Original Article

Association of sleep duration, sleep apnea, and shift work with risk of colorectal neoplasms: a systematic review and meta-analysis

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Background: Although studies have reported that certain sleep characteristics, such as sleep duration and sleep apnea, are linked to the risk of colorectal cancer (CRC), this link remains contentious because of the limited evidence from individual studies. Furthermore, evidence indicated that shift work involving circadian disruption as a probable human carcinogen. This systematic review and meta-analysis aimed to examine the associations between sleep duration, sleep apnea, and shift work with the risk of colorectal neoplasms, including CRC and colorectal adenoma (CRA).

Methods: We conducted a comprehensive literature search in PubMed, Embase, and Web of Science databases. The inclusion criteria were determined using PICOS principles. Observational studies reporting associations of sleep duration, sleep apnea, or shift work with risk of CRC or CRA were included. We assessed the risk of bias on the basis of the Newcastle–Ottawa Scale.

Results: A total of 18 observational studies were included. Of these studies, nine studies reported the effect of sleep duration on risk of colorectal neoplasms, five reported the effect of sleep apnea, and six reported the effect of shift work. The relative risk (RR) for colorectal neoplasms was 1.06 [95% confidence interval (CI): 0.94, 1.20] in the short sleep duration group compared with the moderate sleep duration group. Long sleep duration was associated with an increased risk of colorectal neoplasms (RR: 1.33, 95% CI: 1.07, 1.65). The pooled results showed that sleep apnea was associated with an increased risk of colorectal neoplasms (RR: 1.75, 95% CI: 1.56, 1.97). Furthermore, results showed that the association between shift work and the risk of colorectal neoplasms was not significant (RR: 1.06, 95% CI: 0.95, 1.17). No publication bias was observed in all the analyses (all P>0.05). The sensitivity analysis showed that no individual study substantially influenced the pooled RRs for colorectal neoplasms and CRC.

Conclusions: Our findings suggest the significant positive association of long sleep duration and sleep apnea with risk of colorectal neoplasms and CRC. Given that sleep characteristics may be a potentially modifiable risk factor for colorectal neoplasms, further understanding of its role in carcinogenesis will provide valuable insight for cancer prevention.

Keywords: Sleep duration; sleep apnea; shift work; colorectal neoplasms; meta-analysis

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Introduction

Colorectal cancer (CRC) is the third most common cancer diagnosed worldwide. It was estimated that more than 1.9 million new cases and 935,000 deaths occurred in 2020 (1). Some lifestyle factors and metabolic conditions, including smoking (2), alcohol consumption (3), physical inactivity (4), sedentary behavior (5), diet (6), obesity (7), and diabetes mellitus (8), have been associated with an increased CRC incidence and mortality (9,10). Efforts to prevent CRC by continuing to identify modifiable risk factors are warranted. In recent years, scholars have increasingly focused on the importance of sleep in health promotion. Studies have revealed that excessively short or long sleep durations are associated with increased rates of obesity (11), diabetes mellitus (12), metabolic syndrome (13), cardiovascular disease (14), and elevated levels of inflammatory markers (15). In addition, epidemiological studies have reported that sleep duration is significantly associated with cancer risk and all-cause mortality (16-18).

Although studies have increasingly indicated that certain sleep characteristics, such as sleep duration, sleep disorders, and sleep apnea, are linked to the risk of CRC, this link remains contentious because of the limited evidence from individual studies. A large cohort study involving 75,828 women who had undergone menopause suggested that short sleep durations were associated with an increased risk of CRC (19). Overly long sleep durations have also been reported to be associated with the risk of CRC (19-21). By contrast, several studies did not observe the significant association between short or long sleep duration and risk of CRC (22-24). Moreover, previous population-based cohort and case-control studies have demonstrated sleep apnea to be associated with an increased risk of CRC (25,26). However, other studies have not supported an association between sleep apnea and the risk of CRC (24,27).

At present, evidence on the association of shift work with risk of CRC also remains limited. Based on sufficient experimental data and limited evidence of cancer in humans, International Agency for Research on Cancer (IARC) classified shift work that involves circadian disruption as a possible human carcinogen in 2019 (28). A prospective Nurses' Health Study has shown that a long-term rotating night shift work (more than 15 years) is associated with increased risk of rectal cancer (29). Sleep deprivation, melatonin inhibition and lifestyle changes may be potential mechanisms to explain the possible link between shift work and CRC risk (30). However, several cohort studies did not find any association between shift work and risk of CRC (31-33).

To gain further insight into the association of sleep characteristics including sleep duration and sleep apnea, and shift work with risk of colorectal neoplasm, we conducted a systematic review and meta-analysis of published data. Furthermore, because adenomatous polyps [i.e., colorectal adenoma (CRA)] are critical precursors to most CRCs, they represent an appealing target for interventions and prevention. Therefore, we also included studies that assessed the association of sleep characteristics and shift work with CRA risk in this meta-analysis. We present the following article in accordance with the MOOSE reporting checklist (available at https://jgo.amegroups.com/article/view/10.21037/jgo-22-682/rc).

