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Prospective study of insomnia and incident asthma in adults: the HUNT study

Ben Brumpton[1,2], Xiao-Mei Mai[1], Arnulf Langhammer[1], Lars Erik Laugsand[1], Imre Janszky[1,3] and Linn Beate Strand[1]

Affiliations: [1]Dept of Public Health and General Practice, Faculty of Medicine, Norwegian University of Science and Technology, NTNU, Trondheim, Norway. [2]Dept of Thoracic and Occupational Medicine, Trondheim University Hospital, Trondheim, Norway. [3]Regional Center for Health Care Improvement, St Olav Hospital, Trondheim, Norway.

Correspondence: Ben Brumpton, Dept of Public Health and General Practice, Norwegian University of Science and Technology, NTNU, Postbox 8905, MTFS, NO-7491 Trondheim, Norway.
E-mail: ben.brumpton@ntnu.no

ABSTRACT Insomnia is highly prevalent among asthmatics; however, few studies have investigated insomnia symptoms and asthma development. We aimed to investigate the association between insomnia and the risk of incident asthma in a population-based cohort.

Among 17 927 participants free from asthma at baseline we calculated odds ratios and 95% confidence intervals for the risk of incident asthma among those with insomnia compared to those without. Participants reported sleep initiation problems, sleep maintenance problems and nonrestorative sleep. Chronic insomnia was defined as those reporting one or more insomnia symptom at baseline and 10 years earlier. Incident asthma was defined by questions on asthma at baseline and follow-up (average 11 years).

The prevalence of sleep initiation problems, sleep maintenance problems and nonrestorative sleep were 1%, 1% and 5%, respectively. The multi-adjusted odds ratios were 1.18 (95% CI 0.97–1.44), 1.30 (95% CI 1.03–1.64) and 1.70 (95% CI 1.37–2.11) for people with one, two and three insomnia symptoms, respectively, compared with people without symptoms ($p<0.01$ for trend). The risk of developing asthma in those with chronic insomnia was three times higher (adjusted OR 3.16, 95% CI 1.37–6.40) than those without.

Insomnia symptoms were associated with increased risk of incident asthma in this study.

Introduction

Asthma affects ~300 million people worldwide, and the numbers are increasing rapidly [1]. Proposed risk factors include smoking, obesity and air pollution [2–5], but more recently symptoms of depression and anxiety have been found to be associated with a risk of developing asthma in adulthood [6, 7]. Insomnia, defined as having difficulties initiating sleep, maintaining sleep or having poor sleep quality [8], is also highly prevalent among asthma patients and studies indicate that the prevalence among asthma patients ranges from 44% to 70% [9, 10], compared to 6.6–37.2% in the general population in Westernised countries [11] and 11.9–15.5% in the Norwegian population [12]. However, there is a lack of prospective studies of insomnia and risk of asthma [13, 14].

There is considerable overlap between insomnia symptoms and psychological distress, especially depressive symptoms [15], and insomnia symptoms are very common in several chronic somatic disorders. However, previous reports did not include measures of depression and anxiety, nor did they evaluate the possible role of chronic somatic disorders. Moreover, insomnia is known to have an episodic nature, yet in the previous studies, insomnia was assessed only once.

Therefore, the aim of this study was to investigate the prospective association of repeated self-reported insomnia symptoms with the risk of asthma, taking into account the effects of proposed risk factors for asthma, psychological distress including symptoms of anxiety and depression, and other chronic somatic disorders.

Methods

Study population

The Nord-Trøndelag Health Study (HUNT) is an ongoing health survey of the entire adult population (aged ⩾20 years) of the county of Nord-Trøndelag, Norway. It consists of three surveys: HUNT1 from 1984 to 1986 (n=77 212), HUNT2 from 1995 to 1997 (n=65 237) and HUNT3 from 2006 to 2008 (n=50 807). The HUNT study has been described in more detail elsewhere [16].

We defined our study cohort as those that participated in HUNT2 and HUNT3 and were aged <65 years in HUNT3 (n=25 676). The age limit was set as there is an increased possibility of misclassification of asthma as chronic obstructive pulmonary disease (COPD) in the elderly.

