Sleep Pattern, Lifestyle Pattern, and Risks of Overall and 20 Types of Cancers: Findings From the UK Biobank Cohort

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Objectives: Sleep health and other lifestyle behaviours are gaining increasing attention in public health, particularly for cancer prevention, but a comprehensive assessment is lacking.

Methods: The study included 380,042 UK Biobank participants. A healthy sleep score was constructed based on five sleep factors: chronotype, sleep duration, insomnia, snoring, and daytime dozing. A healthy lifestyle score was constructed based on four lifestyle factors: smoking, alcohol consumption, diet and physical activity. The effect of healthy sleep and lifestyle on cancer risk was examined by Cox proportional hazard models.

Results: Both healthy sleep and lifestyle patterns were significantly associated with a reduced risk of overall cancer and specific cancer sites. Participants with healthy sleep and lifestyle patterns had a lower risk of overall cancer (HR = 0.72, 95% CI = 0.68–0.77), liver cancer (HR = 0.53, 95% CI = 0.31–0.90), bladder cancer (HR = 0.61, 95% CI = 0.47–0.79), lung cancer (HR = 0.22, 95% CI = 0.19–0.27), and colorectal cancer (HR = 0.80, 95% CI = 0.66–0.96) compared to those with unhealthy patterns.

Conclusion: Our findings highlight the importance of public health education and interventions to improve sleep and other lifestyle behaviours for cancer prevention.

Keywords: cancer prevention, UK biobank, healthy sleep pattern, healthy lifestyle pattern, human behaviour

INTRODUCTION

Sleep disorders are increasingly prevalent worldwide [1] and have been linked to numerous chronic health problems like obesity [2], cardiovascular disease [3] and cancers [4–8]. Sleep quality and duration are two main contributors. Previous studies have revealed that long or short sleep duration [4, 5, 8–10], poor sleep quality such as insomnia [11–13] and snoring [14] potentially increase the risk of cancers. However, sleep is multidimensional, and sleep duration, timing, continuity, and sleepiness may interconnect with each other [15] and the comprehensive impact of sleep factors on the risk of cancer remains to be explored.

Other ordinary lifestyle factors, including smoking, alcohol intake, diet habits, as well as exercise engagement, were also related to cancer risk with substantial evidence [16–18]. Lacking physical activity is a well-recognized contributor to various cancers, including colorectal cancer and breast cancer [19]. These lifestyle factors may also have an impact on sleep health. For example, excessive alcohol consumption could disrupt sleep homeostasis, leading to sleep disruptions like snoring [20, 21]. Cigarette smoking has potential associations with poor sleep quality [22, 23]. Moreover, physical exercise has been identified as one of the effective non-pharmacological sleep health interventions [24, 25]. Diet, especially fruit and vegetable intake, may influence sleep quality through the biogenesis of melatonin or polyphenol content [26, 27]. Therefore, the effect of sleep health and other lifestyle factors on cancer risks should be investigated jointly to better explain their roles in cancer development.

In this study, the individual impact of sleep, as well as other lifestyle factors on overall cancer and 20 types of cancers, were initially examined. Subsequently, the combined influence of sleep and lifestyle patterns on cancer risks was also investigated. By converting sleep and other lifestyle factors into measurable scores, we hope to provide a comprehensible explanation of their joint effects on cancer and support guidance on healthy sleep and lifestyle behaviours for reducing cancer risks.

METHODS

Participants

The study population was from the UK Biobank, a large prospective cohort study involving over 500,000 British people between the ages of 37 and 73 years. Eligible participants attended assessment centers across the UK during the baseline assessment period from 2006 to 2010, where they filled in questionnaires and underwent physical measurements. Longitudinal follow-up was facilitated by connecting to national medical and mortality records. Details about the study design and methodology have been described [28]. In this study, participants who had prevalent cancer at baseline were not included (n = 28,699). Subsequently, participants lacking data on the primary exposures to five sleep traits (n = 86,508) or four lifestyle factors (n = 7,118) were also excluded, yielding a participant sample of 380,042 for later analysis (**Supplementary Figure S1**).

