

Research Submission

Is Headache Related to Asthma, Hay Fever, and Chronic Bronchitis? The Head-HUNT Study

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Objectives.—To examine the relationship between migraine and nonmigrainous headache and asthma, hay fever, and chronic bronchitis in a large cross-sectional population-based study.

Background.—Associations between prevalence of migraine and asthma or allergy have been demonstrated in clinic-based and epidemiologic studies whereas studies on chronic bronchitis are scarce.

Methods.—A total of 51,383 subjects completed a headache questionnaire and constituted the “Head-HUNT” Study. Of these 50,401 (98.1%) answered the questions about asthma and chronic bronchitis, and 47,029 (91.5%) answered the question about hay fever. Associations were assessed in multivariate analyses, estimating prevalence odds ratios (ORs) with 95% confidence intervals (CI).

Results.—Both migraine and nonmigrainous headache were approximately 1.5 times more likely among those with current asthma, asthma related symptoms, hay fever, and chronic bronchitis than those without. The association increased with increasing headache frequency.

Conclusions.—This large questionnaire-based study confirms that migraine and other headaches are associated with respiratory and allergic disorders. The magnitude of the association between headache and asthma, hay fever, and chronic bronchitis tended to be in the same order. Headache frequency seems to have a greater impact on the association with respiratory or allergic conditions than headache diagnoses. Whether it is a causal relationship is uncertain, but the results underline the importance of considering comorbid disorders among patients with frequent headache.

Key words: migraine, headache, asthma, chronic bronchitis, hay fever

Abbreviations: COPD chronic obstructive pulmonary disease, HUNT Nord-Trøndelag Health Study (“Helse undersøkelsen i Nord-Trøndelag”), Q questionnaire, IHS International Headache Society, OR odds ratio, CI confidence interval

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Several epidemiologic¹⁻⁶ and clinic-based studies⁷⁻⁹ have demonstrated an association between migraine, asthma, and allergy.¹⁰ In 2 prospective longitudinal studies weak associations between asthma and migraine during childhood and adulthood were found.^{2,5} However, in one epidemiologic study an association between migraine and asthma was found only among women.⁶ Both epidemiologic³ and clinic-based studies⁸ have also investigated the relation between migraine and hay fever, rhinitis, and eczema where associations of approximately the same size as with asthma were found. A few studies have shown an association between headache in general and respiratory or allergic symptoms;^{3,4,6} however, 3 studies did not.¹¹⁻¹³ Furthermore, the impact of frequent headache on the association has been investigated in children⁴ but not in adults. Regarding possible associations between headache and chronic obstructive pulmonary disease (COPD) there are only 2 previous clinic-based studies indicating an association with headache.^{8,14}

The main purposes of the present study were to examine the relationship between headache (both migraine and nonmigrainous headache) and asthma, hay fever, and chronic bronchitis in a large population-based study, and to evaluate the impact of headache frequency on this relationship.

METHODS

Study Population.—In 1995-1997 all inhabitants aged ≥ 20 years in Nord-Trøndelag county were invited to participate in the adult part of the Nord-Trøndelag Health Study (“Helse undersøkelsen i Nord-Trøndelag” = HUNT). The target population, including both participants and nonparticipants, has been described previously.¹⁵ Briefly, 2 questionnaires, including more than 200 health-related questions, were administered to the participants. The first questionnaire (Q1) was enclosed with the invitation and delivered when attending the health examination. All participants received a second questionnaire (Q2) that was returned by mail. The Q1 included 6 questions about cough, previous or present asthma, and asthma related symptoms. The Q2 included 13 questions about headache¹⁶ and questions about hay fever and family history of allergy and asthma.¹⁷ A total of 51,383 sub-

jects completed the headache questionnaire in Q2, and constituted the “Head-HUNT Study.” Of these 50,401 (98.1%) answered the questions about asthma and chronic bronchitis, and 47,029 (91.5%) answered the question about hay fever.

