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Sleep abnormalities in different clinical stages of psychosis: A systematic review and meta-analysis

Joëlle Bagautdinova*[1], MSc, Ahmad Mayeli[2]*[†], PhD, James D. Wilson[2], PhD, Francesco L. Donati[2,3], MD, Rebekah M. Colacot[4], BS, Nicholas Meyer[5], MD, PhD, Paolo Fusar-Poli[6,7], MD, PhD, Fabio Ferrarelli[2†], MD, PhD

[1]Department of Neuroscience, University of Pennsylvania, USA

[2]Department of Psychiatry, University of Pittsburgh, USA

[3]Department of Health Sciences, University of Milan, Italy

[4]Department of Neuroscience, University of Pittsburgh, USA

[5]Department of Psychosis Studies, Institute of Psychology, Psychiatry and Neuroscience, King's College London King's College London, UK

[6]Early Psychosis: Interventions and Clinical-detection (EPIC) Lab, Department of Psychosis Studies, Institute of Psychiatry, Psychology & Neuroscience, King's College London, London, United Kingdom

[7]Department of Brain and Behavioral Sciences, University of Pavia, Pavia, Italy

*** Co-first authors**

Joëlle Bagautdinova and Ahmad Mayeli

[†] **Corresponding Authors:**

Fabio Ferrarelli, MD PhD

3501 Forbes Ave, Suite 456, Pittsburgh, PA 15213

Telephone Number: (412) 864-1668

Email: ferrarellif@upmc.edu

Ahmad Mayeli, PhD

3501 Forbes Ave, Suite 715, Pittsburgh, PA 15213

Email: mayelia@upmc.edu

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Key points

- **Question**: Do sleep abnormalities differ in occurrence and severity in clinical high-risk (CHR-P), early psychosis (EP), and chronic psychosis (CP)?
- **Findings**: Sleep disturbance prevalence across 5135 cases was 50% and was comparable across psychosis stages. Comparing 1575 cases and 977 controls revealed poor self-reported sleep quality throughout stages. CP had more arousal vs. CHR-P and reduced spindle duration vs. EP.
- **Meaning**: These findings indicate that a) sleep disturbances are highly prevalent throughout psychosis stages; b) CHR-P, EP, and CP show common and distinct self-reported and objective sleep alterations, thus representing clinical targets and research domains for psychosis.

Abstract

Importance: Abnormal sleep is frequent in psychosis; however, sleep abnormalities in different stages (i.e., Clinical-High-risk for Psychosis (CHR-P), Early Psychosis (EP), and Chronic Psychosis (CP)) have not been characterized.

Objective: Identify sleep abnormalities across psychosis stages.

Data sources: Web of Science and PubMed were searched between inception and June 15th, 2022.

Study selection: Sleep disturbance prevalence studies and case-control studies reporting sleep quality, sleep architecture, or sleep EEG oscillations in CHR-P, EP, or CP.

Data Extraction and Synthesis: This meta-analysis (PROSPERO; CRD42021240503) followed PRISMA 2020 guidelines. Stage-specific and pooled random-effects meta-analyses were conducted, along with the assessment of heterogeneity, study quality, and meta-regressions (clinical stage, sex, age, medication status, psychotic symptoms).

Main Outcomes and Measures: Sleep disturbance prevalence, self-reported sleep quality, sleep architecture (total sleep time, sleep latency, sleep efficiency, NREM and REM stages, number of arousals), and sleep EEG oscillations (spindle density, amplitude, and duration, and slow wave density).

Results: Fifty-nine studies with up to 6710 cases (N= 5135 for prevalence) and 977 controls were included. Sleep disturbance prevalence in pooled cases was 50% (95%CI=40-61%) and it was similar in each psychosis stage. Sleep quality was worse in pooled cases vs. controls (standardized mean difference, SMD=1.00, 95%CI=[0.70-1.30]). Sleep architecture alterations included: higher sleep onset latency (pooled cases SMD=0.96[0.62-1.30], EP SMD=0.72[0.52-

