Smoking and Incidence of Sleep Disorder: a systematic review and meta-analysis of cohort studies

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Nan Hu, Chunyi Wang, Yan Liao, Qichen Dai, Shiyi Cao

Nan Hu
Huazhong University of Science and Technology

Chunyi Wang
Huazhong University of Science and Technology

Yan Liao
Huazhong University of Science and Technology

Qichen Dai
Huazhong University of Science and Technology

Shiyi Cao
Huazhong University of Science and Technology

caoshiyi@hust.edu.cn Corresponding Author

Prescreen

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Abstract

Background

Both smoking and sleep disorder are worldwide problems and this study aim to investigate the impact of smoking on the incidence of sleep disorder.

Methods

PubMed, EMBASE and OVID were searched through March, 2020. Cohort studies reporting the effect of smoking on the incidence of sleep disorder were included. We quantitatively analyzed the basic framework and study characteristics, and then pooled estimate effects with 95% confidence intervals (CIs) of outcomes of each included studies using fixed-effects meta-analyses.

Results

This systematic review included seven cohort studies involving 17,414 participants. Quantitatively summarized results suggested smoking could increase the incidence of sleep disorder (OR: 1.08, 95%CI: 1.02,1.13). For regular smokers and occasional smokers, significant association between smoking and incidence of sleep disorder was found (regular smoker: OR = 1.07, 95% CI:1.01,1.13; occasional smoker: OR = 1.62, 95% CI:1.15,2.28). As for ex-smokers, the pooled analysis didn’t indicate a positive association (OR = 1.02, 95% CI:0.67,1.54). Subgroup analysis by age, gender ratio and religion showed statistically significant relationship between smoking and incidence of sleep disorder in specific groups.

Conclusions

Integrated longitudinal observational evidence identified smoking as a significant risk factor of sleep disorder. Considering the limited amount of available researches, more high-quality and prospective cohort studies of large sample sizes are needed to explore details of this association.

1. Background

Sleep, a basic and necessary biological process of human being, is crucial for our physical and mental functioning. With the development of society and the improvement of living standard, public attention to our own health and quality of life is gradually increasing. Epidemiologic studies revealed that the prevalence rate of one or more symptoms of sleep disorder ranges from 30–35%[1]. Poor sleep health, defined as sleep of inadequate quality, timing, efficiency or duration to prevent daytime sleepiness, has been identified as a public health issue[2, 3] and approximately $100 billion was spent on conditions associated with sleep disorders in the USA [4]. Besides, studies and official reports in other parts of the world revealed the similar heavy burden of sleep health for the public[5–7]. Therefore, increasing researches were done to study sleep health. According to the Diagnosis and Statistical Manual of Mental Disorders fifth edition (DSM-5), sleep-wake disorders are broadly classified into eleven parts, among which insomnia disorder is mostly concerned by researchers. The experiments about excessive daytime sleepiness(EDS) and frequent nocturnal awakenings were raising in the recent years. It was reported that insomnia was associated with negative outcomes ranging from motor vehicle accidents to suicide[8, 9]. Some chronic diseases have also been observed in relation to sleep disorder, such as hypertension[10], metabolic syndrome[10, 11] and diabetes mellitus[12]. It’s vital to find appropriate ways to improve public sleep health.

To reveal the risky factors of sleep disorder, many associated researches has been done. Alcohol, smoking, depression are widely known as independent factors for sleep disorder[5], among which smoking captured a lot of researchers’ attention in recent years. Cigarette use was reported to associated with poor sleep health in national samples of adolescents [13] and adults[14, 15], including college students[16]. Moreover, compared to nonsmokers, current smokers demonstrated shorter sleep times, longer sleep onset latency, more sleep apneas
and more leg movements during sleep[17]. Several epidemiological evidence also supported the association[6, 18].

Although some precious studies reported positive effects of smoking on sleep, results varied from experiments. Negative results have also been reported. Besides, most of the studies were cross-sectional studies, which couldn’t reflect the sequential order and causal relationship between smoking and sleep disorder. We found several recent reviews which focused on this project but no meta-analysis has been done[19–21]. Substantial association between smoking and sleep disorder is still unclear. Therefore, our studies focused on the association between smoking and incidence of sleep disorder in cohort studies. Details about smoking status, gender, age, religion’s interaction with sleep disorder in smokers would also be discussed in this study. A better understanding of the association between smoking and sleep disorder might offer guidance to public health management.