Headache Diagnoses.—Subjects who answered “yes” to the question “Have you suffered from headache during the last 12 months?” were classified as those with headache. Based on data from the subsequent 12 headache questions, they were classified into 2 groups of either migraine or nonmigrainous headache. The diagnoses were mutually exclusive. Persons were classified as migraineurs if they reported having migraine or fulfilled the following 3 criteria: (i) headache attacks lasting 4-72 hours (<4 hours was accepted for those who reported visual disturbances *often* before headache); (ii) headache with at least 1 of the following 3 characteristics: (a) pulsating quality, (b) unilateral location, (c) aggravation by physical activity; (iii) during headache, at least 1 of the following symptoms: (a) nausea, and (b) photophobia and/or phonophobia. Headaches that did not fulfill the criteria for migraine were classified as nonmigrainous headache. Headache frequency was divided in 3 categories; less than 7 days/month, between 7 and 14 days/month, and more than 14 days/month.

The questions about headache were mainly designed to determine whether the person suffered from headache or not, to determine frequency of headache, and to diagnose migraine according to a modified version of the migraine criteria of the Headache Classification Committee of the International Headache Society (IHS) (1988). The classification of the subjects has been described in detail previously, and has been validated by interview diagnoses.¹⁸

Asthma, Chronic Bronchitis, and Allergy.—Subjects who reported having had asthma at one time or another and attacks of wheezing or breathlessness during the last 12 months were defined as having current asthma.¹⁷ Those who reported attacks of wheezing or breathlessness during the last 12 months, but not having had asthma were defined as having had asthma related symptoms. Those who reported having had asthma, but no symptoms of wheezing or breathlessness during the last 12 months, were defined

as having had asthma previously. Chronic bronchitis was defined as coughing with phlegm in periods of at least 3 months during each of the last 2 years.¹⁹ Those who reported having nose allergy or hay fever were classified as having hay fever. To quantify smoking “pack years” were calculated as number of years of smoking $\times$ number of cigarettes a day/20 cigarettes.

Statistical Analyses.—In the multivariate analyses, using logistic regression, we estimated prevalence odds ratio (OR) with 95% confidence interval (CI) for the association between headache and asthma, chronic bronchitis, and hay fever. Potential confounders as gender, age (10 years categories), educational level, smoking (pack years), smoking category (never smoker, ex-smoker, current smoker), anxiety and depression (assessed with The Hospital Anxiety and Depression Scale),²⁰ and body mass index were tested in the models. Only gender, age, educational level, and smoking stood out as important confounders and were included in the final analyses. When appropriate, headache frequency categories were incorporated in χ^2 test for trend, evaluating the probability of a linear relationship between headache frequency and asthma, hay fever, and chronic bronchitis, respectively. Data analysis was performed with the Statistical Package for the Social Sciences, version 13.0 (SPSS, Chicago, IL, USA).

Ethics.—The HUNT study was approved by the regional committee for ethics in medical research, and by the Norwegian Data inspectorate.

RESULTS

More women than men had current asthma, while the opposite was found regarding chronic bronchitis (Table 1). Subjects with chronic bronchitis had higher mean age and lower level of education than those without such symptoms.

The prevalence of headache was higher among individuals with asthma, hay fever, and chronic bronchitis than among those without such complaints in all age groups (Figures 1–3). In the multivariate analyses, asthma and hay fever were significantly associated with both migraine and nonmigrainous headache (Table 2). Asthma related symptoms were also significantly associated with both headache types, but previous asthma was at the same level as no asthma (Table 2). Also, reported allergy in the family (defined as at least 1 first degree relative with reported allergy) was significantly associated with both headache types, for migraine OR was 1.4 (95% CI 1.3–1.4) and for nonmigrainous headache OR was 1.2 (1.1–1.3).

For both headache types, there was a strong linear trend ($P < .0001$) of higher prevalence OR of current asthma, hay fever, and chronic bronchitis with increasing headache frequency (Table 3).

Table 1.—Sex, Age, and Educational Level Among Subjects With Asthma, Hay Fever, and Chronic Bronchitis

Variables	Sex, Female (%)	Mean Age, Years (SD)	Years of Education (%)		
			≤ 9	10–12	≥ 13
No asthma	54.2	48.7 (16.7)	34.1	44.0	21.9
Previous asthma	49.7	47.3 (16.8)	34.0	44.4	21.7
Asthma-related symptoms	50.8	51.7 (19.2)	43.6	41.8	17.2
Current asthma	55.0	51.1 (17.6)	41.6	41.8	14.6
Hay fever					
No	53.4	49.2 (16.8)	35.3	44.0	20.7
Yes	58.6	44.8 (15.9)	28.2	45.8	26.0
Chronic bronchitis					
No	54.3	46.8 (16.7)	34.0	44.0	22.0
Yes	46.6	54.5 (16.3)	48.0	38.3	13.7

Current patients with asthma were defined as those who answered “yes” to questions about previous or present asthma and attacks of wheezing or breathlessness last 12 months. Those without respiratory symptoms answered “no” to both questions. “Chronic bronchitis” was defined as coughing with phlegm in periods of at least 3 months during each of the last 2 years.

