Anxiety mediates the effect of smoking on insomnia in people with asthma: evidence from the HUNT3 study

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Objectives: The aim of this study was to investigate factors related to insomnia in a cohort of people with asthma.

Design: This secondary analysis utilized cross-sectional data from the Norwegian Nord-Trøndelag Health Study, a population-based health survey (n=50,807).

Participants: We used self-reported data from 1,342 men and women with a physician-confirmed asthma diagnosis ranging in age from 19.5 to 91 years.

Measurements: Data on sleep, lifestyle variables (smoking and exercise), anxiety, and depression were included. An insomnia scale and asthma impact scale were constructed using factor analysis. Hierarchical series of multiple regression models were used to investigate direct and mediational relationships between the study variables and insomnia.

Results: The hierarchical models revealed significant independent contributions of female sex, higher age, not exercising, asthma impact, anxiety, and depression on insomnia (R²=25.2%). Further, these models suggested that the impact of smoking on insomnia was mediated by anxiety, and that the beneficial impact of exercise was mitigated by depression symptoms.

Conclusion: Smokers with asthma have more insomnia, and this relationship may be mediated by anxiety. Further, people with asthma who experience depression symptoms are less likely to benefit from physical exercise as a method to enhance sleep quality. Our findings would suggest that helping smokers to manage their anxiety and depression through behavioral methods may reduce their insomnia symptoms, and enable them to engage in other health-enhancing pursuits, such as physical exercise.

Keywords: insomnia, asthma, anxiety, depression, smoking, mediation

Introduction
Sleep problems are widespread both in general population and in clinical practice. Insomnia is the most common sleep disorder, and is characterized by subjective complaints about dissatisfaction with sleep quality or duration, as well as difficulty with initiating sleep, maintaining sleep at bedtime, waking up in the middle of the night or too early in the morning, or nonrestorative, poor quality of sleep.1 Population studies show that up to 48% of adults report “some insomnia problems over the past year”, and 6%–15% report chronic insomnia.2

Sleep patterns change throughout life. Sleep problems are common in adolescents,3 possibly because of the puberty-related circadian shift toward being a “night owl”.4 Menopausal transition status is also related to severe self-reported sleep difficulty,5 6
In order to improve interventions, it is important to understand social and mental health determinants of insomnia. Determinants of insomnia in asthma are not well understood. Therefore, the aim of this study was to investigate factors related to insomnia in a cohort of people with asthma.

Materials and methods

Data source

We analyzed data from the third wave of the Nord-Trøndelag Health Study (HUNT study), which is a large population database for medical and health-related research. The present study uses data from the most recent survey, HUNT3, which was carried out between October 2006 and June 2008. Nord-Trøndelag is located in central Norway. The area is fairly representative of Norway in terms of geography, economy, industry, and sources of income, as well as in terms of the age distribution, morbidity, and mortality rates of its inhabitants. The present study was approved by the Regional Committee for Ethics in Medical Research (2015/660) and by the HUNT Publication Review Board.

Study sample

All inhabitants in the county were invited to participate. From among 93,860 who were eligible for participation, 50,807 (54.1%) responded to the first questionnaire (Q1) that was enclosed with the invitation letter. The data were collected in each of the 24 municipalities in the county by using temporarily located health examination sites staffed by certified fieldwork teams. A second questionnaire (Q2) focusing more on symptoms and diseases was handed out to everyone to be completed at home, and returned by mail in a prepaid envelope. Respondents with lung diseases also participated in a substudy (n=12,128). Our data came from this substudy. Eligibility criteria for inclusion in our study sample were: 1) having a physician-confirmed diagnosis of asthma and 2) endorsing having had asthma symptoms in the year prior to the interview. Those who reported having a diagnosis of chronic obstructive pulmonary disease, chronic bronchitis, or emphysema were excluded from the study sample.

Measures

Insomnia

Participants were asked four questions on insomnia symptoms, which included how often during the last 3 months they had 1) experienced difficulties with falling asleep at night; 2) woke up repeatedly during the night; 3) woke up too early without being able to get back to sleep; and 4) felt sleepy...
during the day. Response options were: 1 (never/seldom), 2 (occasionally), or 3 (several times a week). A factor analysis yielded one component with an eigenvalue greater than 1.0 (Table 1). We computed a total sum score representing insomnia from these four items. This score ranged from 4 to 12, with higher scores reflecting more severe insomnia. The summary score had acceptable internal consistency reliability (Cronbach’s $\alpha=0.68$). Thus, the HUNT3 questions assessing insomnia symptoms generated a unidimensional score with high internal consistency, and were a sound psychometric composite for analysis.

