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Original Article

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Sex-specific associations between habitual snoring and cancer prevalence: insights from a US Cohort Study

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Abstract

Study Objectives: To investigate the sex-specific association between habitual snoring and overall cancer prevalence and subtypes, and to examine the influence of age, body mass index (BMI), and sleep duration on this association.

Methods: This study utilized data from the National Health and Nutrition Examination Survey cycles between 2005 and 2020 and included 15 892 participants aged 18 and over. We employed inverse probability of treatment weighting based on propensity scores to adjust for confounders when comparing the prevalence of cancer between habitual snorers and non-habitual snorers for each sex and cancer type. Subgroup analyses were conducted based on sleep duration, age, and BMI categories.

Results: The cohort (mean age 48.2 years, 50.4% female, and 30.5% habitual snorers) reported 1385 cancer cases. In men, habitual snoring was linked to 26% lower odds of any cancer (OR 0.74, 95% CI: 0.66 to 0.83), while in women, it showed no significant difference except lower odds of breast cancer (OR 0.77, 95% CI: 0.63 to 0.94) and higher odds of cervix cancer (OR 1.54, 95% CI: 1.18 to 2.01). Age and sleep duration significantly influenced the snoring-cancer relationship, with notable variations by cancer type and sex.

Conclusions: Habitual snoring exhibits sex-specific associations with cancer prevalence, showing lower prevalence in men and varied results in women. These findings emphasize the critical need for further research to uncover the biological mechanisms involved. Future investigations should consider integrating sleep characteristics with cancer prevention and screening strategies, focusing on longitudinal research and the integration of genetic and biomarker analyses to fully understand these complex relationships.

Key words: cancer prevalence; sex differences; snoring; propensity score; inverse probability of treatment weighting; sleep duration; age; population-based

Statement of Significance

With cancer continuing to challenge global health, the elucidation of contributing factors, including those from common conditions like habitual snoring, remains a crucial yet underexplored area. While the snoring-cancer link is hypothesized to involve obstructive sleep apnea and its accompanying intermittent hypoxia, the current understanding of snoring's independent role, absent sleep apnea, is still limited. This gap is particularly pronounced when examining sex-specific cancer risks. This research contributes to the understanding of how habitual snoring could reflect broader health implications beyond known sleep disorders, specifically indicating differential cancer associations across genders. These insights reinforce the need for future research to unravel these connections. They could inform sex-specific novel preventive and screening initiatives tailored to individual risk profiles based on sleep patterns.

Cancer is the leading cause of mortality worldwide, responsible for nearly one in six deaths in 2020 [1]. The burden of cancer incidence and mortality is not only expanding across the world but also exhibits a disproportionate distribution, with countries with higher human development levels having a greater share of the overall cancer incidence burden [2, 3]. In the United States,

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there were an estimated 1.9 million new cancer cases and 609 360 cancer-related deaths in 2022 [4]. Lung cancer remains the most lethal, with prostate and breast cancers following in male and female populations, respectively [4].

Sleep, as a critical determinant of health, has garnered attention for its potential role in cancer etiology. Habitual snoring, which may affect up to 45% of adult males and 28% of adult females [5], is increasingly recognized as a significant risk factor for cancer [6, 7]. The proposed mechanism linking snoring to cancer remains largely unknown but is hypothesized to involve obstructive sleep apnea (OSA) [8–10]—a condition characterized by disrupted sleep and intermittent hypoxia [10]—and other carcinogenic risk factors such as aging, obesity, cardiometabolic disease, and lifestyle factors [11, 12]. However, the specific relationship between non-apneic snoring and cancer or its subtypes is less understood.

Habitual snoring results from the passage of air through the upper airway during sleep, leading to tissue vibration and noise [13]. It is essential to distinguish this from the cyclical snoring seen in OSA, which includes alternating periods of snoring and silence and may trigger concern in observers due to its severity [14]. Past research on the association between snoring and cancer risk has often neglected to adjust for the presence of sleep apnea or other sleep disorders such as insomnia [6, 7], casting uncertainty on whether it is snoring per se or its common association with OSA that elevates cancer risk.

Sex differences in cancer susceptibility and mortality are among the most consistent observations in cancer epidemiology [15]. For example, males have a higher incidence of colorectal, stomach, and liver cancers and a higher mortality rate from cancers such as lung, colorectal, and stomach compared to females [16]. Yet it is unknown that habitual snoring contributes to the risk of cancer equally for men and women.

To bridge these gaps in knowledge, our study investigated the sex-specific associations of habitual snoring with overall cancer prevalence and cancer subtypes, within a diverse US general adult population. Additionally, we explored whether these associations are influenced by age, body mass index (BMI), and sleep duration, thereby providing a more nuanced understanding of the interplay between habitual snoring and cancer risk across different life stages, BMI subgroups, and sleep duration.

Methods

Data sources and study population

This study utilized participant data derived from the National Health and Nutrition Examination Survey (NHANES), specifically from 2005 to 2008, 2007 to 2008, and 2015 to 2020 cycles. These cycles were selected for their extensive sleep assessment protocols, which offered a more robust dataset for our analysis. NHANES, a nationally representative cross-sectional survey conducted by the Centers for Disease Control and Prevention [17], employed a stratified, multistage, probability cluster sampling method [18]. Detailed descriptions of NHANES design and methods have been documented in prior publications [17]. Participants in NHANES undergo a two-stage evaluation process: an initial household interview followed by a physical examination and further interviews conducted at a mobile examination center [17]. Ethical approval for the NHANES protocol was obtained from the National Center for Health Statistics Research ethics review board, and written informed consent was obtained from participants. As the NHANES data is de-identified and publicly available, the Purdue University Committee on Human Research did not deem additional IRB review necessary for our study. For the purposes of this analysis, we excluded any data pertaining to pregnant individuals and minors under the age of 18 years.

