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The association of insomnia with future mental illness: Is it just residual symptoms?☆

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ABSTRACT

Objectives: To evaluate whether the prospective association between insomnia and mental illness in the general population remained after controlling for multiple confounders, or whether this represented partly remitted prior mental illness.
Design: Cohort study.
Setting: Australian general population.
Participants: The participants were 10,444 people aged 15 or older in the Household, Income and Labour Dynamics in Australia (HILDA) survey who did not meet K10 criteria for likely mental illness at baseline (2013–14).
Measurements: The prospective associations of insomnia (yes/no) at baseline with mental illness (yes/no) approximately 2 years later (2015–16), determined from scores on the K10, were evaluated using logistic regression. These were then adjusted for potential confounders including sociodemographic factors, physical health and health behaviors, and baseline and past mental health.
Results: Insomnia at baseline increased risk of mental illness onset at two-year follow up (OR 2.23, 95% CI 1.91–2.59, $P < .001$). This relationship was attenuated but still significant after adjustment for confounding variables (OR 1.72 95% CI 1.46–2.02). Accounting for reverse causality from prior mental ill health and baseline symptoms reduced this further but the relationship remained (OR 1.30, 95% CI 1.09–1.55, $P = .003$). This effect appeared more robust among those <65 years of age.
Conclusions: Insomnia has a consistent prospective relationship with mental illness at two-year follow-up. Insomnia did not appear to be simply a symptom of past, or baseline subclinical, mental illness. This supports the specific targeting of insomnia symptoms in selective preventive mental health initiatives, particularly among those under 65 years of age.

Introduction

Thomas Dekker, 17th century dramatist, wrote that sleep is "*that golden chain that ties health and our bodies together*".[1] Multiple studies have since confirmed that disturbed sleep is associated with poor mental as well as physical health.[2–4]

The most common sleep disorder, insomnia, is experienced by an estimated 7% to 20% of adults in Western countries[3,5–10] with similar prevalence estimates being reported in developed Eastern countries.[11,12] The core symptoms of the disorder as defined by international classification systems include difficulty initiating or maintaining sleep, resulting in sleep that is insufficient in quality and/or quantity, and accompanying daytime dysfunction.[13–15]

Among those without current mental ill health, insomnia is associated prospectively with both incidence and relapse of mental disorders. For example, recent meta-analyses indicate that in non-depressed individuals, current insomnia is associated with an approximately two-fold risk of future major depression.[16,17] Large-scale studies also show that in non-anxious populations current insomnia is associated with increased risk of future anxiety disorder[18] or high levels of anxiety symptoms.[19] Given the ubiquity of insomnia symptoms across psychiatric disorders, it has been suggested that future research considers a preventive role of insomnia treatment for mental ill-health.[16] However, it is possible that rather

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than causing future mental illness, alternative explanations may underlie the apparent prospective relationship.

As well as predicting future incidence of depression, there is also evidence that insomnia increases the risk of relapse following remission.[20–23] This is significant, as sleep disturbance is one of the most common residual symptoms of depression. For example, approximately 70% of participants with remitted depression following the large-scale STAR*D trial continued to experience sleep disturbance.[24] Insomnia also appears to be associated with relapse of PTSD,[25,26] though this is not a consistent finding.[27] Thus this association may reflect a partly resolved prior episode with the insomnia being a residual symptom, that is, reverse causality.

Baglioni et al.[16] have expressed that there is a need for future studies to assess the prospective relationship between sleep and mental illness controlling rigorously for related confounders, including alcohol use, somatic and psychiatric illness, and medication status. While numerous studies have explored the association of insomnia and mental illness, there is substantial variability between which confounders are taken into account.[17] Importantly few have controlled for both past and current mental health as covariates in analyses,[28–34] and in such studies other important demographic or physical health variables have been omitted. Finally studies specifically of mental ill health or sleep may induce response or selection biases overinflating associations. The current study seeks to address these three issues together by using a large multi wave nationally representative panel survey with very high response rates which has income and employment as its primary focus, yet ascertains both sleep and mental health, and a very broad range of potential confounders of this association.

Aims

To address the identified gap and recommendations, we aimed to evaluate prospective associations between insomnia and onset of mental illness among those with good mental health, using a dataset that allowed for addressing multiple potential confounders.