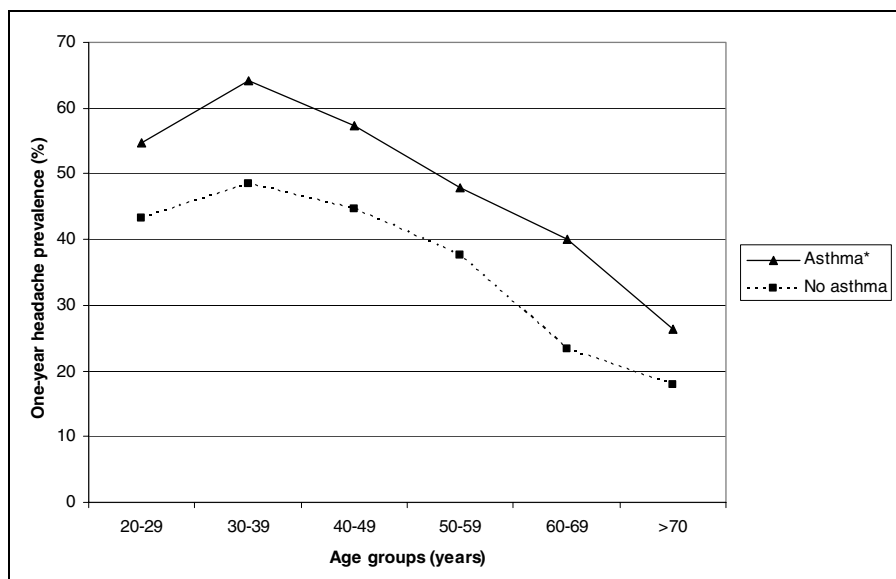


Fig 1.—One-year prevalence of headache (%) related to age in those with asthma and in those with no asthma symptoms.* Current patients with asthma were defined as those who answered yes to questions about present or previous asthma and attacks of wheezing or breathlessness during the last 12 months. The group with no asthma had negative answers in both questions.

COMMENTS

This large-scale population-based cross-sectional study shows that migraine and nonmigrainous headache is approximately 1.5 times more likely among those with current asthma, asthma related symptoms, hay fever, and chronic bronchitis than among those without these disorders. The association increases with increasing headache frequency, and the

magnitude of the increase is similar for both headache categories. Thus, headache frequency seems to have a greater impact on the association with respiratory and allergic conditions than the headache diagnoses.

Our findings of associations between headache and asthma and asthma related symptoms are in accordance with other epidemiologic studies.^{1,2,5,6,10} This has also been seen in several clinic-based studies both

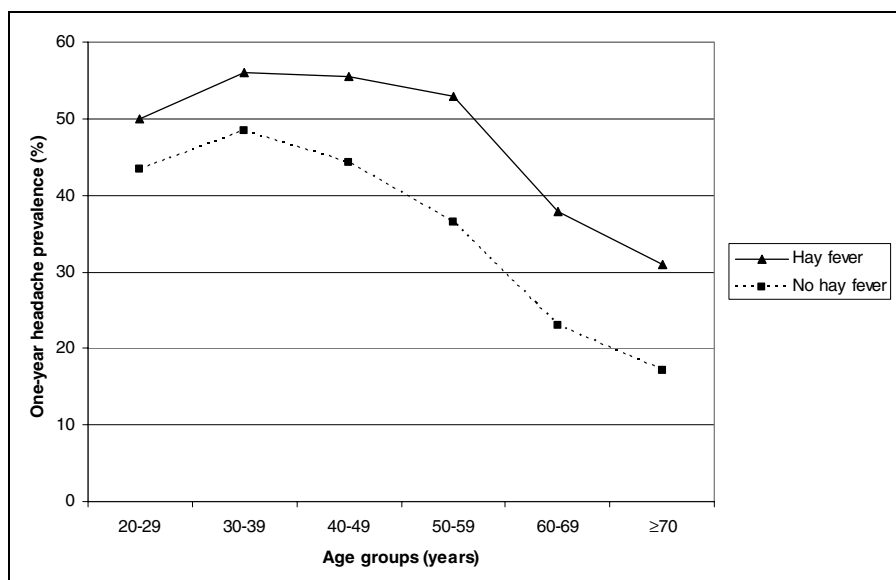


Fig 2.—One-year prevalence of headache (%) related to age in those with and without self-reported hay fever.