Definition of habitual snoring and other sleep characteristics

In the NHANES interview, participants reported snoring frequency over the past 12 months using a scale ranging from "never" to "frequently" (5–7 nights per week) [19]. Habitual snoring was defined as "frequent" snoring. Participants who reported "never," "rarely," or "occasionally" snoring were categorized as the non-habitual snoring comparison group. Sleep duration was self-reported as the average number of hours slept per night on weekdays or workdays, categorized as short (<7 hours), long (>9 hours), or average (7 to 9 hours) [20]. Additionally, participants were asked if a healthcare professional had diagnosed them with a sleep disorder, with affirmative responses prompting further inquiry into specific disorders, such as sleep apnea, insomnia, restless legs syndrome, or other sleep-related conditions.

Assessment of cancer status

Cancer status was determined by participants' affirmative response to whether a doctor or other health professional had ever diagnosed them with cancer or a malignancy. Those who answered "yes" to this question were then asked to specify the type(s) of cancer diagnosed, with the provision to list up to three distinct cancer types.

Covariates

Covariates in this study included sociodemographic factors, behavioral determinants, and clinical characteristics. Sociodemographic factors included age, sex, race/ethnicity (categorized as non-Hispanic whites, non-Hispanic blacks, Hispanic, and non-Hispanic others), marital status, family income (quantified using the poverty-income ratio, PIR), education level, and health insurance status (categorized as uninsured, private insurance, government insurance, or a combination thereof).

Behavioral determinants included alcohol use and smoking status; the latter was ascertained by serum cotinine levels, with levels≥10 ng/mL indicating active smoking [21]. Clinical characteristics included BMI, presence of cardiometabolic syndrome, and history of hypertension and diabetes. The presence of cardiometabolic syndrome was defined using the National Cholesterol Education Program Adult Treatment Panel III criteria with the presence of three or more metabolic abnormalities: waist circumference >102 cm for men and >88 cm for women; blood pressure ≥130 mmHg systolic and or ≥85 mm Hg diastolic; fasting glucose ≥100 mg/dL; triglycerides ≥150 mg/dL; HDL cholesterol <40 mg/dL for men and <50 mg/dL for women [22]. The presence of diagnosed sleep disorders including sleep apnea, insomnia, restless leg syndrome, and other sleep disorders were also included.

Statistical Analysis

In our observational cross-sectional analysis, participants were categorized by snoring status, and subject characteristics were compared using standardized mean differences. We summarized rates of cancer, any and by subtypes, sex, and snoring frequency.

To balance demographic, clinical, and behavioral risk factors, separate propensity score models were constructed for men and women, with snoring status as the outcome and participant

Table 1. Participants Characteristics of Cohorts by the Presence of Habitual Snoring (N = 15 892)

Characteristics	No Snoring *n* (%) or mean (sd)	Habitual Snoring *n* (%) or mean (sd)	Standardized mean difference (SMD)	Propensity score weighted SMD
N	11 048 (69.5%)	4844 (30.5%)		
Demographics				
Female	6006 (54.4)	2002 (41.3)	0.263	0.033
Age, mean, years	46.1 (19.9)	50.8 (16.8)	0.253	0.026
Poverty			0.016	0.027
Below poverty threshold	2093 (18.9)	948 (19.6)		
Average poverty threshold	964 (8.7)	459 (9.5)		
Above poverty threshold	4120 (37.3)	1912 (39.5)		
Race			0.091	0.044
Non-Hispanic white	4713 (42.7)	2049 (42.3)		
Non-Hispanic black	2563 (23.2)	1030 (21.3)		
Mexican American	1825 (16.5)	886 (18.3)		
Other Hispanics	840 (7.6)	449 (9.3)		
Other race	1107 (10.0)	430 (8.9)		
Education			0.130	0.018
Less than high school	2743 (24.8)	1433 (29.6)		
High school	2746 (24.9)	1242 (25.6)		
Some College	3218 (29.1)	1318 (27.2)		
College & above	2329 (21.1)	845 (17.4)		
Married or with partner	3183 (28.8)	1376 (28.4)	0.001	0.001
With health insurance	8752 (79.2)	3835 (79.2)	0.004	0.016
Clinical factors				
Hypertension	3279 (29.7)	1407 (29)	0.053	0.020
Asthma	1460 (13.2)	767 (15.8)	0.075	0.001
Diabetes	853 (7.7)	701 (14.5)	0.216	
Cardiometabolic disease	1162 (10.5)	998 (20.6)	0.290	0.011
BMI	27.6 (6.3)	31.4 (7.5)	0.538	0.060
Lifestyle factors				
Alcohol use	5566 (50.4)	2784 (57.5)	0.080	0.010
Smoking status	4223 (38.2)	2490 (51.4)	0.240	0.022
Sleep-related characteristics				
Restless leg syndrome	23 (0.2)	14 (0.3)	0.017	0.035
Insomnia	101 (0.9)	55 (1.1)	0.022	0.056
Sleep apnea	207 (1.9)	248 (5.1)	0.216	0.013
Sleep duration categories			0.146	0.014
Short	3479 (31.5)	1858 (38.4)		
Average	5963 (54.0)	2368 (48.9)		
Long	1573 (14.2)	600 (12.4)		

Numbers in the table do not add up due to missing values.
Abbreviations: BMI, body mass index; N, number of participants; SMD, standardized mean difference.

characteristics as predictors. To account for missing covariates, we used multiple imputations with 20 imputations, constructing a separate logistic regression model on each imputed dataset. The propensity model included all demographic and clinical factors in Table 1. Recognizing OSA as a potential confounder due to its association with increased cancer risk and hypoxic burden [23–25], we included OSA as a variable in our propensity model to help balance this confounder across snorers and non-snorers. Predicted probabilities were then used as the inverse probability of treatment weights (IPTW) in subsequent analyses, with analyses performed separately on each imputation set and the results pooled.