We excluded participants with self-reported asthma in HUNT2 and missing information on asthma status in HUNT2 or HUNT3, or missing information on insomnia and covariates in HUNT2 (n=17 927).

Asthma ascertainment

In both HUNT2 (1996–1997) and HUNT3 (2006–2008), subjects were asked "Do you have or have you had asthma?". Cumulative incident asthma was defined from the survey questionnaires as those who did not report asthma at HUNT2, but reported asthma at HUNT3 (an average of 11 years later). Additionally, we used a stricter definition of asthma, *i.e.* self-reported asthma and use of asthma medication during the past 5 years at follow-up, without report of attacks of wheezing at baseline *versus* the reference group with no asthma and no wheeze at baseline. In Norway asthma medication must be prescribed by a doctor.

Insomnia

Insomnia disorder is characterised by a subjective feeling of having difficulties initiating or maintaining sleep or having a feeling of nonrestorative sleep [8]. The HUNT1 questionnaire included one question in regard to insomnia symptoms: "During the last month, have you had any problems falling asleep or sleep disorders?" with the response options "never", "sometimes", "often" and "almost every night". The HUNT2 questionnaire included three questions directly related to insomnia symptoms. The participants answered how often during the past month they had experienced difficulties initiating sleep at night and how often during the past month they had experienced difficulties maintaining sleep and had woken up too early and not been able to go back to sleep. These two questions had the response options "never", "occasionally", "often" and "almost every night". The participants also answered how often they suffered from poor sleep. This question had the response options "never or a few times a year", "1–2 times per month", "about once a week" and "more than once a week".

We further defined chronic insomnia as those reporting at least one symptom in HUNT2 and responding "almost every night" to the question "During the last month, have you had any problems falling asleep or sleep disorders?" in HUNT1 (1984–1986). Only participants who had valid data at both HUNT1 and HUNT2 were defined as having chronic insomnia.

Covariates

Information on potential confounders was collected from administrative questionnaires and clinical examinations at HUNT2. Sociodemographics included age, sex, body mass index (BMI), years of education

(<10, 10–12 or ⩾13 years) and whether subjects were having economic difficulties. Participants with economic difficulties were those who reported difficulties meeting the cost of food, transport and/or housing. Lifestyle factors included smoking (never, former or current). The participants were also asked whether they worked shifts and whether they had used sleeping medications daily or almost daily during any period in the past 12 months. The participants were extensively assessed and reported their medical history regarding chronic somatic disorders.

Anxiety and depression symptoms were measured at HUNT2 using the Hospital Anxiety and Depression Scale (HADS) [17]. The HADS consists of 14 questions, of which seven measure anxiety symptoms and seven measure depression symptoms, experienced during the preceding week. Each question is answered on a scale of 0–3, giving a total score for anxiety of 21 and a total score for depression of 21.

Statistical analysis

We used logistic regression to examine the association of insomnia symptoms with subsequent risk of incident asthma and presented adjusted odds ratios with 95% confidence intervals. For tests of linear trend, we treated the insomnia response categories as continuous variables.

We dichotomised each insomnia symptom and those in the highest response categories, *i.e.* having difficulties initiating sleep almost every night, difficulties maintaining sleep almost every night and having nonrestorative sleep more than once a week, were considered to have the respective insomnia symptom. We then combined the dichotomised insomnia symptoms and calculated the risk associated with an increasing number of insomnia symptoms.

In all analyses, we adjusted for age and sex in model 1. In model 2 we included age, sex, education, economic difficulties, smoking and BMI as potentially confounding factors. As it is not clear whether psychological distress is a cause or a consequence of sleep disorders, we adjusted for symptoms of depression and anxiety in model 3.

We conducted several stratified analyses to assess whether the association of insomnia symptoms with asthma could be modified by other factors. Thus, we investigated potential effect modification by sex, BMI (dichotomised at 30 kg·m^{-2}), education (dichotomised at 12 years) and age (dichotomised at age 45 years in HUNT3). In these analyses we used the insomnia trend variable as defined above and included covariates from model 2.

