No rest for the weary: Prevalence, impact and nature of sleep problems among young people at risk of psychosis

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Abstract
Aims: Sleep problems are common in people with a psychosis-spectrum diagnosis and are associated with worse psychotic symptoms and lower quality of life. Sleep problems are also frequent in individuals at a clinical high risk for psychosis (CHR-P) however, less is known about the prevalence and association with symptoms in this population. This study investigates the prevalence of sleep problems within CHR-P individuals and the associations with attenuated positive symptoms, transition to psychosis, time to transition to psychosis and functioning.

Methods: The clinical records interactive search (CRIS) tool was used to carry out a retrospective study of 795 CHR-P individuals. Sleep problems, subsequent psychotic diagnoses, attenuated positive symptoms and Health of The Nation Outcome Scale scores were extracted. Regression models were used to examine the association between sleep problems and clinical outcomes.

Results: 59.5% of CHR-P individuals experienced sleep problems. Perceptual abnormality severity (OR = 1.24, 95% CI = 1.05–1.48) and frequency (OR = 1.31, 95% CI = 1.08–1.58) as measured by the Comprehensive Assessment of At-Risk Mental State interview, predicted sleep problems. Sleep problems were not associated with transition to psychosis; however, they were significantly associated with a shorter time to transition in individuals who developed psychosis (HR = 1.4, 95% CI = 1.05–1.88) and higher follow-up Health of the Nation Outcome Scale scores (MD = 2.26, 95% CI = 0.55–3.96).

Conclusions: The high prevalence of sleep problems, along with the association with positive symptoms and worse functioning, highlights the need for effective sleep interventions in this population. Further research is needed to better understand the relationship between sleep problems and transition to psychosis.

Keywords
psychotic disorders, risk factors, sleep, sleep deprivation, young adult
INTRODUCTION

Sleep problems are highly prevalent in people who have experienced psychosis (Lunsford-Avery et al., 2015), with reports of up to 80% of people with a schizophrenia diagnosis (Cohrs, 2008) and 78.8% of people who have experienced a first episode of psychosis (FEP; Ma et al., 2018). Evidence suggests an association between disturbed sleep and the occurrence of positive and negative psychotic symptoms in populations with schizophrenia spectrum diagnoses (Afonso et al., 2014; Blanchard et al., 2020). Along with distressing unusual experiences, sleep problems have also been independently associated with poorer quality of life (Xiang et al., 2009) and more frequent relapse in people with a diagnosis of schizophrenia (Eisner et al., 2013). Preliminary research suggests that sleep problems may be a predisposing and precipitating factor for the development of psychosis (Ruhmann et al., 2010; Waite et al., 2020).

Clinical high risk for psychosis (CHR-P) refers to individuals who are at a much higher risk of developing psychosis than people in the general population and can be identified using semi-structured clinical interviews such as the comprehensive assessment of at risk mental states (CAARMS; Yung et al., 2005) or the structured interview for prodromal symptoms (SIPS; Miller et al., 2003). Most people with this clinical syndrome will experience distressing attenuated psychotic symptoms which are not frequent and/or severe enough to meet criteria for a psychotic disorder, yet warrant intervention (Fusar-Poli et al., 2013, 2020). Consistent with findings in established psychosis samples, there is convincing cross-sectional evidence showing that distressing attenuated psychotic symptoms are associated with several sleep disturbances (e.g., day/night reversal and shorter sleep duration) in CHR-P populations (Lunsford-Avery et al., 2013; Poe et al., 2017; Reeve et al., 2019), with more severe sleep problems associated with more severe attenuated psychotic symptoms (Goines et al., 2019). In addition, (Ruhmann et al., 2010) found that disturbed sleep at the CHR-P stage was predictive of transition to psychosis within an 18-month period. This is consistent with longitudinal studies that have suggested that disturbed sleep in CHR-P youth predicts worsening symptom severity over time (Lunsford-Avery et al., 2015).

Considering the established role disturbed sleep has in relapses for people who have experienced frank psychosis (Eisner et al., 2013), it is key to further explore the role of sleep problems in the development of psychosis within CHR-P populations using larger sample sizes and longer follow-up periods.