For hypothesis testing, IPTW logistic regression models were employed to evaluate cancer risk by snoring status, calculating odds ratios (ORs) with 95% confidence intervals (95% CIs) for each sex and cancer type. Subgroup analyses were conducted based on sleep duration (short, long, and average), age (<50, 50–64, and 65 years and above), and BMI categories (underweight, healthy, overweight, and obese) to assess the consistency of associations. Additionally, dose–response relationships were explored by analyzing cancer risk across frequencies of snoring (never, 1–2, 3–4, or 5–7 nights a week). All analyses were performed using Stata version 18 (StataCorp, College Station TX).

Results

Participants characteristics

A total of 15 892 individuals, with or without habitual snoring, were analyzed. The mean (standard deviation) age was 48.2 (19.4) years, and 50.4% were female. Cohort characteristics before multivariable adjustment by snoring status are summarized in Table 1. Individuals with habitual snoring were more likely to have income below poverty levels and were less likely to be married or cohabiting. Additionally, they were less likely to have hypertension compared to those without habitual snoring. Differences in the presence of sleep disorders were noted, with individuals reporting habitual snoring showing a higher likelihood of restless leg syndrome and insomnia than their counterparts without habitual snoring ($p < .05$). Stratified analysis by sex revealed a consistent pattern in most characteristics differentiating habitual snorers from non-snorers (Supplementary Tables 1 and 2). Notably, among women, those with habitual snoring had a higher incidence of alcohol consumption compared to non-snorers (44.7% vs. 43.6%, standardized mean difference [SMD]: 0.023).

Unadjusted relationship between habitual snoring and cancer

Within the analytical cohort, a total of 1385 cancer cases were reported (Supplementary Table 3). Men with habitual snoring exhibited a lower prevalence of any type of cancer compared to non-habitual snorers (non-snoring vs. snoring: 9.1% vs. 7.5%, $p < .001$), while women with habitual snoring showed a higher prevalence (8.0% vs. 11.4%, $p < .001$). Additionally, the prevalence of cervical cancer differed significantly between women with and without habitual snoring, with the former reporting higher prevalence (1.9% vs. 0.9%, $p < .001$).

Sex-specific IPTW-weighted associations of habitual snoring with cancer

In the IPTW-weighted analysis of the entire cohort, we observed significant variations in cancer risks associated with habitual snoring. The adjusted odds of overall cancer, prostate cancer, breast cancer, and liver cancer were notably lower in habitual snorers compared to non-snorers, with odds ratios of 0.88 (95% CI: 0.81 to 0.95), 0.80 (95% CI: 0.67 to 0.97), 0.80 (95% CI: 0.66 to 0.98), and 0.22 (95% CI: 0.06 to 0.90), respectively. Conversely, the risk for cervix cancer was higher among habitual snorers, with an odds ratio of 1.49 (95% CI: 1.14 to 1.94). These findings provide a foundational context for our sex-stratified analyses, illustrating differential cancer risks associated with snoring across different types (Table 2). For men, habitual snoring was associated with a 26% reduction in the odds of overall cancer compared to non-habitual snorers (OR 0.74, 95% CI: 0.66 to 0.83). In men, the association between habitual snoring and cancer varied across cancer subtypes, showing lower odds for lung cancer, colon and rectum cancer, skin cancer, melanoma, and leukemia. In contrast, among women, no significant difference was observed in the odds of overall cancer prevalence between habitual and non-habitual snorers (OR 1.03, 95% 0.92 to 1.15), except for breast cancer and cervix cancer. Habitual snoring in women was associated with 23% lower odds of breast cancer (OR 0.77, 95% CI: 0.63, 0.94), while the odds of cervix cancer increased by 54% among women with habitual snoring (OR 1.54, 95% CI: 1.18, 2.01). Exploring the dose–response relationship between snoring frequency and overall cancer prevalence in men and women, we found that increasing snoring frequency nights per week reduced the likelihood of overall cancer in men, while such gradation in the association was not evident in women (Figure 1).

Roles of age and BMI in sex-specific associations between habitual snoring and cancer

As shown in Tables 3 and 4, the results indicate that age and BMI play important roles in the sex-specific associations between habitual snoring and cancer prevalence. In our IPTW-weighted subgroup analysis by age, we observed different associations of habitual snoring with overall cancer risk across age groups in men. An inverse association was observed in men aged ≤49 years (OR 0.62, 95% CI [0.41, 0.95]) and those aged 65 and above (0.70, 95% CI [0.60, 0.82]; Table 3). However, this association was not statistically significant for men aged 50 to 64 years, although still inverse (OR 0.79, 95% CI[0.62, 1.00]). In terms of specific cancer types, lower odds of colon and rectum cancer, skin cancer, and melanoma associated with habitual snoring were significantly noted only in older males (≥65 years). Age also modified the association of habitual snoring and cancer in women, with increased odds of overall cancer, ovary cancer, melanoma, uterine cancer, and cervical cancer observed predominantly in the younger age groups (≤49 years). Conversely, the inverse associations between habitual snoring and breast and ovary cancer were significant for those aged 65 years and above.

In men, lower odds of overall cancer were consistent across subgroups stratified by BMI but were not significant among those underweight (Table 4). In women, BMI did not modify the association between habitual snoring and the prevalence of most cancers, except for cervix cancer. The positive association of snoring and cervix cancer was observed only for women in the healthy, overweight, and obese groups, with the strength declining with increasing BMI (OR 3.90 [2.00, 7.61] for healthy; 2.86 [1.46, 5.59] for overweight; and 2.17 [1.21, 3.90] for obese).

Roles of short and long sleep duration in sex-specific association between habitual snoring and cancer

To delineate the roles of short and long sleep duration in the sex-specific association between habitual snoring and cancer prevalence, we stratified the unadjusted and IPTW-weighted analyses by sleep duration. In the unadjusted analysis, males sleeping less than 7 hours per night showed significant differences in overall cancer and lung cancer prevalence between those with and without habitual snoring, with lower prevalence among snorers (Supplementary Table 4). Conversely, among females sleeping more than 9 hours per night, significant differences in overall cancer, uterine, and ovary cancer prevalence were noted, with snorers exhibiting higher cancer prevalence.