Sleep Traits Assessment, Sleep Score Calculation and Sleep Pattern Definition

According to the touchscreen questionnaires collected at baseline, five sleep traits were measured, which consisted of sleep duration, chronotype, insomnia, daytime dozing, and snoring. The detailed questionnaire, along with definitions of each item, can be found in **Supplementary Table S1**. In brief, we defined a sleep duration of 7–8 h each day as a healthy sleep factor, while sleep durations longer or shorter were considered unhealthy. The preference for a morning chronotype was categorized as a healthy sleep factor. Additionally, participants who reported not having usual

insomnia symptoms were defined as exhibiting a healthy sleep factor, and participants who did not receive complaints about snoring from others were also classified as having a healthy sleep factor. Moreover, the absence of excessive daytime dozing was considered a healthy sleep factor. Participants were assigned a score of 1 for each sleep factor when their answer was categorized as "healthy sleep factor" and otherwise a score of 0. A healthy sleep score was generated based on the summation of five individual scores of healthy sleep factor, which ranged between 0 and 5. A healthy sleep pattern was characterized by a total sleep score of 4 or higher, whereas an unhealthy sleep pattern was characterized by a score of 3 or lower [15].

Lifestyle Factor Assessment, Lifestyle Score Calculation and Lifestyle Pattern Definition

This study evaluated four lifestyle factors by self-reported questionnaire, including cigarette smoking, alcohol consumption, fruit and vegetable intake, and physical activity. These specific factors were selected according to the guidelines established by the World Cancer Research Fund/American Institute of Cancer Research [WCRF/AICR (Arlington, VA)] [29] and had been incorporated into a score in several healthy lifestyle-related studies [29–32]. The definition of healthy lifestyle factors included no current smoking, low to moderate alcohol intake (0–14 UK units/week), regular physical activity (≥600 MET-mins/week), and a diet abundant in fruits and vegetables (over 5 servings daily). Detailed definitions of each item can be found in **Supplementary Table S2**. Participants were assigned a score of 1 when their answer was categorized as "healthy" for each lifestyle factor and otherwise will be assigned a score of 0. The healthy lifestyle score was determined by totaling the scores of four distinct healthy lifestyle factors, which ranged between 0 and 4. A healthy lifestyle pattern was characterized by a total score of ≥ 3, an intermediate lifestyle pattern was characterized by a total score of 2, and an unhealthy lifestyle pattern was characterized by a total score of ≤1 [15].

Outcomes

Cancer diagnoses among participants were ascertained through the hospital, national cancer registries, and death records, with cancer cases classified according to the International Classification of Diseases, 9th or 10th revision (ICD9 or ICD10). Participants were follow-up until the endpoint, which was defined as the earliest occurrence of four scenarios: cancer diagnosis, death, loss or the end of the follow-up period (October 2015 in Scotland and March 2016 in England and Wales). Finally, we defined "overall cancer" as all malignant neoplasms except those coding as C44, defined as "Other and unspecified malignant neoplasms of skin." We also included 20 types of common tumors, encompassing cancers affecting various regions of the body such as the head and neck, esophagus, stomach, colon and rectum, liver, pancreas, breast, uterus, ovary, prostate, lung, kidney, bladder, brain and central nervous system, thyroid, as well as non-Hodgkin's lymphoma, multiple myeloma, leukemia, melanoma, mesothelioma. The ICD9 and ICD10 codes for each

TABLE 1 | Baseline characteristics of the participants (n = 380,042) by sleep patterns (United Kingdom, 2006–2016).

