Association of sleep disorders with asthma: a meta-analysis

Xueqian Liu,1 Cheng Hong,2 Zhiyu Liu,3 Lihua Fan,2 Moqing Yin,2 Yunhu Chen,2 Xiang Ren,1,Xuefang Gu4

ABSTRACT
Background Animal experiments and clinical trials have revealed a potential relationship between sleep disorders and asthma. However, the associations between these factors remain unclear.

Material and methods We searched PubMed, Embase, Web of Science and Cochrane Library databases for eligible studies published before 30 December 2022. Studies investigating the association between sleep disorders (insomnia, poor sleep quality and insufficient sleep time) and asthma were selected. Sleep disorders were assessed using questionnaires, interviews, or medical records. Asthma was diagnosed based on medical history and drug use. The Newcastle-Ottawa Scale and the Agency for Healthcare Research and Quality checklist were employed for quality assessment. We used OR with 95% CI as the effect measures and forest plots to display the results. Heterogeneity was evaluated using I² statistics and subgroup analyses were performed for bias analysis. Publication bias was evaluated using the funnel plots and Egger’s test.

Results Twenty-three studies were included in the primary analysis, which suggested a positive association between sleep disorders and asthma (OR: 1.38, 95% CI 1.10 to 1.74). Subgroup analyses were conducted according to the study design, age, family history of asthma and type of sleep disorders. We did not find any association between sleep disorders and asthma in children aged <12 years (OR: 1.13, 95% CI 0.97 to 1.32). The association was insignificant in studies where the family history of asthma was adjusted for (OR: 1.16, 95% CI 0.94 to 1.42). Funnel plot and Egger’s test indicated a significant publication bias.

Conclusion Sleep disorders are associated with an increased prevalence and incidence of asthma. However, the quality of the evidence was low because of potential biases.

WHAT IS ALREADY KNOWN ON THIS TOPIC
⇒ Sleep disorders are highly prevalent in patients with asthma and often result in poor asthma control. Whether sleep disorders are associated with an increased risk of asthma remains indeterminate.

WHAT THIS STUDY ADDS
⇒ Sleep disorders are associated with an increased prevalence and incidence of asthma. However, the quality of evidence was low because of potential biases.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY
⇒ Although more studies are required to confirm the current findings, sleep disorders should be seriously considered in patients with asthma or in healthy subjects.

INTRODUCTION
Bronchial asthma is a heterogeneous disease clinically characterised by variable airway obstruction, with interrupted wheezing and chest tightness being its major symptom.1 Although the pathogenesis of asthma is still not fully understood, airway inflammation plays a key role.2 Medication, especially glucocorticoids, has shown significant benefits, and the mortality rate from asthma has decreased by 26.7% from 1990 to 2015.3 However, the prevalence has increased by 12.6%,3 bringing huge health hazards and economic burdens. Therefore, an increased focus on risk factors for asthma is urgent and essential.

Sleep disorders are highly prevalent in patients with asthma and often result in poor asthma control.4 These findings have led to speculation about the relationship between sleep and asthma risk.5 Two prospective cohort studies have found that chronic insomnia symptoms significantly increased the risk of asthma.6 7 However, other studies have indicated that asthma is not associated with poor sleep quality.8–12 Moreover, several large-scale cross-sectional studies8 10 13–20 have investigated the association between insufficient sleep and asthma, with widely divergent results. Some studies have suggested a positive association16 18 21 while others have indicated that the association is not significant.8 17 A Korean study also indicated that catch-up sleep decreases the incidence of asthma.15

The conclusions of the observational studies were inconsistent, and the results were easily confounded. We hypothesised that the association between sleep disorders and asthma may be subject to population specificity (eg,
age, sex and family history), the study design and type of sleep disorders. Therefore, we conducted a meta-analysis to test the hypothesis.

**MATERIALS AND METHODS**

The meta-analysis was conducted according to the recommendations of the Meta-analysis of Observational Studies in Epidemiology (MOOSE) Group,22 and was reported following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.23 The MOOSE checklist is provided in online supplemental material 1.

**Patient and public involvement**

No patients were involved.