In weighted analyses, inverse associations between habitual snoring and overall cancer and lung cancer were observed only in males sleeping less than 7 hours (Supplementary Table 5). Conversely, among females sleeping more than 9 hours per night,

Table 2. IPTW-Weighted Association Between Habitual Snoring and Prevalent Cancer, Stratified by Sex

Cancer types	Odds Ratios (95% CI)	P value
All participants		
Cancer of any types	0.88 (0.81, 0.95)	**.002**
Lung cancer	0.65 (0.41, 1.04)	.072
Prostate cancer	0.80 (0.67, 0.97)	**.020**
Breast cancer	0.80 (0.66, 0.98)	**.030**
Liver cancer	0.22 (0.06, 0.90)	**.034**
Colon and rectum cancer	0.92 (0.71, 1.18)	.501
Non-melanoma skin cancer	0.93 (0.79, 1.09)	.342
Melanoma	0.76 (0.56, 1.03)	.077
Uterine cancer	1.26 (0.87, 1.82)	.226
Pancreas cancer	2.21 (0.37, 13.27)	.386
Leukemia	0.46 (0.20, 1.05)	.066
Lymphoma	0.61 (0.36, 1.03)	.065
Cancer of the brain and nervous systems	1.55 (0.57, 4.21)	.390
Cancer of the mouth/tongue/lips/Larynx	0.55 (0.24, 1.29)	.169
Kidney cancer	0.76 (0.46, 1.25)	.278
Stomach cancer	0.84 (0.34, 2.09)	.710
Cervix cancer	1.49 (1.14, 1.94)	**.003**
Ovary cancer	0.95 (0.61, 1.47)	.802
Testis cancer	3.38 (0.65, 17.72)	.149
Males		
Cancer of any types	0.74 (0.66, 0.83)	**<.001**
Lung cancer	0.35 (0.18, 0.70)	**.003**
Prostate cancer	0.84 (0.70, 1.01)	.066
Liver cancer	0.50 (0.12, 2.05)	.338
Colon and rectum cancer	0.58 (0.39, 0.85)	**.005**
Non-melanoma skin cancer	0.81 (0.66, 1.00)	**.050**
Melanoma	0.50 (0.32, 0.79)	**.003**
Leukemia	0.17 (0.04, 0.73)	**.017**
Lymphoma	0.76 (0.39, 1.51)	.439
Cancer of the brain and nervous systems	4.58 (0.85, 24.74)	.077
Cancer of the mouth/tongue/lips/Larynx	0.58 (0.22, 1.51)	.263
Kidney cancer	0.51 (0.26, 0.99)	.046
Stomach cancer	1.12 (0.36, 3.50)	.840
Testis cancer	3.38 (0.65, 17.72)	.149
Females		
Cancer of any types	1.03 (0.92, 1.15)	.583
Lung cancer	1.38 (0.64, 2.94)	.410
Breast cancer	0.77 (0.63, 0.94)	**.011**
Colon and rectum cancer	1.33 (0.93, 1.90)	.118
Non-melanoma skin cancer	1.10 (0.85, 1.41)	.471
Melanoma	1.25 (0.80, 1.94)	.327
Uterine cancer	1.26 (0.87, 1.82)	.222
Leukemia	1.32 (0.41, 4.26)	.637
Lymphoma	0.47 (0.20, 1.10)	.081
Thyroid cancer	0.86 (0.50, 1.51)	.608
Cancer of the brain and nervous systems	0.43 (0.08, 2.30)	.323
Cancer of the mouth/tongue/lips/Larynx	0.67 (0.12, 3.76)	.652
kidney cancer	1.41 (0.58, 3.40)	.444
stomach cancer	0.50 (0.10, 2.56)	.404
Cervix cancer	1.54 (1.18, 2.01)	**.002**
Ovary cancer	0.96 (0.61, 1.50)	.852

Variables included in propensity model: demographics-Sex, age, poverty levels, race/ethnicity, education, marital status, health insurance status; clinical factors-hypertension, asthma, diabetes, cardiometabolic disease, BMI; lifestyle factors-alcohol use, smoking status; sleep-related characteristics: restless leg syndrome, sleep apnea. Significant *P* values are denoted by bold type.

increased odds of uterine cancer and overall cancer prevalence were significant, while lower odds of breast cancer prevalence associated with habitual snoring were observed among those females sleeping less than 7 hours per night.

Discussion

Our retrospective cohort study reveals significant sex disparities in the relationship between habitual snoring and cancer prevalence. Using IPTW-weighted analysis to balance demographic, clinical, lifestyle, and sleep-related characteristics, we observed a 26% reduction in overall cancer odds among men with habitual snoring, particularly in lung, colon and rectum, skin, melanoma, and leukemia subtypes. Conversely, among women, no significant difference was observed in overall cancer prevalence except for breast and cervix cancers. Drawing from a dataset of 15 892 nationally representative adults, we also found age played a crucial role in habitual snoring-cancer relationships, with inverse associations noted in men aged ≤49 years and ≥65 years, and positive associations in young and middle-aged women. Sleep duration further influenced these associations, with shorter duration (<7 hours) linked to lower overall and lung cancer prevalence among snoring men, and longer duration (>9 hours) associated with higher overall and uterine cancer prevalence among snoring women. These nuanced findings underscore the complex interplay between habitual snoring and cancer risk across different life stages, sleep durations, and BMI subgroups, emphasizing the need for individualized evaluation and consideration of sex, age, and sleep-related factors in future mechanistic research.