2. Methods

This work was performed according to the MOOSE (Meta-analysis Of Observational Studies in Epidemiology) guidelines[22].

2.1 Literature Search

We identified relevant studies published from 1946 to March 2020 by searching on PubMed, EMBASE and OVID. Studies were restricted to human species. We used the keywords “Sleep Disorder” or “Insomnia” in combination with “Smoking”. The full electronic search strategy for PubMed is: ((((((((Sleep Disorder[MeSH Terms]) OR Sleep Disorder[Title/Abstract]) OR Sleep Disorders[Title/Abstract]) OR Disorder Sleep[Title/Abstract]) OR Sleep Disturbance[Title/Abstract]) OR Disturbance Sleep[Title/Abstract]) OR Night Terroris[Title/Abstract]) OR Insomnia[Title/Abstract]) OR Insomnias[Title/Abstract]) OR Sleeplessness[Title/Abstract]) OR Insomnia Disorders[Title/Abstract]) OR Insomnia Disorder[Title/Abstract]) OR Sleep Health[Title/Abstract]) AND ((((((((Smoke[MeSH Terms]) OR Smoking[Title/Abstract]) OR Smokeable[Title/Abstract]) OR Smokes[Title/Abstract]) OR Tobacco Smoking[Title/Abstract]) OR Smk[Title/Abstract]) OR Cigarette [MeSH Terms]) OR Cigarette Smoking[Title/Abstract]) OR Cigar[Title/Abstract]) OR Cigars[Title/Abstract]).

No filter for study designs was applied. Pertinent studies were also identified during the screen of reviews and reference lists of search results. After the exclusion of duplications, titles and abstracts were screened during the initial selection. Further review was based on the full text. Nan Hu and Chunyi Wang screened all the articles independently. Their results reached consensus. A senior reviewer (Shiyi Cao) would check the article and make decisions if there was disagreement. (Fig. 1)

2.2 Inclusion and Exclusion Criterion

Studies were included if they satisfied the following criteria: 1. Cohort studies. 2.Studies designed to examined the relationship between smoke exposure and incidence of sleep disorder among healthy populations. 3. Comparators defined as nonsmokers or never smokers. 4. Studies that provide clear hazard ratio(HR) or odds ratio(OR) with 95% confidence interval(CI). The exclusion criterion included: 1. Duplications or same cohorts with similar study period, unless they had different points. 2. Studies which did not provide clear hazard ratio(HR) or odds ratio(OR) with 95% confidence interval(CI), and could not retrieve by contacting with the authors. 3. Studies which restricted the population to specific patients, such as patients with depression at the start.

2.3 Data Extraction

Data extraction was carried out by two reviewers (Nan Hu and Chunyi Wang ) independently. From each eligible study, we collected authors, publication year, geographical region, gender ratio (women/men), mean age, smoking status, study period, study design, sample size, endpoints, diagnostic criteria of sleep disorder or insomnia, HRs or ORs with 95% CI. While there were results of different calculation models, we extracted the HR or OR fully adjusted for covariates. If necessary, we tried to contact the corresponding author of relevant articles.
2.4 Quality assessment

Used Newcastle-Ottawa Quality Assessment Scale (NOS) (http://www.ohri.ca/programs/clinical-epidemiology/oxford.asp) as reference according to our included study design, we assessed the quality of the eligible studies from 3 individual perspectives: the population selection; the comparability in study design; and the ascertainment of outcome or exposure. Two reviewers Nan Hu and Chunyi Wang ) performed the assessment separately and a senior reviewer (Shiyi Cao) resolved disagreement. (Table 1 and Supplementary File Table 1)

2.5 Definition

We included studies that fit the definition of sleep disorder: a chronic state of sleep deprivation and subsequent daytime sleepiness, including insomnia and excessive daytime sleepiness. And literatures included must provide the diagnostic standard which has been tested or used by other studies or acknowledged by public. The diagnostic standards are provided in Table 1. Besides, according to DSM-III-R, insomnia symptoms were divided into several types which were further discussed in our study: (a) Difficulty getting to sleep; (b) Wake up during the night and have a hard time getting back to sleep; (c) Wake up repeatedly and can’t get back to sleep; (e) Not feel rested during the day, no matter how many hours of sleep you had. For each symptom, responders indicated the frequency with which it was experienced: very frequent (16 or more days or nights per month), frequent (5–15 days or nights per month), infrequent (2–4 days or nights per month), rare (1 or fewer days or nights per month).

