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Short communication

Insomnia and the incidence, recurrence and persistence of common mental disorders: Sex-differences in the general population

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ABSTRACT

Insomnia is common throughout the population and thought to be a risk factor for mental disorders. We assessed the association of insomnia symptoms with incidence, recurrence and persistence of mood, anxiety and substance use disorders. In 4007 participants (55 % women, mean age 51.0 ± 12.3) of the population-based Netherlands Mental Health Survey and Incidence Study (NEMESIS), having insomnia symptoms increased the odds of developing, recurring and persisting mood disorders, mostly in men. Insomnia only associated with recurring anxiety disorders, particularly in women, and not with substance use disorders. Treating insomnia may aid recovery and prevention of mental disorders, particularly mood disorders.

1. Introduction

Insomnia is a well-known risk factor for the development of mood disorders (Baglioni et al., 2011; Li et al., 2016; Zhang et al., 2022). It has also been suggested to be a risk factor for other common mental disorders (Atwood, 2022; Hertenstein et al., 2023; Pigeon et al., 2017) such as anxiety disorders and substance use disorders, although the latter two have been studied much less extensively than mood disorders. Additionally, insomnia may not only be a risk factor for new onset mental disorders, it may also play a role in the recurrence and persistence of these disorders (Atwood, 2022; Pigeon et al., 2008; Roehrs et al., 2021), for example as a transdiagnostic process (Hertenstein et al., 2023).

As insomnia can be treated well in most persons (Riemann et al., 2017) and can be targeted at large scale (Luik et al., 2017), insomnia may be particularly interesting as a modifiable risk factor. Treating insomnia has also been shown to alleviate symptoms of mood and anxiety disorders directly (Espie et al., 2019), and suggested to prevent the development of mood disorders (Boland et al., 2023).

Research on the association of insomnia with recurrence and persistence of mental disorder has so far typically been done in clinical samples but this might not be translatable to the general population where insomnia complaints are common (Kocevska et al., 2021) and disorders are often less severe. Population-based studies on the incidence of mental disorders typically only assessed symptoms of mental disorders with questionnaires, therefore lacking the possibility to study diagnoses and the rigour of a clinical interview. This is however particularly relevant for the association of insomnia symptoms and mental disorders, as insomnia symptoms may be a symptom of the mental disorder per se. Moreover, information is limited on sex differences (Bao et al., 2017), even though we know that insomnia symptoms and mental disorders are more common in women. Therefore we assessed the association of insomnia symptoms with the incidence, recurrence and persistence of mood disorders, anxiety disorders and substance use disorders in a population-based cohort, hypothesizing that insomnia symptoms lead to increased risks for these disorders. Additionally, we studied if these associations differ between women and men.

2. Methods

This study is embedded within the second cohort of the population-based Netherlands Mental Health Survey and Incidence Study (NEMESIS-2) (de Graaf et al., 2010a, 2010b), the only exclusion criteria employed were insufficient mastery of Dutch and being homeless or

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Table 1
Association of insomnia with development of a first onset, recurrent or persistent mental disorder over 12 months for the overall sample, women and men.