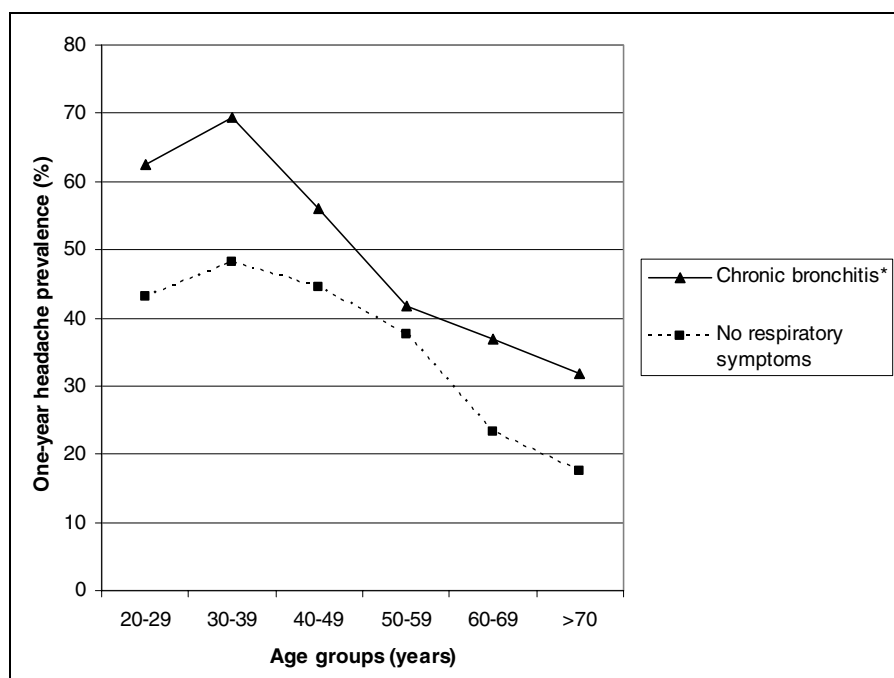


Fig 3.—One-year prevalence of headache (%) related to age in those with chronic bronchitis and in those with no respiratory symptoms.* “Chronic bronchitis” was defined as coughing with phlegm in periods of at least 3 months during each of the past 2 years. “No respiratory symptoms” was defined as no asthma or chronic bronchitis symptoms.

among children and adults with higher rates of allergy or asthma among headache subjects when compared to controls.⁷ Only a few clinic-based studies have failed to demonstrate any associations but these were small and performed before the introduction of the IHS criteria.¹¹⁻¹³

Most of the previous studies, however, have focused on migraine in relation to asthma^{1,2,6,8} and a few studies on headache in general.^{3,5,8} In one recent clinic-based study which has compared atopy among different headache categories, considerably more atopic disorders were found among patients with migraine than among those with chronic tension type headache.⁹ This may seem to be in contrast to the results of the present study where no significant difference was seen between migraine and nonmigrainous headache, but methodological differences may account for this, as chronic tension type headache constituted only a small part of the group with nonmigrainous headache and the study population was much larger in the present study.

Through the present and previous studies, the association between headache and asthma and allergy

seems well documented, but the cause of the association is still unknown. First, since both diagnoses in the present study are self-reported, one cannot exclude the possibility of information bias related to a tendency to report different symptoms in some individuals, ie, those who report their headache complaints are more likely to report also other complaints such as respiratory problems.²¹ This may create strong associations that reflect personality traits rather than biological mechanisms.²² In the present study there was a tendency of more somatic complaints as fatigue, chronic joint pain, low back pain, heartburn, and insomnia among those with symptoms of asthma, hay fever, and chronic bronchitis. Some previous studies have shown that somatization is more common in patients who report frequent respiratory symptoms.^{23,24}