Methods

Literature search

The PubMed, Embase, and Web of Science databases were systematically searched for observational studies from inception through May 2021, using the following terms: ("sleep duration" OR "sleep time" OR "sleep apnea" OR "sleep quality" OR "sleep disorders" OR "insomnia" OR "sleep dysfunction" OR "sleep impairment" OR "shift work") AND ("colorectal cancer" OR "colorectal tumor" OR "colorectal neoplasms" OR "colorectal adenoma"). No language restrictions were imposed. Furthermore, the reference lists of eligible studies and other potentially relevant review articles were manually searched.

Inclusion criteria

The inclusion criteria were as follows: (I) observational study, including prospective cohort, case-control, case-cohort, or nested case-control study; (II) the subject of interest was sleep duration, sleep apnea, or shift work; (III) the outcome of interest was CRC or CRA; (IV) odds ratio (OR), relative risk (RR) or hazard ratio (HR) with 95% confidence interval (CI) were reported; (V) participants were free of disease at baseline. Furthermore, if we found more than one articles reported the same study, we used the results from the largest sample size or the latest published articles. All identified studies that met the inclusion criteria were independently reviewed by two investigators. Any

disagreements were resolved through consensus.

Data extraction and quality assessment

Data extraction was done by two authors independently. The information extracted from each study was as follows: author, publication year, country, age of participants, gender, follow-up period, number of participants, exposure details, assessment of outcome, and adjusted variables. The moderate sleep duration group was defined as the reference group, and we extracted the ORs, RRs or HRs with 95% CI for the longest (long sleep duration) or shortest sleep duration (short sleep duration) *vs.* the reference. Furthermore, we examined the association between sleep apnea and shift work and the risk of colorectal neoplasms and CRC. We chose the most adequately adjusted model to evaluate the risk value for the final analysis when extracting data.

The basis of each study included in the meta-analysis was assessed independently two authors using the Newcastle-Ottawa Scale (NOS) (34). The scale ranges from 0 to 9 stars and involves three main quality parameters: four items for selection, two items for comparability, three items for exposure (case-control study) or outcome (cohort study) evaluation. A score of $\geq$7 is considered to be of high quality in the present meta-analysis.

Statistical analysis

As the prevalence of colorectal neoplasms was relatively low, the ORs were considered as RRs (35,36). Furthermore, the HRs was also considered equivalent to RRs (37). The pooled RR with its corresponding 95% CI was calculated to assess the association between sleep duration and sleep apnea with the risk of colorectal neoplasms. Heterogeneity was determined with the *Q* test and quantified with the I^2 statistic. The presence of substantial heterogeneity was defined by $P_Q<0.05$ or $I^2>50\%$, and the random-effects model was adopted as the pooling method. Otherwise, the fixed-effects model was used. Subgroup analyses were conducted to investigate the potential sources of heterogeneity. To examine the influence of single studies on the overall results, a sensitivity analysis was performed using the single study removal method. The stability of the results was assessed by excluding studies that reported CRAs. Publication bias was assessed using the Egger regression test and visual inspection of the funnel plots. We used STATA version 12.0 (StataCorp LP, College Station, TX, USA) to analyze the data, and a two-tailed $P<0.05$ was considered statistically significant.

Results

Study description

The flow diagram for the screening and selection process of the studies is shown in *Figure 1*. We initially identified 928 potentially eligible studies after the removal of duplicates via through database searching. After title and abstract review, we excluded 815 studies because they were not observational studies or were not relevant to the purpose of this meta-analysis. After full-text review, 97 articles were further excluded according to the inclusion and exclusion criteria. Among the excluded articles, 35 were non-observational studies, 29 did not have relevant outcomes, 11 did not have relevant exposure, 20 were review articles, and 2 were duplicated reports. In addition, we identified 346 potentially eligible studies after the removal of duplicates via citation searching. We assessed full-text articles among 38 articles, and then 36 articles were further excluded due to without relevant outcome or exposure. Finally, we identified 18 observational studies that evaluated the association of sleep duration, sleep apnea, or shift work with the risk of colorectal neoplasms (published between 2010 and 2021) (19-27,31-33,36,38-42).

The characteristics of the studies, including author, publication year, country, age of participants, gender, follow-up period, number of participants, exposure details, assessment of outcome, and NOS quality scores, are summarized in *Table 1*. Of the 18 observational studies, four involved women only (19,22,31,36), one study involved men only (32), and 13 involved both men and women (20,21,23-27,33,38-42). Furthermore, 11 studies used a cohort study design (19,20,22,23,26,31-33,36,38,42), five used a case-control study design (16,21,24,39,41), and two used a nested case-control study (25,27). Seven studies reported an association between sleep duration and risk of CRC (19-23,38,40), and two studies reported the risk of CRA (24,36). Five studies reported the association between sleep apnea and the risk of colorectal neoplasms (24-27,39). Furthermore, six studies reported the association between shift work and the risk of colorectal neoplasms (31-33,36,41,42). All included studies scored 7–9 stars in quality assessment, and were considered as high the quality study.