Characteristics	All	Sleep patterns		P value
		Healthy (n = 221,913)	Unhealthy (n = 158,129)	
Age, year (mean, SD)	56.23 (8.11)	56.07 (8.22)	56.46 (7.93)	<0.001
Male (n, %)	173,368 (45.62)	95,967 (43.25)	77,401 (48.95)	<0.001
Townsend Deprivation Index (mean, SD)	−1.42 (3.02)	−1.57 (2.94)	−1.23 (3.12)	<0.001
Sedentary time, hour/day (mean, SD)	4.81 (2.39)	4.59 (2.28)	5.11 (2.51)	<0.001
Ethnicity (n, %)				<0.001
White	359,944 (94.71)	210,703 (94.95)	149,241 (94.38)	
Non-white	15,977 (4.20)	8,964 (4.04)	7,013 (4.43)	
Unknown/Missing	4,121 (1.08)	2,246 (1.01)	1,875 (1.19)	
Education (n, %)				<0.001
College	126,594 (33.31)	79,103 (35.65)	47,491 (30.03)	
Less than college	250,628 (65.95)	141,195 (63.63)	109,433 (69.20)	
Missing	2,820 (0.74)	1,615 (0.73)	1,205 (0.76)	
Employment (n, %)				<0.001
Working	225,628 (59.37)	134,969 (60.82)	90,659 (57.33)	
Retired	121,561 (31.99)	70,456 (31.75)	51,105 (32.32)	
Other	32,853 (8.64)	16,488 (7.43)	16,365 (10.35)	
BMI, kg/m^2 (n, %)				<0.001
<25	126,215 (33.21)	83,693 (37.71)	42,522 (26.89)	
25–29.9	161,448 (42.48)	93,748 (42.25)	67,700 (42.81)	
≥30	90,592 (23.84)	43,532 (19.62)	47,060 (29.76)	
Missing	1,787 (0.47)	940 (0.42)	847 (0.54)	
Smoking (n, %)				<0.001
Never	208,255 (54.80)	129,582 (58.39)	78,673 (49.75)	
Former	132,349 (34.82)	73,667 (33.20)	58,682 (37.11)	
Current	39,438 (10.38)	18,664 (8.41)	20,774 (13.14)	
Drink alcohol, UK unit (n, %)				<0.001
≤14	204,408 (53.79)	122,256 (55.09)	82,152 (51.95)	
14–28	91,764 (24.15)	55,401 (24.97)	36,363 (23.00)	
≥28	83,870 (22.07)	44,256 (19.94)	39,614 (25.05)	
Fruit and vegetable intake serving (n, %)				<0.001
≥5	158,786 (41.78)	96,069 (43.29)	62,717 (39.66)	
2–5	193,195 (50.84)	112,435 (50.67)	80,760 (51.07)	
<2	28,061 (7.38)	13,409 (6.04)	14,652 (9.27)	
Physical activity, MET-mins/week (n, %)				<0.001
≥1,800	132,645 (34.90)	80,813 (36.42)	51,832 (32.78)	
600–1,800	134,895 (35.49)	81,128 (36.56)	53,767 (34.00)	
0–600	112,502 (29.60)	59,972 (27.03)	52,530 (33.22)	
Healthy lifestyle pattern				<0.001
Healthy	245,911 (64.71)	151,829 (68.42)	94,082 (59.50)	
Intermediate	103,832 (27.32)	56,362 (25.40)	47,470 (30.02)	
Unhealthy	30,299 (7.97)	13,722 (6.18)	16,577 (10.48)	

SD, standard deviation; BMI, body mass index; MET, metabolic equivalent.

cancer and the numbers of cases are shown in **Supplementary Table S3**. Participants diagnosed with multiple cancers on the same date (n = 67) were excluded from the analysis of specific types of cancers but were retained as a case for the overall cancer study.

Statistical Analysis

Baseline characteristics of the study population were described using mean and standard deviation (SD) for continuous variables, along with frequency and the corresponding percentages for categorical data. The follow-up period was calculated from the recruitment date to the earliest date among the four scenarios: cancer diagnosis, death, loss or the end of the follow-up period. The Cox proportional hazard model was used to explore the separate and joint association of sleep and lifestyle patterns with

cancer risk. Assumptions of proportional hazards were examined by Schoenfeld residuals. Three models were employed to analyze the link between sleep patterns and cancer risks. As for the first model, only sex and age were used as covariates. The second model was adjusted for sex, age, socioeconomic conditions (measured by Townsend deprivation index, TDI), ethnicity (white, non-white or unknown/missing), sedentary time (sum of hours spent on activities such as television and computer usage, driving per day), employment status (working, retired, or others), education (college, less than college), and body mass index (BMI) (<25, 25–29.9, or ≥30). The third model includes additional covariates of lifestyle pattern (healthy, intermediate, unhealthy). For the analysis of an individual sleep factor, all the other sleep factors were included as covariates. For the analysis of a healthy sleep pattern, the above covariates were

TABLE 2 | Associations of high-risk groups of sleep pattern, sleep factors, lifestyle pattern, and lifestyle factors with overall cancer, liver cancer, bladder cancer, lung cancer and colorectal cancer (United Kingdom, 2006–2016).