**Literature search**

Databases including PubMed, Embase, Cochrane Library and Web of Science were searched without language restrictions for articles published before 30 December 2022. We used the following items as keywords: (“insomnia” OR “sleep duration” OR “sleep time” OR “sleep restriction” OR “sleep loss” OR “lack of sleep” OR “insufficient sleep” OR “sleep deprivation” OR “sleep disturbances” OR “sleep quality” OR “initiate sleep” OR “initiating sleep” OR “maintain sleep” OR “maintaining sleep”) AND “asthma”. A complete search strategy is provided in online supplemental material 2.

**Inclusion and exclusion criteria**

Observational studies (cohort, case-control, longitudinal, or cross-sectional) designed to evaluate the association between sleep disorders and the incidence (or prevalence) of asthma were included. Sleep disorders included insomnia, poor sleep quality and insufficient sleep duration. Insomnia was defined as disturbance of sleep onset or sleep maintenance, or poor sleep quality.24 Insufficient sleep was defined as sleep duration shorter than the recommended sleep time at different ages. In adults, sleep durations <7 hours were regarded as insufficient sleep.25 Sleep quality was assessed based on face-to-face interviews or questionnaires from subjects. No restrictions were imposed on the effect measures used in the included studies. Letters, comments, conference abstracts and studies with incomplete data were excluded.

**Data extraction and risk of bias assessment**

Literature search, data extraction and quality assessment of the included studies were performed independently by two researchers (XL and CH). When the researchers disagreed, a third researcher (ZL.) was consulted. The extracted information included author, region, study design, population characteristics of each study (eg, age and sex), diagnosis of asthma, ascertainment of sleep disorders and adjusted covariates.

The methodological quality of the cohort or case-control studies was assessed using the Newcastle-Ottawa Scale (NOS), designed for non-randomised controlled trials (RCTs). It considered three parts as follows: selection bias, information bias and confounding bias. Details of the NOS scale and grading standards are provided in online supplemental table 1. The checklist recommended by the Agency for Healthcare Research and Quality (AHRQ)26 was employed for the quality assessment of cross-sectional studies, and the standards were as follows: low quality, 0–3; moderate quality, 4–7; high quality, 8–11. It consists of 11 items and the details are provided in online supplemental table 2.

Observational studies are easily subject to confounders, and subgroup analyses are performed. The cross-sectional design only describes coexistence relationships rather than causal relationships. Patients with asthma often experience sleep disorders. Therefore, the study design was considered a source of bias. In the present meta-analysis, sleep disorders were associated with poor sleep quality and insufficient sleep duration. The type of sleep disorders can also lead to bias. In addition, we hypothesised that the following population characteristics might confound the relationship between sleep disorders and asthma: (1) age, (2) race, (3) body mass index (BMI) and (4) family history of asthma.

**Quality of evidence assessment**

Two researchers (XL and CH) independently evaluated the quality of evidence for all outcomes based on the Grading of Recommendation Assessment, Development, and Evaluation (GRADE) methodology.27 The following factors were considered: risk of bias, inconsistency in results, indirectness of evidence, imprecision and reporting bias. The quality of the evidence was classified as high, moderate, low or very low.

**Data synthesis and analysis**

All data analyses were performed using Stata V.15.0 (Stata Corp). Forest plots were used to display the individual and pooled results for the association between sleep disorders and asthma. OR with 95% CI were used as effect measures. In individual studies, 19 reported ORs, 2 reported relative risk (RR) and 2 reported HRs. In pooled analyses of epidemiological studies, distinctions among the effect measures can be ignored if the outcomes are uncommon.28 Among studies that reported RRs or HRs, the incidence of asthma was low (<10%). Thus, RR and HR were regarded directly as OR in our study. Forest plots were used to display the individual and pooled results. Heterogeneity was assessed using $I^2$ statistics. The random-effect model was selected because of the clinical heterogeneity in the definitions of asthma, sleep quality and sleep duration. A sensitivity analysis was conducted to assess the robustness of the results. Publication bias was evaluated using funnel plots and Egger’s test.
RESULTS
Study selection
A PRISMA statement flow chart of the study selection process is shown in figure 1. We obtained 1854 publications after eliminating duplicates. We identified 216 potentially eligible articles by reviewing titles and abstracts. Ultimately, 23 studies met the eligibility criteria and were included in the meta-analysis.