Smoker is defined as people who have/had experience of smoking or exposure to cigarette or tobacco. Different types of smoking status are classified by smoking period and number of tobaccos people smoke/smoked each day. No smoker is defined as never users and current smoker is defined as present users which includes regular smoker and occasional smoker and ex-smoker is people who ever smoked but stopped later at the endpoint including the quitters/decreasers. Regular smokers are people who started smoking before and stayed at a level of daily smoking at the endpoint. According to the time of initiation, regular smokers are divided into two types: heavy/continuous smokers are people who started smoking early, reached their maximum level (i.e., about one pack a day or more) in their late twenties, and then maintained that level into their thirties (the endpoint). Late starters are people who started smoking in late adolescence but reached the same level of smoking (i.e., about one pack a day) as the heavy/continuous smokers in the late twenties and then maintained that level till the endpoint. The occasional smokers are people who increased the amount of smoking from adolescence to the early twenties and then stayed at a level of less than daily smoking during adulthood.

2.6 Statistical analysis

Because of low heterogeneity (I² = 31.8%), we chose fixed-effects model to calculate the pooled HR/OR and 95% CI. Heterogeneity was tested with the I² statistic. We combined Funnel plot asymmetry and Egger's regression to detect publication bias, and defined significant publication bias as a p value < 0.1. Sensitivity analysis was used to examine the stability of the pooled results, whereby each study was omitted at a time and recalculated the pooled HR of the rest studies. Meta-analysis was performed with Stata software (version 16.0; College station, TX, USA). All p values were two-side with a significant level at 0.05.

3. Results

3.1 Literature selection

A total of 592 studies were included in our study, including the results of keywords search (n = 586) and additional records identified from reference lists of other studies (n = 6). After the detailed reading of full texts, six articles[23–28] were potentially eligible for meta-analysis (Fig. 1) and one other article[29] was eligible for systematic review. Finally, a total of 7 cohort studies were included in our analysis. Six included studies [23–27, 29] reported the relationship between smoking and incidence of insomnia, among which one study[29] divided
insomnia into different symptoms. One study[28] reported the relationship between smoking and incidence of excessive daytime sleepiness (EDS). The main information of eligible studies was given in Table 1. We assessed the quality of included studies from 3 aspects and their scores were no less than 7 points (total score = 9 points) (Table 1 and Supplementary File Table 1).

| Study             | Area            | Study Period  | Total Sample | Mean Age (Years) | Gender (woman/man) | Smoking Status                  |
|-------------------|-----------------|---------------|--------------|------------------|--------------------|---------------------------------|
| Jaussent et al (2017) | France         | 2012-2017     | 1453         | 51               | 678/775            | Regular smoker                   |
| Brook et al (2015)   | USA            | 1983-2013     | 528          | From 14.1 to 42.7| Not given          | Heavy/continuous smoker          |
| Haario et al (2013)  | Finland        | 2002-2007     | 6458         | ≥40              | 5248/1210          | Smoker                           |
| Fernandez et al (2012) | USA            | 1990/1999-2000/2003 | 1246     | 45.4             | 517/729            | Current smoker                   |
| Zhang et al (2012)   | China-Hong Kong| 2006-2011     | 1611         | From 9.0-13.7    | 822/789            | Current smoker                   |
| Janson et al (2001)  | Sweden          | 1984-1994     | 2602         | ≥30              | All men             | Ex- smoker                       |
| Wetler et al (1994)  | USA            | 1994          | 3516         | ≥18              | 1840/1666          | Smoker                           |

Abbreviation: USA the United States; EDS excessive daytime sleepiness; ESS the Epworth sleepiness scale; DSM the Diagnostic and Statistical Manual of Mental Disorders
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including current smoker and ex-smoker

3.2 Risk of bias assessment for included studies

3.2.1 Bias from character of population

Cohorts of five included studies[23–25, 27, 28] were representative of general community population, whereas other two studies[26, 29] restricted their cohorts to specific population, such as adult employers. One study[27] didn’t provide gender information. The diversity of included population means potential different educational level, socioeconomic status and mental health level, which might contribute to the bias of synthesized results.

