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

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 (caoshiyi@hust.edu.cn)
Huazhong University of Science and Technology

Research article

Keywords: smoking, insomnia, meta-analysis

Posted Date: October 7th, 2020

DOI: https://doi.org/10.21203/rs.3.rs-27889/v4

Version of Record: A version of this preprint was published at Public Health on September 1st, 2021. See the published version at https://doi.org/10.1016/j.puhe.2021.07.012.

Abstract

Background: Both smoking and insomnia are worldwide problems and this study aims to investigate the impact of smoking on the incidence of insomnia.

Methods: PubMed, EMBASE and OVID were searched through March, 2020. Cohort studies reporting the effect of smoking on the incidence of insomnia 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 six cohort studies involving 12445 participants. Quantitatively summarized results suggested smoking could significantly increase the incidence of insomnia (OR: 1.07, 95%CI: 1.02,1.13). Regular smoking was significantly associated with incidence of insomnia (OR=1.07, 95% CI:1.01,1.13). As for occasional smokers and ex-smokers, the pooled analysis didn't indicate a significant association (occasional smoker: OR=2.09, 95% CI:0.44,9.95; ex-smoker; OR=1.02, 95% CI:0.67,1.54). Subgroup analysis by age, gender ratio and region showed statistically significant relationship between smoking and incidence of insomnia in specific groups.

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

1. Background

Insomnia disorders, namely insomnia, is characterized by sleep of inadequate quality, timing and efficiency. Epidemiologic studies revealed that the prevalence rate of one or more symptoms of insomnia disorder ranges from 30% to 35% [1]. It was reported that approximately $100 billion was spent on conditions associated with insomnia as a public health issue in the USA [2-4]. Studies and official reports in other parts of the world revealed the similar heavy burden of sleep health for the public [5-7]. Besides, 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 insomnia including hypertension[10], metabolic syndrome[11] and diabetes mellitus[12]. It's vital to find appropriate ways to reduce the incidence of insomnia and improve public sleep health.

Emerging studies have been done to reveal the risky factors of insomnia. Alcohol, smoking, depression are widely known as independent factors for insomnia [5], among which smoking might be the most concerned. 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 previous studies suggested that smoking might be a contributing factor for insomnia, there were considerable differences among the results of studies [14, 19, 20]. Besides, most of the studies were cross-sectional studies, which couldn't reflect the sequential order and causal relationship between smoking and insomnia. We found several recent reviews which focused on this project but no meta-analysis has been done [21-23]. Therefore, our study focused on the association between smoking and incidence of insomnia of cohort studies. Besides, it has been reported that demographic factors including gender, age might be associated with insomnia [24, 25] and the degree of correlation between smoking and insomnia varied with region [1, 26], which were discussed in our study through subgroup analysis. Smoking status were also discussed for more specific results and guidance to public health management.

2. Methods

This work was performed according to the MOOSE (Meta-analysis Of Observational Studies in Epidemiology) guidelines[27].

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. Following search keywords were used for searching: (1) smoking, smoker, cigar and their synonyms; (2) insomnia and its synonyms. 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. NH and CYW screened all the articles independently. Their results reached consensus. A senior reviewer (SYC) would check the article and make decisions if there was disagreement. (Figure 1)

2.2 Definition and Study selection

We included studies that fit DSM (The Diagnostic and Statistical Manual of Mental Disorders) -5 for diagnostic criterion of insomnia: difficulty initiating or maintaining sleep in addition to impaired daytime functioning or clinically significant discomfort because of sleep problems[28]. And literature 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) The feeling of not having enough rest 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).

Smokers are people who have 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. A non smoker is defined as a person who never smokes and ex-smoker is people who ever smoked but stopped when the data was collected. 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.

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 insomnia 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. 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 baseline.

The study was independently screened by two authors (NH and CYW) using the criteria described above and the different opinions encountered in the study screening would be discussed throughout the process until authors reached a mutual consensus.

2.3 Data Extraction

Data extraction was c0onducted by two reviewers (NH and CYW) 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 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 for information.