Exposure	%[a]	Overall cancer		Liver cancer		Bladder cancer		Lung cancer		Colorectal cancer	
		HR (95% CI)[b]	P value	HR (95% CI)[b]	P value	HR (95% CI)[b]	P value	HR (95% CI)[b]	P value	HR (95% CI)[b]	P value
Sleep patterns											
Unhealthy sleep pattern	41.61	Reference	—	Reference	—	Reference	—	Reference	—	Reference	—
Healthy sleep pattern	58.39	**0.95 (0.93, 0.98)**	**<0.001**	**0.73 (0.57, 0.94)**	**0.015**	**0.82 (0.73, 0.93)**	**0.002**	**0.90 (0.81, 0.99)**	**0.030**	**0.92 (0.85, 0.99)**	**0.036**
Healthy sleep factors											
Healthy sleep duration	68.46	0.99 (0.97, 1.02)	0.664	**0.73 (0.57, 0.95)**	**0.020**	**0.87 (0.76, 0.99)**	**0.032**	**0.89 (0.80, 0.99)**	**0.030**	0.93 (0.85, 1.01)	0.066
Morning chronotype	62.74	**0.96 (0.94, 0.99)**	**0.003**	0.98 (0.75, 1.27)	0.863	0.94 (0.83, 1.07)	0.368	**0.87 (0.79, 0.97)**	**0.009**	0.98 (0.90, 1.06)	0.579
No usual insomnia	72.61	**0.97 (0.94, 1.00)**	**0.045**	0.78 (0.60, 1.02)	0.067	0.93 (0.81, 1.07)	0.297	0.98 (0.88, 1.09)	0.659	1.09 (1.00, 1.19)	0.060
No self-reported snoring	62.70	0.99 (0.96, 1.01)	0.322	1.08 (0.83, 1.40)	0.555	0.90 (0.79, 1.02)	0.089	0.98 (0.89, 1.09)	0.769	0.96 (0.88, 1.04)	0.293
No excessive daytime dozing	97.31	0.93 (0.87, 1.00)	0.051	0.67 (0.40, 1.15)	0.145	1.03 (0.73, 1.44)	0.870	0.92 (0.71, 1.19)	0.536	0.91 (0.74, 1.13)	0.385
Lifestyle patterns											
Unhealthy	7.97	Reference	—	Reference	—	Reference	—	Reference	—	Reference	—
Intermediate	27.32	**0.84 (0.80, 0.88)**	**<0.001**	**0.65 (0.43, 0.98)**	**0.041**	**0.78 (0.63, 0.96)**	**0.019**	**0.44 (0.38, 0.50)**	**<0.001**	1.00 (0.87, 1.16)	0.968
Healthy	64.71	**0.77 (0.73, 0.80)**	**<0.001**	**0.65 (0.44, 0.95)**	**0.028**	**0.70 (0.58, 0.86)**	**<0.001**	**0.24 (0.21, 0.28)**	**<0.001**	**0.86 (0.74, 0.98)**	**0.028**
Healthy lifestyle factors											
Not current smoker	89.62	**0.73 (0.70, 0.76)**	**<0.001**	0.82 (0.56, 1.19)	0.295	**0.53 (0.45, 0.63)**	**<0.001**	**0.18 (0.17, 0.20)**	**<0.001**	0.92 (0.81, 1.05)	0.218
Low/moderate alcohol consumption	77.93	**0.95 (0.92, 0.98)**	**<0.001**	1.09 (0.81, 1.47)	0.573	1.07 (0.93, 1.23)	0.356	**0.85 (0.76, 0.95)**	**0.004**	**0.76 (0.69, 0.82)**	**<0.001**
Regular physical activity	70.40	**0.97 (0.94, 0.99)**	**0.015**	**0.65 (0.50, 0.84)**	**<0.001**	1.04 (0.91, 1.20)	0.557	**0.85 (0.77, 0.95)**	**0.003**	1.00 (0.91, 1.08)	0.925
Healthy diet	41.78	**0.96 (0.94, 0.99)**	**0.002**	1.06 (0.82, 1.37)	0.654	0.93 (0.82, 1.06)	0.296	**0.86 (0.77, 0.95)**	**0.004**	1.01 (0.94, 1.10)	0.732