Participants and methods

Data

Data for this study were obtained via the ongoing Household, Income and Labour Dynamics in Australia (HILDA) panel survey.[35–37] Since 2001 this household-based panel study has annually collected information about labour market dynamics, economic and personal well-being, and family life. The survey employs a multi-stage sampling approach, resulting in a nationally representative sample of households (the sampling unit was the household). Selected households were sent information via mail, and later invited to participate directly by interviewers. The reference population for wave 1 consisted of all residents living in private dwellings in Australia, excluding small groups such as short-term visitors.[37] At wave 1 (2001–02), 19,914 individuals comprising 7682 households participated in the survey (household response rate 66%, individual response rate 61%). In 2011–12 (Wave 11) a further 5451 persons (2153 households) were added to the cohort (response rate 69%). Baseline (T1) data for the current study were collected in 2013–14 (wave 13), the only timepoint at which sleep was ascertained. Follow up (T2) data were obtained in 2015–16 (wave 15). Wave 14 data (2014–15) was not used for follow-up outcome data as the primary outcome measure for the current study (the Kessler 10 or K10) was not administered at this wave. Data from Wave 7 (2007–8), Wave 9 (2009–10), and Wave 11 (2011–12) were also used, as these were the only pre-baseline waves at which the K10 was administered.

Fig. 1 summarizes the selection of participants into the study, which resulted in a final sample of N = 10,444 participants aged 15 to 96 years. This figure included n = 531 individuals 18 years of age or younger. While adolescents experience distinct biological and circadian rhythm changes related to sleep,[38] the decision was made to include these participants as evidence suggests sleep disturbance is also prospectively associated with mental illness among this group.[39,40]

Interviews were almost all conducted at participants' household address, with a small proportion conducted in other locations according to participants' availability, and< 10% conducted via phone at each wave. The survey consists of two sections. Each member of a participating household over the age of 15 was invited to complete the first section of the survey with an interviewer, and the second section alone (without the interviewer administering items). The second section, referred to as the 'self-completion questionnaire', was comprised of mainly attitudinal questions which respondents may be more comfortable answering alone. After completion, this section was either left with the interviewer, collected by an interviewer at a later date, or returned by mail. A minority of respondents (~19%) completed the second section before the first section. The average duration between T1 and T2 self-completion questionnaire was 23.8 months (SD 1.1; 3.8% missing at least one date). The majority of participants (98.6%) completed the T2 outcome measure between 20 and 28 months after T1.

Mental illness

The Kessler 10 or K10[41] is a validated measure of psychological distress with ability to discriminate between cases and non-cases of mental illness in the general population. The measure asks respondents to indicate how frequently over the four weeks prior to administration they have experienced symptoms such as feelings of hopelessness, depression, amotivation, and nervousness on a 5-point Likert scale. Potential responses include 'none of the time', 'a little of the time', 'some of the time', 'most of the time', and 'all of the time'. The measure demonstrates excellent internal consistency reliability (Cronbach's $\alpha = 0.93$).[41] It is also commonly used among adolescents and has been observed to discriminate between cases and non-cases of major depressive disorder in this population.[42] Based on validation studies and how the K10 is used in general practice,[43,44] scores of 20 or greater were classified as probable cases of mental illness. This cut-off point was found to be associated with sensitivity of 66% and specificity of 92% for identifying people who meet DSM-IV[45] criteria for any anxiety or affective disorder,[43] and is thus a conservative measure. Participants were classified in this manner at T1 and T2.

Insomnia

The key ICSD-3[13] and DSM-V[14] criteria for insomnia include subjective problems with sleep initiation or maintenance at least 3 times per week. Participants reported how frequently over the past month they a) had trouble sleeping because they cannot get to sleep within 30 minutes, and b) had trouble sleeping because they wake up in the middle of the night or early morning. Potential responses on a 5-point scale included 'not during the past month', 'less than once a week', 'once or twice a week', 'three or four times a week', and 'five or more times a week'. In line with diagnostic criteria for insomnia, experiencing either difficulty at least 3 nights per week was categorized as *difficulty initiating or maintaining sleep.*[13] We also took into account the fact that many individuals may experience difficulties initiating or maintaining sleep but have no complaint[13] by incorporating subjective sleep quality into our assessment of insomnia. Participants rated their overall sleep quality during the past month on

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