In one sensitivity analysis we included the stricter definition of asthma. In another sensitivity analysis, we excluded for other known chronic disorders, such as stroke, myocardial infarction, angina pectoris, diabetes mellitus, goitre, hypo- and hyperthyroidism, fibromyalgia, arthritis, ankylosing spondylitis, cancer, epilepsy and osteoporosis. In addition, we adjusted for the use of sleep medication and shift work in separate models. In addition, we conducted sensitivity analysis excluding participants who reported COPD at follow-up. The statistical analyses were conducted using R 3.2.3. This study was approved by the regional committee for medical research ethics and all participants gave informed written consent.

Results

The prevalence of having any problems falling asleep or sleep disorders almost every night in HUNT1 was 1%. The prevalence of having difficulties initiating sleep almost every night, having difficulties maintaining sleep almost every night and having nonrestorative sleep more than once a week in HUNT2 were 1%, 1% and 5%, respectively.

The characteristics of the participants by number of insomnia symptoms are described in table 1. Those with three insomnia symptoms were more likely to be older, have more symptoms of anxiety and depression, to be male, have a low level of education, have economic difficulties and more likely to smoke than those without any insomnia symptoms.

Among the 17 927 participants included in our analysis, 686 were diagnosed with asthma during the 11-year follow-up.

Table 2 presents the odds ratios and 95% confidence intervals for incident asthma in relation to each insomnia symptom from our three different models. Participants reporting to have had difficulties falling asleep "often" or "almost every night" during the past month had a 65% (OR 1.65, 95% CI 1.18–2.25) and 108% (OR 2.08, 95% CI 1.27–3.24) increased risk of developing new onset asthma over the next 11 years, respectively (model 2). Similarly, those reporting having awakened too early without being able to go back to sleep "often" and "almost every night" in the past month had a 92% (OR 1.92, 95% CI 1.40–2.59) and 36% (OR 1.36, 95% CI 0.67–2.48) increased risk of developing asthma, respectively. For nonrestorative sleep, a similar pattern was shown, with those reporting nonrestorative sleep "more than once a week" having a 94% increased risk of developing asthma (OR 1.94, 95% CI 1.46–2.53).

TABLE 1 Descriptive statistics of the Nord-Trøndelag Health Study (HUNT) at baseline (1995)

	Symptoms n			
	0	**1**	**2**	**3**
Age years	38.4±8.6	40.3±8.8	40.1±8.8	42.7±8.1
BMI kg·m^{-2}	25.5±3.6	25.8±3.8	25.6±3.7	25.9±4.0
HADS-A	3.1±2.6	4.1±2.9	5.0±3.2	6.4±3.8
HADS-D	2.2±2.2	2.9±2.6	3.5±2.8	4.6±3.4
Sex				
Male	4171 (55.2)	2778 (54.1)	1450 (56.4)	1588 (59.7)
Female	3392 (44.8)	2354 (45.9)	1122 (43.6)	1072 (40.3)
Education				
Low	1148 (15.2)	933 (18.2)	482 (18.7)	740 (27.8)
Mid-range	4167 (55.1)	2735 (53.3)	1433 (55.7)	1311 (49.3)
High	2248 (29.7)	1464 (28.5)	657 (25.5)	609 (22.9)
Economic difficulties				
No	5495 (72.7)	3496 (68.1)	1595 (62.0)	1603 (60.3)
Yes	2068 (27.3)	1636 (31.9)	977 (38.0)	1057 (39.7)
Smoking status				
Never	3902 (51.6)	2437 (47.5)	988 (38.4)	1062 (39.9)
Former	1771 (23.4)	1383 (26.9)	639 (24.8)	732 (27.5)
Current	1890 (25.0)	1312 (25.6)	945 (36.7)	866 (32.6)
Total	7563 (42.2)	5132 (28.6)	2572 (14.3)	2660 (14.8)

Data are presented as mean±SD or n (%). BMI: body mass index; HADS-A: Hospital Anxiety and Depression Scale-Anxiety; HADS-D: Hospital Anxiety and Depression Scale-Depression. n=17 927

