Headache and insomnia in population-based epidemiological studies

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Abstract
Background: Several epidemiological studies on the association between primary headaches and insomnia have been published in recent years. Both disorders are frequent, and our purpose was to review results from population-based studies exploring this association.
Methods: We performed a literature search in PubMed for “insomnia” (or sleep disturbance) and “headache” (or migraine) linked with “epidemiology.” Two hundred and eight records were identified. Three longitudinal and 10 cross-sectional studies met our inclusion criteria: population-based design with at least 200 participants including a numerical estimate of the association between headache and insomnia.
Results and conclusions: In nearly all studies, primary headaches, including migraine and tension-type headache, were significantly related to insomnia symptoms with OR estimates ranging from 1.4 to 1.7. The odds were even greater, from 2.0 to 2.6, for frequent, comorbid or severe headache. Recent large longitudinal studies from Norway found a bidirectional, possibly causal, association between headache and insomnia. However, not all studies used standardized diagnostic criteria for either headache or insomnia. Further research should use well defined and validated diagnostic criteria both for insomnia and headache types in order to improve the comparability between studies, investigate causality and clarify the relevance of the findings for clinical practice.

Keywords
Insomnia, headache, epidemiology, population, migraine, sleep

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Introduction
A connection between headache and sleep disturbance was suggested as early as the 19th century (1,2), and associations were initially described in clinical reports, reviews and patient-based populations (3–5). More recently, epidemiological methods have been applied. Most population-based studies, the majority of them cross-sectional, have focused on the association between headache and insomnia symptoms, sleep apnea or restless legs syndrome, whereas few studies have evaluated the association with other sleep disorders like hypersomnias and parasomnias (5).

Previously, the criteria for the diagnosis of primary headaches and sleep disorders have varied between studies. More recently, operational diagnostic criteria have been introduced for headache (6) and sleep disorders (7), including insomnia (8). Although somewhat arbitrary, these criteria provide a more precise framework for reliable estimates in epidemiological studies.

With these instruments one may potentially even investigate possible causal relationships between headaches and sleep disorders in prospective epidemiological designs. However, since questionnaires used in large epidemiological studies often are abbreviated versions of published criteria, validation is often deemed necessary in order to estimate the diagnostic accuracy of the specific questions as a diagnostic tool (9,10). This brief
review will focus on the results and applied methodology in population-based studies of the association between insomnia symptoms and primary headaches in adults.

Methods
A PubMed search for population-based studies was performed in April 2014: “sleep disturbance” OR insomnia) AND (headache OR migraine) AND epidemiology with 208 hits. Studies that obviously were not population-based original articles were excluded by title or abstract, including reviews and drug trials (Figure 1). The following two criteria had to be fulfilled: 1) a population-based study with more than 200 participants and 2) the association between insomnia and headache had been calculated. We were particularly interested in studies with 1000 individuals or more because this will provide numerically precise estimates with margins of error around 2%–3% (11). A number as low as 200 was nevertheless chosen to be able to include cross-sectional validation studies in which a limited number of participants undergo both questionnaires and clinical interviews and investigations (12,13), while the numerical margins of error remain below 5%–7% for prevalent disorders like headache and insomnia (11). Papers based on selected (patient) populations were excluded. Thirteen population-based studies remained for the present review: three longitudinal (12–14) and 10 cross-sectional studies (10,15–23) (Table 1).

Results
Unspecified headache
Cross-sectional studies. In multivariate analyses, the strength of the association between unspecified headache and insomnia expressed by adjusted odds ratio (OR) was 1.7 in two studies (15,19) Odds were generally slightly larger when severe headache was investigated, i.e. 2.5–2.6 (21) and 2.4 (18). Sex differences for the association strength have not been observed (18). In a study using headache diagnosis based on a face-to-face interview with a neurologist, the unadjusted prevalence of insomnia was 1.7 times higher among headache sufferers compared to headache-free subjects (74.5% versus 45.5%, \( p < 0.01 \)) (10).

Figure 1. Flowchart describing the selection of reviewed population-based studies.
Longitudinal studies. Three longitudinal studies performed in Norway had a large sample size with a follow-up time of 11 years (12–14). These studies examined the risk of headache in insomnia, and the risk of insomnia in headache patients, respectively. Insomnia at baseline increased the risk for headache after 11 years (relative risk (RR) 1.6 (12) and OR 1.5 (14). Conversely, Ødegård et al. found that headache at baseline increased the risk for insomnia 11 years later (OR 1.5 (13) (Table 1). OR estimates were marginally higher for women than for men; however, confidence interval (CI) overlaps (not tabulated) were substantial (14).