### Asthma impact

Questions on the impact of asthma included how much they had experienced asthma symptoms in the last 7 days, and use of asthma medication. Specific questions were: 1) How many of the last 7 days have you noticed symptoms from your respiratory disease? 2) How many of the last 7 days have breathlessness restricted your normal activities (school, sport, work, housekeeping, etc)? and 3) How many of the last seven nights did you wake up/were affected by breathlessness (including cough)? A factor analysis generated one component (eigenvalue =1.78; Cronbach’s $\alpha=0.61$; Table 1). We thus created a subscale by adding the three asthma items into an asthma impact score, ranging from 0 to 21. Higher scores reflect more asthma symptoms. Thus, the HUNT3 questions assessing asthma impact generated a unidimensional score with high internal consistency, and were a sound psychometric composite for analysis.

### Anxiety and depression

The Hospital Anxiety and Depression Scale$^{35}$ was used to assess self-reported symptoms of anxiety and depression. The questionnaire consisted of 14 questions: seven for anxiety and seven for depression. Response options were on a 4-point scale ranging from 0 (not at all) to 3 (very often). Recall time was the last week. Responses were summed to provide separate scores for anxiety and depression symptoms, with possible scores ranging from 0 to 21 for each scale. Higher scores indicate greater likelihood of depression or anxiety.$^{35,36}$ The psychometric properties of the scale have been validated previously.$^{36,37}$ Cronbach’s $\alpha$ was 0.82 for the anxiety score and 0.76 for the depression score. A cutoff score of 8 on both subscales has been shown to give an optimal balance between sensitivity and specificity at $\sim 0.80$ for depression, according to the *Diagnostic and Statistical Manual of Mental Disorders* (III and IV) and the International Classification of Disorders (ICD-8 and 9).$^{38}$ The anxiety and depression

### Table 1 Items and factor structure for insomnia and asthma impact measures

| Scale      | Item                                                                 | % Respondents | Eigenvalue | Cronbach’s $\alpha$ | Factor loading |
|------------|-----------------------------------------------------------------------|---------------|------------|----------------------|----------------|
| Insomnia   | How often in the last 3 months have you had difficulties with…       |               |            |                      |                |
|            | Never/seldom                                                         | 41            |            |                      |                |
|            | Sometimes                                                             | 43            |            |                      |                |
|            | Several times a week                                                  | 16            |            |                      |                |
|            | falling asleep                                                        | 0.81          |            |                      |                |
|            | nocturnal awakening                                                    | 26            |            |                      |                |
|            | waking too early                                                       | 50            |            |                      |                |
|            | daytime                                                               | 46            |            |                      |                |
|            | sleepiness during daytime                                              | 40            |            |                      |                |
|            |                                                                      | 14            |            |                      |                |
|            |                                                                      |               | 0.75       |                      |                |
|            |                                                                      | 14            |            |                      |                |
|            |                                                                      | 0.73          |            |                      |                |
|            |                                                                      | 20            |            |                      |                |
|            |                                                                      | 60            |            |                      |                |
|            |                                                                      | 20            |            |                      |                |
|            |                                                                      | 0.45          |            |                      |                |
| Asthma impact| How many of the last 7 days (0–7):                                    | 2.05 (2.85)   |            | 0.62                 |                |
|            | Have you noticed symptoms from your respiratory disease?              |               | 0.59 (0.43)| 0.63                 |                |
|            | Have breathlessness restricted your normal activities?                 |               | 0.36 (1.79)| 0.52                 |                |
|            | Did you wake up/were affected by your breathlessness?                  |               | 1.78       | 0.61                 |                |
scores were dichotomized according to this cutoff score for the present analyses.36,37

Demographic and lifestyle variables
The following variables were included to characterize the sample. Age was categorized in 6 decades, from 19 to 79 years, and one additional group with those 80 years and older. Partnership was dichotomized into those living with a partner and those living alone. Data on education were obtained from the National Population Registry of Norway, and highest completed education was classified as: 0, primary and lower secondary school – up to 10 years; 1, high school – 11–13 years; 2, university and high school, short; and 3, university and high school, long. Physical activity was assessed by the single item “How often do you perform exercise?” with response options as: 0, never; 1, less than once a week; 2, once a week; 3, two to three times a week; and 4, almost every day. Smoking was characterized as either “never smoking”, “quit smoking”, “now and then”, or “daily”, with yes/no response options. For daily smokers, number of cigarettes per day was also recorded. Questions on medications included use of prophylactic- and symptom-reducing medication.