0.92], CP SMD=1.36[0.66-2.05]), higher wake after sleep onset (pooled cases SMD=0.5[0.29-0.71], EP SMD=0.62[0.34-0.89], CP SMD=0.51[0.09-0.93]), higher number of arousals (pooled cases SMD=0.45[0.07-0.83], CP SMD=0.81[0.30-1.32]), higher stage 1 sleep (pooled cases SMD=0.23[0.06-0.40], EP SMD=0.34[0.15-0.53]), lower sleep efficiency (pooled cases SMD=-0.75[-0.98 to -0.52], EP SMD=-0.90[-1.20 to -0.60], CP SMD=-0.73[-1.14 to -0.33]), and lower rapid eye movement density (pooled cases SMD=0.37[0.14-0.60], CP SMD=0.48[0.19-0.77]). Spindle parameter deficits included density: pooled cases SMD=-1.06[-1.50 to -0.63], EP SMD=-0.80[-1.22 to -0.39], CP SMD=-1.39[-2.05 to -0.74]; amplitude: pooled cases SMD=-1.08[-1.33 to -0.82], EP SMD=-0.86[-1.24 to -0.47], CP SMD=-1.25[-1.58 to -0.91]; and duration: pooled cases SMD=-1.21[-1.69 to -0.73], EP SMD=-0.71[-1.08 to -0.34], CP SMD=-1.74[-2.10 to -1.38]. Furthermore, CP had more frequent arousals vs. CHR-P ($z=2.24$, $p=0.02$), and reduced spindle duration vs EP ($z=-3.91$, $p<0.001$).

Conclusion: Sleep disturbances are highly prevalent throughout the course of psychosis, and different psychosis stages show both shared and distinct abnormalities in sleep quality, architecture, and spindles. Thus, sleep should become a core clinical target and research domain from at-risk to early and chronic stages of psychosis.

Introduction

Sleep abnormalities have been observed in psychotic disorders since the dawn of psychiatric literature[1]. Sleep disturbances, such as insomnia, are commonly reported by individuals with chronic psychosis (CP)[2] and are associated with subsequent relapse[3]. Altered sleep often precedes a psychotic episode in early psychosis (EP)[4], and disrupted sleep contributes to predicting transition to psychosis in youth at clinical high risk (CHR-P)[5]. Thus, sleep abnormalities not only co-occur with psychotic symptoms but are also implicated in the development, manifestation, and recurrence of psychosis[6].

Sleep disturbance prevalence, which is usually assessed with self-reported questionnaires (e.g., the Pittsburgh Sleep Quality Index, PSQI)[7] is ~25% in the general population[7,8]. Several studies have reported higher sleep disturbance prevalence in psychosis, although rates vary substantially (21-100%)[9–11] and have thus far never been meta-analyzed in different psychosis stages.

Altered sleep patterns across psychosis stages can also be examined in case control comparisons. Several case control studies have used subjective sleep assessments (e.g., PSQI), which are inexpensive and easy to implement in large clinical cohorts, and have reported worse sleep quality in CHR-P[12], EP[13], and CP[14] vs. healthy comparison groups. Other sleep studies have utilized actigraphy, electroencephalography (EEG), and polysomnography (PSG) to objectively quantify altered sleep characteristics in psychosis. Traditionally, these studies have focused on sleep architecture. Meta-analyses of sleep architecture findings from actigraphy[15] and PSG/EEG studies[16–18] revealed shorter total sleep time and longer sleep onset latency and wake after sleep

onset in CP. PSG/EEG studies also showed decreased deep NREM sleep and reduced latency and duration of REM sleep in these patients[18]. Furthermore, shorter total sleep time and larger wake after sleep onset were reported in EP and CHR-P[19], suggesting that altered sleep architecture is an early feature of psychosis.

More recently, several studies investigated sleep-specific EEG oscillations, including spindles, in psychosis. Deficits in spindle parameters (i.e., density, amplitude, and duration) were established in CP[20] and EP[21,22]. Furthermore, a recent meta-analysis reported reduced spindle density in psychotic disorders that yielded large effect sizes and was associated with disease progression[23].

Systematically investigating the occurrence and severity of sleep abnormalities in CHR-P, EP, and CP may therefore help differentiate sleep dysfunctions associated with chronicity and long-term medication exposure (i.e., observed only/primarily in CP) from those implicated in the manifestation of full-blown psychosis (i.e., occurring first in EP) and from sleep alterations related to vulnerability to psychosis (i.e., present since CHR-P)[24]. This meta-analysis assessed, for the first time, the prevalence of sleep disturbances, along with subjective and objective sleep alterations throughout the course of psychosis, including CHR-P, EP, and CP.

Methods

This meta-analysis followed the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) 2020[25] guidelines. The protocol was registered in PROSPERO (CRD42021240503).