Characteristics of included studies
Table 1 summarises the authors, regions and population characteristics (eg, age and sex) of each study. Five cohort studies and 18 cross-sectional studies were included in the meta-analysis. Sleep disorders were assessed using questionnaires, face-to-face interviews or medical records. Asthma diagnosis was based on medical records, drug use, questionnaires or interviews regarding relevant medical history. In addition, multiple covariates...
<table>
<thead>
<tr>
<th>Author</th>
<th>Region</th>
<th>Study design</th>
<th>Age</th>
<th>Gender, male (%)</th>
<th>Diagnosis of asthma</th>
<th>Exposure</th>
<th>Measure of exposure</th>
<th>OR with 95% CI</th>
<th>Adjusted covariates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brumpton et al</td>
<td>Norway</td>
<td>Prospective cohort study</td>
<td>20–65 years</td>
<td>55.7</td>
<td>Questionnaire about physician diagnosis and prescription of asthma drugs</td>
<td>Insomnia</td>
<td>Questionnaire</td>
<td>2.67 (1.15 to 5.45)</td>
<td>Age, gender, BMI, education, economics, smoking, anxiety and depression</td>
</tr>
<tr>
<td>Han et al</td>
<td>Korea</td>
<td>Cross-sectional study</td>
<td>12–18 years</td>
<td>50.2</td>
<td>Questionnaire about physician diagnosis</td>
<td>Insufficient sleep</td>
<td>Questionnaire</td>
<td>&lt; 5 hours, 1.09 (1.04 to 1.14); 6 hours, 1.05 (1.00 to 1.10)</td>
<td>Age, gender, BMI, smoking, alcohol use, regular physical activity, economics, residence, school type, sexual experience, drug use, academic achievement, family structure, stress, health status, happiness, depression, suicidal idea, suicidal plan and suicidal attempt</td>
</tr>
<tr>
<td>Bakour et al</td>
<td>The United States</td>
<td>Cross-sectional study</td>
<td>High school students</td>
<td>50.3</td>
<td>Questionnaire about physician diagnosis</td>
<td>Insufficient sleep</td>
<td>Questionnaire</td>
<td>1.22 (1.07 to 1.40)</td>
<td>Age, gender, race, smoking, alcohol use, marijuana use, physical activity</td>
</tr>
<tr>
<td>Bakour et al</td>
<td>The United States</td>
<td>Longitudinal cohort study</td>
<td>12–18 years</td>
<td>50.1</td>
<td>Questionnaire about physician diagnosis</td>
<td>Insufficient sleep</td>
<td>Questionnaire</td>
<td>1.52 (1.11 to 2.10)</td>
<td>Age, gender, race, BMI, smoking, alcohol, physical activity, parental income, parental education, pubertal development, family history of asthma</td>
</tr>
<tr>
<td>Björnsdóttir et al</td>
<td>Multicenter</td>
<td>Cross-sectional study</td>
<td>39–67 years</td>
<td>52.3</td>
<td>Questionnaire about physician diagnosis</td>
<td>Insufficient sleep</td>
<td>Questionnaire</td>
<td>0.97 (0.62 to 1.52)</td>
<td>Gender, age, marital status, exercise, smoking, BMI</td>
</tr>
<tr>
<td>Dashti et al</td>
<td>The United States</td>
<td>Cross-sectional study</td>
<td>≥ 18 years</td>
<td>57.6</td>
<td>Medical record</td>
<td>Insufficient sleep</td>
<td>Questionnaire</td>
<td>1.23 (1.09 to 1.38)</td>
<td>Age, gender, race, BMI</td>
</tr>
<tr>
<td>Dai et al</td>
<td>The United States</td>
<td>Cross-sectional study</td>
<td>≥ 18 years</td>
<td>43.6</td>
<td>Medical record</td>
<td>Insufficient sleep</td>
<td>Questionnaire</td>
<td>&lt; 5 hours, 1.7 (1.1 to 2.4); 6 hours, 1.2 (0.8 to 1.7)</td>