Statistical analysis
Hierarchical series of multiple regression analyses were performed with insomnia as dependent variable. Mediation was tested by a multistage regression approach outlined by Baron and Kenny,39 in which the three regression equations were estimated: first, regressing the mediator (M) on the independent variable (X); second, regressing the dependent variable (Y) on the independent variable (X); and third, regressing the dependent variable (Y) on both the independent variable (X) and on the mediator (M).39 The mediator has been called an intervening or process variable. Complete mediation is the case in which variable X no longer affects Y after M has been controlled and so path $c'$ is zero. Partial mediation is the case in which the path from X to Y is reduced in absolute size but is still different from zero when the mediator is introduced.40 The type I error rate was set to $P<0.05$, and all tests were two-tailed. The statistical analyses were carried out using SPSS 22.0 for Windows (IBM Corporation, Armonk, NY, USA).41

Results
From the 3,348 participants who reported that they had, or ever had asthma, only those with a current asthma diagnosis, and with no missing data on sleep questions were included. The final asthma sample included 1,342 persons. The age range was 19–91 years (mean 53.0, standard deviation 1.8). The majority was female (60.3%), and there was a high prevalence of current tobacco smokers (33% smoking daily, and now and then). Approximately 11% reported a high level of depression and 18% had a high level of anxiety (Table 2). The asthma sample did not differ from the HUNT3 in age, partnership, or smoking. However, the asthma sample had more women ($P=0.001$), a higher prevalence of insomnia ($P=0.001$), and fewer people with more than 20 years of education compared

| Table 2 Description of study population |
| Variables | N (%) |
| --- | --- |
| **Age years mean (SD)** | 1,342 (100) |
| Range | 53.0 (15.8) |
| **Sex** | 19.5–91.0 |
| Female | 830 (61.8) |
| Partnered | 798 (59.5) |
| Yes | 542 (40.4) |
| No | 2 (0.1) |
| No information | 2 (0.1) |
| **Age groups (years)** | |
| 19–29 | 105 (7.9) |
| 30–39 | 167 (12.4) |
| 40–49 | 238 (17.7) |
| 50–59 | 237 (17.0) |
| 60–69 | 25 (19.0) |
| 70–79 | 162 (12.1) |
| >80 | 42 (3.1) |
| **Education** | |
| Primary and lower secondary school, up to 10 years | 317 (23.6) |
| High school, up to 13 years | 706 (52.6) |
| University and high school, short | 273 (20.3) |
| University and high school, long | 34 (2.5) |
| **Smoking** | |
| Never | 543 (40.5) |
| Quit smoking | 438 (32.6) |
| Now and then | 131 (9.8) |
| Daily | 291 (21.6) |
| Cigarettes per day (among smokers only, n=260) mean (SD) | 11.8 (6.2) |
| **Depression** | |
| Low score (<8) | 1,195 (89.0) |
| High score (≥8) | 147 (11.0) |
| **Anxiety** | |
| Low score (<8) | 1,099 (81.9) |
| High score (≥8) | 243 (18.1) |
| **Use of asthma prophylactic medication** | |
| Last 6 months | 737 (43.6) |
| Last week | 739 (43.8) |
| Last 3 days | 705 (41.7) |
| Today | 566 (33.5) |
| **Use of asthma symptom-reducing medication** | |
| Number of days last week mean (SD) | 3.3 (3.0) |
| Last 3 days | 372 (27.7) |
| Today | 248 (18.5) |

Abbreviation: SD, standard deviation.
with the HUNT3 (P=0.035). Further, those with asthma had more anxiety (P=0.001) and depression (P=0.001), which is consistent with the research literature. Univariate regressions suggested that reporting insomnia was associated with being female, older, less educated, and/or a smoker. It was also associated with never exercising, having worse reported asthma symptom impact, and reporting anxiety or depression (Table 3). Of study participants, more than 40% used asthma prophylactic medication, and nearly 28% reported that they had used a medication to reduce asthma symptoms in the past 3 days. We evaluated the medication variables in the univariate models, but they showed no significant association with insomnia, and were not kept for later models.