[a]Percentage referred to the proportion of healthy responders for a given sleep factor among 380,042 participants.
[b]The hazard ratios (HRs), corresponding 95% confidence intervals (CIs) and P values were calculated using Cox regression model adjusting for sex, age, Townsend Deprivation Index, ethnicity, sedentary time, employment, education, BMI, and mutually adjusted for sleep pattern or lifestyle pattern as appropriate.
Bold values provided P value < 0.05.

used in the second model in addition to sleep pattern (healthy or unhealthy). The Kaplan-Meier plot was employed to illustrate the cumulative cancer incidences across different sleep pattern groups or different lifestyle pattern groups. In the sensitivity analysis, incident cancers that occurred in the first 2 years during follow-up were excluded. The examination of the relationship between sleep pattern and lifestyle pattern with cancer risks was stratified by gender. To mitigate the risk of inflated false-positive results, we utilized the Benjamini-Hochberg procedure and presented adjusted P values for the primary analyses. R software (version 4.1.2) was used for all statistical analyses, and P < 0.05 was considered statistically significant.

RESULTS

The number of cases for overall cancer, 20 types of cancers, and controls were grouped by the sleep and lifestyle score and are presented in **Supplementary Tables S4, S5**. The final study sample included 380,042 participants (24,618 incident cancer cases, mean age = 56.2 years old, 45.6% males). The average follow-up duration was 6.9 years. An overview of the demographical features of the study population is shown in **Table 1**. Up to 58.4% of participants had a healthy sleep pattern, with this group characterized by a higher proportion of females, younger age, and lower BMI compared to individuals in the unhealthy sleep pattern group. As for socioeconomic factors, the healthy sleep pattern group exhibited lower socioeconomic deprivation, a higher percentage of college degree attainment, and a higher percentage of employment at work. In terms of lifestyle factors, the participants with a healthy sleep pattern had less sedentary time, consume more vegetables and fruits, were less likely to smoke, drink less alcohol, and participate in more physical activities.

The Relationship Between Healthy Sleep, Lifestyle Factors and Cancers

The associations between sleep pattern and lifestyle pattern with the risk of cancer are displayed in **Table 2** and **Supplementary**

Tables S6, S7. The overall cancer risk was associated with both healthy sleep pattern (HR = 0.95, 95% CI = 0.93–0.98) and healthy lifestyle pattern (HR = 0.77, 95% CI = 0.73–0.80). Additionally, the healthy sleep and lifestyle pattern also showed protective effects on four types of cancer, including liver cancer (HR = 0.73, 95% CI = 0.57–0.94 for healthy sleep pattern; HR = 0.65, 95% CI = 0.44–0.95 for healthy lifestyle pattern), bladder cancer (HR = 0.82, 95% CI = 0.73–0.93 for healthy sleep pattern; HR = 0.70, 95% CI = 0.58–0.86 for healthy lifestyle pattern), lung cancer (HR = 0.90, 95% CI = 0.81–0.99 for healthy sleep pattern; HR = 0.24, 95% CI = 0.21–0.28 for healthy lifestyle pattern) and colorectal cancer (HR = 0.92, 95% CI = 0.85–0.99 for healthy sleep pattern; HR = 0.86, 95% CI = 0.74–0.98 for healthy lifestyle pattern). The cumulative incidences of cancers in different sleep pattern and lifestyle pattern subgroups are detailed in **Supplementary Figures S2, S3**.