The cumulative number of insomnia symptoms was related to incident asthma in a linear fashion ($p<0.01$ for linear trend) in all models, although the odds ratios were somewhat weakened when adjusting for potential confounders (table 3). The odds ratios (95% CI) for 1, 2 and 3 symptoms in the age- and sex-adjusted model (model 1) were 1.23 (1.01–1.50), 1.44 (1.14–1.81) and 1.90 (1.53–2.35), respectively. The corresponding odds ratios (95% CI) in model 2 were 1.18 (0.97–1.44), 1.30 (1.03–1.64) and 1.70 (1.37–2.11), respectively ($p<0.01$ for trend).

The risk of developing asthma was three times higher (OR 3.16, 95% CI 1.37–6.40) in those with chronic insomnia compared to those without chronic insomnia (table 4, model 2). When adjusting for symptoms of depression and anxiety at baseline, this association was somewhat attenuated.

We found no statistical evidence for effect modification of the association between insomnia symptoms and incident asthma by sex, age, BMI or education, based on stratified analyses and formal testing of statistical interactions (p-values 0.7, 0.3, 0.4 and 0.4, respectively, for interaction term).

Restricting our analysis to those reporting asthma and use of asthma medication at follow-up, without report of asthma or wheeze at baseline generally increased the strength of our estimates (online supplementary table S1). Additionally, after excluding those with other known chronic disorders, or adjusting our results for use of sleep medication, shift work or restricting our analysis to those that did not report COPD at follow-up, did not change our estimates considerably (online supplementary tables S2–S5).

Discussion

In the 11-year follow-up, we found that those having problems initiating sleep often or almost every night, waking up too early without being able to go back to sleep often and experiencing nonrestorative sleep more than once a week had an increased risk of developing asthma, compared with those never or almost never having these symptoms. The cumulative number of insomnia symptoms was associated with an increased risk of incident asthma in a dose-dependent manner.

Our study in the context of previous studies

To the best of our knowledge, this is the first study to investigate the prospective association of repeated assessments of self-reported insomnia symptoms with risk of subsequent development of asthma while adjusting for important risk factors for asthma and psychological distress and taking into account the effects of comorbid chronic disorders. One study has previously investigated this association in the HUNT study [13], reporting an 18% increased risk of developing asthma (OR 1.18, 95% CI 1.08–1.30) among

TABLE 2 The association between insomnia symptoms and incident asthma in the Nord-Trøndelag Health Study (HUNT) (1995–2008)

	Subjects	Asthma cases	Model 1[#]	p-value	Model 2[¶]	p-value	Model 3[+]	p-value
Sleep initiation problems								
Never	10 669	365	Ref.		Ref.		Ref.	
Occasionally	5644	253	1.31 (1.11–1.54)	<0.01	1.22 (1.03–1.44)	0.02	1.14 (0.96–1.36)	0.12
Often	692	47	1.97 (1.42–2.67)	<0.01	1.65 (1.18–2.25)	<0.01	1.4 (0.99–1.93)	0.05
Almost every night	236	21	2.59 (1.59–4.01)	<0.01	2.08 (1.27–3.24)	<0.01	1.71 (1.03–2.69)	0.03
Continuous	17 927	686	1.37 (1.23–1.51)	<0.01	1.26 (1.13–1.40)	<0.01	1.18 (1.05–1.32)	0.01
Sleep maintenance problems								
Never	10 384	367	Ref.		Ref.		Ref.	
Occasionally	5913	257	1.26 (1.07–1.48)	0.01	1.23 (1.04–1.45)	0.02	1.16 (0.98–1.37)	0.09
Often	741	52	2.05 (1.50–2.76)	<0.01	1.92 (1.40–2.59)	<0.01	1.65 (1.19–2.26)	<0.01
Almost every night	203	10	1.48 (0.73–2.69)	0.23	1.36 (0.67–2.48)	0.35	1.13 (0.55–2.08)	0.71
Continuous	17 927	686	1.29 (1.15–1.44)	<0.01	1.25 (1.12–1.40)	<0.01	1.17 (1.04–1.32)	0.01
Nonrestorative sleep								
Never or a few times a year	12 772	438	Ref.		Ref.		Ref.	
1–2 times per month	2670	127	1.40 (1.14–1.70)	<0.01	1.33 (1.08–1.62)	0.01	1.24 (1.01–1.53)	0.04
About once a week	937	54	1.68 (1.25–2.23)	<0.01	1.52 (1.12–2.02)	0.01	1.38 (1.01–1.85)	0.03
More than once a week	862	67	2.27 (1.72–2.94)	<0.01	1.94 (1.46–2.53)	<0.01	1.67 (1.24–2.22)	<0.01
Continuous	17 927	686	1.32 (1.21–1.42)	<0.01	1.25 (1.15–1.35)	<0.01	1.19 (1.09–1.29)	<0.01