<td>Gender, age, race, education, economics, employment status, depression</td>
</tr>
<tr>
<td>Choi et al</td>
<td>Korea</td>
<td>Cross-sectional study</td>
<td>19–39 years</td>
<td>41.8</td>
<td>Questionnaire about physician diagnosis</td>
<td>Insufficient sleep</td>
<td>Questionnaire</td>
<td>&lt; 5 hours, male, 1.265 (0.79 to 2.206); &lt; 5 hours, female, 1.553 (1.023 to 2.359); 6 hours, male, 1.299 (0.959 to 1.759); 6 hours, female, 1.06 (0.757 to 1.484)</td>
<td>Age, BMI, smoking, alcohol use, physical activity, economics, serum 25(OH)D level, stress level</td>
</tr>
<tr>
<td>Zhang et al</td>
<td>Hong Kong, China</td>
<td>Prospective cohort study</td>
<td>Adults, 40.7±5.4 (mean±SD)</td>
<td>46.5</td>
<td>Questionnaire about physician diagnosis</td>
<td>Insomnia syndrome</td>
<td>Questionnaire</td>
<td>17.9 (2.28 to 140)</td>
<td>Age, gender, education, economics, drug use</td>
</tr>
<tr>
<td>Nutakor et al</td>
<td>Multicenter</td>
<td>Cross-sectional study</td>
<td>≥ 50 years</td>
<td>53.5</td>
<td>Internet interview</td>
<td>Insufficient sleep</td>
<td>Internet interview</td>
<td>1.34 (0.75 to 2.40)</td>
<td>Gender, residence, age, marital status, education, economics</td>
</tr>
<tr>
<td>Stangenes et al</td>
<td>Norway</td>
<td>Cross-sectional study</td>
<td>&lt; 11 years</td>
<td>NA</td>
<td>Questionnaire about physician diagnosis and prescription of asthma drugs</td>
<td>Poor sleep quality and insufficient sleep</td>
<td>Questionnaire</td>
<td>Poor sleep quality, 1.1 (0.5 to 2.5); insufficient sleep, 2.6 (0.9 to 7.6)</td>
<td>Gender, single parenthood, maternal education</td>
</tr>
<tr>
<td>Author</td>
<td>Region</td>
<td>Study design</td>
<td>Age</td>
<td>Gender, male (%)</td>
<td>Diagnosis of asthma</td>
<td>Exposure</td>
<td>Measure of exposure</td>
<td>OR with 95% CI</td>
<td>Adjusted covariates</td>
</tr>
<tr>
<td>-----------------</td>
<td>-------------------------</td>
<td>----------------------</td>
<td>-----------</td>
<td>------------------</td>
<td>--------------------------------------</td>
<td>--------------------------------------------------------------------------</td>
<td>----------------------------------------------------------------------------------</td>
<td>----------------------------------------------------------------------------------</td>
<td></td>
</tr>
<tr>
<td>Seow et al⁸</td>
<td>Singapore</td>
<td>Cross-sectional study</td>
<td>≥ 18 years</td>
<td>49.6</td>
<td>Poor sleep quality and insufficient</td>
<td>Questionnaire</td>
<td>Questionnaire</td>
<td>Poor sleep quality, 1.011 (0.784 to 1.304); insufficient sleep, 1.174 (0.899 to 1.534)</td>
<td>Sociodemographic and lifestyle factors, physical and mental disorder</td>
</tr>
<tr>
<td>Blank et al²⁵</td>
<td>The United States</td>
<td>Cross-sectional study</td>
<td>13–18 years</td>
<td>48.6</td>
<td>Face-to-face interview</td>
<td>Insomnia</td>
<td>Face-to-face interview</td>
<td>1.53 (1.19 to 1.96)</td>
<td>Age, gender, race</td>
</tr>
<tr>
<td>Lim et al³⁰</td>
<td>Korea</td>
<td>Cross-sectional study</td>
<td>12–18 years</td>
<td>51.6</td>
<td>Questionnaire about physician diagnosis</td>
<td>Insufficient sleep</td>
<td>Questionnaire</td>
<td>&lt; 6 hours, 1.38 (1.15 to 1.65); 6 to 7 hour, 1.07 (0.9 to 1.27)</td>