Inclusion and exclusion criteria

For inclusion, studies had to be published between inception and June 15th, 2022, and written in English. Diagnosis of stages of psychosis was established using a recognized clinical assessment tool (see eMethods for *Clinical Stages* definition). Studies needed to provide measures of the prevalence of sleep disturbances in individuals at different psychosis stages and/or quantification of sleep characteristics in these individuals, assessed with PSG, EEG, actigraphy, or self-reports. Inclusion and exclusion criteria are explained in greater detail in the eMethods.

Search strategy

One author (JB) performed the literature search on the Web of Science and PubMed from inception until June 15th, 2022. The description of study search terms is provided in the eMethods. A manual search of the references of included articles and of relevant prior reviews/meta-analyses were also performed.

The eMethods contain details on study selection and data extraction.

Methodological quality appraisal

Quality appraisal was assessed using the Agency for Healthcare Research and Quality (AHRQ)[26] methodology checklist for cross-sectional/prevalence studies. For additional details, see eMethods.

Statistical analysis

Sleep disturbance prevalence was evaluated in three distinct analyses: 1) a pooled cases analysis of sleep disturbance prevalence aggregating all psychosis stages; 2) a stage-specific cases analysis of sleep disturbance; and 3) a moderator analysis comparing clinical stages with one another. We also performed a secondary analysis in a subgroup of studies assessing insomnia. Sleep disturbance prevalence effect sizes were analyzed as logit transformed values, quantifying the log odds of sleep disturbance.

Sleep architecture and oscillatory alterations were evaluated in three different analyses: 1) a pooled case-control comparison of each sleep variable aggregating all psychosis stages; 2) a stage-specific case-control analysis of sleep abnormalities; and 3) a moderator analysis comparing clinical stages with one another. Sleep architecture and sleep oscillatory parameters were analyzed as standardized mean differences across groups using the Hedges' g statistic[27]. For all hypothesis testing, we used two-sided tests with statistical significance at the $P<.05$ level. A random effects linear regression model was fitted for each sleep parameter, and calculated effect sizes were weighted according to inverse variance to account for the variability of each study[28]. Meta-analysis models were estimated using restricted maximum likelihood estimation using the *rma* function in the R *metafor* package in R software v. 4.1.0 (method = "PLO" for prevalence analyses; method = "SMD" for case-control comparisons).

The recovery of missing or partial data from studies and the assessment of study heterogeneity using funnel plots, Cochran's Q statistic[29], I^2 statistic[30] and Egger tests[31] are further discussed in the eMethods.

Moderator analyses were conducted to assess the influence of clinical stage (i.e., CHR-P, EP, and CP), age (i.e., mean age across the study), sex (i.e., proportion of males in the study), antipsychotic medications (i.e., proportion of each study sample taking antipsychotics) and positive and negative symptoms severity on sleep parameters using linear mixed effect meta-analysis models. For each sleep parameter, we regressed the differences between patient and control groups from the available sample on each moderator variable. For prevalence, we regressed the log odds of sleep disturbances on each moderator variable. To further investigate the interactions of age, sex, and medication with staging, we applied linear mixed effect models regressing sleep parameter differences on age, sex, medication, and positive and negative symptom severity moderator variables for each stage separately. A threshold of $P<0.017$ was used to establish statistical significance after correcting for multiple comparison for three explanatory variables (i.e., sex, age, and proportion medicated) using Bonferroni correction. We also examined the effects of psychotic symptoms (i.e., Positive and Negative Syndrome Scale [PANSS]), and a Bonferroni corrected P threshold of 0.025 was used to establish statistical significance.

Results

The initial search yielded 7418 records (Figure 1). After removing duplicates, 4863 publications were screened, resulting in 236 studies considered for full-text review. Twelve additional articles were identified through reference checking. After a full-text review, 59 articles were included, with 21 studies assessing sleep disturbance prevalence in 5135 patients (eTable 1) and 39 studies measuring sleep alterations subjectively (e.g., sleep quality) and/or objectively (e.g., sleep architecture and sleep oscillatory measures) in 1575 patients and 977 controls (eTable 2).

Prevalence of sleep disturbances and insomnia

The pooled (i.e., combined CHR-P, EP and CP) prevalence of sleep disturbances was 50% across clinical stages (95% CI 40% to 61%, Q = 611.28, df = 20, Figure 2A). Stage-specific analyses yielded a sleep disturbance prevalence of 54% in CHR-P (95% CI 40% to 67%, Q = 13.66, df = 3), 68% in EP (95% CI 32% to 90%, Q = 21.2, df = 3), and 44% in CP (95% CI 32% to 57%, Q = 432.73, df = 12, Figure 2A); eFigure 1 shows forest plots of individual studies. Furthermore, prevalence of insomnia as the primary sleep disturbance was 34% (95% CI 24% to 45%) of pooled cases, 48% (95% CI 37% to 59%) of EP, and 27% (95% CI 20% to 35%) of CP (Figure 2B, see eFigure 2 for individual studies forest plot). Moderator analysis yielded no sleep disturbance or insomnia differences between clinical stages (eTable 3).