Sleep duration and risk of colorectal neoplasms

Nine studies examined the association between sleep

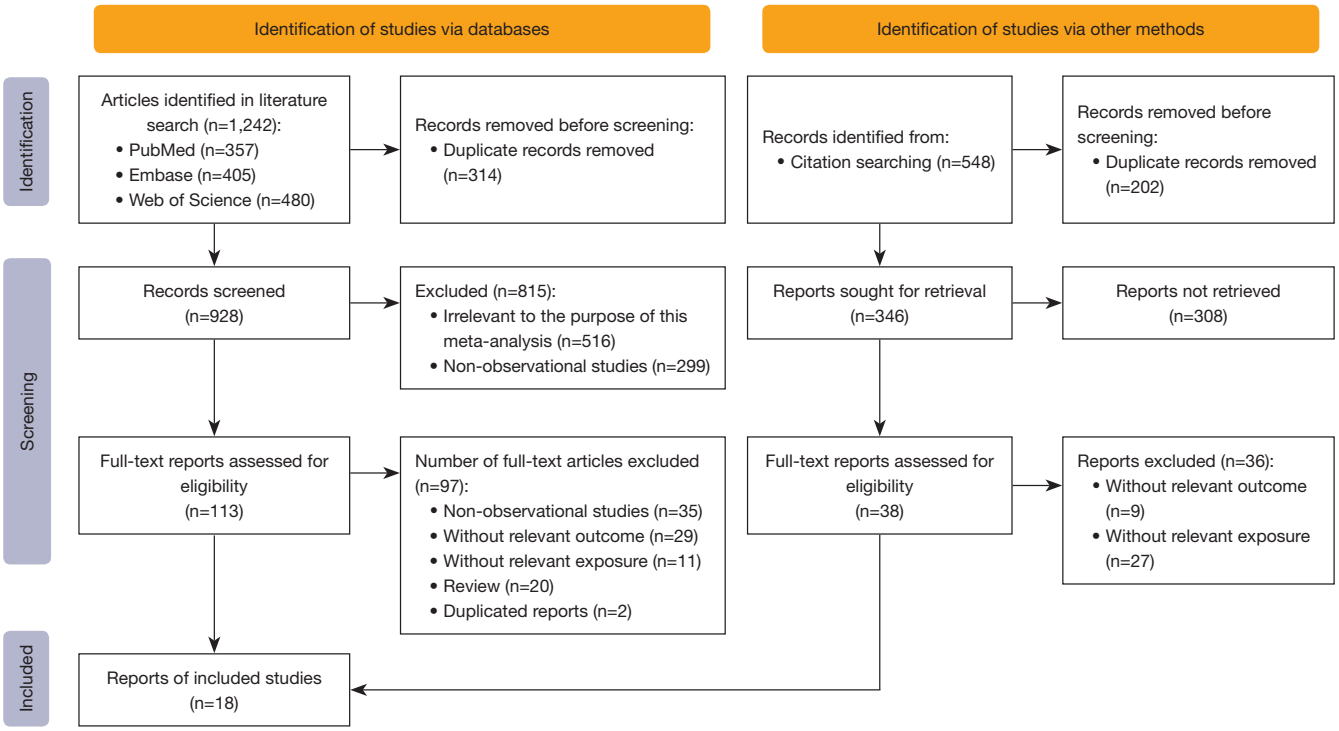

Figure 1 Flow diagram of the literature search and selection.

duration and the risk of colorectal neoplasms. The RR for risk of colorectal neoplasms was 1.06 (95% CI: 0.94, 1.20, P=0.348) in the short sleep duration group compared with the moderate sleep duration group (*Figure 2A*). Significant heterogeneity existed between the nine studies, so a random effects model was used to pool the RRs (I^2=47.7%, P_Q=0.046). No publication bias was detected by visual inspection of the funnel plots or the Egger test (P=0.426). Compared with moderate sleep duration, long sleep duration was associated with an increased risk of colorectal neoplasms (RR: 1.33, 95% CI: 1.07, 1.65, P=0.011) (*Figure 2B*). Statistical heterogeneity was identified (I^2=80.6%, P_Q<0.001), but no publication bias was detected (P=0.323). The sensitivity analysis of the association between short or long sleep duration and risk of colorectal neoplasm showed that the pooled RR significance did not change after the sequential removal of each individual study. Interestingly, when the subgroup analyses were performed according to the study design, there was no significant heterogeneity among the subgroups in the cohort or case-control studies.

After excluding the study on CRA, short sleep duration was not significantly associated with an increased risk of CRC compared with moderate sleep duration (RR: 1.07, 95% CI: 0.98, 1.17, P=0.132) (*Figure 3A*). Statistical heterogeneity was not identified (I^2=12.7%, P_Q=0.331), and no publication bias was detected by the funnel plots or Egger test (P=0.791). However, long sleep duration was associated with an increased risk of CRC compared with moderate sleep duration (RR: 1.41, 95% CI: 1.13, 1.75, P=0.002) (*Figure 3B*). Statistical heterogeneity was identified (I^2=74.4%, P_Q<0.001), but no publication bias was detected by the funnel plots or Egger test (P=0.581).