Migraine

Cross-sectional studies. The strength of the associations (OR) between migraine and insomnia were, respectively, 1.65 (16), 1.4 (19.23) and 2.6 (22). Ødegård et al. (10) also found 1.4 times higher prevalence in univariate analyses (Table 1) although the difference was not significant probably because of the limited sample size.

Longitudinal studies. Insomnia was found to be a risk factor for migraine 11 years later (RR 1.7) (12). Conversely, migraineurs also had increased insomnia risk at follow-up (OR 1.7 (13)). The associations were stronger for those with headache ≥7 days per month (OR 2.2, 95% CI 1.9–2.6) and for those with coexisting muscular pain (OR 2.0, 95% CI 1.8–2.2).

Tension-type headache (TTH)

In a cross-sectional study (10), the unadjusted prevalence of insomnia was 1.8 times higher in TTH compared to headache-free subjects (Table 1). In one longitudinal study insomnia had a 40% higher risk for developing TTH after 11 years (RR 1.4) (12). The association between insomnia and migraine tended to be stronger than the association between insomnia and TTH, particularly when insomnia was rated as severe (OR 2.9 for migraine and 1.9 for TTH) or moderate (OR 2.2 for migraine and 1.5 for TTH) (12).

Headaches with specific presentations

Our search identified two studies that focused on (unspecified) headache presentations: Chronic morning headaches (17) and nocturnal awakening with headache (20). These are neither defined headache entities in International Classification of Headache Disorders, third edition beta (ICHD-3(beta)) (24) nor in the very recent International Classification of Sleep Disorders, third edition (ICSD-3) (25). However, since both presentations are associated with sleep disorders (26–28) and with migraine or TTH (29–33), they have been included in this review. Ohayon (17) found that subjects with chronic morning headache were twice as likely to have insomnia (OR 2.14; Table 1).

Lucchesi et al. (20) found that subjects with nocturnal awakening with headache were more than two times as likely to have Diagnostic and statistical manual of mental disorders, fourth edition (DSM-IV) insomnia (OR 2.2; Table 1).

Discussion

Among population-based studies meeting our criteria, the oldest was published in 2001 and most were from 2010 or later. This is surprisingly late, as ICHD-1 was published in 1988 (3) and ICSD-1 in 1990 (4), providing a good foundation for population-based studies on headache and insomnia. However, a number of informative reviews (4,5,30–32) and studies based on clinical cohorts (3,33,34) have also been published. Moreover, no population-based study on the association between rarer primary headache types and insomnia has seemingly been published.

Consistent and similar significant associations between insomnia and headache and between insomnia and migraine, with OR ranging between 1.4 and 1.7, have been found in the presently reviewed studies. For frequent, severe or headache comorbid with muscular pain, the associations appeared slightly stronger with OR between 2.0 and 2.6 (Table 1). Studies reflect different populations and cultures in Asia, the United States and Europe, and estimates have also been adjusted for different confounders. In this perspective, the observed relative consistency strengthens the concept of primary headaches as a universal neurobiological trait.

Some of the remaining differences in OR between studies are probably due to different diagnostic criteria. The time frame for questions, e.g. one month (15), three months (18), or one year (21) and the specific phrasing, e.g. neural question “headache yes/no” (15) or “frequent and severe headache” (21), varied. The diagnosis of migraine varied from self-reported migraine (19) to strict use of ICHD-2-based face-to-face interview by neurologists (10). Nine studies used more standardized criteria either for headache or insomnia but almost never for both disorders simultaneously. Only one cohort study was based both on ICHD-2 criteria and the validated Karolinska Sleep Questionnaire (35) (Table 1). Such a variation in criteria makes comparison between studies difficult.