Standardized mean differences in sleep quality

Sleep quality was assessed comparing total PSQI scores between clinical and control groups. Results indicated a significant SMD in pooled cases versus controls (SMD [95% CI] = 1.00 [0.70, 1.30], $P < 0.001$). Each clinical group showed poorer sleep quality compared to controls (CHR-P vs control: SMD [95% CI] = 1.25 [0.83, 1.67], $P < 0.001$; EP vs control: SMD [95% CI] = 1.17 [0.33, 2.01], $P = 0.006$; CP vs control: SMD [95% CI] = 0.65 [0.4, 0.89], $P < 0.001$;

Figure 3, see eFigure 3 for forest plot of individual studies). Moderator analysis revealed no PSQI scores differences between different clinical stages (eTable 3).

Standardized mean differences in sleep architecture

Pooled cases had higher effect sizes for sleep onset latency (SMD = 0.96 [0.62, 1.30], P < 0.001), wake after sleep onset (SMD = 0.50 [0.29 , 0.71], P < 0.001), number of arousals (SMD = 0.45 [0.07, 0.83], P = 0.019), Stage 1 NREM sleep (SMD = 0.23 [0.06, 0.40], P = 0.008), and REM density (SMD = 0.37 [0.14, 0.60], P = 0.002) vs. controls. Conversely, effect sizes were lower in pooled cases vs control groups for sleep efficiency (SMD = -0.75 [-0.98, -0.52], P < 0.001) and slow wave sleep (SMD = -0.24 [-0.44, -0.03], P = 0.023). Furthermore, total sleep time, Stage 2 sleep, and REM latency did not differ between groups (Figure 4; eFigures 4-13 contain forest plots of studies for each sleep architecture variable).

Stage-specific case-control comparisons revealed no sleep architecture differences in CHR-P vs. controls. EP had higher sleep onset latency (SMD = 0.72 [0.52, 0.92], P < 0.001), wake after sleep onset (SMD = 0.62 [0.34, 0.89], P < 0.001), and Stage 1 (SMD = 0.34 [0.15, 0.53], P < 0.001), along with lower total sleep time (SMD = -0.56 [-0.99, -0.12], P = 0.012) and sleep efficiency (SMD = -0.90 [-1.20, -0.60], P < 0.001) compared to controls. CP showed higher sleep onset latency (SMD = 1.36 [0.66, 2.05], P < 0.001) and wake after sleep onset (SMD = 0.51 [0.09, 0.93], P = 0.018), combined with lower sleep efficiency (SMD = -0.73 [-1.14, -0.33], P < 0.001) vs. controls. CP also showed more arousals (SMD = 0.81 [0.30, 1.32], P = 0.002) and REM density (SMD = 0.48 [0.19, 0.77], P = 0.001) compared to controls. Moderator analysis revealed more frequent arousals in CP compared to CHR-P (z = 2.24, p = 0.02, eTable 3).

Standardized mean differences in spindle and slow wave parameters

Pooled cases showed lower spindle density (SMD = -1.06 [-1.50, -0.63], P < 0.001), spindle amplitude (SMD = -1.08 [-1.33, -0.82], P < 0.001), and spindle duration (SMD = -1.21 [-1.69, -0.73], P < 0.001, Figure 5) compared to controls. Stage-specific case-control comparisons revealed that spindle parameters were lower in both EC and CP relative to controls (Figure 5, see eFigures 14-16 for forest plots of individual studies). Furthermore, moderator analysis showed no differences between EP and CP in spindle density or amplitude (eTable 3) but lower spindle duration in CP compared to EP (z = - 3.91, p < 0.001).

Finally, slow wave density was not altered in patient groups relative to controls (Figure 5; eFigure 17 contains a forest plot of individual studies for slow wave density).

Supplementary Materials contain results for meta-regressions accounting for medication, age, sex, and positive and negative symptoms (eResults and eTables 4-8), study heterogeneity and publication bias (eResults, eFigure 18), study quality appraisal (eTables 9-10) and the PRISMA 2020[25] checklist (eTable 11).

Discussion

This meta-analysis investigated sleep abnormalities across clinical stages of psychosis and identified both uniformly present and stage-specific sleep disruptions.