While the current literature has suggested that there is a high prevalence of sleep problems in CHR-P groups (Kaskie et al., 2017; Stowkowy et al., 2020; Tan et al., 2001), this finding needs to be replicated in a larger, non-convenience sample. Establishing the prevalence of sleep problems in the CHR-P population is important in encouraging clinicians to offer targeted evidence-based treatment where sleep problems exist (Kaskie et al., 2017). As such, the present study will extract participant data from the clinical records of the Outreach and Support in South London (OASIS), a large service for CHR-P people (Fusar-Poli et al., 2020).

In addition to determining the prevalence of sleep problems within a CHR-P population, the present study aims to: (1) examine the association between attenuated positive psychotic symptoms (unusual thought content, non-bizarre ideas, perceptual abnormalities and disorganized speech) and sleep problems; (2) examine the association between sleep problems and the development of psychosis; (3) examine the association between sleep problems and time to transition to psychosis; and (4) examine the association between sleep problems and functioning at follow-up.

METHODS

2.1 Study design

This was a retrospective study which used the clinical records of residents living within the boundaries of South London and Maudsley NHS Foundation Trust (SLaM). Clinical records of service users under the care of the OASIS team between 01 January 2007 and 31 December 2017 were retrieved. OASIS is an established outreach community mental health team that offers care to young people aged 14–35 who are identified as being CHR-P and offers psychological, vocational and pharmacological interventions (Fusar-Poli et al., 2020).

2.2 Data source

Clinical records were accessed using the Clinical Records Interactive Search tool (CRIS) developed at SLaM and used at the Biomedical Research Centre Nucleus (Perera et al., 2016). CRIS was first developed in 2006 and holds an inventory of all electronic clinical records in a de-identified format, which is updated in real-time and has been expanding since development (Jackson et al., 2017). Data were extracted from structured and unstructured text fields and used natural language processing (NLP) to extract relevant data.

2.3 Study sample

Individuals accepted into the OASIS caseload between 01 January 2007 and 31 December 2017 were included. Clinical and demographic data was derived from service users’ care episode within OASIS and following their discharge if they continued to access SLaM services. In line with standard CRIS procedure, service user consent was not required for the study. In total, 795 client records were included in the initial dataset.

2.4 Study approval

Project approval was obtained from the CRIS oversight committee (ref number: 18-129).
2.5 | Procedure

2.5.1 | Demographic information

Age at the date of acceptance to OASIS team, gender, ethnicity, and length of treatment within OASIS was collected from structured fields and did not require manual validation.

2.5.2 | Attenuated psychotic symptoms

Positive symptoms were assessed using scores on the CAARMS (Yung et al., 2005). The positive symptoms domain consists of four subscales: Unusual Thought Content (UTC), Non-Bizarre Ideas (NBI), Perceptual Abnormalities (PA) and Disorganized Speech (DS). These are rated in terms of severity and frequency both on a 7-point Likert scale.

CRIS carried out a keyword search whereby all electronic notes that contained the word CAARMS within accepted OASIS cases were reported. These were then manually checked by the first author (E.N.), and any CAARMS positive symptom scores present were recorded. If a service user had more than one set of CAARMS scores, their earliest assessment was recorded.

2.5.3 | Sleep problems

This variable identified individuals experiencing disturbed sleep and/or insomnia using natural language processing and were manually validated. Sleep problems were defined as present when the clinician reported that the service-user was experiencing any form of insomnia or disturbed sleep that happened more than once and was having an impact on the client’s life.

2.5.4 | Transition to psychosis

The earliest psychotic diagnosis that occurred following acceptance to an OASIS team was extracted using structured and unstructured fields and were manually validated by the first author (E.N.) and confirmed with experienced clinicians (S.T., I.A., T.S.) before being included within the analysis. The number of days between acceptance to OASIS and the first psychotic diagnosis was calculated, which represented the time taken to transition to psychosis.

2.5.5 | Health of the nation outcome scale

The Health of the Nation Outcome Scale (HoNOS) is a clinician rated measure which was developed in order to measure and track the mental health and social functioning of people with a mental health disorder, where higher scores indicate more severe difficulties (Wing et al., 1998). The CRIS tool extracted the follow-up HoNOS score for each service-user.

2.5.6 | Cognitive Behavioural therapy

The use of cognitive behavioural therapy for insomnia (CBT-I) was extracted using the structured event field which recorded Cognitive Behavioural Therapy (CBT) sessions. For individuals who received CBT after the date of onset of insomnia, the written report of CBT sessions was examined by the first author (E.N.) in order to identify whether elements of CBT-I were being used.