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 (NH and CYW) performed the

assessment separately and a senior reviewer (SYC) resolved disagreement. (Table 1 and Supplementary Table 1)

2.5 Statistical analysis

Because of low heterogeneity (I^2 =14.9%, p=0.310), we chose fixed-effects model to calculate the pooled HR/OR and 95% CI. Heterogeneity was tested with the I^2 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 based on the results of quality assessment, whereby each study was omitted at a time and recalculated the pooled OR of the rest studies. We also performed subgroup analysis by age, gender ratio, region and smoking status to examine details about the association. 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, five articles[29-33] reported the relationship between smoking and incidence of insomnia were potentially eligible for meta-analysis (Figure 1) and one other article[34] was eligible for further discussion as it divided insomnia into different symptoms. The main information of eligible studies was given in Table 1. We assessed the quality of included studies from three aspects and their scores were no less than seven points (total score=seven points) (Table 1 and Supplementary Table 1).

3.2 Risk of bias assessment for included studies

3.2.1 Bias from character of population

Cohorts of four included studies [29-31, 33] were representative of general community population, whereas other two studies [32, 34] restricted their cohorts to specific population, such as adult employers. One study [33] 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. All five studies [29-34] adjusted the results for age and two studies [30, 33] adjusted the result for gender. One study [32] further adjusted the result for baseline insomnia symptoms, marital status, occupational class, sleep duration and common mental disorders, one study [30] further adjusted for parental education, family income, and

parent-reported poor health condition at baseline and one study [29] further adjusted for medical disorder, BMI, physical inactivity, alcohol. One study [31] adjusted for sampling weight.

3.2.3 Bias from definition of endpoint

Although included studies [29-34] all provided clear definition of insomnia, the definition varied from studies which might contribute to the bias of synthesized results.

3.3 Smoking and Insomnia Incidence

Figure 2 showed the ORs of five studies about smoking and incidence of insomnia. The pooled OR for smoking was 1.07 (95% CI:1.02, 1.13), which indicated a significant association between smoking and incidence of insomnia. The heterogeneity was not significant (I^2=14.9%, p=0.310). Funnel plot and Egger's regression revealed that there was no significant evidence for publication bias (Egger's regression: p>0.1, Supplementary figure 1). Sensitivity analysis indicated heterogeneity was mainly from one study [31] (Figure 1 and Supplementary figure 2). After reviewing the whole article, we noticed that in this study, participants which had a poor quality of sleep while didn't meet the criterion of insomnia at the baseline were also included in the analysis while in other included studies, this part of participants was excluded. Besides, PSG (polysomnography) was used to diagnose insomnia in this study, which might find out potential insomnia that was neglected in other included studies. All these factors might cause the heterogeneity.

Subgroup-analysis by smoking status showed significant association between regular smoking and incidence of insomnia (OR=1.07, 95% CI:1.01, 1.13). As for occasional and ex-smokers, the pooled analysis didn't indicate a significant association (occasional smoker: OR=2.09, 95% CI:0.44, 9.95; ex-smoker: OR=1.02, 95% CI:0.67, 1.54) (Figure 2).

Subgroup-analysis by age suggested significant association both in adults (>18) (OR=1.06, 95%CI: 1.02,1.13) and juveniles (≤18) (OR=3.97, 95%CI: 1.04,15.18) (Table 2 and Figure 1). The subgroup-analysis by gender ratio suggested significant association in population with gender ratio (women/men) <1 (OR=1.06, 95%CI: 1.01,1.13), but not in population with gender ratio (women/men) ≥1 (OR=1.08, 95%CI: 0.93,1.25) (Table 2 and Figure 2). However, the pooled result in population with gender ratio (women/men) ≥1 showed a high heterogeneity (I2=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 smoking and incidence of insomnia was not significant in Europe (OR=1.09, 95% CI: 0.96, 1.25) (Table 2).

Wetler et al (1994) [34] 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 Table 2)

4. Discussion

In this systematic review and meta-analysis, we quantitatively summarized available results from five cohort studies including about 12.5 thousand people to reveal the substantial association between smoking and incidence of insomnia. The results showed that smoking was significantly associated with incidence of insomnia. The heterogeneity was not considerable and was mainly from one study [31].