Our study represents the first to document a significant inverse association between habitual snoring and cancer prevalence in men, particularly among males aged ≥65 years or with short sleep duration. While we adjusted for OSA diagnosis, our study, akin to prior epidemiologic research, cannot discern the impact of simple snoring versus snoring with OSA on cancer prevalence. Moreover, underdiagnosis of OSA is prevalent in the general population, with an estimated 93% of women and 82% of men with moderate-to-severe OSA being unaware of their condition [26, 27]. Existing studies on the potential link between OSA and cancer exhibit inconsistency, and sex-specific aspects of this association remain poorly studied [28]. For instance, a study of 267 849 individuals from the Korea National Health Insurance Service registry indicated a lower risk of lung cancer development in males with OSA but not in females, especially those aged>65 years [29]. However, the study's generalizability was limited by

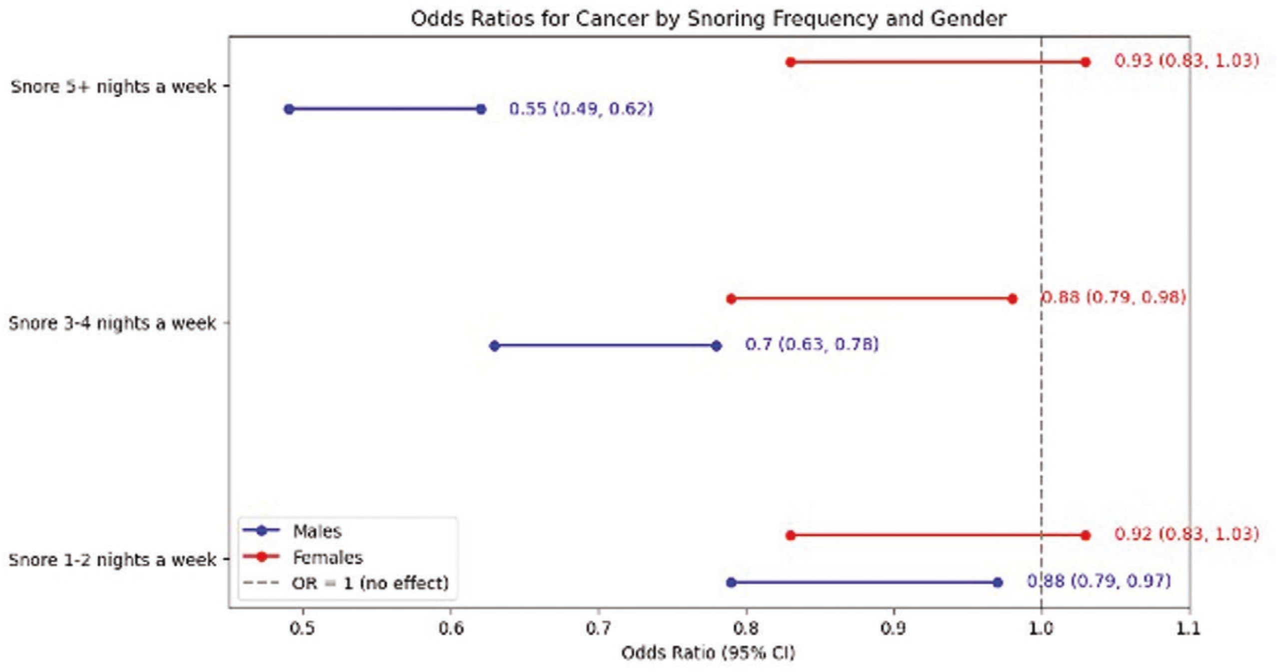

Figure 1. IPTW-weighted relationship between snoring frequency and cancer prevalence, stratified by sex. Variables included in the propensity model: demographics-sex, age, poverty levels, race/ethnicity, education, marital status, health insurance status; clinical factors-hypertension, asthma, diabetes, cardiometabolic disease, BMI; lifestyle factors-alcohol use, smoking status; sleep-related characteristics: restless leg syndrome, sleep apnea.

its failure to account for major behavioral and clinical lung cancer risk factors and its homogenous sample [29]. Our findings extend these insights by incorporating demographic, lifestyle, clinical, and sleep-related factors into the analyses, exploring snoring-related cancer prevalence across diverse patient populations. Additionally, an analysis involving 4580 individuals aged 65 and above from the Cardiovascular Health Study highlighted an inverse association between snoring and incident overall cancer risk, considering gender, age, BMI, diabetes, physical activity, and alcohol use [30]. This analysis suggests that the type of cancer and age might influence the epidemiological association with sleep problems and that older age could confer protection against intermittent hypoxia-induced carcinoma growth [30, 31]. These assumptions align with our observed inverse association between habitual snoring and overall cancer, colon and rectum, skin, melanoma cancer in males aged 65 and above, and breast cancer in women aged 65 and above.

A surprising finding of this study was the lower cancer prevalence among habitual snorers compared to non-habitual snorers, particularly in men. While snoring is widely recognized as a primary symptom of OSA [32, 33]—a condition linked to increased cancer risk [8, 23–25, 34]—our findings suggest a more complex relationship. Previous studies have indicated that the association between OSA and cancer typically emerges in more severe cases of apnea, as evidenced by elevated cancer risks in patients with moderate to severe OSA compared to those with mild OSA [25]. Hypoxia and sleep fragmentation are considered to be the main pathologic link in the OSA-cancer incidence relationship [35, 36]. In murine-based reports implicating sleep fragmentation and intermittent hypoxia components of OSA, fragmented sleep accelerates tumor growth and progression through tumor-associated macrophage recruitment and TLR4 signaling [35]. On the other hand, hypoxia increases angiogenesis into the tumoral tissue and induces overexpression of transcription factors, such as hypoxia-inducible factor-1, which are known to trigger upregulation of proangiogenic mediators, such as vascular endothelial growth factor in tumor cells, and enhance tumor progression [36, 37].

Notably, snoring alone does not necessarily indicate the presence of OSA [33]. Advanced signal processing algorithms-based studies have demonstrated only a weak positive correlation between snoring frequency and the apnea–hypopnea index (AHI), a standard measure of OSA severity [33]. This suggests that snoring without accompanying severe apnea may not significantly elevate cancer risk, a hypothesis supported by our data and other population-based studies [38]. For instance, Gozal et al. identified selective cancer risks associated with OSA using a nationwide employee-sponsored health insurance database, where certain cancers like pancreatic and kidney cancers showed increased risk, whereas others like colorectal and breast cancers demonstrated lower risks among those diagnosed with OSA [38]. This aligns with our findings of reduced colorectal and breast cancer prevalence in men and female habitual snorers, respectively, potentially highlighting a complex interplay of factors beyond simple hypoxia-induced carcinogenesis.