Sleep apnea and risk of colorectal neoplasms

Five studies examined the association between sleep apnea and the risk of colorectal neoplasms (*Figure 4*). The pooled results showed that participants with sleep apnea had an increased risk of colorectal neoplasms (RR: 1.75, 95% CI: 1.56, 1.97, P<0.001). No significant heterogeneity was found (I^2=9.7%, P_Q=0.354). The sensitivity analysis showed that no individual study substantially influenced the pooled RRs for colorectal neoplasms. There was no evidence of publication bias from either visual inspection of the funnel plots or the Egger test (P=0.890).

Table 1 Description of the studies included in the meta-analysis

Author, year, country	Study population and design	Age, sex	No. of participants	Exposure details	Outcome	NOS quality scores
Zhang *et al.*, 2013, China (20)	HPFS and NHS, cohort study	Median age was 53 for women and 56 for men	HPFS: 30,121; NHS: 76,368	Sleep duration: ≤5 *vs.* 7 h and ≥9 *vs.* 7 h	CRC	7
Jiao *et al.*, 2013, USA (19)	WHI-OS, cohort study	Mean age was 63.5 years, women	75,828	Sleep duration: ≤5 *vs.* 7 h and ≥9 *vs.* 7 h	CRC	8
McNeil *et al.*, 2020, Canada (23)	ATP, cohort study	NR, men and women	21,804	Sleep duration: <7 *vs.* 7–9 h and >9 *vs.* 7–9 h	CRC	8
Hurley *et al.*, 2015, USA (22)	CTS, cohort study	Mean 52 [20–104] years, women	101,609	Sleep duration: 3–6 *vs.* 7–9 h and ≥10 *vs.* 7–9 h	CRC	8
Lin *et al.*, 2018, China (21)	Population-based, case-control study	Case: 57.50±10.72 years; controls: 55.58±9.68 years, men and women	166/166	Sleep duration: <6 *vs.* 6–9 h and >9 *vs.* 6–9 h	CRC	7
Gu *et al.*, 2016, USA (38)	NIH-AARP Diet and Health, cohort study	Aged 50–71 years, men and women	297,185	Sleep duration: <5 *vs.* 7–8 and >9 *vs.* 7–8 h	CRC	8
Papantoniou *et al.*, 2021, Austria (40)	MCC-Spain, case-control study	Aged 20–85 years, men and women	2,008/3,598	Sleep duration: <5 *vs.* 7 h and ≥9 *vs.* 7 h	CRC	8
Devore *et al.*, 2017, USA (36)	NHS II, cohort study	Aged 25–42 years, women	49,231	Sleep duration: ≤5 *vs.* 7 h and ≥9 *vs.* 7 h; shift work: nightshift work duration ≥10 years *vs.* never	CRA	7
Thompson *et al.*, 2011, USA (24)	Screening colonoscopy-based, case-control study	Case: 57.3±8.0 years; controls: 54.7±8.8 years, men and women	338/902	Sleep duration: <6 *vs.* >7 h and sleep apnea	CRA	7
Chen *et al.*, 2020, China (26)	NHIRD, cohort study	NR, men and women	16,720	Sleep apnea	CRC	8
Lee *et al.*, 2017, Korea (39)	Screening colonoscopy-based, case-control study	Case: 54.9±14.5 *vs.* control: 63.0±10.9, men and women	111/52	Sleep apnea	CRC	7
Fang *et al.*, 2015, China (27)	NHIRD, nested case-control study	≥18 years, men and women	68,422/136,844	Sleep apnea	CRC	7
Lin *et al.*, 2019, China (25)	Taiwan's National Health Insurance program, nested case-control study	Mean 63.05±14.52 years, men and women	36,775	Sleep apnea	CRC	7
Walasa *et al.*, 2018, Austria (41)	Australian population-based, case-control study	Aged 40–79 years, men and women	350/410	Graveyard shift work ≥7.5 *vs.* none	CRC	8
Yong *et al.*, 2014, Germany (32)	Workers in a German chemical company, retrospective cohort study	Case: 39.5 years *vs.* control: 40.5 years, men	27,828	Rotating shift *vs.* day workers	CRC	7

Table 1 *(continued)*

Table 1 *(continued)*

Author, year, country	Study population and design	Age, sex	No. of participants	Exposure details	Outcome	NOS quality scores
Wichert *et al.*, 2020, Germany (42)	HNR and SHIP, cohort study	Aged 55 years, men and women	6,903	Duration of rotating shift work ≥10 years *vs.* never	CRC	9
Shi *et al.*, 2020, Austria (31)	NHS, cohort study	Age 30–55 years, women	121,700	Nightshift work duration ≥15 years *vs.* never	CRC	8
Arafa *et al.*, 2020, Japan (33)	JACC, cohort study	Age 40–79 years, men and women	45,390	Rotating shift work *vs.* day work	CRC	8

NR, not reported; HPFS, The Health Professionals Follow-up Study; NHS, The Nurses' Health Study; NIH-AARP, National Institutes of Health–American Association of Retired Persons; MCC, multi case-control; NHS II, The Nurses' Health Study II; WHI-OS, The Women's Health Initiative–Observational Study; ATP, Alberta's Tomorrow Project Cohort; CTS, California Teachers Study; NHIRD, National Health Insurance Research Database; HNR, the Heinz Nixdorf Recall Study; SHIP, the Study of Health in Pomerania; JACC, Japan Collaborative Cohort Study. CRC, colorectal cancer; CRA, colorectal adenoma.