The sensitivity study involved excluding incident cancer cases within the first 2 years following the baseline. Consistent and significant effects on overall cancer risk were observed with adherence to a healthy sleep or lifestyle pattern (HR = 0.95, 95% CI = 0.92–0.98 for healthy sleep pattern; HR = 0.77, 95% CI = 0.73–0.81 for healthy lifestyle pattern). Similar consistent results were also observed for bladder and lung cancers. While the correlation between liver cancer and the healthy lifestyle pattern remained significant, the association between liver cancer and the healthy sleep pattern was no longer significant. In addition, the relationship between colorectal cancer and sleep pattern remained statistically significant, whereas no significant association between colorectal cancer and lifestyle pattern was found (**Supplementary Tables S8, S9**).

Stratification analysis by gender was conducted and the results are shown in **Supplementary Tables S10, S11**. The association of healthy sleep pattern and healthy lifestyle pattern with overall cancer remained statistically significant in both males and females. For females, the associations of healthy sleep and lifestyle patterns with lung cancer risk were consistently observed, while no statistical significance was observed for liver, colorectal and bladder cancer. For males, healthy sleep pattern was significantly associated with colorectal cancer and bladder cancer, and healthy lifestyle pattern was significantly associated with liver, bladder and lung cancers.

Using the healthy sleep score and as healthy lifestyle score continuous variables, consistent results were found on overall cancer, as well as bladder, liver and lung cancer in Model 3. However, no association between healthy sleep and lifestyle factors with colorectal cancer risk was found (**Supplementary Tables S12, S13**). After excluding incident cancer cases in the first 2 years, the associations remained statistically significant except for liver cancer. However, no significant association was observed between the two scores and colorectal cancer, and this result should be interpreted with caution.

We also evaluated the effects of various healthy sleep factors and healthy lifestyle factors on the risk of overall cancer and the likelihood of developing four cancers, including liver cancer, bladder cancer, lung cancer and colorectal cancer (**Table 2**). We found that individuals with morning chronotype (HR = 0.96, 95% CI = 0.94–0.99) or no usual insomnia (HR = 0.97,

95% CI = 0.94–1.00) showed a reduced risk of overall cancer. Besides, a healthy sleep duration was linked to a reduced liver cancer risk (HR = 0.73, 95% CI = 0.57–0.95), bladder cancer risk (HR = 0.87, 95% CI = 0.76–0.99), and lung cancer risk (HR = 0.89, 95% CI = 0.80–0.99). Furthermore, all four lifestyle factors showed significant protective effects on both overall cancer and lung cancer. Results for the overall cancer, as well as all 20 specific cancer sites, are displayed in **Supplementary Figures S4, S5**.

Joint Association of Sleep Pattern and Lifestyle Pattern With Cancers

The joint association of sleep pattern and lifestyle pattern with cancers was additionally evaluated. Compared with the unhealthy sleep - unhealthy lifestyle group, participants with healthy sleep and healthy lifestyle pattern could reduce the risk of overall cancer by 28% (HR = 0.72, 95% CI = 0.68–0.77), liver cancer by 47% (HR = 0.53, 95% CI = 0.31–0.90), bladder cancer by 39% (HR = 0.61, 0.47–0.79), lung cancer by 78% (HR = 0.22, 95% CI = 0.19–0.27), and colorectal cancer by 20% (HR = 0.80, 95% CI = 0.66–0.96) (**Table 3**). After excluding cancer cases diagnosed in the first 2 years post-baseline, consistent results were observed (**Supplementary Table S14**).

DISCUSSION

This study provides new insights into the relationship between sleep patterns, lifestyle patterns, and cancer risk. Using the UK Biobank, one of the largest cohort studies, we examined the individual effects of sleep and lifestyle patterns on the risk of overall cancer and 20 cancer types, as well as the combined impact of these patterns on cancer development. By constructing separate comprehensive scores for sleep and lifestyle patterns, we found that participants with healthier sleep or lifestyle patterns had reduced risks of overall cancer and four specific types—liver, bladder, lung, and colorectal cancers. The joint association analysis consistently supported these findings.

