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Differences in anxiety levels among symptoms of insomnia. The HUNT study

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ABSTRACT

Objectives: This study aim is to compare anxiety levels among individuals experiencing different symptoms of insomnia.
Design: Case-control study.
Setting: The Nord-Trøndelag Health Study (the HUNT3 study, Norway).
Participants: Of the 50,802 individuals taking part in the HUNT3 study, the current sample comprised 7933 individuals, including 4317 cases with insomnia and 3616 controls.
Measurements: Symptoms of anxiety were assessed using Hospital Anxiety and Depression Scale, whereas insomnia symptoms were assessed according to the core *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition,* nocturnal symptoms. Anxiety levels of the 4317 individuals reporting at least 1 insomnia symptom were compared with the 3616 controls reporting no symptoms. Level of anxiety among participants experiencing combinations of insomnia symptoms was also investigated.
Results: Anxiety levels were significantly higher in individuals reporting insomnia symptoms ($M = 2.5$, SD = 2.4) compared to controls (5.5, SD = 3.7, $P < .001$). Anxiety levels also differed significantly between different insomnia symptoms ($P < .001$). Participants reporting all 3 insomnia symptoms had the highest anxiety score ($M = 6.8$, SD = 4.3), followed in decreasing order by sleep onset insomnia with terminal insomnia ($M = 6.7$, SD = 4.0), sleep onset insomnia with sleep maintenance insomnia ($M = 6.3$, SD = 3.8), sleep onset insomnia only ($M = 5.8$, SD = 3.7), sleep maintenance insomnia with terminal insomnia ($M = 5.6$, SD = SD = 3.4), terminal insomnia ($M = 5.2$, SD = 3.4), and sleep maintenance insomnia only ($M = 4.5$, SD = 3).
Conclusions: Difficulties initiating sleep, both alone and in combination with 1 or 2 of the other symptoms, seem to play a key role in rising anxiety levels.
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Introduction

Insomnia and anxiety are interlinked throughout the lifespan,[1] with 20%-30% of people with insomnia also presenting with significant anxiety. Insomnia and anxiety do not merely co-occur; they also seem to influence each other over time, and there is increasing evidence that the relationship between insomnia and anxiety is most likely bidirectional.[2,3] The 2 conditions are hypothesized to be either different expressions of the same response to psychological distress, or distinct conditions with shared symptoms or other underlying common factors.[3]

From a biological point of view, the co-occurrence of insomnia and anxiety may be caused by dysregulation of specific corticolimbic circuits responsible for both emotional responses and sleep.[4] Genetic studies support[5] this theory, reporting common predisposing genetic variations for these conditions. The corticotrophin-releasing hormone system is another biological element wiring insomnia and

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anxiety, which is involved in promoting psychological arousal. In a state of anxiety, catecholamines are released, resulting in psychological and physiological alertness and hence anxiety and insomnia.[6]

An often overlooked aspect of insomnia is that people with the disorder may present with 1 symptom only or a combination of several. According to the *Diagnostic and Statistical Manual of Mental Disorders*, *Fifth Edition* (DSM-5),[7] there are 3 principal nocturnal symptoms of insomnia: difficulties in falling asleep (or sleep onset insomnia), difficulty staying asleep (or maintenance insomnia), and terminal insomnia (terminal insomnia). Although most researchers treat these symptoms equivalently or combine them to produce a joint operationalization of an insomnia disorder, few studies have examined each insomnia symptom individually in this context.

The established relationship between insomnia and anxiety is based on studies that do not consider possible differences in the symptoms. Comparing different symptoms with regard to their consequences and background is necessary to validate the customary treatment of these symptoms as equal. In one such study, Canivet and colleagues brought evidence of a different risk of somatic and mental disorders among the aforementioned insomnia symptoms.[8] For example, men reporting sleep onset insomnia or terminal insomnia were 3 times more likely than healthy sleepers to receive a disability pension due to mental problems, whereas maintenance insomnia gave a considerably lower risk. These findings suggest that different insomnia symptoms may have different implications and consequences, including different patterns of anxiety. Few studies[9–11] have reported anxiety levels for single symptoms of insomnia, but small sample size and low resolution in defining the 3 symptoms and their combinations call for further investigations.