4.1 Association between smoking and incidence of insomnia

Consistent with our result, several cross-sectional studies and epidemiological investigations suggested that smoking might be an independent risk factor for insomnia [19, 20, 35]. However, the difference in incidence of insomnia between smokers and non-smokers was very small (OR=1.07) which might limit the public health implications of the result. Firstly, since about 30% people might suffer from insomnia [1] and billions of dollars were spent on it [2-4], a small improvement of sleep health though anti-smoking could also create considerable public health benefits. Secondly, it was reported that insomnia was a risk factor of smoking among students [36] and there might be a vicious circle between smoking and insomnia [37], which further highlighted the importance of understanding the relationship between smoking and incidence of insomnia.

For more specific and quantitative results, we further conducted the stratified analysis by smoking status. The results showed significant association between regular smokers and incidence of insomnia. Several previous studies reported similar association[23, 35]. The association between occasional smokers and incidence of insomnia was not significant. The main cause of smoking's negative effect on sleep is associated with chemicals in it, so after quitting or decreasing, the impact might reduce. However, one study demonstrated that sleep architecture disturbances among current smokers were not influenced by the amount of smoking quantified by pack-years [38], which indicated there might be other mechanisms of smoking' impact on sleep. Besides, it was reported that occasional smoking was significantly associated with excessive daytime sleepiness while regular smoking was not [39]. Firstly, there were only three cohorts in the regular-smoking subgroup and the heterogeneity was minimal. Therefore, we confirmed the result was authentic. There was only one included study in the occasional subgroup which might reduce the credibility of the outcome due to the differences in demographic factors among studies. Secondly, since the effects of smoking were associated with nicotine-acetylcholine receptors in our brain [38], 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 could alleviate the effects of nicotine on sleep health. There is still no satisfied explanation based on existing studies. More work on the association between the amount of smoking quantified by pack-years and insomnia 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 significant 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[40]. Another study showed that longer sleep duration was associated with successful smoking cessation[41]. All these suggested that quitting smoking might be beneficial to sleep health and current smokers might improve sleep quality by quitting smoking.

4.2 Subgroup analysis

The region-specific analysis found significant association between smoking and incidence of insomnia in North America and Asia. Epidemiological investigations and cross-sectional studies in these places reported similar conclusion[6, 18]. However, the Asian subgroup included only one study and focused on insomnia in adolescents around 13 years old. We needed to be cautious about the result as the age difference of the participants might result in the inhomogeneity. The association was not significant in Europe. Consistent with our result, several prior studies[25, 42] showed that there was no significant association between smoking and insomnia in Europe. Differences in living habits, social atmosphere and gene might contribute to the different results between areas. We noticed that Mediterranean diet, which was popular in Europe, was possibly beneficial factor for sleep health[43]. The pace of life in Europe was much slower than in other areas and lifestyle has been reported to related to insomnia[5]. Besides, genetic diversity might also have an influence on how human organism reacted to chemicals in cigars[44]. Therefore, it is possible for people to prevent insomnia by changing living habits including diet or slowing down the pace of live.

Subgroup analysis based on age suggested significant association both in adults (>18) and juveniles (≤18). Similar results were reported by other studies[7, 45, 46]. Considering only one included study focused on juveniles, the result might be influenced by region and smoking status which was associated with the effect of smoking on insomnia as discussed above. More work remained to be done to reveal the association between smoking and insomnia in juveniles. A cohort study of the foetus reported the adverse influence of in utero exposure to smoking on sleep patterns in preterm neonates[47], which suggested that smoking might influence sleep health at a very early age. Therefore, people of all ages should try to avoid smoking for improving the sleep health.

Because included studies 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 insomnia 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, smoking has a negative influence on sleep in population which

males are more than females. The point was reported for the first time. Prior study suggested that females were more likely to suffer from insomnia[24]. 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)[48] suggested that both for males and females, current smoking was associated with several 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 smoking and incident insomnia, the other didn't. As there were only two studies in the subgroup, different region, mental disorder and social status might all contribute to the high heterogeneity, which reduced the credibility of the result. Passive smoking has also been associated with sleep disturbance among pregnant women[49]. To better understand the interaction between gender, smoking and insomnia, more work with female populations and comprehensive analysis of all-cause insomnia incidence remained to be done.