Our study refines this perspective by incorporating IPTW to control for important confounders such as smoking, BMI, race/ethnicity, and other demographic characteristics, unlike previous studies that might not have fully accounted for these variables [38]. Despite this, the pathophysiological mechanisms underlying the reduced risk of certain cancers in snorers remain speculative. It is hypothesized that varying cancer types may interact differently with hypoxia-inducible factors, which play critical roles in tumor progression and response to hypoxia [38–41]. Given these complexities, the findings necessitate cautious interpretation, particularly due to the cross-sectional design of our study which limits causal inferences. Future research should aim to replicate these results in larger, prospective cohorts with objective measures of snoring and OSA severity, alongside detailed cancer

Table 3. IPTW-Weighted Sex-Specific Relationship Between Habitual Snoring and Cancer, Stratified by Age Groups

Age groups	≤49 years		50–64 years		65 years and above	
Males	**OR (95% CI)**	**P-value**	**OR (95% CI)**	**P-value**	**OR (95% CI)**	**P-value**
Lung cancer	na		0.10 (0.02,0.54)	.007	0.70 (0.33,1.46)	.340
Prostate cancer	na		0.77 (0.50,1.18)	.230	0.83 (0.67,1.03)	.083
Liver cancer	na		na		0.46 (0.11,1.97)	.292
Colon and rectum cancer	0.93 (0.37,2.34)	.881	0.78 (0.32,1.89)	.582	0.52 (0.32,0.84)	.008
Non-melanoma skin cancer	1.27 (0.63,2.57)	.500	0.88 (0.55,1.39)	.573	0.71 (0.55,0.92)	.010
Melanoma	0.36 (0.06,2.17)	.266	1.92 (0.76,4.83)	.166	0.30 (0.16,0.55)	<.001
Leukemia	1.00 (1.00,1.00)	.	1.00 (1.00,1.00)	.	1.00 (1.00,1.00)	.
Lymphoma	1.00 (1.00,1.00)	.	0.65 (0.19,2.15)	.478	1.47 (0.55,3.98)	.445
Cancer of the brain and nervous systems	na		na		4.54 (0.92,22.48)	.064
Cancer of the mouth/tongue/lips/Larynx	1.06 (0.10,11.76)	.961	1.00 (1.00,1.00)	.	0.57 (0.18,1.77)	.332
Kidney cancer	0.64 (0.09,4.51)	.652	0.50 (0.15,1.62)	.247	0.44 (0.18,1.07)	.071
Stomach cancer	1.22 (0.12,12.67)	.865	1.00 (1.00,1.00)	.	3.12 (0.47,20.53)	.237
Testis cancer	na		1.08 (0.13,8.80)	.942	1.00 (1.00,1.00)	.
Cancer of any type	0.62 (0.41,0.95)	.027	0.79 (0.62,1.00)	.053	0.70 (0.60,0.82)	<.001
Females						
Lung cancer	6.25 (0.85,46.03)	.072	0.35 (0.06,2.02)	.238	0.90 (0.27,2.97)	.857
Breast cancer	0.50 (0.24,1.04)	.064	0.86 (0.60,1.22)	.400	0.69 (0.53,0.91)	.007
Liver cancer	1.00 (1.00,1.00)	.	na		1.00 (1.00,1.00)	.
Colon and rectum cancer	2.44 (1.00,5.95)	.049	0.68 (0.31,1.50)	.338	1.54 (0.98,2.41)	.060
Non-melanoma skin cancer	1.18 (0.62,2.26)	.617	1.35 (0.76,2.40)	.304	0.94 (0.68,1.29)	.693
Melanoma	1.00 (1.00,1.00)	.	3.95 (1.53,10.21)	.005	1.01 (0.57,1.79)	.978
Uterine cancer	2.39 (0.90,6.31)	.080	1.98 (1.14,3.45)	.016	0.55 (0.29,1.06)	.073
Leukemia	1.00 (1.00,1.00)	.	1.00 (1.00,1.00)	.	1.00 (1.00,1.00)	.
Lymphoma	1.00 (1.00,1.00)	.	1.00 (1.00,1.00)	.	0.86 (0.33,2.25)	.761
Thyroid cancer	1.65 (0.68,3.99)	.270	0.45 (0.17,1.17)	.101	1.04 (0.33,3.29)	.951
Cancer of the brain and nervous systems	1.00 (1.00,1.00)	.	1.66 (0.16,16.90)	.667	na	
Cancer of the mouth/tongue/lips/Larynx	2.28 (0.23,22.15)	.478	1.00 (1.00,1.00)	.	na	
Kidney cancer	na		1.20 (0.25,5.72)	.822	1.72 (0.61,4.84)	.302
Stomach cancer	na		1.00 (1.00,1.00)	.	1.51 (0.19,12.05)	.696
Cervix cancer	2.34 (1.67,3.28)	<.001	1.09 (0.64,1.85)	.756	0.54 (0.21,1.39)	.203
Ovary cancer	2.18 (1.02,4.63)	.043	1.00 (0.50,2.01)	.989	0.31 (0.11,0.89)	.029
Cancer of any type	1.34 (1.08,1.68)	.009	0.99 (0.80,1.21)	.892	0.88 (0.75,1.05)	.152

Abbreviations: CI, confidence intervals; IPTW, inverse probability of treatment weighting; *N*, number of participants; na, information not available due to insufficient sample size to calculate the odds ratios; ORs, odds ratios.
Variables included in propensity model: variables included in the propensity model: demographics-sex, age, poverty levels, race/ethnicity, education, marital status, health insurance status; clinical factors-hypertension, asthma, diabetes, cardiometabolic disease, BMI; lifestyle factors-alcohol use, smoking status; sleep-related characteristics: restless leg syndrome, sleep apnea.

diagnoses, to better delineate the relationships and underlying mechanisms at play.

