sleep associated with CMDs risks were not considered in this sleep pattern, such as restless legs syndrome and sleep apnea syndrome [54, 55]. Finally, although we adjusted for covariables in multiple aspects, other residual confounding effects might remain from unknown or unmeasured factors.

In this cohort study, our results addressed the gap of the role of this healthy sleep pattern on the progression from hypertension to overall CMM and highlighted the significance of sleep health again. Individuals with an unhealthy sleep pattern might improve sleep by improving diet, physical activity, weight condition, and sleep environment, as previous studies found that these factors were associated with good sleep quality [56–59]. However, whether these associations could be interpreted as causal relationships still needs further investigation. Additionally, the potential protective role of other uninvolved dimensions of healthy sleep in reducing the risk of CMM among hypertensives might remain. Future cohort studies are needed to explore a more complete healthy sleep pattern to strengthen the conclusion of our research.

Supplementary Material

Supplementary material is available at *SLEEP* online.

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