3.2.2 Bias from covariates adjustment
Different studies provided different information of covariates adjustment. Five studies[23, 24, 26, 27, 29] adjusted the results for age and three studies[24, 26, 27] adjusted the result for gender. One[26] further adjusted the result for baseline insomnia symptoms, marital status, occupational class, sleep duration and common mental disorders, one[24] further adjusted for parental education, family income, and parent-reported poor health condition at baseline and one[23] further adjusted for medical disorder, BMI, physical inactivity, alcohol. One[25] adjusted for sampling weight.

### 3.2.3 Bias from definition of endpoint

Although included studies all provided clear definition of insomnia and sleep disorder, the definition varied from studies which might contribute to the bias of synthesized results.

### 3.3 Smoking and Sleep Disorder Incidence

Figure 2 showed the ORs of six studies about smoking and incidence of sleep disorder. The pooled OR for smoking was 1.08 (95% CI:1.02, 1.13), which indicated a positive association between exposure to smoking and incidence of sleep disorder. The heterogeneity of these studies was not significant ($I^2 = 31.8\%$, $p = 0.145$). Funnel plot and Egger’s regression suggested that there might be publication bias (Egger’s regression: $p = 0.035$, Fig. 1). Sensitivity analysis indicated heterogeneity was mainly from one study (Fig. 1 and Supplementary File Fig. 2). For individuals who smoke regularly and occasionally, significant association between smoking and incidence of sleep disorder was found (regular smoker: OR = 1.07, 95% CI:1.01, 1.13; occasional smoker: OR = 1.62, 95% CI:1.15, 2.28). As for ex-smokers, the pooled analysis didn’t indicate a positive association (OR = 1.02, 95% CI:0.67, 1.54) (Fig. 2).

The subgroup-analysis by age suggested significant association both in adults (> 18) (OR = 1.07, 95%CI: 1.02,1.13) and juveniles (≤ 18) (OR = 3.97, 95%CI: 1.04,15.18) (Table 2 and Fig. 1). The subgroup-analysis by gender ratio suggested significant association in population with gender ratio (women/men) < 1 (OR = 1.07, 95%CI: 1.02,1.13), but not in population with gender ratio (women/men) ≥ 1 (OR = 1.08, 95%CI: 0.93,1.25) (Table 2 and Fig. 2). However, the pooled result in population with gender ratio (women/men) ≥ 1 showed a high heterogeneity ($I^2 = 72.8\%$, $p = 0.055$). Because there were only two studies in this subgroup and they reported different results, we failed to exclude any one of them to reduce heterogeneity. The region-specific analysis suggested a positive association in North America (HR: 1.06, 95% CI: 1.01, 1.13) and Asia (only one study) (OR = 3.97, 95%CI: 1.04,15.18). The association between smoke and incidence of sleep disorder was not significant in Europe (OR = 1.12, 95% CI: 1.00, 1.25) (Table 2).
Table 2
Subgroup-analysis of smoke and incidence of sleep disorder.

| Subgroup                      | Stratum         | Number of studies | Pooled OR (95%CI) | Text of heterogeneity |
|-------------------------------|-----------------|-------------------|-------------------|-----------------------|
| Age                           | >18 years old   | 3                 | 1.07(1.02,1.13)   | 23.4                  | 0.258                |
|                               | ≤18 years old   | 1                 | 3.97(1.04,15.18)  |                       |                      |
| Gender ratio(women/man)       | <1              | 3                 | 1.07(1.02,1.13)   | 38.5                  | 0.164                |
|                               | ≥1              | 2                 | 1.08(0.93,1.25)   | 72.8                  | 0.055                |
| Region                        | Europe          | 3                 | 1.12(1.00,1.25)   | 31.3                  | 0.213                |
|                               | North America   | 2                 | 1.06(1.01,1.13)   | 12.7                  | 0.333                |
|                               | Asia            | 1                 | 3.97(1.04,15.18)  |                       |                      |

Abbreviations: OR, Odds ratio. CI, Confidence interval.