	Mood disorder		Anxiety disorder		Substance use disorder	
	Model 1 OR [95% CI]	Model 2 OR [95% CI]	Model 1 OR [95% CI]	Model 2 OR [95% CI]	Model 1 OR [95% CI]	Model 2 OR [95% CI]
Total population						
Without history of mental disorder[a]	*N* = 2951		*N* = 2984		*N* = 3197	
Probable Insomnia	2.47*** [1.46,4.16]	2.18** [1.27,3.74]	1.92* [1.09,3.38]	1.39 [0.76,2.53]	1.62 [0.81,3.24]	1.46 [0.70,3.03]
Insomnia Symptoms	1.09*** [1.04,1.15]	1.08** [1.02,1.14]	1.09** [1.03,1.15]	1.06 [1.00,1.12]	1.04 [0.97,1.11]	1.02 [0.95,1.09]
History of mental disorder[a] (> 12 months)	*N* = 861		*N* = 787		*N* = 692	
Probable Insomnia	1.72* [1.09,2.72]	1.61 [1.00,2.61]	2.11** [1.34,3.31]	2.10** [1.31,3.38]	1.45 [0.66,3.18]	1.68 [0.74,3.81]
Insomnia Symptoms	1.08*** [1.04,1.13]	1.07** [1.02,1.12]	1.06** [1.02,1.11]	1.05* [1.00,1.10]	1.02 [0.95,1.10]	1.04 [0.96,1.12]
Current mental disorder[a] (=<12 months)	*N* = 195		*N* = 236		*N* = 118	
Probable Insomnia	2.81** [1.48,5.34]	2.51* [1.17,5.37]	1.32 [0.76,2.27]	1.13 [0.61,2.09]	0.60 [0.21,1.71]	0.49 [0.15,1.63]
Insomnia Symptoms	1.07* [1.01,1.12]	1.04 [0.98,1.11]	1.03 [0.98,1.08]	1.01 [0.96,1.07]	1.00 [0.92,1.09]	1.00 [0.90,1.10]
Women						
Without history of mental disorder[a]	*N* = 1513		*N* = 1550		*N* = 1959	
Probable Insomnia	1.93 [0.95,3.90]	1.83 [0.87,3.85]	1.63 [0.82,3.24]	1.21 [0.58,2.51]	1.89 [0.73,4.92]	2.19 [0.81,5.94]
Insomnia Symptoms	1.07 [1.00,1.15]	1.07 [0.99,1.15]	1.08* [1.01,1.15]	1.05 [0.98,1.12]	1.07 [0.98,1.18]	1.09 [0.98,1.20]
History of mental disorder[a] (> 12 months)	*N* = 584		*N* = 508		*N* = 224	
Probable Insomnia	1.25 [0.72,2.18]	1.17 [0.66,2.09]	2.47** [1.41,4.32]	2.48** [1.39,4.43]	2.21 [0.73,6.67]	2.44 [0.77,7.77]
Insomnia Symptoms	1.06* [1.00,1.12]	1.05 [0.99,1.11]	1.08** [1.02,1.14]	1.06* [1.01,1.13]	1.03 [0.93,1.15]	1.06 [0.94,1.19]
Current mental disorder[a] (=<12 months)	*N* = 129		*N* = 168		*N* = 43	
Probable Insomnia	2.24* [1.01,4.99]	2.24 [0.88,5.73]	1.64 [0.85,3.14]	1.28 [0.59,2.75]	0.53 [0.09,3.14]	NA[b]
Insomnia Symptoms	1.05 [0.98,1.12]	1.03 [0.96,1.12]	1.05 [0.99,1.12]	1.02 [0.96,1.09]	1.02 [0.88,1.18]	NA[b]
Men						
Without history of mental disorder[a]	*N* = 1438		*N* = 1434		*N* = 1238	
Probable Insomnia	3.31** [1.56,7.05]	2.58* [1.16,5.75]	2.75* [1.03,7.31]	2.20 [0.77,6.31]	1.47 [0.53,4.04]	1.07 [0.35,3.27]
Insomnia Symptoms	1.12** [1.04,1.21]	1.10* [1.02,1.19]	1.12* [1.02,1.22]	1.08 [0.99,1.19]	1.01 [0.91,1.11]	0.97 [0.87,1.08]
History of mental disorder[a] (> 12 months)	*N* = 277		*N* = 279		*N* = 468	
Probable Insomnia	3.47** [1.55,7.76]	3.81** [1.47,9.84]	1.63 [0.72,3.66]	1.60 [0.64,4.00]	0.90 [0.26,3.17]	0.90 [0.23,3.51]
Insomnia Symptoms	1.14** [1.05,1.23]	1.14** [1.04,1.25]	1.03 [0.95,1.12]	1.02 [0.93,1.12]	1.01 [0.90,1.12]	1.00 [0.89,1.13]
Current mental disorder[a] (=<12 months)	*N* = 66		*N* = 68		*N* = 75	
Probable Insomnia	3.93* [1.33,11.62]	6.80* [1.20,38.65]	0.80 [0.29,2.24]	0.38 [0.08,1.85]	0.68 [0.18,2.55]	0.73 [0.14,3.70]
Insomnia Symptoms	1.08 [1.00,1.18]	1.07 [0.95,1.22]	0.98 [0.90,1.08]	0.89 [0.77,1.04]	1.00 [0.89,1.11]	1.01 [0.87,1.16]

Model 1: adjusted for sex and age.
Model 2: adjusted for variables in model 1 and additionally for educational level, living situation, employment, negative life events, any chronic somatic disorder, smoking, psychotropic medication and other 12-month mental disorders (e.g. in the model with mood disorder as dependent variable these are any anxiety disorder and any substance use disorder).
Probable insomnia refers to the dichotomized score, insomnia symptoms to the continuous score.
[a] Mental disorder refers to the disorder investigated in the association, so for the association with mood disorders it refers tot mood disorder, but for anxiety disorder to anxiety disorders.
[b] Not applicable, could not be computed due to small cell sizes.
* $p<0.05$.
** $P<0.01$.
*** $P<0.001$.

institutionalized for a long time-period. It includes those who participated at the third (2013–2015) and fourth (2016–2018) interview rounds ($N = 4007$) during which insomnia symptoms were assessed. At each round, participants completed a 1.5 h interview. NEMESIS was approved by the Medical Ethical Review Committee for Mental Health Institutions (METIGG). All participants provided written informed consent to participate at each interview round in the study.

To determine whether participants met the DSM-IV diagnostic criteria (American Psychiatric Association, 1994) for mood, anxiety and/or substance use disorders, which largely overlap with the criteria from the updated DSM-5, participants were assessed with the Composite International Diagnostic Interview (CIDI 3.0) (Haro et al., 2006; Kessler et al., 2005). Symptoms of insomnia were measured using the Women's Health Initiative Insomnia Rating Scale (Levine et al., 2003). This questionnaire consists of five questions assessing symptoms in the past month, answered on a scale of 0–4, where higher scores indicate more severe symptoms of insomnia (Cronbach's alpha = 0.76). Probable insomnia was defined as a total score ≥9 (Levine et al., 2003). Additionally, information was collected on sex, age, education, living situation, employment, smoking, somatic diseases, negative live events (Brugha et al., 1985), and use of medication for mental disorders.