Another limitation regarding the interpretation and comparability between studies is caused by the focus on unspecified headache presentations that are not recognized as entities in ICHD-2 or ICHD-3 (beta). Chronic morning headache was defined as answering...
<table>
<thead>
<tr>
<th>Ref./Country</th>
<th>Design&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Age(s)</th>
<th>Participants</th>
<th>Headache type&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Headache diagnosis&lt;sup&gt;c&lt;/sup&gt;</th>
<th>Insomnia/sleep disturbance measure&lt;sup&gt;d&lt;/sup&gt;</th>
<th>Results&lt;sup&gt;e&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ødegaard, 2011/</td>
<td>L</td>
<td>≥20</td>
<td>15,268</td>
<td>H, M, TTH</td>
<td>ICHD-2 based</td>
<td>Two items (graded frequency). (last month)</td>
<td>For insomnia, risk for headache after 11 years; H: RR 1.6 (CI 1.3–2.0) TTH: RR 1.4 (CI 1.1–1.9) Migraine: RR 1.7 (CI 1.2–2.5)</td>
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<td>Norway (12)</td>
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<tr>
<td>Ødegaard, 2013/</td>
<td>L</td>
<td>≥20</td>
<td>19,271</td>
<td>M, NMH</td>
<td>Modified ICHD-1</td>
<td>Three items, graded frequency (last three months)</td>
<td>For headache, risk for insomnia after 11 years in: NMH: OR 1.5 (CI 1.3–1.6) Migraine: 1.7 (CI 1.5–2.0)</td>
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<tr>
<td>Sivertsen, 2014/</td>
<td>L</td>
<td>19–67</td>
<td>24,715</td>
<td>H</td>
<td>Yes/No</td>
<td>DSM-IV</td>
<td>For insomnia, risk for headache after 11 years: OR 1.5 (CI 1.2–1.9) Headache in insomnia: OR 1.7 (CI 1.3–2.2) Migraine in insomnia OR 1.65 (99% CI 1.3–2.0)</td>
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<td>Norway (14)</td>
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<td>Kim, 2001/</td>
<td>CS</td>
<td>≥20</td>
<td>3030</td>
<td>H</td>
<td>Yes/no, last month</td>
<td>3 items, graded frequency, last month</td>
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<td>Japan (15)</td>
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<td>Sutton, 2001/</td>
<td>CS</td>
<td>≥15</td>
<td>11,924</td>
<td>M</td>
<td>Yes/no (current)</td>
<td>Yes/no (current)</td>
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<tr>
<td>Ohayon, 2004/</td>
<td>CS</td>
<td>≥15</td>
<td>18,980</td>
<td>CMH</td>
<td>Graded frequency</td>
<td>DSM-IV</td>
<td>Insomnia in CMH: OR 2.1 (CI 1.8–2.6)</td>
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<td>multiple (17)</td>
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<td>Strine, 2006/</td>
<td>CS</td>
<td>≥18</td>
<td>29,828</td>
<td>SH (incl M)</td>
<td>Yes/no, last 3 months</td>
<td>One item, (graded frequency) last 12 months</td>
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<td>United States (18)</td>
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<tr>
<td>Sivertsen, 2009/</td>
<td>CS</td>
<td>20–89</td>
<td>47,700</td>
<td>H, M</td>
<td>H: yes/no, M: self-reported</td>
<td>Two items (graded frequency), last month</td>
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<td>Norway (19)</td>
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<td>yes/no, last month</td>
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<tr>
<td>Ødegaard, 2010/</td>
<td>CS</td>
<td>≥20</td>
<td>297</td>
<td>H, M, TTH</td>
<td>ICHD-2, face to face interview</td>
<td>Three KSQ items (graded frequency last three months)</td>
<td>Insomnia prevalence in H: 1.7 times higher (74% vs. 45%, p &lt; 0.01), in M:1.4 times higher (65% vs. 45%, p &gt; 0.05), and in TTH: 1.8 times higher (80% vs. 45%, p &lt; 0.01)</td>
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<td>Norway (10)</td>
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<td>Lucchesi, 2010/</td>
<td>CS</td>
<td>20–80</td>
<td>1101</td>
<td>NAH</td>
<td>One item, graded frequency</td>
<td>DSM-IV</td>
<td>Insomnia in NAH: OR 2.2 (CI 1.0–4.8)</td>
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<td>Brazil (20)</td>
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<tr>
<td>Lateef, 2011/</td>
<td>CS</td>
<td>≥18</td>
<td>5692</td>
<td>SH, SM</td>
<td>Modified ICHD-2, last year</td>
<td>Three items + daytime fatigue last 12 months</td>
<td>Insomnia (≥ 3 of 4 symptoms) in SH: OR 2.5 (CI 2.0–3.1) Migraine: OR 2.6 (CI 2.0–3.4)</td>
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<td>United States (21)</td>
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<tr>
<td>Budhiraja, 2011/</td>
<td>CS</td>
<td>16–65</td>
<td>3282</td>
<td>M</td>
<td>Self-reported yes/no (lifetime)</td>
<td>DSM-IV (including daytime consequences), last three months</td>
<td>Insomnia in migraine: OR 1.8 (CI 1.5–2.1)</td>
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<td>United States (22)</td>
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<tr>
<td>Huang, 2013/</td>
<td>CS</td>
<td>≥15</td>
<td>5519</td>
<td>M</td>
<td>ICHD-2, face to face</td>
<td>Unspecified</td>
<td>Insomnia in migraine: OR 1.4 (CI 1.1–1.7)</td>
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<td>China (23)</td>
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<sup>a</sup>CS: cross-sectional; L: longitudinal.

<sup>b</sup>H: any headache; TTH: tension-type headache; M: migraine; NMH: non-migraineous headache; SH: severe headache; SM: severe migraine; NAH: nocturnal awakening with headache; CMH: chronic morning headache.

<sup>c</sup>ICHD: International Classification of Headache Disorders.