Data are presented as n or OR (95% CI), unless otherwise stated. Ref: reference. [#]: adjusted for age and sex; [¶]: adjusted for age, sex, body mass index, education, economic difficulty and smoking status; [+]: adjusted for age, sex, body mass index, education, economic difficulty, smoking status, anxiety and depression.

TABLE 3 The association between the number of insomnia symptoms and incident asthma in the Nord-Trøndelag Health Study (HUNT) (1995–2008)

	Subjects	Asthma cases	Model 1[#]	p-value	Model 2[¶]	p-value	Model 3[+]	p-value
Insomnia symptoms n								
0	7329	234	Ref.		Ref.		Ref.	
1	4941	191	1.23 (1.01–1.50)	0.04	1.18 (0.97–1.44)	0.09	1.14 (0.93–1.39)	0.20
2	2460	112	1.44 (1.14–1.81)	<0.01	1.30 (1.03–1.64)	0.03	1.21 (0.95–1.53)	0.11
3	2511	149	1.90 (1.53–2.35)	<0.01	1.70 (1.37–2.11)	<0.01	1.49 (1.17–1.87)	<0.01
Continuous	17 927	686	1.23 (1.15–1.32)	<0.01	1.18 (1.10–1.27)	<0.01	1.13 (1.05–1.22)	<0.01

Data are presented as n or OR (95% CI), unless otherwise stated. Ref: reference. [#]: adjusted for age and sex; [¶]: adjusted for age, sex, body mass index, education, economic difficulty and smoking status; [+]: adjusted for age, sex, body mass index, education, economic difficulty, smoking status, anxiety and depression.

those reporting experiencing one or more of the insomnia symptoms, *i.e.* problems falling asleep at night and waking up too early without being able to fall back asleep "often" or "almost every night". However, this study was exploratory and simultaneously looked for several associations without testing any predefined hypothesis, did not adjust for potential confounders specific to the insomnia–asthma association, included only one definition of insomnia and did not use repeated measures. Another study undertaken in Hong Kong on ~2300 middle-aged adults reported that those suffering from one insomnia symptom (*i.e.* difficulties initiating sleep, difficulties maintaining sleep or early-morning awakenings) in addition to daytime sleepiness at baseline, had 18 times the risk of developing asthma at follow-up 5.2 years later on average (OR 17.9, 95% CI 2.28–140) [14]. Neither of these studies accounted for increasing severity of the insomnia, nor did they adjust for risk factors including smoking or shift work, and did not exclude other known chronic disorders (online supplementary tables S2 and S5).

Additionally, due to the episodic nature of insomnia disorder, one measurement might not capture it. Any reported symptoms may stop and never return, in which case no adverse health effects would be expected. In our study, we had the opportunity to investigate chronic insomnia symptoms over a 10-year period and we found that those reporting chronic insomnia had more than double the risk of developing asthma compared to those without chronic insomnia. We also found that when adjusting for symptoms of anxiety

TABLE 4 The association between chronic insomnia and incident asthma in the Nord-Trøndelag Health Study (HUNT) (1984–2008)