2.6 | Statistical analyses

All statistical tests were carried out using STATA software version 12. Descriptive statistics were performed for age, gender, days in OASIS treatment, follow-up HoNOS scores, CAARMS scores, time to psychosis diagnosis and proportion of service users that had insomnia and have received one or more CBTi sessions. Regression models were used to test if there were significant associations between gender or age. Ethnicity was not used as a confounder because the data was inconsistently recorded (see Supporting Information).

Regression models were used to assess the association between (1) the severity and frequency of attenuated positive symptoms and sleep problems; (2) the extent to which sleep problems predicted transition to psychosis; (3) time to transition to psychosis; and (4) follow-up HoNOS scores. For aims 1–3, the statistical analyses were carried out across the entire sample (n = 795). For aim 4, only individuals who were in the service for longer than 6 months were analysed (n = 360). As we aimed to examine the association sleep has with follow-up HoNOS scores, we were interested in exploring this among individuals who were in receipt of care from OASIS for a significant time period. In addition, the full sample had a high level of missing data in the follow-up HoNOS scores (n = 449 out of 795 service-users).

For aim (1), sleep problems were the outcome variable and had two levels respectively (0 = no sleep problems, 1 = sleep problems). In order to address aim (1), we performed a logistic regression with attenuated positive symptoms as predictor variables. For aim (2), a logistic regression was used with transition to psychosis (0 = no transition, 1 = transition) as the outcome variable and sleep problems as the predictor variable. This analysis was adjusted for the severity and frequency of positive symptoms. For aim (3), a Cox proportional hazards model was used to look at the impact of sleep problems on survival time, that is, days to transition to psychosis, where sleep problems were entered as the predictor variable. Finally, to address aim (4), a linear regression was performed with follow-up HoNOS as the outcome variable and sleep problems the predictor variable. For every aim, each predictor was first entered into univariate logistic regression models unadjusted for confounders age and gender, and again as multivariate models adjusted age and gender.
RESULTS

3.1 | Sample characteristics

Between 01 January 2007 and 31 December 2017, there were 448 males and 347 females between the ages of 13 and 36 that were under the care of OASIS services. Table 1 contains information on demographic clinical variables for the sample. Following validation, 474 (59.47%) service users met criteria for sleep problems (see Table 1 for further details regarding the breakdown of prevalence between disturbed sleep and insomnia). There were 186 (23.4%) individuals who developed psychosis following the commencement of treatment in OASIS and up until the point of data extraction (07 February 2020).

The association between CAARMS scores and sleep problems.

There were 201 sets of CAARMS scores in the sample (see Table S1). When adjusted for age and gender (Table 2), there were positive associations between perceptual abnormalities frequency scores and sleep problems (OR = 1.31, 95% CI = 1.08-1.58) and perceptual abnormalities severity scores and sleep problems (OR = 1.24, 95% CI = 1.05-1.48). This meant that increasing frequency and severity of perceptual abnormalities predicted a higher likelihood of sleep problems. There were no significant associations between non-bizarre ideas, disorganized speech and unusual thought content with sleep problems (p > .05).

The association between sleep problems and transition to a psychotic diagnosis.

There were no significant associations between sleep problems and transition to psychosis (p > .05, Table 3).

The association between sleep problems and time to transition.

### Table 1 Descriptive statistics for the sample

| Variable | Overall sample (n = 795) | Sample without sleep problems (n = 321) | Sample with sleep problems (n = 474) |
|----------|--------------------------|----------------------------------------|-------------------------------------|
| Female [n (%)] | 347 (43.65%) | 133 (41.43%) | 214 (45.15%) |
| Age [mean (SD)] | 22.72 (4.89) | 22.45 (4.61) | 22.89 (5.06) |
| Days in OASIS service [mean (SD)] | 287.58 (313.80) | 151.69 (245.33) | 373.87 (322.1) |
| Sleep problems [n (%)] | 474 (59.55%) | - | 474 (100%) |
| Insomnia [n (%)] | 175 (22.01%) | - | 175 (100%) |
| Disturbed sleep [n (%)] | 462 (58.11%) | - | 462 (100%) |
| Received CBT-I and had insomnia [n (%)] | 38 (4.78%) | - | 38 (8.02%) |
| Follow-up HoNOS for those in service >6 months [mean (SD)] | 9.48 (5.44) | 7.51 (5.42) | 9.86 (5.37) |
| Transition [n (%)] | 186 (23.4%) | 92 (28.66%) | 94 (19.83%) |
| Days to transition [mean (SD)] | 1349.16 (1099.05) | 1601.75 (1080.43) | 1101.94 (1065.23) |

Abbreviations: CBT, cognitive behavioural therapy; CBT-I, Cognitive Behavioural Therapy for Insomnia; HoNOS, Health of The Nation Outcome Scale; NICE, National Institute of Health and Care Excellence; SD, standard deviation.