5. Biological Mechanisms

Our study identified smoking, especially regular smoking as a risk factor for insomnia. The specific biological mechanism of smoking to particulate matters is still evolving. So far, nicotine, the primary addictive component of cigarettes or tobacco, was the most concerned. Nicotine has a known potential for enhancing attention and maintaining a certain level of arousal [50]. 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 that nicotine has on cholinergic neurotransmission in the basal forebrain responsible for cortical arousal[50]. In relation to insomnia, nicotine can regulate and change the normal neurotransmitter and disturb sleep architecture both in the early[38] and later stages of the sleep[48]. 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[51, 52].

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 [5]. 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 insomnia.

6. Strengths And Limitations

There are several strengths in our study. Firstly, the five 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 insomnia. 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 insomnia, 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 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, 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. Besides, insomnia might be a predictive factor for smoking behaviors and we didn't conduct a further discussion due to the limited number of relevant studies. Alcohol, tea, social status, depression and other factors might also have an interaction with smoking and insomnia, which were not discussed in the study. Lastly, there might be grey literature that was not included in this study, leading to potential publication bias.

7. Recommendations For Future Studies

7.1 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.

7.2 Smoking status

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

7.3 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.

7.4 Definition of endpoints

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

8. Conclusions

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

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 analyzed during this study are included in published articles

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.

Acknowledgments

Authors would like to thank all the authors of the original articles.

Funding

This work was supported by the Fundamental Research Funds for the Central Universities, Huazhong University of Science and Technology (2020WKZDJC015).

Competing interests

None declared

References

1. Roth, T., *Insomnia: definition, prevalence, etiology, and consequences.* J Clin Sleep Med, 2007. **3**(5 Suppl): p. S7-10.
2. Buysse, D.J., *Sleep health: can we define it? Does it matter?* Sleep, 2014. **37**(1): p. 9-17.
3. Barnes, C.M. and C.L. Drake, *Prioritizing Sleep Health: Public Health Policy Recommendations.* Perspect Psychol Sci, 2015. **10**(6): p. 733-7.
4. Pollack, M., et al., *Insomnia-related comorbidities and economic costs among a commercially insured population in the United States.* Curr Med Res Opin, 2009. **25**(8): p. 1901-11.
5. Bixler, E., *Sleep and society: an epidemiological perspective.* Sleep Med, 2009. **10 Suppl 1**: p. S3-6.
6. Doi, Y., *[Epidemiologic research on insomnia in the general Japanese populations].* Nihon Rinsho, 2009. **67**(8): p. 1463-7.
7. Kim, W.J., et al., *Factors Associated with Insomnia among the Elderly in a Korean Rural Community.* Psychiatry Investig, 2017. **14**(4): p. 400-406.
8. Bernert, R.A., et al., *Sleep disturbances as an evidence-based suicide risk factor.* Curr Psychiatry Rep, 2015. **17**(3): p. 554.
9. Watson, N.F., et al., *Recommended Amount of Sleep for a Healthy Adult: A Joint Consensus Statement of the American Academy of Sleep Medicine and Sleep Research Society.* Sleep, 2015. **38**(6): p. 843-4.
10. Gangwisch, J.E., et al., *Short sleep duration as a risk factor for hypertension: analyses of the first National Health and Nutrition Examination Survey.* Hypertension, 2006. **47**(5): p. 833-9.
11. Hall, M.H., et al., *Self-reported sleep duration is associated with the metabolic syndrome in midlife adults.* Sleep, 2008. **31**(5): p. 635-43.
12. Gangwisch, J.E., et al., *Sleep duration as a risk factor for diabetes incidence in a large U.S. sample.* Sleep, 2007. **30**(12): p. 1667-73.
13. Terry-McElrath, Y.M., et al., *Sleep and Substance Use among US Adolescents, 1991-2014.* Am J Health Behav, 2016. **40**(1): p. 77-91.
14. Sabanayagam, C. and A. Shankar, *The association between active smoking, smokeless tobacco, second-hand smoke exposure and insufficient sleep.* Sleep Med, 2011. **12**(1): p. 7-11.
15. McNamara, J.P., et al., *Sleep disturbances associated with cigarette smoking.* Psychol Health Med, 2014. **19**(4): p. 410-9.
16. Boehm, M.A., et al., *Depression, anxiety, and tobacco use: Overlapping impediments to sleep in a national sample of college students.* J Am Coll Health, 2016. **64**(7): p. 565-74.
17. Jaehne, A., et al., *How smoking affects sleep: a polysomnographical analysis.* Sleep Med, 2012. **13**(10): p. 1286-92.
18. Huang, Y.S., C.H. Wang, and C. Guilleminault, *An epidemiologic study of sleep problems among adolescents in North Taiwan.* Sleep Med, 2010. **11**(10): p. 1035-42.
19. Brett, E.I., et al., *Electronic cigarette use and sleep health in young adults.* J Sleep Res, 2020. **29**(3): p. e12902.