<td>Age, genders, region, economics, smoking, physical activity, sitting time, obesity</td>
</tr>
<tr>
<td>Estanislau et al⁰</td>
<td>Brazil</td>
<td>Cross-sectional study</td>
<td>12–17 years</td>
<td>43.8</td>
<td>Questionnaire about physician diagnosis</td>
<td>Insufficient sleep</td>
<td>Questionnaire</td>
<td>1.17 (1.01 to 1.35)</td>
<td>Age, gender, type of school, mental disorders, excess weight</td>
</tr>
<tr>
<td>Gureje et al³⁵</td>
<td>Nigeria</td>
<td>Cross-sectional study</td>
<td>≥ 65 years</td>
<td>46.2</td>
<td>Face-to-face interview</td>
<td>Insomnia</td>
<td>Face-to-face interview</td>
<td>2.1 (1.4 to 3.1)</td>
<td>Age, gender</td>
</tr>
<tr>
<td>Basnet et al⁴</td>
<td>Finland</td>
<td>Cross-sectional study</td>
<td>25–74 years</td>
<td>47.3</td>
<td>Questionnaire about physician diagnosis</td>
<td>Poor sleep quality</td>
<td>Questionnaire</td>
<td>1.435 (0.96 to 2.14)</td>
<td>Age, gender, living status, education, region, smoking, alcohol intake, physical activity, BMI</td>
</tr>
<tr>
<td>Ma et al⁹</td>
<td>China</td>
<td>Cross-sectional study</td>
<td>3–6 years</td>
<td>51.7</td>
<td>Questionnaire about physician diagnosis</td>
<td>Insufficient sleep and difficulty maintaining sleep</td>
<td>Questionnaire</td>
<td>Insufficient sleep, 0.95 (0.49 to 1.84); difficulty maintaining sleep, 1.49 (1.05 to 2.13)</td>
<td>Age, gender, region, maternal education, BMI, delivery mode, birth weight, maternal tobacco exposure during pregnancy, feeding pattern before 6 months</td>
</tr>
<tr>
<td>Chen et al¹⁰</td>
<td>China</td>
<td>Cross-sectional study</td>
<td>12–18 years</td>
<td>64.4</td>
<td>Questionnaire about physician diagnosis</td>
<td>Poor sleep quality</td>
<td>Questionnaire</td>
<td>Difficulty falling asleep, 1.00 (0.77 to 1.31); difficulty maintaining sleep, 1.25 (0.94 to 1.67)</td>
<td>Demographic characteristics, family structure, gestation, delivery, feeding, socioeconomic status, health problems, daily activity and behaviour routine</td>
</tr>
<tr>
<td>Lin et al³²</td>
<td>Taiwan, China</td>
<td>Prospective cohort study</td>
<td>All ages</td>
<td>40.0</td>
<td>Medical record</td>
<td>Insomnia</td>
<td>Medical record</td>
<td>1.89 (1.64 to 2.17)</td>
<td>Age, gender, comorbidity, region, economics</td>
</tr>
<tr>
<td>Chen et al⁹⁹</td>
<td>Taiwan, China</td>
<td>Prospective cohort study</td>
<td>12–17 years</td>
<td>51.2</td>
<td>Questionnaire about physician diagnosis</td>
<td>Poor sleep quality</td>
<td>Questionnaire</td>
<td>1.10 (1.03 to 1.17)</td>
<td>Age, sex, parental education, economics</td>
</tr>
<tr>
<td>Chen et al¹²</td>
<td>China</td>
<td>Cross-sectional study</td>
<td>≤2 years</td>
<td>51.1</td>
<td>Medical record</td>
<td>Poor sleep quality</td>
<td>Face-to-face interview</td>
<td>Difficulty falling asleep, 1.05 (0.89 to 1.24); difficulty maintaining sleep, 1.06 (0.81 to 1.39)</td>
<td>Gender, maternal age, maternal education level, economics, family history of allergy, delivery mode, household secondhand smoke</td>
</tr>
<tr>
<td>Hu et al¹³</td>
<td>China</td>
<td>Cross-sectional study</td>
<td>All ages</td>
<td>46.5</td>
<td>Questionnaire about physician diagnosis</td>
<td>Insufficient sleep</td>
<td>Questionnaire</td>
<td>1.72 (1.32 to 2.24)</td>
<td>Gender, age, smoking, alcohol, region, BMI</td>
</tr>
</tbody>
</table>