Second, since the study is cross-sectional, it cannot be determined whether frequent headache causes respiratory and/or allergic distress or vice versa or whether other risk factors or a shared susceptibility causes these associations. Several biological explanations for the comorbidity of asthma and headache have been introduced in previous reports, such as genetic

Table 2.—Prevalence OR of Headache Related to Asthma, Hay Fever, and Chronic Bronchitis

Variables	Total	All Headache Types		%	Migraine		Nonmigrainous Headache	
		%	OR [†] (95% CI)		%	OR [†] (95% CI)	%	OR [†] (95% CI)
No asthma	42,472	37.3	1.0 (reference)	11.7	1.0 (reference)	25.6	1.0 (reference)	
Previous asthma	1740	38.8	1.1 (1.0-1.2)	11.0	1.0 (0.8-1.1)	27.8	1.1 (1.0-1.3)	
Asthma-related symptoms	3678	48.6	1.9 (1.7-2.0)	15.5	1.6 (1.4-1.8)	33.1	1.5 (1.4-1.7)	
Current asthma	2511	47.6	1.7 (1.6-1.9)	15.3	1.5 (1.3-1.7)	32.2	1.5 (1.3-1.6)	
Missing	982	36.2	1.1 (1.0-1.3)	10.3	1.0 (0.8-1.2)	25.9	1.1 (1.0-1.3)	
Hay fever								
No	38,061	36.5	1.0 (reference)	11.1	1.0 (reference)	25.4	1.0 (reference)	
Yes	8969	50.0	1.6 (1.5-1.7)	17.4	1.5 (1.4-1.6)	32.6	1.3 (1.3-1.4)	
Missing	4353	33.4	1.1 (1.1-1.2)	9.1	1.1 (1.0-1.2)	23.9	1.1 (1.0-1.2)	
Asymptomatic [‡]	41,806	37.2	1.0 (reference)	11.7	1.0 (reference)	25.5	1.0 (reference)	
Chronic bronchitis	1734	46.3	1.9 (1.7-2.1)	13.6	1.6 (1.3-1.8)	32.8	1.6 (1.5-1.8)	

[†]In the analyses of asthma and chronic bronchitis ORs were adjusted for sex, age, education level, and smoking (pack years), but hay fever ORs were not adjusted for smoking (multiple logistic regression).

[‡]In the analyses of chronic bronchitis the reference group consisted of those who reported neither symptoms of chronic bronchitis nor asthma/asthma-related symptoms (all smoking categories included). Missing cases and those without chronic bronchitis who reported previous asthma or asthma symptoms last year ($n = 7843$) were not included in the analyses of chronic bronchitis.

disposition,^{1,25} mast cell activation,²⁶ functional abnormality in smooth muscle in blood vessels and airways,²² vasoactive mediators,^{9,25} and deranged arachidonic acid metabolism.²⁷ In addition, one may assume that having 2 unpredictable attack disorders may entail a considerable psychological stress that may trigger or aggravate both asthma and headache attacks. One could also speculate that medication could be involved. It is well known that use of β -blockers, sal-

icylates, and nonsteroidal anti-inflammatory drugs in treatment of migraine may trigger asthma,^{27,28} but this seems to be a problem in only a small subgroup of those with asthma.²⁸ In the present study, we do not have data on medication use to address this issue.

The strengths of this study were the large and unselected population and the use of validated headache diagnoses, but there are limitations that must be taken into account. The questionnaire-based headache

Table 3.—Prevalence ORs of Asthma, Hay Fever, and Chronic Bronchitis in Different Headache Frequency Categories

Variables	Current Asthma			Hay Fever			Chronic Bronchitis		
	Total No.	%	OR [†] (95% CI)	Total No.	%	OR [‡] (95% CI)	Total No.	%	OR [†] (95% CI)
Headache-free	29,815	4.9	1.0 (reference)	29,815	16.0	1.0 (reference)	28,336	3.5	1.0 (reference)
Migraine									
<7 days/month	3807	6.4	1.6 (1.4-1.9)	4120	25.4	1.5 (1.4-1.7)	3640	3.4	1.5 (1.4-1.7)
7-14 days/month	931	8.7	2.2 (1.7-2.8)	1047	29.7	1.9 (1.7-2.2)	888	6.3	2.7 (2.1-3.7)
>14 days/month	286	14.6	2.9 (2.0-4.2)	322	34.8	2.6 (2.1-3.3)	273	11.4	4.3 (2.9-6.4)
Nonmigrainous headache									
<7 days/month	8793	6.1	1.5 (1.3-1.7)	9518	22.8	1.4 (1.3-1.5)	8481	4.4	1.7 (1.5-1.9)
7-14 days/month	1350	8.6	2.0 (1.6-2.4)	1467	24.7	1.6 (1.4-1.8)	1284	6.2	2.2 (1.7-2.8)
>14 days/month	658	11.1	2.4 (1.8-3.0)	740	26.1	1.9 (1.6-2.3)	638	9.9	3.0 (2.3-3.9)