Sleep disturbance prevalence is consistently high throughout psychosis stages

Sleep disturbance prevalence has been commonly found to be higher in psychosis compared to the general population[7,8], although prior studies reported a variable incidence (21-100%)[9–11]. Here, we established that sleep disturbances were present in 50% of pooled clinical cases, with similar prevalence in different psychosis stages, including at-risk individuals. This suggests that sleep disturbances are not only present throughout the course of psychosis, including before the manifestation of a psychotic episode, but are also consistently high in each psychosis stage, thus representing a critical issue that should be addressed in these individuals.

Sleep quality is poor throughout stages of psychosis

Case-control comparisons of self-reported sleep quality indicated poorer subjective sleep quality in pooled cases and in each clinical stage. Therefore, in addition to sleep disturbances being common, the intensity of perceived sleep distress is also more severe throughout the course of psychosis, including CHR-P, corroborating prior meta-analyses of sleep quality in CHR-P[9,19]. Notably, in CHR-P poorer sleep quality leads to worse negative symptoms[33] and contributes to predicting transition to psychosis[5]. Together, these findings expose the need to address subjective sleep complaints throughout the course of psychosis, even in the at-risk stage. It would therefore be important for primary care and mental health providers to systematically screen for sleep disturbances and to promote sleep hygiene practices (e.g., abstaining from caffeine, nicotine, and

alcohol near bedtime, avoiding napping, and maintaining regular sleep and rise times and exposure to daylight) in prodromal individuals.

Shared and distinct sleep architecture alterations are present in EP and CP but not in CHR-P

Consistent with prior meta-analyses[15–18], case-control comparisons of sleep architecture revealed increased sleep onset latency, wake after sleep onset, number of arousals, Stage 1 sleep and REM density, along with lower sleep efficiency and slow wave sleep in pooled clinical cases.

Prior work furthermore suggested the presence of specific sleep alterations in early stages of psychosis[10,19]. However, comparisons from at-risk to chronic stages had thus far not been performed. Here, stage-specific case-control comparisons showed that sleep architecture abnormalities were absent in CHR-P and driven by EP and CP stages. Altered sleep characteristics shared among EP and CP included increased sleep onset latency, increased wake after sleep onset, and reduced sleep efficiency. These findings are consistent with insomnia, as well as other disturbances including circadian phase delay, which is supported by recent studies reporting an association between evening chronotype in at-risk [34] and full-blown psychosis[35]. Together, these results suggest that difficulties in initiating and maintaining sleep first occur in full-blown psychosis and remain relatively stable throughout the course of the disorder, as none of the measures worsened in CP vs. EP.

EP also showed a reduction in total sleep time and a higher percentage of Stage 1 sleep, a pattern that was not observed when comparing other clinical stages to their respective control groups. A plausible interpretation of these findings is that individuals in the early course of psychosis suffer from considerable sleep loss and overall shallower sleep, a pattern that is furthermore

corroborated by the higher rates of insomnia in EP found in this study. Sleep disruptions in these individuals are also likely involved in psychotic symptomatology, where psychotic experiences worsen sleep and sleep exacerbates psychotic symptoms[6,36]. From a treatment perspective, early-course patients may therefore benefit from routine insomnia screening and targeted sleep interventions, including cognitive-behavioral therapy for insomnia (CBT-I), which is effective in ameliorating difficulties in initiating and maintaining sleep[37,38].

CP was the only clinical group with more arousals and increased REM density compared to controls. Higher REM density has been associated with increased suicidality in psychotic patients[39], and pharmacological reviews indicated that antipsychotic medications can enhance REM density, although effects vary between antipsychotic compounds[11,40]. Weight gain is a frequent side effect of long-term antipsychotic treatment[41] and has been associated with sleep apnea in schizophrenia[42]. Brief awakenings can help restore airflow in such conditions, which may account for the increased frequency of arousals in CP. Moderator analyses further indicated that CP had more arousals compared to CHR-P and that the number of arousals was significantly affected by medication ($p=0.001$), above and beyond disease effects ($z=-3.01$ for medication vs. $z=2.37$ for pooled cases vs. controls). Altogether, these findings indicate that the effects of antipsychotic medications on sleep should be closely monitored, especially in CP, and proper medication adjustments (e.g., decrease medication doses, switch to a different compound) should be considered based on their impact on these sleep patterns.