\(\chi^2\) is the value of total variation clarified by heterogeneity

Weter et al (1994)[29] suggested that current smoking was related to very frequent (OR = 2.32, 95%CI:1.04,5.16), frequent (OR = 1.56, 95%CI:1.02,2.38), and infrequent difficulty getting to sleep (OR = 1.44, 95%CI:1.05,1.98) for males. For females, current smoking was associated with very frequent (OR = 1.88, 95%CI:1.09,3.23), frequent (OR = 1.78, 95%CI:1.26,2.52) difficulty getting to sleep. Besides, current smoking was associated with very frequent nonrestorative sleep (OR = 2.20, 95%CI:1.15,4.19) for males and very frequent (OR = 2.61, 95%CI:1.62,4.19), frequent (OR = 1.73, 95%CI:1.24,2.40), and infrequent (OR = 1.81, 95%CI:1.37,2.41) nonrestorative sleep for females. Current smoking was associated with excessive daytime sleepiness for females (very frequent: OR = 2.61, 95%CI:1.43,4.78, frequent: OR = 1.48, 95%CI:1.04,2.09, and infrequent: OR = 1.47, 95%CI:1.12,1.91) but not for males. (Supplementary File Table 2)

### 4. Discussion

Our meta-analysis has quantitatively examined the association between smoking and sleep disorder. The pooled analysis included six cohort studies including about 13 thousand people. The results showed that smoking was significantly associated with incidence of sleep disorder. Sensitivity analysis revealed heterogeneity was mainly from one study [25]. After review the whole article, we noticed in this study, pool sleepers at the baseline who developed insomnia at the endpoint were also included in the analysis while in other included studies, this part of participants were excluded. Besides, PSG was used to diagnose insomnia in this study, which might detected potential insomnia in other included studies. All these factors might cause the heterogeneity.

The stratified analysis according to smoking status found significant association between current smokers and incidence of sleep disorder, both for regular smokers and occasional smokers. Many previous studies reported similar association[7, 30]. The association between occasional smokers and incidence of sleep disorder was more significant than regular smokers. This point was the first time to be reported. The main cause of smoking’
negative effects on sleep is associated with chemicals in it, so after quitting or decreasing, the impact should reduce. However, one study demonstrated that sleep architecture disturbances among current smokers were not influenced by the amount of smoking quantified by pack-years [31], which indicated there might be other mechanisms of smoking’ impact on sleep. Because the effects were associated with nicotine-acetylcholine receptors in our brain[31], as the daily amount of smoking increased, this kind of receptors might be saturated at some point and the effects of smoking might reach the maximum. The effects of nicotine on our brain were nonspecific, so while its concentration in the blood reached a certain value, other effects might gradually emerge which might alleviate the effects of nicotine on sleep health. There is still no better explanation according to existing researches. More works on the association between the amount of smoking quantified by pack-years and sleep disorder were needed to be done. To better understand the etiology, concentration of nicotine and other chemicals in cigarette needed to be tested among insomnia population so their effects on sleep could be analyzed.

The pooled analysis didn’t indicate a positive association in ex-smokers. It was also reported that there were not significant differences between former smokers and never smokers for the prevalence of trouble sleeping[32]. Another study has shown that longer sleep duration was associated with successful smoking cessation[33]. Besides, insomnia symptoms were also risk factors for cessation failure following smoking treatment[34]. The effects were mutual and might create a vicious circle between smoking and insomnia. This suggested that quitting smoking might be beneficial to sleep health and current smokers might improve sleep quality by quitting smoking.

The region-specific analysis found significant association between smoking and incidence of sleep disorder in North America and Asia. Epidemiological investigations and cross-sectional studies in these places reported similar conclusion[6, 18]. The association was not significant in Europe. This point was consistent with previous studies[35, 36], which in Europe didn’t suggest that smoking was an independent risk factor for sleep disorder or insomnia either. The different results between areas might due to differences in living habits, social atmosphere and gene. We noticed that Mediterranean diet, which was popular in Europe, was possibly beneficial factor for sleep health[37]. The pace of life in Europe was much slower than in other areas and lifestyle has been reported to related to sleep disorder[5]. Besides, genetic diversity might also have an influence on how human organism reacted to smoking[38]. These factors might decrease the effect of smoking on sleep, but couldn’t offset it. One included study[29] showed that excessive daytime sleepiness was related to smoking for females while nightmares and disturbing dreams were related to smoking among males. More work needed to be done to reveal the substantial association between smoking and sleep disorder. Cross-sectional studies and epidemiological researches in other areas revealed the negative effect of smoking on sleep health[7, 30]. Sleep disorder and smoking are both worldwide problems. Our study showed the conclusion that prohibiting smoking was beneficial to sleep health was widely applicable.