The overall aim of this study was to report and compare anxiety levels among individuals reporting different symptoms of insomnia using a large population-based sample, the Nord-Trøndelag Health Study (HUNT). This large dataset gives the unique opportunity to investigate this very relationship, as it has collected data from inhabitants on both insomnia symptoms and anxiety.

Methods

Participants

This study is part of the Nord-Trøndelag Health Study (the HUNT study, Norway) that includes data from 3 cohorts. In the present

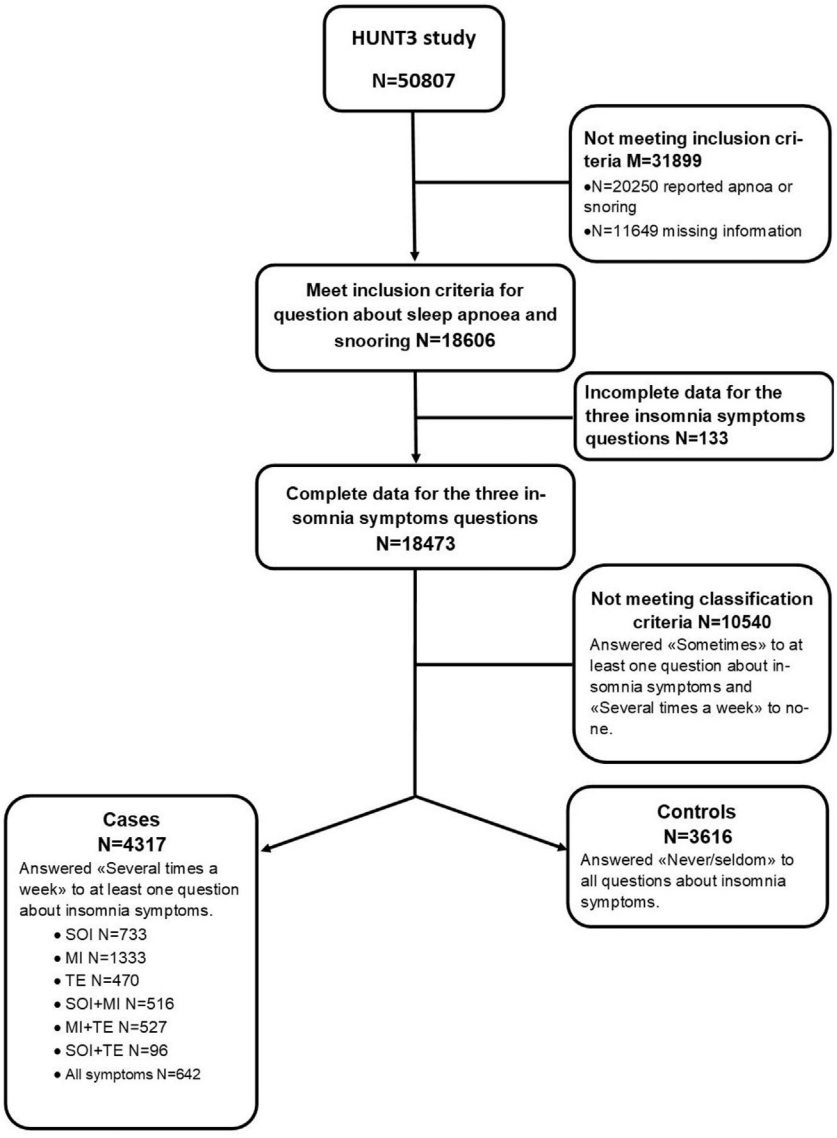

Fig. 1. Study design and participant flow of the study sample. SOI, sleep onset insomnia; MI, maintenance insomnia; TE, terminal insomnia.

study, we used data from the HUNT3 cohort (2006-2008) which comprised 50 807 participants. As with the first 2 HUNT cohorts, in HUNT3, all citizens (N = 93 860) from the Norwegian region of Nord-Trøndelag aged 20 years or more were invited to provide extensive health information and biological samples. Detailed information about the HUNT studies has been summarized by Krokstad et al.[12]

Figure 1 shows the design and participant flow of the current sample. Of 50 807 participants, 50 802 individuals provided valid responses on the relevant HUNT3 questionnaires. Of these, we selected 18 606 individuals (36.6%) who answered "Never/Seldom" to questions regarding the frequency of snoring or interrupted breathing during the night (ie, possible proxy for sleep apnea) during the past month. Of these, participants with complete data for all 3 symptoms of insomnia (n = 18 473, 97.3%) were selected and comprised the current study sample.