[†]OR adjusted for sex, age, education level, and smoking (pack-years) (multiple logistic regression).

[‡]OR adjusted for sex, age, and education level (multiple logistic regression). P -trend value <.0001 for all the variables.

diagnoses were not optimal compared to the interview diagnoses.¹⁸ In order to reduce misclassification bias with regard to headache diagnosis we used a simplified headache classification. The potential for accurate questionnaire-based diagnoses was influenced by the formulations of the questionnaire. The headache questionnaire had to be adapted to the other questions in HUNT, and the number of items was limited. Thus, the intention was to clarify whether the participants suffered from headache or not, to categorize those with headache according to headache frequency, and finally, to clarify whether this headache was migraine or not. Due to limited space, the questionnaire did not allow a further differentiation of headache diagnoses, or to diagnose more than 1 headache type in each patient.

There is a possibility of nondifferential diagnostic misclassification which might weaken real associations, but we think this is a minor problem as the prevalence of migraine in the current population is consistent with data from other population-based studies in the Western countries.²⁹ The impact of nonparticipants has been discussed in more detail previously.¹⁶ Briefly, 13,177 individuals who did not answer the questions about headache in Q2, had completed the Q1 with information about general health and somatic pain. There were more participants than these partial participants who reported good or very good health. However, more specific questions about pain in shoulder, neck, or back revealed no significant differences. Previously, a strong association between headache and neck or shoulder pain has been found.³⁰ We may therefore assume that the results are fairly representative of all participants in Q1. Whether the results also apply to those who did not answer Q1 (complete nonparticipants, $n = 28,006$) remains uncertain. There is probably no interest-related selection bias since headache and respiratory and allergic conditions were 2 out of many objectives of the study.¹⁷

The prevalence of asthma in the present study was higher than in some Scandinavian studies dating some years back³¹ but comparable to more recent ones.^{17,32} The questions about asthma, hay fever, and chronic bronchitis used in the present study were similar to those used in other epidemiologic studies on respiratory and allergic symptoms.^{6,17,19,33,34} In previ-

ous studies different criteria for the asthma diagnosis have been used, and among subjects above 40 years COPD has often been misdiagnosed as asthma. However, stratifying our analyses by age did not change the estimates. In the previous studies on comorbidity of headache and allergies or asthma, different ways to ask about headache and respiratory and allergic symptoms have been used. Nevertheless, the results regarding associations between headache and respiratory and allergic symptoms are quite similar.^{5,6,8} Although the information on hay fever was limited in the present study, the prevalence was comparable to other questionnaire-based studies.^{35,36}

Studies on chronic bronchitis in relation to headache are scarce. However, various respiratory symptoms in addition to asthma have been associated with headache in different studies.³ In a case-control study the relative risk of COPD in patients with migraine was 1.2.⁸ Furthermore, in a study of patients with moderate to severe COPD, headache, mainly of tension type, was a common problem.¹⁴ The association between chronic bronchitis and headache demonstrated in the present study might be explained by a specific comorbidity, by common life-style, environmental, or occupational factors.³⁷ Smoking might be a possible explanation as chronic bronchitis and COPD in Norway is mainly caused by smoking and smoking seems to be associated with headache.³⁸ However, adjusting the analyses for smoking did not change the results substantially. Furthermore, respiratory stress in chronic bronchitis often leads to impaired sleep, which may also trigger headache.³⁹

In conclusion, this large study confirms that migraine and other headaches are associated with respiratory and allergic disorders. Furthermore, it shows that headache frequency has a greater impact on the association than headache diagnoses. Whether it is a causal relationship is unknown, but the results of the present study underline the importance of considering comorbid disorders among patients with frequent headache. Follow-up assessments of this cohort may provide further information on the cause of the associations.

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Conflict of Interest: None

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