Sleep spindles, but not slow waves, are severely altered in EP and CP

Meta-analyses of sleep oscillations revealed no alteration in slow wave parameters in clinical cases vs. controls. In contrast, decreased spindle density, spindle amplitude, and duration were observed in pooled cases vs. controls. Stage-specific analyses further indicated that these deficits were present in both EP and CP and yielded some of the largest effect sizes in case-control comparisons (z=-4.93 to -8.31). Of note, spindle measures could not be assessed in CHR-P, as only one study reported spindle measures in this group[43]. Moderator analyses further indicated that CP patients showed a more pronounced reduction of spindle duration compared to EP. Worsening of spindle deficits in chronic stages of psychosis were also reported by a recent meta-analysis on sleep spindles[23], although the clinical groups (schizophrenia, first-episode psychosis, and familial risk) and spindle measure (spindle density) only partially overlapped with our study. Furthermore, our moderator analyses revealed considerably larger effect sizes in spindle measures for case-control comparisons (z=-4.93 to -8.31) relative to the effect sizes for the proportion medicated (z=-1.14 to -2.13), and prior studies have consistently shown an absence of correlation between antipsychotic medication and spindle deficits in chronic patients[44,45]. Together, these findings indicate that spindle deficits are unlikely to be related to antipsychotic medications and may represent a neurophysiological biomarker that could be used to monitor the course of psychotic disorders. Furthermore, given increasing evidence for an association between spindle deficits and clinical and cognitive dysfunction in individuals with psychosis[24,46], spindles may represent a promising target for novel treatment interventions. In this context, non-invasive brain stimulation has shown promise to restore sleep oscillations, including spindles[47].

Limitations

The current meta-analysis presents some limitations. First, while included studies were selected based on comparable sleep assessment tools, substantial variability in across-study methodology remained. This was most pronounced in sleep disturbance prevalence studies, as sleep disorders were assessed with established diagnostic tools (e.g., DSM criteria for insomnia) in only one study[48]. Similarly, across-study methods employed to measure sleep oscillations varied considerably (e.g., manual vs. automated spindle detection, 2-256 electrodes). Notwithstanding this methodological variability, we reported robust, consistent findings, especially regarding spindle deficits in clinical vs. control groups. Second, a few of the included studies were rated as "poor" (N=2), and several were rated as "weak" (N=26). However, the quality of most of these studies was "good" (N=27) or "excellent" (N=5). Third, some analyses had limited statistical power. Specifically, pooled sample sizes of clinical groups included larger samples in CHR-P and CP individuals in prevalence studies, with relatively few prevalence studies in EP. Conversely, for sleep quality and architecture studies, CHR-P sample sizes were smaller compared to EP and CP, indicating that objectively measured sleep is understudied in at-risk populations. The same applied to sleep spindles, which were reported in only one study in CHR-P[43]. Fourth, due to insufficient data availability, spindles were not stratified into fast and slow spindles, although some evidence suggests that distinct alterations in these two types of spindles may occur in psychosis[49] (see eDiscussion). Similarly, while acute psychosis is likely associated with specific sleep alterations[50,51], insufficient data was available to incorporate this factor in the current meta-analysis. Fifth, the sleep assessments presented here were based on cross-sectional data rather than on longitudinal evaluations. Nonetheless, this meta-analysis represents the most

comprehensive effort to date to delineate sleep abnormalities along the course of psychosis, from at-risk to chronic stages.

Conclusion

This study demonstrates that sleep disturbances are highly prevalent throughout the course of psychosis and that different stages of psychosis show both shared and distinct abnormalities in sleep quality, sleep architecture, and sleep spindle parameters.

Altogether, these findings indicate several prospective research directions. To begin with, future studies should use standardized, validated tools to report the prevalence of well-established sleep disorders, as these are common in psychosis but have been rarely assessed in specific clinical stages of psychosis. Moreover, longitudinal sleep studies following at-risk populations through illness stages are necessary to further characterize the interplay between sleep abnormalities and psychosis. To achieve this, research efforts should move beyond conventionally assessed sleep measures and evaluate different sleep patterns using emerging mobile technologies to assess sleep in the home environment[3]. Future work is also needed to further delineate sleep alterations specific to acute and remitted psychosis, as well as the impact of psychotic symptoms severity. Additionally, future studies should better understand the role of antipsychotic medications and different medication types throughout different stages of psychosis. Finally, given the pervasive spindle alterations in EP and CP, an important future direction involves examining spindle properties from CHR-P[52] to CP stages to determine whether spindle alterations may represent risk/susceptibility, monitoring, and/or prognostic biomarkers for psychosis. In doing so, studies should differentiate between fast and slow spindles to accurately delineate psychosis-related

386 sleep alterations. Findings from these studies will help establish sleep as a core clinical target and
387 research domain from prodromal to early and chronic stages of psychosis.