Insomnia

Three questions in the HUNT3 Questionnaire 2 (Sleep section,[13] the 3 items can be found in section S1 of Supplementary material) cover the principal symptoms of insomnia as stated in the DSM-5[7]: difficulties falling asleep (sleep onset insomnia), woken up repeatedly during the night (maintenance insomnia), and woken too early and could not get back to sleep (terminal insomnia). These questions investigate the frequency of the symptoms during the previous 3 months using the following response options: "Never/seldom," "Sometimes," and "Several times a week."

Study participants were classified into insomnia cases and controls. Those who answered "Several times a week" to at least 1 symptom were classified as cases (n = 4317), and those who answered "Never/Seldom" to all 3 questions constituted the controls (n = 3616). The rest of the respondents answering "Sometimes" to at least 1 question and "Several times a week" to none of them were excluded. Cases were further assigned to 1 of 7 subgroups, according to the combinations of the reported insomnia symptoms.

Anxiety measure

The Hospital Anxiety and Depression Scale (HADS)[14] is a 14-item questionnaire used to evaluate symptoms of depression and anxiety and is a popular tool among both clinicians and researchers.[15] In this study, we used the sum of the 7 items related to anxiety (HADS-A), giving a sum score in the range from 0 to 21.

Analyses

A total of 493 individuals (2.7%) in our working dataset lacked data on 1 or more HADS-A items. We used single imputation (expectation-maximization algorithm) to singly impute these missing data. The imputation model included the variables age and HADS-A items.

Student *t* test was used to compare HADS-A scores between cases and controls. We used linear regression with HADS-A as dependent variable and type of sleep symptoms as an 8-category covariate, adjusting for sex and age. Differences in HADS-A levels among cases in subgroups were compared using Bonferroni adjustment accounting for all the pairwise comparison between the 7 groups. Separate analyses for men and women were conducted in the same way. Because the residuals were not normally distributed, we used bootstrapping with 1000 bootstrap samples.

Separately, participants were classified according to HADS-A score into 4 groups by increasing severity: normal (0-7), mild (8-10), moderate (11-14), and severe (15-21), according to the earlier published classification criteria.[14] Frequencies of the insomnia symptoms and their combination were examined for each group.

We compared HADS-A scores and age between cases, controls, and excluded individuals using analysis of variance with 1000 bootstrap samples. A χ^2 test was used to examine differences in distribution of sexes among the 3 groups.

All analyses were conducted using IBM SPSS 25 (SPSS Inc, Chicago, IL).

Results

Overall, our sample (n= 7933) included more women (66.2%) than men. Sixty-four percent of women were classified as insomnia cases compared to 48.2% of men (χ^1 =144, 6, $P < .001$). Mean age for the sample was 50.2 years (SD = 16.2, range: 19.2-96.8). Cases were significantly older ($M = 54$) than controls ($M = 45$) (t[7931] =26.29, $P < .001$). As detailed in Table 1, the level of anxiety was significantly higher (t[7931] =41.65, $P < .001$, mean difference = 3) in cases ($M = 2.5$, SD = 2.4) than controls ($M = 5.5$, SD = 3.7).

HADS-A levels were significantly higher in women for both cases and controls. When analyzing single symptoms separately, anxiety levels were significantly higher in women experiencing from sleep onset insomnia (t[731] =1.9, P= .049) and maintenance insomnia (t[761.2] =4.6, $P < .001$).

The regression results showed that the level of anxiety differed significantly among the types of insomnia symptoms after controlling for sex and age (F[6, 4317] = 43.92, $P < .001$). Table 2 shows the results for Bonferroni-corrected group comparisons. Participants reporting all 3 insomnia symptoms had the highest anxiety score ($M = 6.8$, SD = 4.3), followed in decreasing order by sleep onset insomnia with terminal insomnia ($M = 6.7$, SD = 4.0), sleep onset insomnia with sleep maintenance insomnia ($M = 6.3$, SD = 3.8), sleep onset insomnia only ($M = 5.8$, SD = 3.7), sleep maintenance insomnia with terminal insomnia ($M = 5.6$, SD = 3.4), terminal insomnia ($M = 5.2$, SD = 3.4), and sleep maintenance insomnia only (M = 4.5, SD = 3). Mean anxiety score for maintenance insomnia differed significantly from all other symptoms except terminal insomnia

Table 1
Descriptive statistics by subgroups of symptoms of insomnia.