BMI, body mass index; NA, not applicable.
were adjusted for in the individual studies, and the details are presented in table 1.

All cohort studies,6 7 21 29 32 were considered high quality according to the NOS assessment (online supplemental table 3). Eleven cross-sectional studies,6 8 10 12 16 17 19 20 34–36 were considered as high quality, and seven studies,8 11 14 15 30 31 33 were considered moderate quality, according to the AHRQ 11-item checklist (online supplemental table 4).

Meta-analysis
Twenty-three studies,6–17 19–21 29–36 contributed to the primary analysis, suggesting that sleep disorders were associated with an increased incidence (or prevalence) of asthma (OR: 1.38, 95% CI 1.10 to 1.74, figure 2). The sensitivity analysis indicated robust results (online supplemental figure 1). Next, subgroup analyses were conducted according to the study design, type of sleep disorders, race, age, BMI, and family history of asthma.

Sleep disorders were associated with asthma in the meta-analysis of cohort studies (OR: 1.73, 95% CI 1.16 to 2.57), and the results were consistent in the analysis of cross-sectional studies (OR: 1.20, 95% CI 1.14 to 1.28; online supplemental figure 2). Insufficient sleep duration (OR: 1.20, 95% CI 1.13 to 1.28) or poor sleep quality was associated with asthma (OR: 1.10, 95% CI 1.05 to 1.16; online supplemental figure 3). The association of sleep disorders with asthma was significant in European/American subjects (OR: 1.34, 95% CI 1.21 to 1.48) and Asian subjects (OR: 1.21, 95% CI 1.12 to 1.31; online supplemental figure 4). Sleep disorders were associated with increased incidence (or prevalence) of asthma in adults (>18 years, OR: 1.36, 95% CI 1.18 to 1.57) and...
adolescents (12–18 years, OR: 1.15, 95% CI 1.08 to 1.21), but not in children (<12 years, OR: 1.13, 95% CI 0.97 to 1.32; figure 3). The association between sleep disorders and asthma was significant in studies where family history of asthma was not adjusted (OR: 1.27, 95% CI 1.18 to 1.36), while the association was not significant in those where family history of asthma was adjusted (OR: 1.16, 95% CI 0.94 to 1.42; figure 4). Additional details of the subgroup analyses are presented in table 2. Funnel plots (figure 5) and Egger’s test (p=0.001) also indicated a significant publication bias.

**Quality of evidence**

In the overall analysis, the quality of evidence was regarded as very low. In the subgroup analyses, the grade levels of evidence ranged from low to very low. The classification of the GRADE evidence for all outcomes is presented in table 3.

**DISCUSSION**

To our knowledge, this is the first meta-analysis evaluating the relationship between sleep disorders and asthma. After a comprehensive review of the current literature, we found that sleep disorders were positively associated with asthma. However, this association was significant in studies where family history of asthma was not adjusted. In addition, this relationship was not significant in children.

Several subgroup analyses were performed to interpret the high heterogeneity observed in the primary analysis. Our meta-analysis included 23 studies, most of which were cross-sectional. Such a study design cannot describe...
a causal relationship; however, a pooled analysis of cohort studies indicated that sleep disorders significantly increased the incidence of asthma. Similarly, another 7-year prospective cohort study that recruited 7655 individuals discovered that healthy-long sleep duration, compared with short sleep time, decreased the incidence of asthma in adults.37 Moreover, two Mendelian randomisation studies demonstrated the causality between insomnia and asthma from a genetic perspective. These findings suggest that sleep disorders may be a risk factor for asthma.

We also speculate that an association between sleep disorders and asthma might exist in a partial population owing to the contradictory results of individual studies. Obesity is believed to play a role in the development of asthma. A cross-sectional survey by Bakour et al.,19 including 16728 participants in Florida, concluded that short sleep duration was related to asthma only in adolescents with obesity. However, our subgroup analyses indicated that sleep disorders were associated with asthma, regardless of whether BMI was adjusted. We also found that the association between sleep disorders and asthma was insignificant in children aged <12 years. In these studies, the measurements of sleep disorders were mainly based on questionnaires completed by parents rather than on self-reported results, which may have led to bias. It should also be noted that the incidence of asthma could have been underestimated because the diagnosis was mainly based on relevant symptoms such as wheezing.38 Therefore, this result should be interpreted with caution. In addition, the present meta-analysis suggests that the association between sleep disorders and asthma is modified by genetic factors since this association was not significant in studies that adjusted for a
family history of asthma. Nevertheless, only two studies were included in the secondary analysis, which may have been underpowered to reach a definitive conclusion.