Table 3 shows the results of the hierarchical multiple regression analyses modeling the prediction of insomnia. Because all of the bivariate correlations between variables used in the analysis were r<0.7, we assumed no multicollinearity of variables (Table 3). Inspection of residuals indicated no violation of regression assumptions.

In step 1, controlling for demographic and lifestyle variables, female sex, higher age, current smoking, and never doing physical activity, were all independently associated with insomnia (P<0.001 for all variables). In step 2, asthma impact was entered into the model and was found to have an independent effect on insomnia (β=0.14, P<0.001). In step 3, depression was entered into the model and was found to have an independent effect on insomnia (β=0.36, P<0.001). Further, exercise was no longer a significant predictor of insomnia, suggesting that the beneficial impact of exercise was mitigated by depression symptoms. In step 4, anxiety was entered into the model along with the step 1 and step 2 covariates, and was found to have an independent effect on insomnia (β=0.39, P<0.001). In step 5, depression and anxiety were entered together into the model and were found to have independent effects on insomnia (β=0.20 and 0.28, respectively; P<0.001 in both cases). In step 6, two interaction terms were entered into the model (anxiety x asthma impact, and depression x asthma impact); both were not statistically significant.

Sociodemographic and lifestyle variables (step 1) explained 6.8% of the variance in explaining insomnia, whereas asthma impact (step 2) added only 1.9%. Anxiety and depression accounted for 16.6% variance (step 5), adding most to the explained 25.0% variance in the total model.

This hierarchical approach to modeling insomnia revealed that when anxiety was entered into the model (step 3), the previously significant direct relationship between smoking and insomnia (β=0.06, P<0.01) was no longer significant (β=0.05 in both steps 4 and 5; P=0.06 in step 4 and 0.08 in step 5). This pattern suggests that anxiety mediated the relationship between smoking and insomnia. Figure 1 displays the mediation model.

**Discussion**

Our findings from this large population-based survey suggest that insomnia in people with asthma is associated with

| Variables | Univariate models | Hierarchical models |
|-----------|-------------------|---------------------|
|           | Step 1 | Step 2 | Step 3 | Step 4 | Step 5 | Step 6 |
| Sex (female =0) | -0.18 ***** | -0.19 ***** | -0.18 ***** | -0.20 ***** | -0.15 ***** | -0.17 ***** | -0.17 **** |
| Age | 0.11 *** | 0.13 *** | 0.11 *** | 0.06 ** | 0.16 **** | 0.12 **** | 0.12 **** |
| Education (low–high) | -0.09 *** | -0.04 | -0.02 | 0.00 | 0.00 | 0.01 | 0.01 |
| Partnership (living with a partner =0) | 0.04 ** | 0.05 * | 0.05 * | 0.02 | 0.02 | 0.02 | 0.02 |
| Smoking (not smoking =0) | 0.12 *** | 0.09 *** | 0.09 *** | 0.06 ** | 0.05 * | 0.05 * | 0.05 * |
| Exercise (never =0) | -0.09 **** | -0.09 **** | -0.08 **** | -0.03 | -0.07 **** | -0.05 * | -0.05 * |
| Step 2. Asthma impact | 0.12 **** | 0.14 **** | 0.09 **** | 0.06 ** | 0.05 * | 0.05 * | 0.05 * |
| Step 3. Depression alone (low–high) | 0.39 **** | 0.36 **** | 0.39 **** | 0.20 **** | 0.20 **** | 0.20 **** |
| Step 4. Anxiety alone (low–high) | 0.41 **** | | | | | |
| Step 5. Anxiety and depression together (low–high) | | | | | | 0.28 **** |
| Step 6. Interaction terms added (depression x asthma impact; interaction anxiety x asthma impact) | | | | | | -0.01; -0.01 |
| Explained variance (R²) | 6.80% | 8.60% | 20.30% | 22.70% | 25.20% | 25.00% |
| Change of variance (R² change) | 1.90% | 11.70% | 11.4% | 4.90% | 0 |
| P-value of R² change | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 | ns |