		Sleep onset (SOI)	Maintenance (MI)	Terminal (TI)	SOI + MI	MI + TI	SOI+ TI	All symptoms	Tot. cases	Controls	Total
n		733	1333	470	516	527	96	642	4317	3616	7933
Female %		72	71.6	62.1	80.8	69.6	80.2	81.9	73.2*	57.9	66.2
Age (y), *M* (SD)		49.2	53.9	57.2	52.4	56.1	58.3	55.4	53.9	45.1	50.2
		(17.8)	(16.3)	(15.2)	(15.3)	(14.2)	(18.1)	(15.4)	(16.2)*	(14.7)	(16.2)
HADS-A M (SD)	Tot.	5.9	4.5	5.2	6.3	5.7	6.5	7	5.6	2.5	4.3
		(3.8)	(3.3)	(3.4)	(3.8)	(3.4)	(3.5)	(4.4)	(3.8)*	(2.4)	(3.6)
	Female	6.0***	4.7**	5	6.4	5.7	6.6	7	5.7	3.9**	4.7**
	Male	5.4	3.9	5.2	5.9	5.6	7.4	6.3	5.1	2.8	3.9

* P value < .001 for case-control comparison.
** P value < .001 for male-female comparison.
*** P value = .049 for male-female comparison.

Table 2
Results for Bonferroni-corrected pairwise comparisons of symptoms of insomnia subgroups for HADS-A scores

Pairwise comparisons		MD	*P* value	95% CI
Onset	Maintenance*	1.3	<.001	[1 to 1.6]
	Terminal*	0.7	.029	[0.2 to 1.1]
	Onset + maintenance	−0.5	.518	[−0.9 to −0.1]
	Maintenance + terminal	0.1	1.0	[−0.2 to 0.5]
	Onset + terminal	−1.0	.324	[−1.9 to −0.1]
	All symptoms*	−1.0	<.001	[−1.5 to −0.6]
Maintenance	Terminal*	−0.6	.028	[−1 to −0.3]
	Onset + maintenance*	−1.8	<.001	[−2.1 to −1.4]
	Maintenance + terminal*	−1.2	<.001	[−1.5 to −0.8]
	Onset + terminal*	−2.3	<.001	[−3.2 to −1.4]
	All symptoms*	−2.4	<.001	[−2.7 to −2]
Terminal	Onset + maintenance*	−1.2	<.001	[−1.6 to −0.7]
	Maintenance + terminal	−0.5	.397	[−1 to −0.1]
	Onset + terminal*	−1.6	.001	[−2.5 to −0.8]
	All symptoms*	−1.7	<.001	[−2.2 to −1.3]
Onset + maintenance	Maintenance + terminal	0.6	.133	[0 to 2.1]
	Onset + terminal	−0.5	1.000	[−1.4 to 0.5]
	All symptoms	−0.6	.149	[−1.1 to −0.1]
Maintenance + terminal	Onset + terminal	−1.1	.133	[−2.1 to −0.2]
	All symptoms*	−1.2	<.001	[−1.6 to −0.8]
Onset + terminal	All symptoms	−0.1	1.000	[−0.9 to 0.8]

Differences in mean values can be considered as effect measure for the pairwise comparisons.[24] MD, mean difference.
* Significant results.

only (Table 2). Other groups significantly different from one another are reported in Table 2.

Results from pairwise comparison of mean anxiety level among insomnia subgroups differed in some cases between men and women (Table S2 of Supplementary Material).

The distribution of insomnia symptoms according to the 4 HADS-A levels is reported in Figure 2.

Analysis of variance results for differences in HADS-A levels among cases, controls, and individuals excluded from the study were significant ($F[2, 18\,470] = 1055.45$, $P < .001$). Post hoc analysis showed that HADS-A mean score for each group significantly differed from one another, with excluded individuals ($M = 3.6$) lying between controls ($M = 2.4$) and cases ($M = 5.5$). Age followed a different trend ($F[2, 18470] = 367.97$, $P < .001$) with excluded participants presenting the highest mean age ($M = 54$), followed by cases ($M = 52$) and controls ($M = 45$). Finally, excluded participants showed a percentage of women significantly higher (73.2%) than the others groups (66.3% in cases and 58% in controls), $\chi^2 = 207.2$, $P < .001$.