Author Contributions

***Concept and design*:** Fabio Ferrarelli, Ahmad Mayeli, and Joëlle Bagautdinova.

***Acquisition, analysis, or interpretation of data*:** All authors.

***Drafting of the manuscript*:** Joëlle Bagautdinova, Ahmad Mayeli, James D. Wilson, Francesco L. Donati, Fabio Ferrarelli.

***Critical revision of the manuscript for important intellectual content*:** Nicholas Meyer, Paolo Fusar-Poli, and Fabio Ferrarelli.

***Statistical analysis*:** Ahmad Mayeli, James D. Wilson, Rebekah M Colacot, and Nicholas Meyer

***Obtained funding*:** Fabio Ferrarelli.

Administrative, technical, or material support: James D. Wilson, Nicholas Meyer, and Fabio Ferrarelli.

Supervision: Fabio Ferrarelli.

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Conflicts of interest

The authors have no conflicts of interest to declare that are relevant to the content of this article.

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Figure Legends

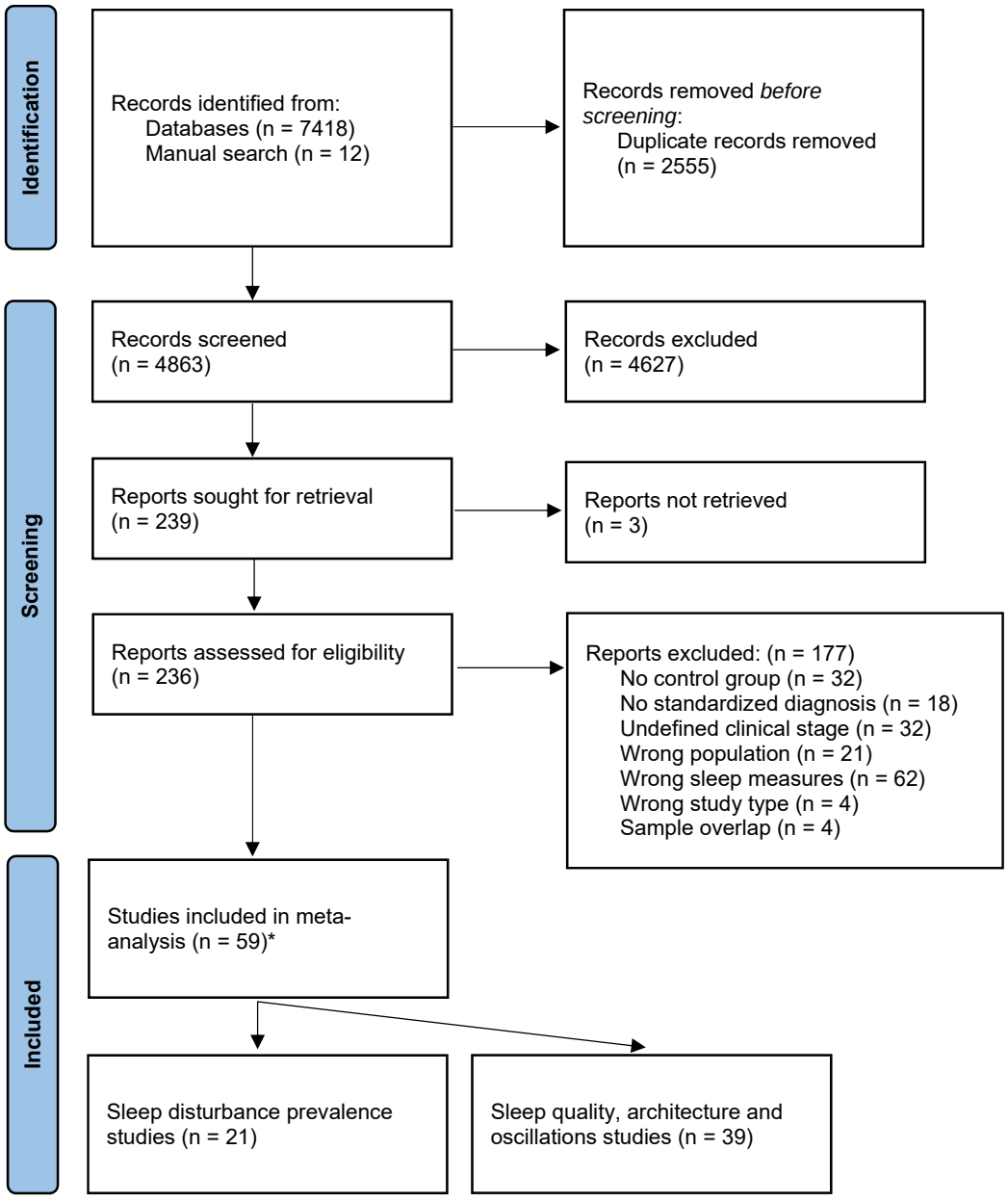
Figure 1. PRISMA workflow of study selection. *Of note, one study[32] was included in both the prevalence and sleep architecture analyses.