	Subjects	Asthma cases	Model 1[#]	p-value	Model 2[¶]	p-value	Model 3[+]	p-value
Chronic insomnia								
No	10256	361	Ref.		Ref.		Ref.	
Yes	65	8	3.77 (1.65–7.53)	<0.01	3.16 (1.37–6.40)	<0.01	2.67 (1.15–5.45)	0.01

Data are presented as n or OR (95% CI), unless otherwise stated. Ref: reference. [#]: adjusted for age and sex; [¶]: adjusted for age, sex, body mass index, education, economic difficulty and smoking status; [+]: adjusted for age, sex, body mass index, education, economic difficulty, smoking status, anxiety and depression.

and depression at baseline, the risk of developing asthma attenuated slightly. No previous studies have looked at chronic insomnia and risk of asthma before and our findings should be confirmed by further studies.

Possible mechanisms

Asthma is considered an inflammatory disorder [18]. Pro-inflammatory cytokines generated in the process of the immune response result in cellular infiltration and inflammation of the airways [18]. Several studies have suggested that insomnia symptoms are linked to chronic inflammation [19, 20], and that they are associated with changes in the production of pro-inflammatory cytokines [20, 21]. In the morning after a night of sleep loss, mononuclear cell nuclear factor (NF)-κB activation has been found to be considerably greater compared with morning levels following uninterrupted baseline or recovery sleep [21]. Consequently, this change in mononuclear cell NF-κB activation may interfere with regulation of inflammatory proteins, which could play a role in asthma and other inflammatory disorders [22, 23]. Therefore, a state of inflammation due to the insomnia symptoms might be the underlying pathophysiology for the association we observed. Moreover, insomnia symptoms may lead to metabolic changes including reduced glucose tolerance and changes in hormones controlling hunger [24–26], and insulin resistance, weight change and obesity have been associated with asthma development [5, 27–29], which might be a pathway for the association we observed.

Insomnia is also a disorder of hyperarousal accompanied by chronic activation of stress responses with increased activity in the hypothalamic–pituitary–adrenal axis and the sympathetic nervous system [30]. For example, sleep disturbances are correlated with decreased morning awakening salivary cortisol [31]. Such stress responses may lead to irregular levels of circulating cortisol, and a glucocorticoid-insensitive state [32–35], which may increase the risk of inflammatory disorders [36]. Thus, abnormalities in the neuroendocrine system may represent a biologically plausible causal link between insomnia and asthma. However, the exact mechanisms linking insomnia symptoms to the development of asthma remain unknown.

Additionally, when insomnia symptoms become chronic over a 10-year period, these changes in the body may accumulate and result in more severe harmful effects on the airways. Finally, due to the close relationship between insomnia symptoms and depression [37], it is possible that the association we see between the insomnia symptoms and asthma reflects the already established association between depression and asthma. However, we have adjusted for symptoms of depression in model 3, and although the associations were slightly attenuated, they still remained strong and depression is unlikely to explain the observed association between the insomnia symptoms and asthma.

Strengths and limitations

Despite the obvious strengths, including the large sample size, the high number of potential confounders included in the models and that we were able to look at both increasing number of insomnia symptoms and chronic insomnia over a 10-year period, this study also has some important limitations.

Lack of a gold standard for asthma diagnosis is a potential barrier to epidemiological research and a limitation of our study. We did not have a registered diagnosis from a general practitioner or any assessment of asthma severity, and the use of self-reported asthma may have resulted in misclassification. However, we did include a stricter definition of asthma in the sensitivity analyses, where incident cases reported the use of asthma medication during the past 5 years at follow-up and did not report attacks of wheezing at baseline, *versus* the references group with no asthma and no wheeze at baseline (online supplementary table S1). Additionally, among those with incident asthma in HUNT3 with follow-up information (n=425), 84% confirmed, in a clinical interview, that the diagnosis was given by a medical doctor. There was a low participation rate at the clinical interview due to long queues, therefore we did not include this information in the study. Additionally, previous studies suggest that the sensitivity and specificity of self-reported asthma are acceptable. For example, in a validation study of the asthma

questions used in the Tasmanian Long Term Health Survey, which were not unlike ours, the sensitivity and specificity were 0.80 and 0.97, respectively [38]. Furthermore, in a review of validation studies, the sensitivity of single questions on wheeze and shortness of breath were both 1.00; however, specificity was low, at 0.75 and 0.83, respectively [39]. To reduce misclassification of COPD as asthma we excluded participants who reported ever having chronic bronchitis, emphysema or COPD in HUNT3 (online supplementary table S5). Additionally, our cohort was restricted to those aged <65 years in HUNT3 and we repeated the main analyses in those aged <45 years in HUNT3 (data not shown). Sensitivity analyses supported our original findings and in most sensitivity analyses we found stronger results.