### Table 2 Results of adjusted logistic regression predicting sleep problems

| OR (95% CI) |
|----------------|
| Unusual thought content severity | 1.03 (0.86, 1.24) |
| Unusual thought content frequency | 1.04 (0.87, 1.25) |
| Perceptual abnormalities severity | 1.24* (1.05, 1.48) |
| Perceptual abnormalities frequency | 1.31* (1.08, 1.58) |
| Non-bizarre ideas severity | 1.02 (0.85, 1.23) |
| Non-bizarre ideas frequency | 1.07 (0.89, 1.28) |
| Disorganized speech severity | 1.13 (0.89, 1.43) |
| Disorganized speech frequency | 1.09 (0.91, 1.30) |

Abbreviations: CI, confidence interval; DSF, disorganized speech frequency; DSS, disorganized speech severity; HONOS, Health of the Nation Outcome Scale; NBIF, non-bizarre ideas frequency; NBIS, non-bizarre ideas severity; OR, odd’s ratio; PAF, perceptual abnormality frequency; PAB, perceptual abnormality severity; UTCF, unusual thought content frequency; UTCS, unusual thought content severity *p < .05.

Using a Cox proportional hazards model and adjusting for age and gender, a significant association between sleep problems with time to transition was observed (Hazard ratio = 1.4, 95% CI = 1.05–1.88); indicating that the presence of sleep problems significantly reduced the time to transition to psychosis.
TABLE 3: Results of adjusted regression models of sleep problems predicting clinical outcomes

| Outcome                                  | HR (95% CI)        | MD (95% CI)      | OR (95% CI)      |
|------------------------------------------|--------------------|------------------|------------------|
| Sleep problems (days to transition)      | 1.40* (1.05, 1.88) | -                 | -                |
| Sleep problems (follow-up HoNOS; sample of individuals in OASIS >6 months) | 2.26* (0.55, 3.96) | -                 | -                |
| Sleep problems (transition)              | 0.56 (0.22, 1.46)  | -                 | -                |

Abbreviations: CI, confidence interval; HoNOS, Health of The Nation Outcome Scale; HR, hazard ratio; MD, mean difference; OR, odd’s ratio. *p < .05.

The association between sleep problems and follow-up HoNOS scores.

Using linear regression and adjusting for age and gender, there was a significant positive association between sleep problems and follow-up HoNOS scores in the sample of service users in OASIS for longer than 6 months (MD = 2.26, 95% CI = 0.55–3.96, Table 3).

4 | DISCUSSION

The present study aimed to explore the association between sleep problems and positive symptoms, HoNOS scores and transition to psychosis within a large CHR-P sample that were under the care of the OASIS service. Results show that over half of the CHR-P sample experienced sleep problems. Baseline PA was the only positive symptom that was found to predict sleep problems. While sleep problems significantly predicted a shorter time to transition, there was no association between sleep problems and transition to psychosis. Finally, sleep problems were also associated with higher scores on the follow-up HoNOS.

The prevalence of sleep problems in the OASIS sample was 59%, similar to the high prevalence reported in established psychosis (Cohrs, 2008; Ma et al., 2018) and greater than the rates shown in typical young adult populations (Paiva et al., 2015). McDonald et al. (2020) used the CRIS tool to investigate clinical outcomes in adults accessing secondary mental health services and found a 26.6% prevalence of sleep problems, which is substantially lower than what we observed in the present study. The higher prevalence of sleep problems in our sample could be linked to the attenuated psychotic symptoms or to the fact that the complex and thorough nature of OASIS assessments increases the likelihood of clinicians identifying and recording sleep problems.

Baseline PA severity and frequency scores were significantly associated with sleep problems. Attenuated symptoms were separated into four clusters: UTC, NBI, PA and DS, suggesting a specific impact of PA on sleep over any other attenuated symptom. This is consistent with Goines et al. (2019), who used a similar sample size of CHR-P youth and found that sleep problems were specifically associated with hallucinations. While the present study suggests that PA predicts the occurrence of sleep problems, other studies have also highlighted that sleep deprivation can subsequently lead to hallucinations (Waters et al., 2018). Further research is needed to establish the nature and direction of this relationship.