For each of the three mental disorders assessed, three groups were created based on data from the first, second and third round: (i) without a history of the disorder ever in life, (ii) with a history of the disorder (>12 months since the third round), and (iii) with a current disorder (=<12 months at the third round) to be able to assess the development, recurrence and persistence of mental disorders.

Logistic regressions were used in these groups to assess the association between insomnia symptoms (dichotomized and continuous score) at round three and mental disorders at round four. Each analysis was run in two models, first a model corrected for age and sex, and second a model additionally corrected for education, living situation, employment, smoking, somatic diseases, negative live events, and use of medication for mental disorders. Analysis were stratified for sex and STATA (version 16.1) was used.

3. Results

Of the 4007 participants included (55 % women, mean age 51.0 ± 12.3 years), 2.9–5.9 % met criteria for a current and 17.3–21.5 % for a history of the specified mental disorders, see Table 1.

Probable insomnia was associated with developing a mood disorder in those without a history of mood disorder (OR:2.18, 95% CI: 1.46,4.16), recurrent mood disorder (OR:1.61, 95% CI: 1.00,2.61) in

those with a history of mood disorder, and persistent mood disorder (OR:2.51, 95% CI: 1.17,5.37) in those with a current mood disorder after adjustment for confounders (Table). Similar associations were found for insomnia symptoms with mood disorders. Associations were statistically significant in men with more pronounced effect sizes than overall, but not in women, where the effect sizes were also smaller.

Probable insomnia was not statistically significantly associated with developing an anxiety disorder (OR:1.39, 95% CI: 0.76,2.53) and persistent anxiety disorder (OR:1.13, 95% CI: 0.61,2.09), but was associated with recurrent anxiety disorder (OR:2.10, 95% CI: 1.31,3.38) after adjustment for confounders (Table 1). Associations for insomnia symptoms were largely similar. In women the association insomnia with recurring anxiety disorder was significant after adjustment for confounders with a slightly more pronounced effect size than the overall effect size. No other significant associations were found in women or men.

Probable insomnia and insomnia symptoms were not associated with incident, recurrent or persistent substance use disorders.

4. Discussion

In this population-based cohort, insomnia symptoms were most consistently associated with a higher chance of newly developing, recurring and persisting mood disorders, while insomnia symptoms were only associated with recurring anxiety disorders and not with substance use disorders.

Notably, the association between insomnia and mood disorders was most pronounced in men, in line with some previous work suggesting a stronger association for men overall (Byrne et al., 2019) or for men at specific ages (Chen et al., 2017). Mechanisms underlying this difference in risk are unclear and should be further studied as they could be explained by differences in biology or differences in the endorsement of insomnia and depressive symptoms.

An association between insomnia and newly developing anxiety was not found in our study. This is in contrast to the overall effect in a recent meta-analyses (Hertenstein et al., 2023), but in line with the only population-based study using clinical interviews (Ford and Kamerow, 1989) in this meta-analysis. This suggests that sampling and method of study may explain at least some of these differences. Yet, insomnia symptoms were associated with recurrence of anxiety disorder, potentially insomnia is only a risk factor for anxiety disorders if a pre-existing vulnerability (e.g. history of the disorder) is present. This association was more prominent in women than men, opposite to what was seen for mood disorders.

Insomnia symptoms were not related to substance use disorder, which in our study was predominantly alcohol use disorder. Although in contrast to previous suggestions (Roehrs et al., 2021) it is in line with a recent meta-analysis (Hertenstein et al., 2023). Potentially, this association was not found as insomnia symptoms might be more pronounced during the withdrawal period, or because the substance is used to target insomnia symptoms as a form of self-medication for sleep onset latency problems.

Strengths of this study are the population-based setting, longitudinal data collection allowing assessment of temporality, and the use of clinical interviews. It also has limitations as it does not allow for determining causal associations similar to many other studies, has relatively small numbers for assessing the associations with the persistence of mental disorders and has limited information on treatment which might play a role in the persistence of disorders.

Together, this study strengthens the literature on sleep as a risk factor for mood disorders, but cannot confirm consistent associations with other common mental disorders for new development and persistence. Sleep might therefore not be a generic risk factor, but rather heighten the risk of mood and anxiety disorders differently depending on the stage of the disease. This opens up the avenue for treating sleep to aid recovery and prevention of specific mental disorders, particularly mood disorders where associations are most consistent.

CRediT authorship contribution statement

Annemarie I Luik: Conceptualization, Methodology, Writing – original draft, Writing – review & editing. **Judith van der Riet:** Conceptualization, Writing – review & editing, Methodology. **Neeltje M Batelaan:** Conceptualization, Methodology, Writing – review & editing. **Margreet ten Have:** Conceptualization, Data curation, Formal analysis, Methodology, Writing – review & editing.

Declaration of Competing Interest

The authors have no conflict of interest.

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