<sup>d</sup>DSM-IV: Diagnostic and statistical manual of mental disorders. 4th ed. KSQ: Karolinska Sleep Questionnaire.

<sup>e</sup>OR: odds ratio; RR: relative risk; CI: 95% confidence interval. Adjusted model results have been reported (when applicable) in this table.

<sup>f</sup>United Kingdom, Germany, Italy, Portugal and Spain.
“sometimes,” “often” or “always” to the question: “Do you have headaches when you wake up in the morning?” (17). Unfortunately, that study did not contain questions regarding location, intensity, time, etc., that could have permitted more specific headache diagnoses.

Individuals having nocturnal awakenings with headache, disregarding frequency, were defined as having nocturnal awakening with headache in one study (20). This definition is slightly at odds with the description of “Sleep-related headache” in ICSD-3 as: “a group of unilateral or bilateral cephalalgias of varying severity and duration that occur during sleep or upon awakening from sleep,” since the latter also include various secondary morning headaches like the ICS-D-defined “sleep apnoea headache” (24) in addition to primary headaches (migraine, TTH, cluster headache, chronic paroxysmal hemicrania and hypnic headache) (25). However, sleep-related migraine has recently been the focus for several polysomnographic (PSG) studies (27,36,37).

Diagnosing insomnia by the new ICSD-3 (25) or DSM-V criteria (38) will probably more likely identify chronic insomniacs rather than those occasionally experiencing insomnia symptoms. A similar request for improvement in diagnostic precision is relevant for headache. Asking for self-reported migraine probably reveals different results than basing the diagnosis on ICHD-2 (or 3) criteria. In a large population-based study, self-reported migraine identified only half of the migraineurs, compared to the modified ICHD-1 criteria (9).

In spite of the shortcomings, insomnia items used for the diagnosis in the reviewed studies are often similar to those used in DSM-IV/DSM-V and ICSD-3. A common approach has been to define insomnia as “frequently experiencing at least one out of three insomnia symptoms, i.e. difficulty initiating sleep, difficulty staying asleep, and early morning awakening” for some time frame. The new ICSD-3 (25) and DSM-V (38) criteria both use comparable symptoms with frequency ≥3 times per week, symptom duration for at least three months and daytime consequences, for instance, fatigue, to diagnose a chronic insomnia disorder, as opposed to short-term insomnia disorder or other insomnia disorder (25). Terminology differs slightly as DSM-V uses insomnia disorder as the umbrella category with additional specifiers like “episodic” or “comorbidity.”

Can epidemiology enlighten the question about potentially causal relationships between insomnia and headache? First, bidirectionality supports the clinical impression that a one-way causality model is too simplistic. Second, the association between insomnia symptoms and headache generally coexists with similar associations to other painful disorders, fatigue, life stress and mental symptoms in a syndrome-like fashion (12–20), again reinforcing the clinical impression of complex and multifactorial symptomatic traits in several patients. Insomnia is also associated with a variety of medical disorders (22), underlining the fact that insomnia symptoms often are secondary to another disorder. Indeed, if comorbidity is the sole cause for a sleep disturbance, the diagnosis chronic insomnia disorder may not be applicable according to ICSD-3 (25) while DSM-V underscores that insomnia should be diagnosed (and treated) also when comorbidity is present (38). On the other hand, since insomnia seemingly carries a greater risk for the development of migraine than TTH (12), the proposed causality between insomnia and migraine (37) is supported. In summary, improved diagnostic precision using specific, valid instruments will enhance our future knowledge. In addition, new analytical methods have recently appeared, and these may improve our future ability to infer causality (39).

Recent physiological data from PSG studies do support a new hypothesis, that increased strain, relative sleep deprivation and varying robustness of the neurobiological arousal system may be among several causal factors for a migraine attack (40). Thus, a combination of clinical, epidemiological and physiological data can be used to provide new (e.g. “biobehavioral”) (41) models about the relationship between headache and insomnia. Hence, our recently proven new knowledge about bidirectionality (13) and resulting models (40,41) can hopefully also be used as frameworks for more systematic therapeutic studies on how improved sleep quality might relieve the burden of headache in the future.

**Clinical implications**

- The association between headache (or migraine) and insomnia symptoms in population-based epidemiological studies is consistently elevated around the world by 40%–70%.
- The association between headache and insomnia is stronger, elevated by 100%–160%, in subjects with more frequent, severe, or comorbid headache.
- Recent prospective studies have shown bidirectional relationships between headache (or migraine) and insomnia symptoms with risk elevations between 50% and 120%, supporting an old hypothesis: Systematic treatment of insomnia might improve the burden of headache.
- Future epidemiological studies should aim to improve diagnostic precision by validated diagnostic instruments, both regarding insomnia and headache.
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Conflict of interest
None declared.

References


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