The subgroup analysis based on age suggested significant association both in adults (> 18) and juveniles (≤ 18).Similar results were reported by other studies[7, 39, 40]. Considering only one included study focused on juveniles, more works needed to be done in the future. A cohort study of the unborn reported the adverse influence of in utero exposure to smoking on sleep patterns in preterm neonates[41]. These studies suggested that smoking might contribute to incidence of sleep disorder at all ages. Comparatively, the earlier people smoked, the greater effect smoke caused on sleep. Juveniles, especially children ‘respiratory system and nervous system are immature, which might be more sensitive to chemicals in cigarettes.

Because included studied didn’t divide participants into males and females, we couldn’t conduct a subgroup analysis based on gender. To explore whether gender was associated with sleep disorder in smokers, we divided included studies into subgroups by gender ratio (women/men). The result suggested significant association in population with gender ratio (women/men) < 1, but not in population with gender ratio(women/men) ≥ 1, that is, smoke has a negative influence on sleep in population which males are in the majority. The result was reported for the first time. Prior research suggested that females were more likely to have insomnia[42]. After discussion, we concluded that as male smokers were more than female smokers, the sample size of female smokers was not enough in included studies, which might contribute to bias. Wetler et al (1994)[43] suggested that both for males and females, current smoking was associated with some kinds of insomnia symptoms. The association was not significant when we changed the endpoints to other insomnia symptoms. Besides, the frequency of
insomnia symptoms had an influence on the association. The pooled result in population with gender ratio (woman/man) ≥ 1 showed a high heterogeneity and one reported significant association between smoke and incident sleep disorder, the other didn’t. As there were only two studies in the subgroup, different religion, mental disorder and social status may all contribute to the high heterogeneity. Passive smoking has also been found to associate with sleep disturbance among pregnant women[44]. To better understand the interaction between gender, smoking and sleep disorder, more works with female smokers and comprehensive analysis of all-cause insomnia incidence remained to be done.

4.1 Biological mechanisms

A large amount of studies have revealed that smoke, especially long-time smoke, could promote the occurrence of sleep difficulties. Compared with no smoker, the population with smoking experience has a higher incidence of sleep disorder and associated diseases. The specific biological mechanism of smoking to particulate matters is still evolving. So far, researchers mainly focused on nicotine, the primary addictive component of cigarettes or tobacco. Nicotine has a known potential for enhancing attention and maintaining a certain level of arousal. These effects are obtained by the central release of dopamine, norepinephrine, serotonin, acetylcholine, all of which have been implicated in the regulation of wakefulness, and by the stimulant effect nicotine has on cholinergic neurotransmission in the basal forebrain responsible for cortical arousal[45]. In relation to sleep disorder, nicotine can regulate and change the normal neurotransmitter and disturb sleep architecture both in the early[46] and later stages of the sleep[43]. The changes have been detected by sleep parameters analysis (polysomnography, PSG). Furthermore, nicotine could generate a dose-dependent reduction in sleep efficiency, slow-wave-sleep, REM (rapid eyes movement) sleep and total sleep time[47, 48].

Besides, several psychosocial and physiological factors may account for the association between smoking and incident insomnia. Depression and obesity might be underlying factors in the biopsychosocial domain. Cigarette use has been linked to adverse life events and work stress, which are also associated with insomnia symptoms[5]. Future studies are needed to investigate these multiple associations and reveal the biochemical relationship between smoking and sleep disorder.