Shift work and risk of colorectal neoplasms

Six studies examined the association between shift work and the risk of colorectal neoplasms (*Figure 5*). The pooled results showed that the association between shift work and the risk of colorectal neoplasms was not significant (RR: 1.06, 95% CI: 0.95, 1.17, P=0.307). No significant heterogeneity was found (I^2=0.0%, P_Q=0.454). The sensitivity analysis showed that no individual study substantially influenced the pooled RRs for colorectal neoplasms. There was no evidence of publication bias from either visual inspection of the funnel plots or the Egger test (P=0.883).

Subgroup analyses

Subgroup analyses based on population, study design, gender, or sample size showed no significant associations between short sleep duration and risk of colorectal neoplasms (*Table 2*). The significance in the pooled RRs for the association between long sleep duration and colorectal neoplasm risk was not altered among subgroups in the cohort (RR: 1.11, 95% CI: 1.00, 1.22, P=0.041) or case-control (RR: 2.39, 95% CI: 1.01, 5.65, P=0.002) studies. However, subgroup analyses showed that the association between long sleep duration and the risk of colorectal neoplasms was not significant in females, other countries, or in studies with a sample size greater than 50,000.

We also conducted subgroup analyses based on the definition of short or long sleep duration (Figure S1). Short sleep duration was defined as <5 or ≤5 hours per night (19,20,36,38,40), <6 or ≤6 hours per night (21,22,24), and <7 hours per night (23), respectively. Long sleep duration was defined as >9 or ≥9 hours per night (19-21,23,36,38,40) and ≥10 hours per night (22), respectively. When stratified by different definition of short sleep duration, the associations between short sleep duration and colorectal neoplasm risk did not appreciably change among all subgroups. When stratified by different definition of long sleep duration, the result showed that long sleep duration (>9 or ≥9 hours per night) was associated with increased risk of colorectal neoplasm.

Discussion

This meta-analysis suggests that excessively long sleep duration is associated with an increased risk of colorectal neoplasm and CRC. By contrast, we discovered no