The interplay of sleep timing, quality and duration is widely recognized. They jointly interpret healthy sleep patterns and contribute to many diseases. For example, insomnia and late chronotype might lead to oversleepiness during the day, insufficient sleep duration, and disturbed circadian rhythm [15, 33]. Sleep duration and severe insomnia have joint effects on cardiovascular episodes and overall mortality [34]. Therefore, we suggest that building a comprehensive sleep score should better reflect the overall sleep patterns and interpret the relationship with cancer outcomes. The findings of our research indicated that having a healthy sleep behaviour could decrease the risk of overall cancer, along with colorectal, bladder, lung and liver cancer. In particular, sleep duration, quality and timing (chronotype and insomnia) all contribute to cancer risk, suggesting that promoting healthy sleep for cancer prevention should consider improving sleep duration and quality. Nevertheless, some associations did not retain statistical significance in the sensitivity or stratification analysis and

TABLE 3 | The joint associations of sleep pattern and healthy lifestyle pattern with overall cancer, liver cancer, bladder cancer, lung cancer and colorectal cancer (United Kingdom, 2006–2016).

Sleep pattern	Lifestyle pattern	Overall cancer		Liver cancer		Bladder cancer		Lung cancer		Colorectal cancer	
		HR (95% CI)[a]	P value[a]	HR (95% CI)[a]	P value[a]	HR (95% CI)[a]	P value[a]	HR (95% CI)[a]	P value[a]	HR (95% CI)[a]	P value[a]
Unhealthy	Unhealthy	—	—	—	—	—	—	—	—	—	—
	Intermediate	**0.82 (0.77, 0.87)**	**<0.001**	0.71 (0.40, 1.28)	0.260	0.83 (0.63, 1.11)	0.208	**0.47 (0.39, 0.56)**	**<0.001**	1.02 (0.84, 1.24)	0.835
	Healthy	**0.77 (0.72, 0.82)**	**<0.001**	0.91 (0.54, 1.55)	0.732	**0.75 (0.57, 0.97)**	**0.032**	**0.24 (0.20, 0.29)**	**<0.001**	0.86 (0.71, 1.04)	0.125
Healthy	Unhealthy	0.95 (0.87, 1.03)	0.181	1.26 (0.64, 2.50)	0.505	0.94 (0.66, 1.35)	0.734	0.96 (0.78, 1.18)	0.686	0.94 (0.73, 1.22)	0.662
	Intermediate	**0.81 (0.76, 0.86)**	**<0.001**	0.69 (0.38, 1.24)	0.212	**0.66 (0.49, 0.88)**	**0.005**	**0.39 (0.32, 0.47)**	**<0.001**	0.93 (0.76, 1.13)	0.454
	Healthy	**0.72 (0.68, 0.77)**	**<0.001**	**0.53 (0.31, 0.90)**	**0.020**	**0.61 (0.47, 0.79)**	**<0.001**	**0.22 (0.19, 0.27)**	**<0.001**	**0.80 (0.66, 0.96)**	**0.017**

[a]The hazard ratios (HRs), corresponding 95% confidence intervals (CIs) and P values were calculated using the Cox regression model adjusting for sex, age, Townsend Deprivation Index, ethnicity, sedentary time, employment, education, and BMI.
Bold values provided P value < 0.05.

warrant careful explanation, e.g., no association between sleep patterns and liver cancer after excluding incident cancers diagnosed within the first 2 years of follow-up, no association between sleep patterns and liver cancer when stratified by gender. In addition, some unexpected results were observed in our study and should be explained with caution. For example, a previous study used sleep duration as a continuous variable and found prolonged sleep duration was associated with increased breast cancer risk [35]. In our study, we used a different categorization method by comparing healthy sleep duration (7–8 h per day) with shorter or longer sleep durations and found a lower risk for the shorter or longer sleep time group. This discrepant observation may be explained by the "J-shape" relation between sleep duration and breast cancer risk [36]. We also performed an analysis treating sleep duration as a continuous variable and found a risk effect of prolonged sleep time (HR = 1.03, 95% CI = 1.00–1.06 per hour increase, data not shown), which was consistent with the previous studies. Besides, unexpected results were also observed in some sleep factors and cancer risk, e.g., increased corpus uteri and ovarian cancer risk for no usual insomnia and increased ovarian cancer risk for no self-reported snoring. Individuals with usual insomnia may use medications or related therapies (e.g., melatonin supplements), which could have protective effects against cancer through hormonal modulation [37–39]. Snoring is often a symptom of obstructive sleep apnea (OSA), which can disrupt hormonal cycles and lower estrogen exposure levels, which may reduce the risk of hormone-related cancers like ovarian cancer [40, 41]. Since the numbers of corpus uteri and ovarian cancer are small in this study (N = 684 and 471), further study is warranted to investigate the relationship between the two sleep factors and hormone-related cancers risk.