20. Chen, L.J., et al., *Physical activity, smoking, and the incidence of clinically diagnosed insomnia.* Sleep Med, 2017. **30**: p. 189-194.
21. Underner, M., J. Paquereau, and J.C. Meurice, *[Cigarette smoking and sleep disturbance].* Rev Mal Respir, 2006. **23**(3 Suppl): p. 6s67-6s77.
22. Balaguer, C., A. Palou, and A. Alonso-Fernandez, *[Smoking and sleep disorders].* Arch Bronconeumol, 2009. **45**(9): p. 449-58.
23. Deleanu, O.C., et al., *Influence of smoking on sleep and obstructive sleep apnea syndrome.* Pneumologia, 2016. **65**(1): p. 28-35.
24. Theorell-Haglow, J., et al., *Gender differences in obstructive sleep apnoea, insomnia and restless legs syndrome in adults - What do we know? A clinical update.* Sleep Med Rev, 2018. **38**: p. 28-38.
25. Beck, F., J.B. Richard, and D. Leger, *[Insomnia and total sleep time in France: prevalence and associated socio-demographic factors in a general population survey].* Rev Neurol (Paris), 2013. **169**(12): p. 956-64.
26. Wang, Y.M., et al., *Prevalence of insomnia and its risk factors in older individuals: a community-based study in four cities of Hebei Province, China.* Sleep Med, 2016. **19**: p. 116-22.
27. Stroup, D.F., et al., *Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group.* Jama, 2000. **283**(15): p. 2008-12.
28. Olufsen, I.S., M.E. Sørensen, and B. Bjorvatn, *New diagnostic criteria for insomnia and the association between insomnia, anxiety and depression.* Tidsskr Nor Laegeforen, 2020. **140**(1).
29. Janson, C., et al., *Insomnia in men-a 10-year prospective population based study.* Sleep, 2001. **24**(4): p. 425-30.
30. Zhang, J., et al., *Longitudinal course and outcome of chronic insomnia in Hong Kong Chinese children: a 5-year follow-up study of a community-based cohort.* Sleep, 2011. **34**(10): p. 1395-402.
31. Fernandez-Mendoza, J., et al., *Clinical and polysomnographic predictors of the natural history of poor sleep in the general population.* Sleep, 2012. **35**(5): p. 689-97.
32. Haario, P., et al., *Bidirectional associations between insomnia symptoms and unhealthy behaviours.* J Sleep Res, 2013. **22**(1): p. 89-95.
33. Brook, J.S., et al., *Insomnia in adults: the impact of earlier cigarette smoking from adolescence to adulthood.* J Addict Med, 2015. **9**(1): p. 40-5.
34. Wetter, D.W. and T.B. Young, *The relation between cigarette smoking and sleep disturbance.* Prev Med, 1994. **23**(3): p. 328-34.
35. Ali, T. and H. Belete, *Insomnia among Town Residents in Ethiopia: A Community-Based Cross-Sectional Survey.* 2019. **2019**: p. 6306942.
36. Tamaki, T., et al., *Prevalence of and factors associated with smoking among Japanese medical students.* J Epidemiol, 2010. **20**(4): p. 339-45.