Several mechanisms may contribute to the association between asthma and insufficient sleep. In both animal models and human trials, sleep restriction upregulated the levels of inflammatory markers, increased the expression of interleukin subfamily genes, and resulted in an evident shift in the T helper lymphocyte 1/2 cytokine balance. These immune responses are critical for the onset of asthma. Moreover, sleep disorders can result in endocrine and metabolic disorders, such as abnormal lip and glucose metabolism, hormone changes, and insulin resistance. These abnormalities may interact with chronic inflammation ultimately promoting asthma development.

In patients with asthma, nocturnal symptoms often lead to poor sleep. Even among healthy individuals,
the prevalence of insomnia is continuously increasing.48 Therefore, sleep disorders should be considered. Developing proper sleep patterns is important for preventing and controlling asthma. Moreover, our findings provide opportunities for new asthma treatment strategies (ie, sleep-related interventions). Several RCTs have found that hypnotic treatment can improve bronchial hyperresponsiveness.49–51 However, RCTs with small sample sizes may be underpowered to reach definitive conclusions. More well-designed multicentre trials are required to confirm these findings. Although sleeping pills may be a potential pharmacological treatment, the risk of adverse events should be fully evaluated in future studies.

This meta-analysis was based on aggregate rather than individual data. As a result, heterogeneity among the studies was significant for all outcomes. This is an obvious limitation of this study. Another limitation was the potential bias in our meta-analysis, which reduced confidence in our results. There are several possible reasons for this discrepancy. In most studies, asthma is diagnosed based on questionnaires rather than secure records (eg, medical records or drug prescriptions). Thus, the incidence and prevalence of asthma can be inaccurately evaluated. Similarly, the ascertainment of sleep disorders was mainly based on self-reported results, which are susceptible to recall bias. Thus, improved measurements (eg, home polysomnography) are necessary for future studies. However, despite adjusting for numerous covariates, residual confounders were inevitable. For example, obstructive sleep apnoea, a common sleep disorder, has been associated with the development of asthma in previous studies.52 53 However, they are also common in patients with insomnia.54 Thus, it may confound the association between asthma and sleep disorders investigated in this meta-analysis.

**CONCLUSIONS**
We found a positive association between sleep disorders and the increased prevalence and incidence of asthma. However, the quality of evidence is not high and the association between sleep disorders and asthma may be
subject to confounding factors (eg, age and family history of asthma). Further studies are required to confirm these findings.

**Author affiliations**

1Emergency Department, Taicang TCM Hospital Affiliated to Nanjing University of Chinese Medicine, Taicang, Jiangsu, China
2Cardiovascular Medicine Department, Taicang TCM Hospital Affiliated to Nanjing University of Chinese Medicine, Taicang, Jiangsu, China
3Department of Gastroenterology, The Second Affiliated Hospital of Nanjing University of Chinese Medicine, Nanjing, Jiangsu, China
4Outpatient Department, Taicang TCM Hospital Affiliated to Nanjing University of Chinese Medicine, Taicang, Jiangsu, China

**Contributors** XR and XG are responsible for the overall content as the guarantors. XL and CH managed literature search, data extraction and quality assessment. XL and MY contributed to manuscript writing. ZL and LF were in charge of data analysis. YC helped with the language polishing. All authors have read and approved the final manuscript.

**Funding** This study was supported by the 2022 Suzhou (Taicang) Science and Technology Development Plan (Application Number: SKYD20220059), and the 2021 Taicang City Basic Research Program Projects (Application Number: TC2021JOY05 and TC2021JOY23).

**Competing interests** None declared.

**Patient consent for publication** Not applicable.

**Ethics approval** Not applicable.

**Provenance and peer review** Not commissioned; externally peer reviewed. 

**Data availability statement** Data are available in a public, open access repository.

**Supplemental material** This content has been supplied by the author(s) and has not been vetted by BMJ Publishing Group Limited (BMJ) and may not have been peer-reviewed. Any opinions or recommendations discussed are solely those of the author(s) and are not endorsed by BMJ. BMJ disclaims all liability and responsibility arising from any reliance placed on the content. Where the content includes any translated material, BMJ does not warrant the accuracy and reliability of the translations (including but not limited to local regulations, clinical guidelines, terminology, drug names and drug dosages), and is not responsible for any error and/or omissions arising from translation and adaptation or otherwise.

**Open access** This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: http://creativecommons.org/licenses/by-nc/4.0/.

**ORCID iD**

Xiang Ren http://orcid.org/0009-0000-4458-865X

**REFERENCES**