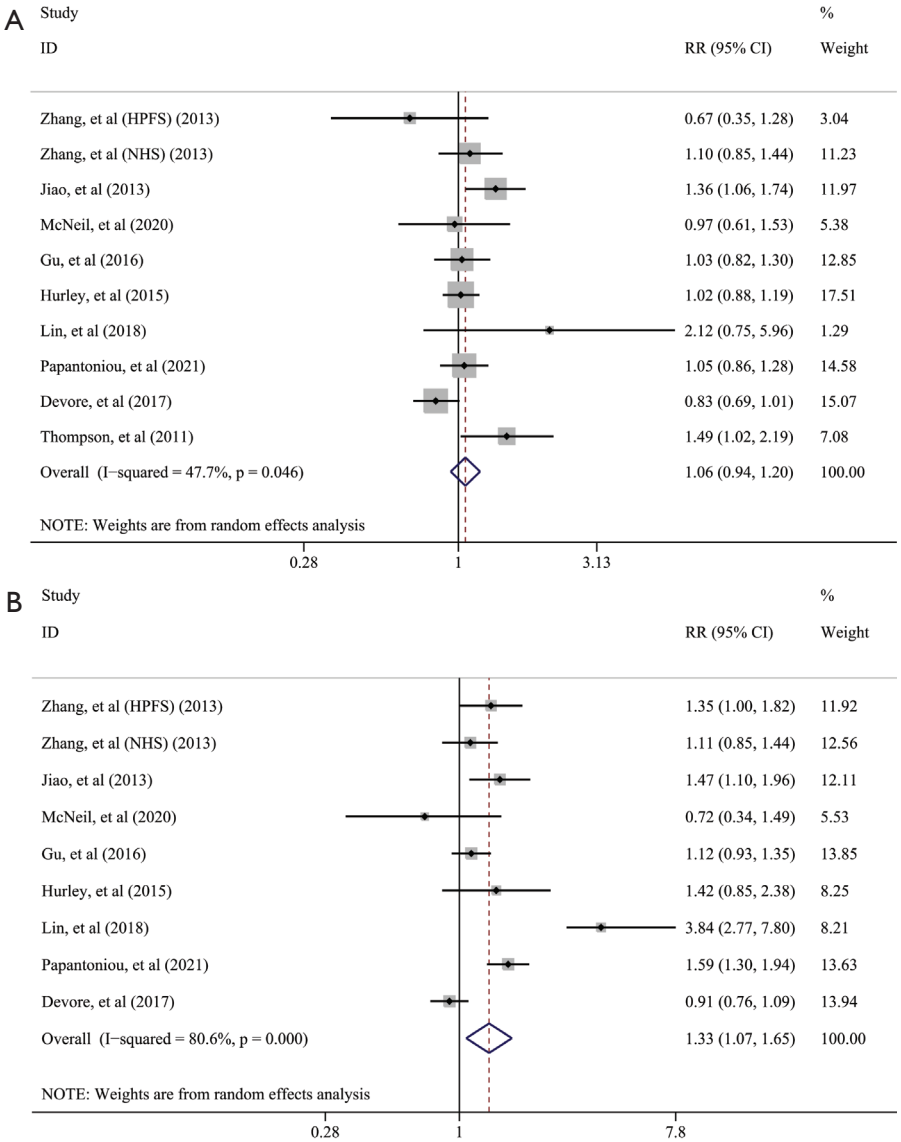

Figure 2 Forest plot of sleep duration and risk of colorectal neoplasm. (A) Short sleep duration. (B) Long sleep duration. RR, relative risk; CI, confidence interval; HPFS, The Health Professionals Follow-up Study; NHS, The Nurses' Health Study.

association between short sleep duration and colorectal neoplasm or CRC risk. We also observed a significant positive association between sleep apnea and colorectal neoplasm risk. The association between shift work and colorectal neoplasm risk was not significant. Furthermore, a significant positive association between long sleep duration and colorectal neoplasm risk was observed among both the cohort and case-control subgroups. The sensitivity analyses indicated that the pooled RRs remained significant after the sequential removal of each individual study, suggesting that the results are reliable.

An increasing number of studies have reported the association between sleep duration and cancer risk. For instance, both shorter and longer sleep durations have been associated with increased lung cancer risk (43), and short sleep duration was considered a risk factor for breast cancer (44). To the best of our knowledge, this systematic review and meta-analysis is the first to comprehensively examine the potential associations of sleep duration and sleep apnea with colorectal neoplasm risk. The mechanism

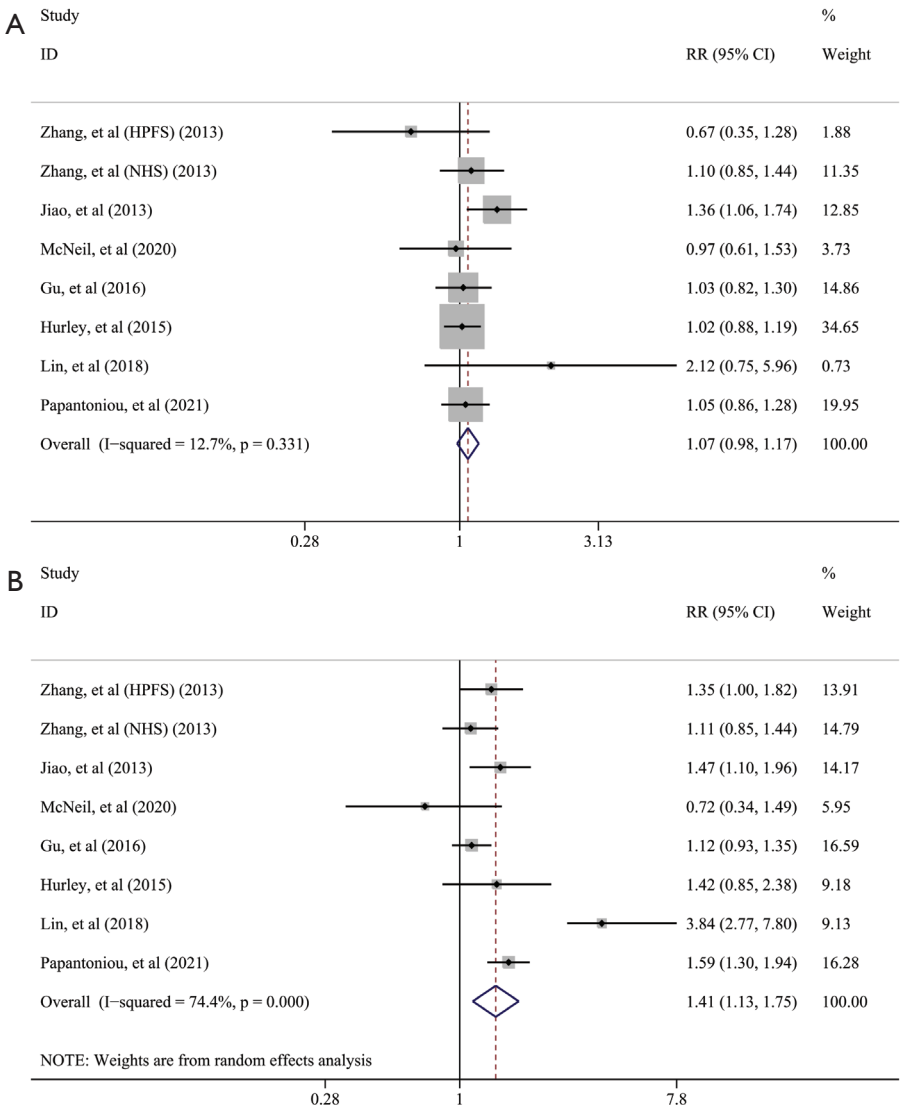

Figure 3 Forest plot of short sleep duration and risk of colorectal cancer. (A) Short sleep duration. (B) Long sleep duration. RR, relative risk; CI, confidence interval; HPFS, The Health Professionals Follow-up Study; NHS, The Nurses' Health Study.