Discussion

The aim of the current study was to investigate the level of anxiety across individual and combinations of symptoms of insomnia using data from a large population-based sample. In short, anxiety levels were higher in participants reporting symptoms of insomnia compared to controls. Moreover, anxiety levels differed among symptoms and their combinations.

First of all, we found anxiety levels to be significantly higher in cases than controls. This is in agreement with a systematic review of the literature conducted by Cox et al,[1] who also reported a higher frequency of sleep disturbances among people affected by

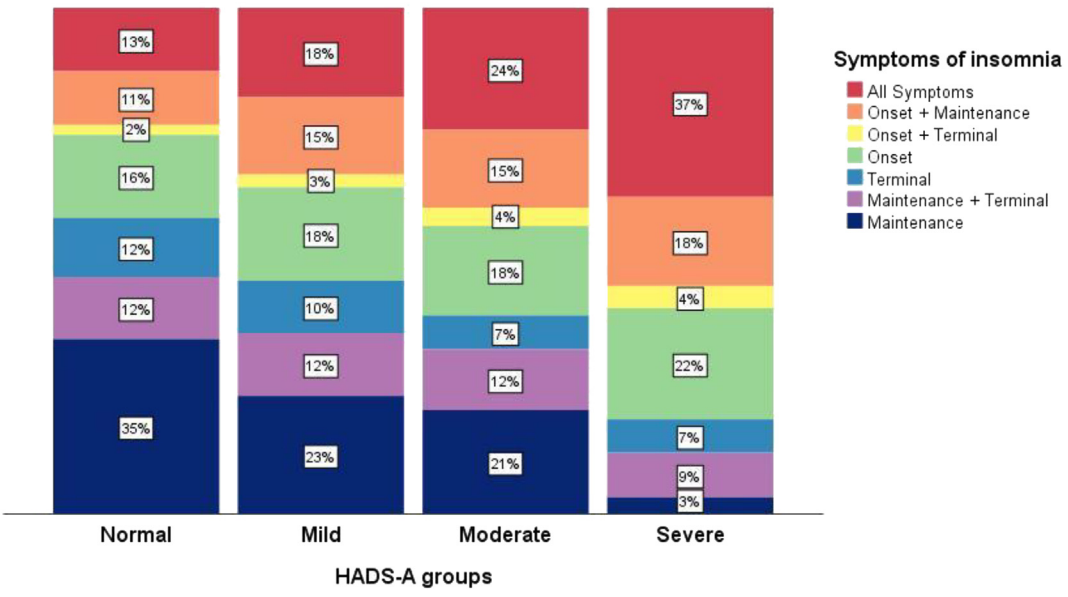

Fig. 2. Distribution of symptoms of insomnia among levels of HADS-A. Normal (0-7), mild (8-10), moderate (11-14), and severe (15-21).

generalized anxiety disorder, panic disorder, and posttraumatic stress disorder than healthy controls.

In our sample, anxiety was significantly lower for maintenance insomnia than terminal insomnia by 0.7 point ($P = .029$) and sleep onset insomnia by 1.4 points ($P < .001$). Studies suggests that the minimal important difference for HADS-A is 1.5 to 2.5[16,17] points; therefore, the difference in anxiety between maintenance and sleep onset insomnia could be considered of borderline importance. To our knowledge, only 3 comparable studies reported anxiety in insomnia symptoms earlier. Cervena et al compared electroencephalographic spectra of people with problems in sleep onset or sleep maintenance and good sleepers and reported mean HADS scores.[9] Taylor et al compared onset, maintenance, and mixed insomnia for demographic and health-related factors including anxiety levels using the State Trait Anxiety Inventory.[10] Finally, a study by Pillai et al[11] compared results of the Beck Anxiety Inventory between subjects reporting sleep onset insomnia and sleep maintenance insomnia. In contrast to ours, none of these studies found a significant difference between individual symptoms of insomnia. These differences might be attributed to the low number of participants in the studies of Cervena et al and Taylor et al ($N = 30$ and $N = 149$) and, generally, to the use of different measurement tools for anxiety and inclusion criteria for the participants.