37. Pasman, J.A., et al., *Causal relationships between substance use and insomnia.* Drug Alcohol Depend, 2020. **214**: p. 108151.
38. Zhang, L., et al., *Power spectral analysis of EEG activity during sleep in cigarette smokers.* Chest, 2008. **133**(2): p. 427-32.
39. Jaussent, I., et al., *Incidence, worsening and risk factors of daytime sleepiness in a population-based 5-year longitudinal study.* Sci Rep, 2017. **7**(1): p. 1372.
40. Prokhorov, A.V., et al., *"Withdrawal symptoms" in adolescents: a comparison of former smokers and never-smokers.* Nicotine Tob Res, 2005. **7**(6): p. 909-13.
41. Rapp, K., G. Buechele, and S.K. Weiland, *Sleep duration and smoking cessation in student nurses.* Addict Behav, 2007. **32**(7): p. 1505-10.
42. Theorell-Haglow, J., E. Lindberg, and C. Janson, *What are the important risk factors for daytime sleepiness and fatigue in women?* Sleep, 2006. **29**(6): p. 751-7.
43. Gianfredi, V., et al., *Sleep disorder, Mediterranean Diet and learning performance among nursing students: inSOMNIA, a cross-sectional study.* Ann Ig, 2018. **30**(6): p. 470-481.
44. Hammerschlag, A.R. and S. Stringer, *Genome-wide association analysis of insomnia complaints identifies risk genes and genetic overlap with psychiatric and metabolic traits.* 2017. **49**(11): p. 1584-1592.
45. Leger, D., et al., *Short sleep in young adults: Insomnia or sleep debt? Prevalence and clinical description of short sleep in a representative sample of 1004 young adults from France.* Sleep Med, 2011. **12**(5): p. 454-62.
46. Yilmaz, K., et al., *Understanding sleep habits and associated factors can help to improve sleep in high school adolescents.* Turk J Pediatr, 2011. **53**(4): p. 430-6.
47. Stephan-Blanchard, E., et al., *The influence of in utero exposure to smoking on sleep patterns in preterm neonates.* Sleep, 2008. **31**(12): p. 1683-9.
48. Wetter, D.W., et al., *Smoking as a risk factor for sleep-disordered breathing.* Arch Intern Med, 1994. **154**(19): p. 2219-24.
49. Ohida, T., et al., *Is passive smoking associated with sleep disturbance among pregnant women?* Sleep, 2007. **30**(9): p. 1155-61.
50. Boutrel, B. and G.F. Koob, *What keeps us awake: the neuropharmacology of stimulants and wakefulness-promoting medications.* Sleep, 2004. **27**(6): p. 1181-94.
51. Davila, D.G., et al., *Acute effects of transdermal nicotine on sleep architecture, snoring, and sleep-disordered breathing in nonsmokers.* Am J Respir Crit Care Med, 1994. **150**(2): p. 469-74.
52. Gillin, J.C., et al., *Dose-dependent effects of transdermal nicotine on early morning awakening and rapid eye movement sleep time in nonsmoking normal volunteers.* J Clin Psychopharmacol, 1994. **14**(4): p. 264-7.

Tables

Table 1

Characteristics of the included studies

y	Area	Study Period	Total Sample	Mean Age(Years)	Gender(woman/man)	Smoking Status	Endpoints	Diagnostic Standard	Study Design
k et al 5)	USA	1983-2013	528	From 14.1 to 42.7	Not given	Heavy/continuous smoker Later smoke starter Occasional smokers Smoke quitters/decreasers	Adult insomnia	Bergen Insomnia Scale	Cohort study
io et al 3)	Finland	2002-2007	6458	≥40	5248/1210	Smoker#	Insomnia	Jenkins Sleep Questionnaire	Cohort study
andez (2012)	USA	1990/1999-2000/2003	1246	45.4	517/729	Current smoker	Insomnia	Full medical evaluation	Cohort study
ıg et al 2)	China-Hong Kong	2006-2011	1611	From 9.0-13.7	822/789	Current smoker	Chronic insomnia	Sleep Questionnaire	Cohort study
on et al 1)	Sweden	1984-1994	2602	≥30	All men	Regular smoker Ex- smoker	Insomnia	Questionnaire that has been proved efficient	Cohort study
er et al 4)	USA	1994	3516	≥18	1840/1666	Smoker	Insomnia	DSM-III-R	Cohort study

Abbreviation: USA the United States DSM the Diagnostic and Statistical Manual of Mental Disorders

including current smoker and ex-smoker

Table 2

Subgroup-analysis of smoking and incidence of insomnia.