underlying the positive correlation between long sleep duration and colorectal neoplasm risk is unclear. Several theories have been postulated to explain the potential role of sleep duration in carcinogenesis, including its influence on immune function regulation, oxidative stress, insulin metabolism, and circadian rhythms mediated by alterations in melatonin secretion (22,45,46). Consistent with prior studies (19), our finding that long sleep duration is positively associated with CRC risk cannot be explained by the melatonin secretion hypothesis. Melatonin is an endogenous hormone with tumor-inhibiting and potentially antiestrogenic properties and is mainly released during night sleep (47). Because melatonin is primarily released during sleep at night, it may provide a greater protective effect in people who sleep longer. Thus, if increasing sleep duration increases melatonin levels, we would expect to observe an inverse association between sleep duration and CRC risk. Furthermore, previous observational studies have reported associations between sleep disorders and risk of CRC (25,48). However, we did not include any studies reporting associations between sleep disorders and colorectal neoplasm in this meta-analysis, given the limited

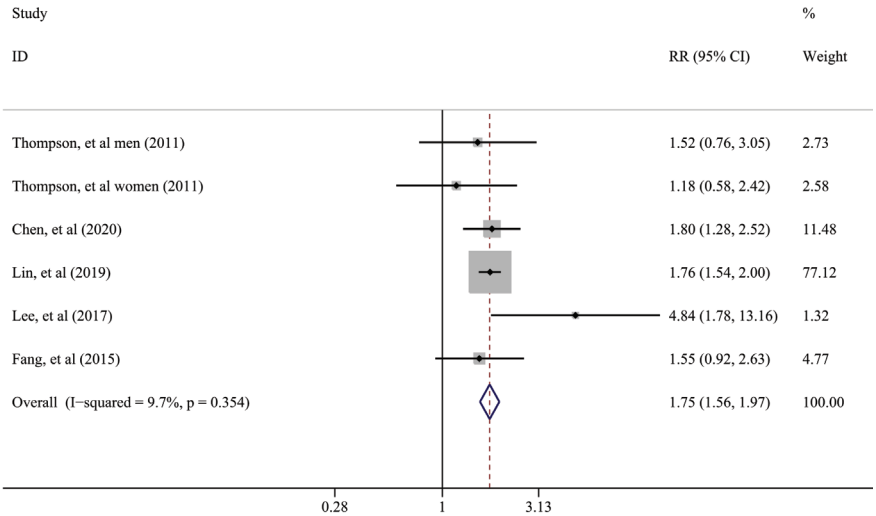

Figure 4 Forest plot of sleep apnea and risk of colorectal neoplasms. RR, relative risk; CI, confidence interval; HPFS, The Health Professionals Follow-up Study; NHS, The Nurses' Health Study.

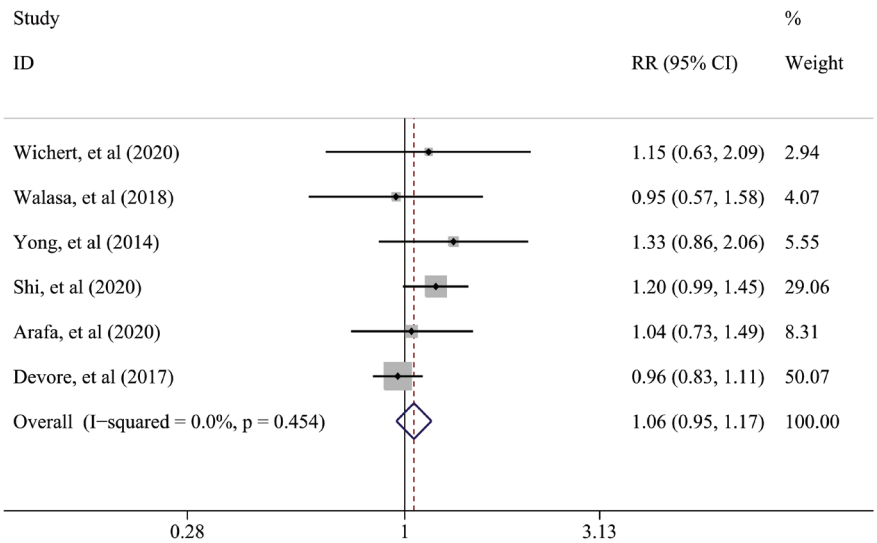

Figure 5 Forest plot of shift work and risk of colorectal neoplasms. RR, relative risk; CI, confidence interval; HPFS, The Health Professionals Follow-up Study; NHS, The Nurses' Health Study.

number of studies.