4.2 Strengths and limitations

There are several strengths in our study. Firstly, the six studies we included for meta-analysis and one for systematic review were all cohort studies. We did not include cross-sectional studies, because they couldn’t reveal the sequence of smoking and sleep disorder. Though there were several reviews of this topic, none of them included meta-analysis. So this article was the first systematic review and meta-analysis in the recent 20 years. Secondly, the quality of included studies were high or moderate, which might contribute to the reliability. Besides, we systematically analyzed the association between smoking status and sleep disorder, which provided extra basis for the public policy of promoting anti-smoking.

We admitted limitations in the following aspects. Firstly, the number of included studies is not enough, especially for the incidence of excessive daytime sleep and subgroup-analysis. Secondly, the pooled result of smoking and incident insomnia in population with gender ratio (woman/man) ≥ 1 showed a high heterogeneity. There were two studies in this subgroup and one suggested significant association and the other didn’t. Excluding any one of them showed different consequences. Thirdly, sleep disorder or insomnia includes different kinds of symptoms. We didn’t find enough studies on specific insomnia symptoms to conduct subgroup analysis while studies focused on different insomnia symptoms might have different results. Lastly, alcohol, tea, social status, depression and other factors might also have an interaction with smoking and sleep disorder, which was not discussed in the study.

4.3 Recommendations for future research

4.3.1 Study design

We suggest high-quality longitudinal studies and cohort studies with detailed baseline information and regular health examination as ideal study method. Population with different features, such as a specific job or different age groups and gender composition, should be recorded and synthesized by stratified analysis. Mental health,
geographical region and other potential factors should be taken into account to improve the representativeness of the study.

### 4.3.2 Smoking status

Future studies should record daily cigarettes that participants smoke and divide them into different groups. The association between smoke and sleep disorder need more quantification.

### 4.3.3 Adjustment by covariates

During the review of eligible studies, we found various covariates which may exert unstable impact on the summary. We recommend standardized covariates included at least age, sex, BMI, smoking status, alcohol consumption, chronic respiratory diseases, mental disorder, socioeconomic status at an individual level. Further adjustment can be performed by personal habits (such as physical activities, diet) and health status (such as diabetes, family history of disorder). This work requires detailed and elaborate baseline information.

### 4.3.4 Definition of endpoints

Though all studies provided definition and diagnostic criteria, some studies lacked preciseness when describing sleep disorder or insomnia. We recommend future studies definite sleep disorder or insomnia according to DSM. And more studies are needed to discuss the relationship between smoking and specific insomnia symptoms.

## 5. Conclusions

Our meta-analysis identified smoking as a significant risk factor of sleep disorder. Considering the limited amount of available researches, more high-quality and prospective cohort studies of large sample sizes are needed to understand details of this association. Since both smoking and sleep disorder are worldwide problems, our study provides new and comprehensive evidence for tobacco control to reduce sleep disorder.

### Abbreviations

OR odds ratio; CI confidence intervals; DSM-5 Mental Disorders fifth edition; EDS excessive daytime sleepiness; MOOSE Meta-analysis Of Observational Studies in Epidemiology; HR hazard ratio; NOS Newcastle-Ottawa Quality Assessment Scale; BMI body mass index; PSG polysomnography; REM rapid eyes movement

### Declarations

**Ethical approval and consent to participate**

Ethical approval and consent to participate were not necessary for this systematic review.

**Consent for publication**

Not applicable

**Availability of data and materials**

All data analysed during this study are included in published articles

**Competing interests**

None declared
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Authors' contributions
Nan Hu: design of the work and the analysis of the data; Chunyi Wang: the analysis of the data; Yan Liao: data collection; Qichen Dai: the analysis of the data; Shiyi Cao: design of the work. All authors have read and approved the manuscript.

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Fig.1. Results of systematic literature search
### Results of systematic literature search

| Study               | ID   |
|---------------------|------|
| >=1                 |      |
| Zhang J (2011)      |      |
| Haario P (2013)     |      |
| Subtotal (I-squared = 72.8%, p = 0.055) | |
| <1                 |      |
| Fernandez-Mendoza J (2012) |  |
| Janson C(ex) (2001) |      |
| Janson C(current) (2001) |   |
| Subtotal (I-squared = 0.0%, p = 0.556) |  |
Heterogeneity between groups: p = 0.885

Overall (I-squared = 17.9%, p = 0.301)

Figure 2
Smoking status and incident sleep disorder

Supplementary Files
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