Subgroup	Stratum	Number of cohorts	Pooled OR (95%CI)	Text of heterogeneity	
				I^2(%)	Pvalue
Age	>18 years old	3	1.06(1.02,1.13)	0.0	0.758
	≤18 years old	1	3.97(1.04,15.18)		
Gender ratio(women/man)	<1	3	1.06(1.01,1.13)	0.0	0.556
	≥1	2	1.08(0.93,1.25	72.8	0.055
Region	Europe	2	1.09(0.96,1.24)	0.0	0.593
	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.

I^2 is the value of total variation clarified by heterogeneity.

Figures

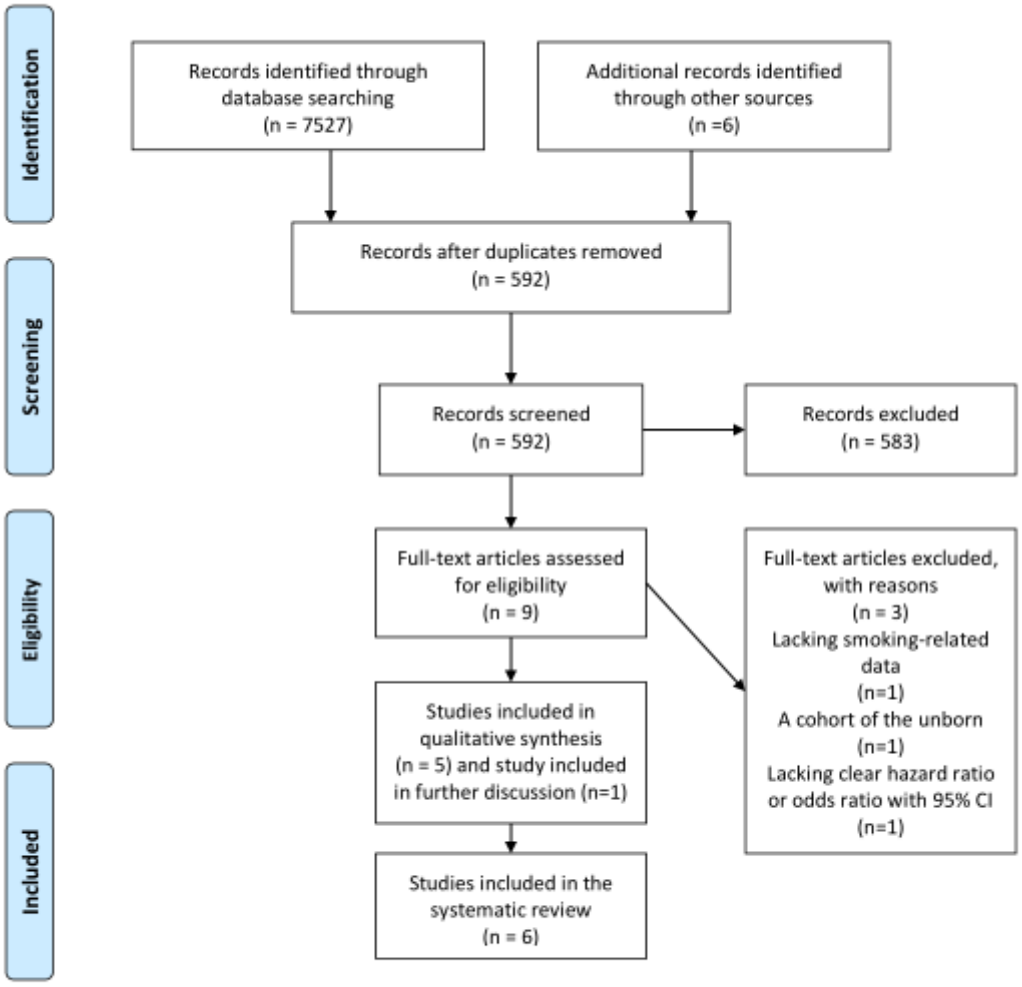