Sex differences in the association between habitual snoring and cancer may stem from distinct effects of carcinogenic risk factors in men and women. Genetic studies suggest that snoring correlates differently with lifestyle and clinical traits in each gender. For instance, while snoring prevalence is typically higher in males, tobacco use appears to have a stronger association with snoring in females, whereas alcohol consumption exerts a greater influence on snoring in males [13, 42]. Additionally, population-based research indicates higher cancer rates among heavy-drinking females compared to males [43, 44]. Moreover, several studies have shown a higher incidence of lung cancer in men than in women with similar tobacco smoking exposure levels [45, 46]. Although genetic evidence supports a causal relationship between BMI or whole-body fat mass and snoring, a prior review suggests a higher overall incidence of obesity-related cancer in females compared to males [13, 47]. Although no clinical studies have directly explored the sex-specific pathologic interaction between habitual snoring, carcinogenic risk factors, and cancer, these previous findings imply that varying carcinogenic potencies may contribute to specific cancer risk in individuals with habitual snoring, depending on gender.

Our findings contribute to the existing literature on the gender-specific influence of sleep duration on cancer risk. For instance, a recent study of 14 851 participants from the China Health and

Table 4. IPTW-Weighted Sex-Specific Relationship Between Habitual Snoring and Cancer, Stratified by BMI Categories

BMI categories	Underweight (BMI < 18.5)		Healthy (BMI: 18.24.9)		Overweight (BMI: 25-29.9)		Obese (BMI ≥ 30)	
Males	**OR (95% CI)**	**P-value**	**OR (95% CI)**	**P-value**	**OR (95% CI)**	**P-value**	**OR (95% CI)**	**P-value**
Lung cancer	na	na	0.68 (0.28,1.70)	.413	0.22 (0.05,1.02)	.054	0.44 (0.12,1.57)	.206
Prostate cancer	1.48 (0.71,3.08)	.296	0.69 (0.45,1.06)	.090	0.74 (0.55,1.00)	.052	0.77 (0.56,1.06)	.114
Colon and rectum cancer	1.14 (0.42,3.08)	.797	1.23 (0.53,2.82)	.627	0.67 (0.36,1.26)	.214	0.21 (0.09,0.49)	<.001
Mon-melanoma skin cancer	1.54 (0.73,3.22)	.257	0.88 (0.54,1.43)	.596	0.64 (0.45,0.91)	.014	0.71 (0.50,0.99)	.045
Melanoma	na	na	0.37 (0.12,1.13)	.082	0.35 (0.17,0.75)	.007	0.75 (0.38,1.47)	.400
Lymphoma	na	na	0.65 (0.16,2.58)	.542	0.90 (0.25,3.27)	.879	0.26 (0.06,1.09)	.065
Kidney cancer	na		na	na	0.91 (0.36,2.28)	.845	0.24 (0.08,0.72)	.011
Cancer of any type	1.42 (0.95,2.14)	.091	0.62 (0.48,0.81)	<.001	0.63 (0.52,0.77)	<.001	0.67 (0.55,0.81)	<.001
Female								
Lung cancer	0.60 (0.23,1.56)	.294	na	na	na	na	na	na
Breast cancer	0.79 (0.64,0.97)	.026	na	na	0.40 (0.10,1.59)	.195	0.78 (0.30,2.04)	.617
Colon and Rectum cancer	1.37 (0.94,2.00)	.098	Na	na	na	na	na	na
Non-melanoma skin cancer	1.04 (0.78,1.37)	.808	2.71 (0.89,8.23)	.078	na	na	0.98 (0.40,2.38)	.963
Melanoma	1.12 (0.67,1.88)	.660	0.88 (0.18,4.36)	.880	na	na	0.93 (0.24,3.64)	.912
Uterine cancer	1.21 (0.81,1.79)	.350	7.90 (1.11,56.25)	.039	na	na	na	na
Thyroid cancer	1.39 (0.70,2.77)	.352	na	na	na	na	1.58 (0.42,6.01)	.502
Cancer of the brain and nervous systems	0.87 (0.13,5.93)	.886	na	na	1.00 (1.00,1.00)	na	na	na
Kidney cancer	1.60 (0.68,3.78)	.283	na	na	na	na	na	na
Cervix cancer	0.75 (0.49,1.16)	.201	3.90 (2.00,7.61)	<.001	2.86 (1.46,5.59)	.002	2.17 (1.21,3.90)	.009
Ovary cancer	1.01 (0.59,1.73)	.978	1.00 (1.00,1.00)	.	2.04 (0.82,5.08)	.127	0.39 (0.06,2.39)	.309
Cancer of any type	0.95 (0.84,1.08)	.456	1.25 (0.81,1.95)	.312	1.14 (0.73,1.77)	.569	1.39 (0.98,1.97)	.067

Abbreviations:.CI, confidence intervals; IPTW, inverse probability of treatment weighting; *N*, number of participants; na, information not available due to insufficient sample size to calculate the odds ratios; OR, odds ratios.
Variables included in the propensity model: demographics-sex, age, poverty levels, race/ethnicity, education, marital status, health insurance status; clinical factors-hypertension, asthma, diabetes, cardiometabolic disease, BMI; lifestyle factors-alcohol use, smoking status; Sleep-related characteristics: restless leg syndrome, sleep apnea.