As in previous population studies, the insomnia symptoms were self-reported and we had no objective measurement of the severity of the symptoms, *i.e.* from polysomnography or a diagnosis from a general practitioner. However, polysomnography is not routinely used for the evaluation of insomnia symptoms [40], and since insomnia disorder is by definition a subjective disease, it cannot readily be measured using objective methods. A patient may have insomnia symptoms despite the failure of objective methods to detect it.

Another important limitation of this study is that it includes nonrestorative sleep as a symptom of insomnia disorder. As opposed to the Diagnostic and Statistical Manual of Mental Disorders (DSM)-4, DSM-5 does not include nonrestorative sleep as a symptom, although it does include "dissatisfaction with sleep quality" in the criteria [41]. Additionally, the International Classification of Sleep Disorders (ICSD)-3 also removed nonrestorative sleep, due to isolated complaints of nonrestorative sleep occurring in conjunction with sleep disordered breathing, other sleep disorders or certain chronic medical conditions such as fibromyalgia or chronic fatigue syndrome [42]. The ICSD-3 also notes that nonrestorative sleep is poorly defined, and may reflect not only sleep disturbance, but also the daytime consequences of poor sleep [42]. While these are limitations to our study, we were able to exclude people with certain chronic medical conditions at baseline, which may have reduced the potential bias due to comorbidities.

In addition, people have different thresholds for consulting a general practitioner, which in turn influences the probability of getting the diagnosis of both insomnia disorder and asthma. We cannot rule out the possibility that such information bias influences our results.

In our study we did not have information on sleep apnoea, a strong correlate of asthma at HUNT2 [43, 44]. Sleep apnoea has been found to overlap with insomnia symptoms [45], making it a potential confounder of the association between insomnia symptoms and asthma. A review found that among >20 000 European subjects, non-insomnia sleep disorders, including sleep apnoea, accounted for ~5% of the reported insomnia symptoms [46]. A more recent review of nine small-scale studies with 1085 participants in total found that the prevalence of obstructive sleep apnoea (OSA) in insomnia patients varied from 15.7% to 75%, depending on the definition of OSA used in the study in question [47]. However, in order to confound the association between the insomnia symptoms and asthma, sleep apnoea must be generally unrelated to the other covariates included in our models. In our study, we adjusted for BMI, a strong correlate of sleep apnoea.

Because some participants with insomnia symptoms at baseline could have had undiagnosed asthma [48], it was important to address the possibility of reverse causation. However, when restricting our analysis to those without wheeze or breathlessness in HUNT2 (both symptoms are common in people with asthma) in a sensitivity analysis (online supplementary table S1), the estimates did not change considerably. This supports the overall conclusion of our study.

Our study was performed in an apparently healthy, socioeconomically homogenous population and our results cannot be directly generalised to less healthy populations or to countries on different latitudes, with a different socioeconomic status or with different sleeping habits.

Conclusions

As one of the first prospective studies on insomnia symptoms and asthma, we found that having problems initiating sleep, waking up too early without being able to go back to sleep and nonrestorative sleep was strongly associated with an increased risk of developing asthma. In addition, there was a dose–response relationship between the number of insomnia symptoms and risk of developing asthma, and those with chronic insomnia had more than triple the risk of developing asthma compared to those without chronic insomnia symptoms. Insomnia is a prevalent and manageable condition, and increased focus on adverse health effects of insomnia could be helpful in the prevention of asthma. Further prospective studies are needed to confirm our findings.

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