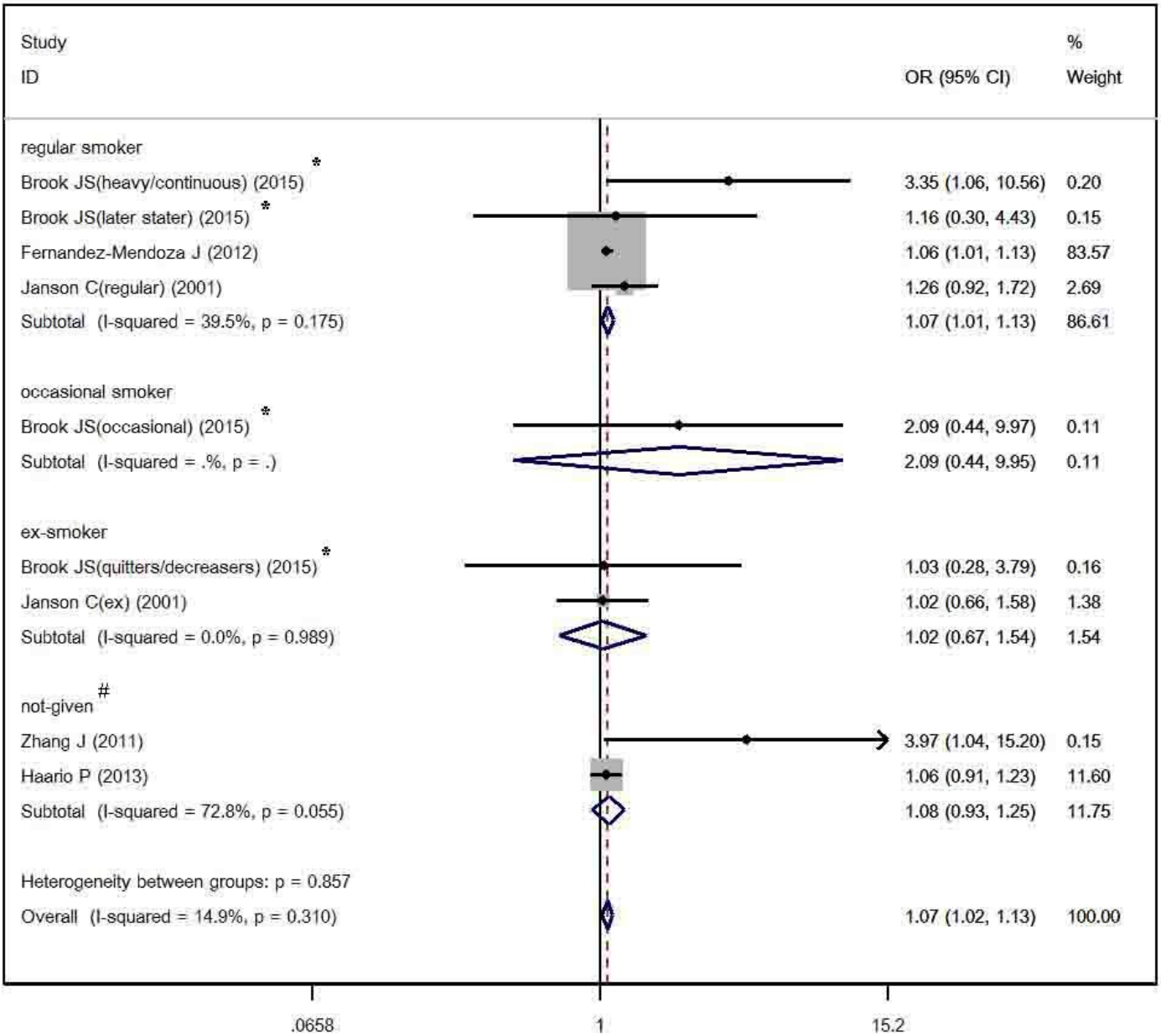


Figure 1. Results of systematic literature search

Figure 1

Results of systematic literature search



Note: # studies that didn't provide necessary information for subgroup analysis *All these cohorts came from subgroups in one study [33].

Figure 2

Smoking status and incident insomnia

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Supplementarfigure1.png
- Supplements.docx
- SupplementaryFiles.docx

- SupplementaryFigure2.png
- PRISMA2009ChecklistMSWord.doc