Notes: **P<0.10, ***P<0.05, ****P<0.01, *****P<0.001. Abbreviation: ns, not significant.
cope or self-medicate by smoking cigarettes to regulate their affect. This approach to managing their anxiety in the short-term may exacerbate their insomnia in the longer-term, and may lead to more negative affect due to the sleep deprivation (insomnia). This escalation in negative affect may in turn lead to more smoking. Future research might utilize longitudinal data from the HUNT study or another data source to investigate causal models of the relationship between smoking, anxiety, asthma symptoms, and insomnia in people with asthma.

**Increase in asthma symptoms significantly associated with insomnia**

In addition to the intriguing mediation effect discussed earlier, we also found robust independent effects of asthma impact on insomnia. Based on these findings, one might speculate that nocturnal asthma—exacerbations of asthma that occur during the night—may further disrupt sleep, causing difficulty initiating and maintaining sleep as well as poor overall sleep quality. Future research might examine the effectiveness of proactive or preventative use of asthma medication (eg, inhalers) just before going to bed at night to reduce insomnia.

**Prescribing physical activity**

Along with identifying health behaviors associated with worse insomnia, our model also identified a robust and independent impact of engaging in physical exercise in reducing insomnia. It is notable that this effect was mediated by depression, suggesting that the salutogenic effect of exercise is explained by (reduced) depression. Thus, engaging in exercise may reduce individuals’ depression symptoms and thus enable a good night’s sleep. When anxiety was entered into the model, this mediation effect was no longer present, suggesting that exercise did not buffer the impact of anxiety on insomnia. Since asthma guidelines aim to help people with asthma to remain active and sleep well, future research might investigate whether exercise-based interventions can be tailored to mitigate both depression and anxiety and thereby improve sleep in people with asthma.

**Strengths and limitations of the study**

This study has a number of notable strengths, including the sample size, the population-based sampling strategy, and the quality of the data collected. Our analyses built on these strengths to ask a research question with clear clinical significance and implications. The limitations of the present study must, however, be acknowledged. First, the main limitation is that the data were not collected for the purpose of the specific

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*Figure 1: Anxiety as a mediator of the relationship between smoking and insomnia. Notes: *P*<0.10, *n*P*<0.001, *n*nP*<0.0001.*
research question for our study. Consequently, the measures might not be the best operationalization of a construct of interest; the sample might not be the most fitting to ask the question (eg, including asthmatics who are using medications that could interfere with sleep). Second, although the HUNT3 has a reasonable compliance rate (54%) for such a large study, nonparticipant analyses suggest that the study sample tends to include relatively healthy people (ie, those with a lower mortality rate), and underrepresents lower socioeconomic status. Third, the flip side of the power advantages of large samples is that analyses of such sample can yield statistically significant findings that have questionable clinical significance. In our analysis, the difference in beta coefficients between model step 1 and 4 was 0.04, yet the significance changed from \( P<0.001 \) to \( P<0.06 \). Future research might replicate these analyses in an independent sample to evaluate their robustness. Finally, our mediation analysis is not able to make causal inferences about the relationships among the study variables. It is intended to suggest causal hypotheses that can be tested in future longitudinal investigations.

**Conclusion**

It is well known that an untreated sleep problem can have a negative effect on an individual’s physical and psychosocial functioning. We found that while the impact of asthma on insomnia is modest, smokers with asthma have more insomnia, and anxiety seems to mediate this relationship. Further, people with asthma who have symptoms of depression do not get the benefit of exercise on insomnia. Our findings would suggest that helping smokers to manage their anxiety and depression through behavioral methods may reduce their insomnia symptoms, and enable them to engage in other health-enhancing pursuits, such as physical exercise. Future research should investigate the impact on sleep and other health behaviors of behavioral interventions aimed at negative-affect reduction in people with asthma.

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**Author contributions**

Both authors contributed to the conception and design, analysis, and interpretation of data. Further, RA drafted the article with substantial contributions from CES, and both authors revised it critically for important intellectual content, and approved the final version. The authors agree that they are accountable for all aspects of the work, confirming that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

**Disclosure**

The authors report no other conflicts of interest in this work.

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