The differences in HADS-A score we observed could be an expression of unequal levels of stress associated with different symptoms of insomnia. Vgontzas and colleagues[18] proposed that objectively shortened sleep is a more severe insomnia subtype compared to subjective shortened sleep because affected individuals experience both psychological and physiological distress. Difficulties in falling asleep may reduce sleep length, whereas very short nocturnal awakenings may not interfere excessively with the amount of sleep and consequently may not create comparable distress. However, our questionnaire did not investigate the length of these nocturnal awakenings, and therefore, these arguments remain speculative.

In our study, participants experiencing any combinations of 2 symptoms concomitantly showed similar anxiety levels with individuals experiencing sleep onset insomnia alone. Moreover, participants reporting sleep onset insomnia alone or in combination with other symptoms constituted 91% of those who were classified as experiencing severe anxiety according to HADS-A (Fig. 2). This suggests that sleep onset insomnia alone is as severe in terms of anxiety as experiencing several symptoms of insomnia at the same time. This is in line with another finding reported in the aforementioned study by Pillai et al that concomitant sleep onset and maintenance symptoms presented significantly higher anxiety scores than single symptoms.[11]

Participants reporting all 3 symptoms of insomnia had the highest mean HADS-A score, but this was not significantly different from combinations of sleep onset with another symptom. Mean HADS-A score for those who were experiencing all 3 symptoms concomitantly was 4.5 points higher than controls, a whole 21% of the full scale. Subjects reporting all 3 symptoms scored also 2.7 points higher than maintenance insomnia, which is 11.4% of the full scale and the highest difference among the symptoms subgroups. Sleep disturbances appear as symptoms of several severe anxiety disorders, and studies showed that, often, both initiation and consolidation of sleep are affected simultaneously in these conditions.[1] Although HADS is not meant as a diagnostic tool and our results should be interpreted primarily as basic research, the measure of these effects exceeding the reported minimal important difference values points to the possible clinical importance of these findings.

In this study, we find differences in HADS-A levels between men and women presenting maintenance insomnia and sleep onset insomnia. Further studies including sex-specific factors are necessary to clarify the nature of these differences.

In terms of clinical importance, these findings suggest that current therapeutic approaches need further definition and personalization. Several studies have examined to what extent monotherapeutic interventions designed specifically for insomnia or anxiety may improve symptoms of the other disorder. However, a meta-analysis from Belleville and colleagues showed that cognitive behavioral therapy for insomnia only had moderate impact on anxiety levels among insomnia patients and that administration of cognitive behavioral therapy for anxiety alone had limited effects on improving insomnia symptoms.[19] This suggests that a more fruitful approach may be to combine interventions for each condition into a more comprehensive treatment approach. For example, research has shown that anxiety management training aimed at reducing bodily tension has beneficial effects on sleep onset insomnia specifically.[20] As such, a closer characterization of the relationship between insomnia symptoms and anxiety might benefit the design of personalized, more effective therapeutic solutions.

Strengths and limitations

Using data from a large population cohort allowed us to include a high number of individuals for each combination of symptoms. Participants in the HUNT study are Norwegian citizens who all reside in the region of Nord-Trøndelag. This granted us genetic and relative environmental homogeneity in the population. Moreover, uniformity in the Norwegian society in terms of socioeconomic status and health care accessibility reduced the confounder potential of these factors.

The HUNT3 study contained only the 3 aforementioned questions on insomnia. Lack of information about sleep length, sleep satisfaction, and duration of the sleep problems did not allow us to refine the characterization of insomnia any further.

The prevalence of insomnia in the HUNT study,[21] the source of our study sample, was similar to other studies that used similar criteria.[22,23] However, our special selection criteria regarding the absence of snoring, interrupted breathing, and how frequent the symptoms occurred make it difficult to compare the frequency of symptoms in our study to other population studies.

As mentioned before, the effect measure of our results suggests a possible clinical relevancy in these findings. However, the use of HADS as a measure of anxiety calls for careful interpretation.

Conclusions

Different symptoms and combinations of symptoms of insomnia are associated with different levels of anxiety. People with difficulties in falling asleep had the highest anxiety levels both alone and in combination with 1 or 2 of the other symptoms. On the contrary, people with maintenance insomnia had the lowest anxiety levels. We believe investigating this relationship between the principal symptoms of insomnia and anxiety may help refine therapeutic approaches not only for anxiety but also for insomnia.

Conflict of interest

The authors have no conflicts of interest to disclose.

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