Moreover, studies have suggested certain unhealthy lifestyle factors, such as low vegetable intake [26], alcohol consumption [42], and smoking [43], could exacerbate the negative effects of sleep behaviours on health risks, while physical activity has been identified as an essential strategy to improve sleep health [24, 25]. The synergistic effects of sleep behaviours and other lifestyle behaviour are worth investigated. In this study, we found

maintaining healthy sleep and lifestyle patterns could jointly decrease the risk of overall cancer and four types of cancers: colorectal, bladder, lung, and liver cancer. This finding highlights the importance of interventions targeting both sleep (e.g., early bedtimes, appropriate sleep duration) and other modifiable lifestyle behaviours (e.g., healthy diet, smoking cessation) for cancer prevention. Nevertheless, some unexpected results were found between lifestyle factors and cancer risks, e.g., increased corpus uteri cancer and melanoma risk for no current smoking, increased kidney cancer and non-Hodgkin lymphoma risk for low/moderate alcohol consumption. These unexpected results were also observed in the previous study. For example, the association of smoking with lower corpus uteri cancer risk was supported by several studies [44, 45]. This observation may be explained by the effect of nicotine on increasing estrogen metabolism and lowering the level of circulating estrogen [46, 47]. The association of smoking with lower melanoma risk was also consistent with a recent review and meta-analysis [48]. The proposed explanation was the reduced cutaneous inflammatory response seen in smokers, which modifies deleterious UV-induced cutaneous immune reactions [49–53]. Alcohol drinking was associated with lower kidney cancer and non-Hodgkin lymphoma risk, which was supported by a systematic review and meta-analysis [54, 55], though the lack of a biological explanation suggests caution in the interpretation of results.

There are several limitations of this study. Firstly, the majority of the study population is White, suggesting more caution when extending the conclusion to other ethnic groups. Secondly, the assessment of sleep traits and other lifestyles was based on a questionnaire and measured at baseline, and a relatively short follow-up time might not have captured the longtime influence of sleep and lifestyle habits on cancer risk. Dynamic evaluation using recorded data from the device is warranted in future studies when available data is obtained. Lastly, the healthy diet factor of this study was only considered based on nutrient intake, but for future research, adhering to nutritious eating habits, such as the Mediterranean diet or following dietary recommendations, is also valuable.

In summary, healthy sleep behaviour and healthy lifestyle jointly contribute to a reduced risk of overall and site-specific cancers, including liver, bladder, lung and colorectal cancer. Health education for keeping a healthy lifestyle or intervention for poor sleep behaviour would be valuable for cancer prevention.

ETHICS STATEMENT

The studies involving humans were approved by the North West Multi-Centre Research Ethics Committee (MREC), UK Biobank as a Research Tissue Bank (RTB) (21/NW/0157), and all participants have provided written informed permission. With this approval, researchers can work under the RTB approval without requiring further ethical permission. The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

T-MW and W-HJ supervised the study. Y-ZZ, W-LZ, and K-WZ performed statistical analysis, interpreted the results, and drafted the paper. Y-QH, W-QX, D-WY, HD, R-WX, YL, and Q-LW contributed to the results interpretation or revision of the manuscript. Upon reviewing the final version of the manuscript, all authors give their approval for submission.

CONFLICT OF INTEREST

The authors declare that they do not have any conflicts of interest.

SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.ssph-journal.org/articles/10.3389/ijph.2024.1607726/full#supplementary-material

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