Retirement Longitudinal Study revealed elevated overall cancer risk among women sleeping less than 6 hours per night, but not in men [48]. Similarly, an analysis of 469 691 individuals in the UK BioBank identified both insufficient and excess sleep duration as independent risk factors for lung cancer, yet did not find an increased risk associated with snoring [49]. However, these studies did not separately investigate the interaction between sleep duration and snoring in cancer risk for men and women. Our weighted analysis, stratified by sleep duration, revealed that the inverse associations between habitual snoring and overall and lung cancer prevalence were observed only in males sleeping less than 7 hours. Conversely, in females, sleeping more than 9 hours per night was associated with increased odds of uterine and overall cancer prevalence. Furthermore, a systematic review and meta-analysis of cohort studies suggest that long sleep duration and sleep disturbance disrupt the immune-inflammation balance, leading to increases in systemic inflammation markers, which are associated with tumorigenesis [50, 51]. While long sleep might be a marker of chronic conditions [52], these findings support the potential role of chronic inflammation in cancer development, and suggest the possibility of using long sleep duration and habitual snoring as screening markers for cancer risk in women. While further research is warranted to explore the exact biological mechanisms, our study provides valuable insights into potential screening strategies for cancer risk.

There is ongoing debate about the impact of sleep duration on cancer risk. Recent analyses, including Mendelian randomization studies and systematic reviews, have further nuanced our understanding of the relationship between sleep duration and cancer risk [53–58]. For instance, Titova et al. (2021), using Mendelian randomization, found suggestive links between genetic predispositions to shorter sleep durations and increased risks of gastrointestinal cancers, although these findings did not withstand multiple testing corrections [53]. Similarly, a pooled analysis of Japanese cohorts indicated a non-linear association, where both very short and long durations of sleep correlated with an increased risk of certain cancers in men and women of certain age and BMI categories [54]. These findings align with our observations that both short and long sleep durations can modulate cancer risks differently across genders and cancer types, potentially through mechanisms involving systemic inflammation and immune function disruption [53, 54]. Notably, while some studies found significant associations for site-specific cancers, comprehensive reviews suggest that the overall cancer risk might not be significantly associated with sleep duration, highlighting the complexity of these relationships and the potential influence of unmeasured confounders [58]. Given these mixed outcomes, our study contributes to the ongoing discourse, suggesting that sleep duration, much like other lifestyle factors, potentially interacts with biological processes in a manner that may increase or decrease cancer risk. Our findings highlight the need to consider habitual snoring as a potential co-factor in these analyses. Future studies should aim to clarify these pathways and consider the impact of circadian rhythm disruptions, providing a more detailed landscape of how habitual behaviors like snoring and variations in sleep duration intersect with cancer epidemiology.

Previous studies have implicated intermittent hypoxia and sleep fragmentation as key mechanisms linking OSA to cancer incidence [28, 29, 59]. Intermittent hypoxia, characterized by repeated episodes of oxygen desaturation followed by reoxygenation, may lead to the generation of reactive oxygen species, similar to reperfusion injury in ischemic stress [60]. This process could predispose individuals to carcinogenesis by promoting reactive oxygen production in vascular endothelial cells [61]. Additionally, intermittent hypoxia may up-regulate hypoxia-inducible factors, altering substrate metabolism, angiogenesis, and cell differentiation, thus promoting cancer development [62]. Sleep fragmentation, on the other hand, has been associated with sympathetic activation, chronic systemic inflammation, and altered immune cell function, all of which may contribute to carcinogenesis in various organs [63, 64]. However, data on sex differences in the association between OSA and cancer are limited [28], and further research is needed to elucidate the potential role of cancer subtype, hormonal influences, and duration of OSA or habitual snoring on sex-specific mechanisms of carcinogenesis.

Limitations

Despite utilizing a large, diverse population sample and employing IPTW-weighted analysis were used in this study, several limitations must be acknowledged. First, sleep-related characteristics and cancer prevalence were self-reported rather than objectively measured, potentially introducing participant-specific recall bias and misclassification of exposure and response variables. While the definition of habitual snoring may misclassify cases where participants lack a bed partner into control, prior studies suggest high accuracy (up to 96%) of self-reported cancer diagnosis [65]. Secondly, our study design was observational, precluding the establishment of causality. Thirdly, the use of simple measures of sleep characteristics in a cross-sectional survey did not account for changes in sleep patterns over time, necessitating longitudinal cohort studies with repeated measures to validate findings. Additionally, our results may be susceptible to residual confounding from unaccounted covariates, such as medication use (e.g. chemotherapy), and genetic factors, which are not included in our dataset. Future studies should consider incorporating these clinical variables to more thoroughly explore the relationship between habitual snoring and cancer prevalence in men and women. Despite efforts to balance demographic, clinical, lifestyle, and sleep-related characteristics through weighted analyses in our main and subgroup analyses, residual confounding remains a possibility.

Conclusions

Our study elucidates sex-specific associations between habitual snoring and cancer prevalence, revealing inverse associations in males, particularly among males aged over 65 years, and varied effects in females, including lower odds of breast cancer but increased odds of cervix cancer. Additionally, we highlight the modifying role of sleep duration, with shorter duration (<7 hours) linked to decreased overall and lung cancer prevalence in snoring men, and longer duration (>9 hours) associated with elevated overall and uterine cancer prevalence in snoring women. Future research exploring the interactions between different sleep characteristics and cancer could have profound implications. Initiating long-term clinical trials to investigate cancer subtype screening based on objective sleep assessment would refine risk delineation, potentially altering prevention and screening strategies in a more accurate and individualized manner. Integration of genetic, circulating biomarkers, and other clinical and behavioral risk factors in future studies could provide insights into shared mechanisms underlying habitual snoring and cancer.

Supplementary Material

Supplementary material is available at *SLEEP Advances* online.

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Author Contributions

Qinglan Ding (Conceptualization [equal], Data curation [lead], Investigation [lead], Methodology [equal], Project administration [lead], Resources [lead], Supervision [lead], Validation [equal], Writing—original draft [lead], Writing—review & editing [lead]), Jeph Herrin (Formal analysis [lead], Methodology [lead], Validation [lead], Visualization [lead], Writing—review & editing [equal]), and Meir Kryger (Conceptualization [lead], Investigation [equal], Methodology [equal], Resources [equal], Supervision [equal], Writing—review & editing [equal])

Data Availability Statement

The data for this study were sourced from NHANES, which is publicly available and can be accessed through the website https://wwwn.cdc.gov/nchs/nhanes/default.aspx.

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