The non-significant association between sleep problems and the development of psychosis was not consistent with previous research (Ruhrmann et al., 2010). However, the current study showed a significant association between sleep problems and days to transition. Our findings may suggest that while sleep problems do not solely lead to psychosis within CHR-P populations, sleep problems exist within a constellation of risk factors that contribute to a transition to psychosis. This is in line with biopsychosocial models of psychosis (e.g., Garety et al., 2000) where psychosis is likely to occur in the context of heightened distress and associated behavioural and physiological consequences (of which poor sleep could be one).

Finally, sleep problems were associated with higher follow-up HoNOS scores, which indicates worse levels of social functioning and greater symptom severity. This is consistent with other studies which show that there is a relationship between sleep problems and overall functioning (Mulligan et al., 2016; Poe et al., 2017). This finding indicates that those with sleep problems experience poorer functioning, and thus sleep difficulties may be an important target for promoting recovery.

4.1 | Strengths and limitations

The present study used a very large cohort (N = 795) of CHR-P service users covering a wide age range of 14–35. The present study accessed anonymised data from everyone that had accessed the OASIS services, which reduced the likelihood of any selection bias that may have occurred in other studies where participants were required to actively enrol in the study.

The study also presents some limitations. Standardized assessments were not employed to identify sleep problems. Therefore, it is possible that the prevalence rate has been overestimated, as some service users may not have met a threshold for sleep problems as defined by structured assessments. It also may have been underestimated, as clinicians may not have assessed or recorded sleep within their consultation. Additionally, while the NLP tool used to extract sleep problems has a high level of performance, this is limited, and it is possible there were more people who reported sleep problems but were not identified by the tool.

It is also important to highlight that this was an observational study where a limited number of variables were examined. As such, there are additional factors that may be confounding our results which we are unaware of. For example, cannabis use has been identified as a risk factor for transition to psychosis and more frequent psychotic relapse (Kraan et al., 2016; Schoeler et al., 2017), however it was not possible to record this in the present study. Additionally,
physical health factors such as obesity can impact sleep quality (Ogilvie & Patel, 2017) which also may have confounded our results. Other risk factors that are commonly associated with transitioning to psychosis, including trauma (Brew et al., 2018), genetic biomarkers (Schneider et al., 2016), and negative psychotic symptoms (Oliver et al., 2020) were not recorded in this study and thus may be an important consideration for future research in this area.

4.2 | Clinical and research implications

The findings of the present study demonstrate the growing need for expanding treatment options in early detection for psychosis services. NICE guidelines recommend the use of CBT-I, which has been found to have benefits when applied within the general population (Trauer et al., 2015). However, there is much less research into its efficacy in the psychosis population. While CBT is often the main form of psychological treatment used in early intervention services, the therapy is usually aimed to target positive symptoms rather than disturbed sleep (Freeman et al., 2015). In the present study, 36% of individuals who had insomnia were found to receive CBT sessions which incorporated elements of CBT-I. Given the potential harmful impact of sleep problems on this population in terms of symptoms and time to transition, incorporating treatment of sleep problems should be a clinical priority. Bradley et al. (2018) conducted a feasibility case-series which found that a trialled CBT-I intervention was effective in improving sleep (large effect size), feasible and acceptable for CHR-P populations. The lack of large-scale research into developing treatments for sleep problems in this population may account for the limited implementation of CBT-I in this setting.

Future studies should continue to explore the relationship between sleep problems and PA, in particular the direction of this relationship in order to determine whether the treatment of attenuated symptoms or the treatment of sleep should be prioritized. The relationship between time to transition and disturbed sleep could be further investigated with the use of longitudinal research and objective measures of sleep. Wearable devices or smartphone apps to monitor sleep would support a more ecologically valid assessment of sleep in this population and has already been used successfully in previous research (Lunsford-Avery et al., 2013; Meyer et al., 2021).

5 | CONCLUSIONS

Sleep problems are highly prevalent among people in the early stages of psychosis. Considering the finding that sleep problems were related to shorter time to transition, it may be that current treatment methods for sleep problems are not effective enough and/or not implemented consistently. Overall, the findings from this study emphasizes the importance of effective and accessible treatment in early intervention services that are able to minimize the harmful impact that sleep problems have on an individual’s quality of life and functioning.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

Research data are not shared.

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