The positive associations of sleep duration and sleep apnea with colorectal neoplasm risk might have several other explanations. First, compared with short sleepers, long sleepers have higher serum cortisol levels and lower killer cell activity, both of which may promote carcinogenesis (49). A cross-sectional study demonstrated that increases in C-reactive protein and interleukin 6 are related to an increase in habitual sleep duration, and the activation of proinflammatory pathways may be the mechanism through which extreme sleep habits adversely affect health (50). Second, a previous study revealed that the severity of oxidative stress increases with the severity of obstructive sleep apnea (51). Hypoxia caused by sleep disorders may explain the increase in reactive oxygen species levels. Overexpression of hypoxia-inducible factor 1 is related to proangiogenic mediators, including vascular endothelial growth factor in tumor cells, as well as apoptosis and cell

Table 2 Subgroup analysis of sleep duration and risk of colorectal neoplasms

Subgroups	Short sleep duration				Long sleep duration			
	No. of sub-groups	RRs (95% CI)	I^2 (%)	P_Q	No. of sub-groups	RRs (95% CI)	I^2 (%)	P_Q
Overall	10	1.06 (0.94, 1.20)	47.7	0.046	9	1.33 (1.07, 1.65)	80.6	<0.01
Study design								
Cohort study	7	1.02 (0.89, 1.16)	48.4	0.071	7	1.11 (1.00, 1.22)	50.6	0.059
Case-control	3	1.27 (0.91, 1.76)	48.8	0.142	2	2.39 (1.01, 5.65)	89.7	0.002
Population								
United States	7	1.06 (0.91, 1.23)	60.8	0.018	6	1.16 (1.00, 1.36)	53.8	0.055
Other countries	3	1.06 (0.89, 1.27)	0	0.393	3	1.70 (0.81, 3.56)	86.8	<0.01
Gender								
Male	3	1.09 (0.73, 1.64)	36.1	0.047	2	1.63 (1.09, 2.43)	62.7	0.101
Female	6	1.11 (0.93, 1.33)	64.7	0.030	5	1.19 (0.95, 1.50)	61.0	0.036
Sample size								
>50,000	4	1.10 (0.97, 1.24)	25.8	0.257	6	1.35 (0.97, 1.88)	87.0	<0.01
<50,000	6	1.02 (0.82, 1.28)	56.3	0.043	3	1.26 (1.04, 1.53)	26.8	0.255

RRs, relative risks; CI, confidence interval.

cycle regulation mediators (52). Additionally, short sleep duration and sleep disturbance have been linked to obesity, metabolic syndrome, and diabetes (11-13), which are independent risk factors for colorectal neoplasm. Although we observed that sleep apnea was associated with an increased colorectal neoplasm risk, the association between short sleep duration and colorectal neoplasm risk was not significant among the cohort study subgroup. By contrast, a significant positive association was identified among the case-control studies. This inconsistency in our meta-analysis requires further investigation in future studies.

There is increasing epidemiologic evidence regarding the association between shift work and cancer risk. A prospective cohort study reported that a long nightshift work history without daytime napping and long nighttime sleep duration were independently and jointly associated with a higher cancer incidence among males (53). This meta-analysis suggests that shift work is not associated with an increased risk of colorectal neoplasm. Similar findings were also reported in previous epidemiologic studies (31-33,36,41). By contrast, a population-based case-control study conducted in Canada demonstrated that an increased duration of night work was associated with an increased colon cancer risk in men (54). However, the mechanisms underlying the association remain unclear but warrant further investigation.

The present meta-analysis is the first to comprehensively examine the associations between sleep duration, sleep apnea, and shift work with colorectal neoplasm risk. Furthermore, our meta-analysis has several strengths. First, the summary risk estimates were based on several large-sample studies, including the Health Professionals Follow-Up Study, the Nurses' Health Study, the Women's Health Initiative Observational Study, and the ATP Study. Second, most included studies had prospective designs and long follow-up durations. Third, all included studies were high quality and adjusted for potential confounding factors, such as obesity, smoking status, physical activity, and diabetes. In addition, our sensitivity analysis indicated that the results were reliable, and no evidence of publication bias was discovered.

Nevertheless, our study has several limitations. First, although the tests for heterogeneity among the included studies were significant, we did not discover the potential source of heterogeneity through the subgroup analyses. Notably, after excluding the study on CRA, no significant heterogeneity in association between short sleep duration and risk of CRC was observed, indicating the pooled of different results, such as CRC and CRA, may lead to increased heterogeneity. Second, only observational studies were included in this meta-analysis, and the number of

eligible studies was limited.

Conclusions

In conclusion, our meta-analysis shows that both long sleep duration and sleep apnea are associated with an increased risk of colorectal neoplasm. We also identified a significant positive association between long sleep duration and CRC risk. By contrast, we found no significant association of short sleep duration and shift work with risk of colorectal neoplasm and CRC. Given that sleep characteristics may be a potentially modifiable risk factor for colorectal neoplasms, further understanding of its role in carcinogenesis will provide valuable insight for cancer prevention.

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Footnote

Reporting Checklist: The authors have completed the MOOSE reporting checklist. Available at https://jgo.amegroups.com/article/view/10.21037/jgo-22-682/rc

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jgo.amegroups.com/article/view/10.21037/jgo-22-682/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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