Figure 2. Forest plots of A) Prevalence of sleep disturbance and B) Prevalence of insomnia in the pooled clinical groups and each psychosis subgroup. Logit transformation was applied for analysis and the final pooled logit was back transformed to proportions for ease of interpretation of the forest plots.

Figure 3. Summary of standardized mean differences in sleep quality as measured by total PSQI in the pooled clinical groups and each psychosis subgroup.

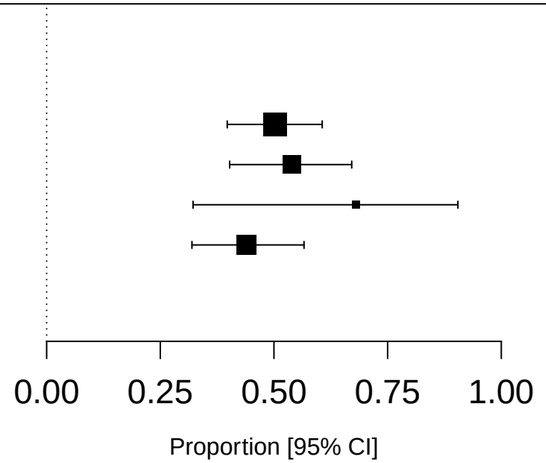
Figure 4. Summary of standardized mean differences for sleep architecture parameters in pooled clinical groups and in each clinical subgroup. Significant ($p < 0.05$) effect sizes between two subgroups are marked with an asterisk.

Figure 5. Summary of standardized mean differences for sleep spindle parameters and slow-wave density in pooled cases and in each clinical subgroup. Significant ($p < 0.05$) effect sizes between two subgroups are marked with an asterisk.


Identification
Records identified from:
Databases (n = 7418)
Manual search (n = 12)
Records removed *before screening*:
Duplicate records removed
(n = 2555)
Screening
Records screened
(n = 4863)
Records excluded
(n = 4627)
Reports sought for retrieval
(n = 239)
Reports not retrieved
(n = 3)
Reports assessed for eligibility
(n = 236)
Reports excluded: (n = 177)
No control group (n = 32)
No standardized diagnosis (n = 18)
Undefined clinical stage (n = 32)
Wrong population (n = 21)
Wrong sleep measures (n = 62)
Wrong study type (n = 4)
Sample overlap (n = 4)
Included
Studies included in meta-analysis (n = 59)*
Sleep disturbance prevalence studies (n = 21)
Sleep quality, architecture and oscillations studies (n = 39)

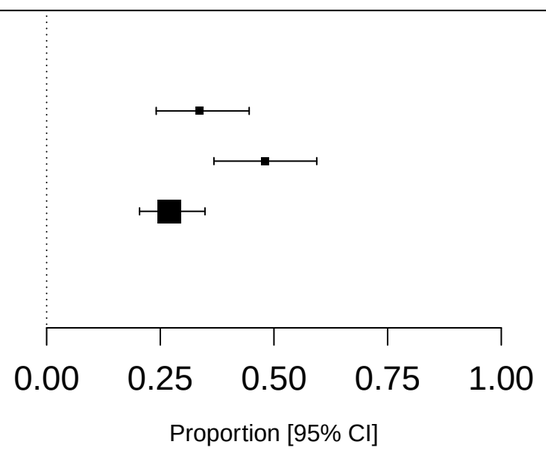
A)

Variable	Number of: Patients	Proportion [95% CI]
Prevalence		
Sleep Disturbance, Pooled Clinical Groups	5135	0.50 [0.40, 0.61]
Sleep Disturbance, CHR−P	1005	0.54 [0.40, 0.67]
Sleep Disturbance, EP	407	0.68 [0.32, 0.90]
Sleep Disturbance, CP	3723	0.44 [0.32, 0.57]

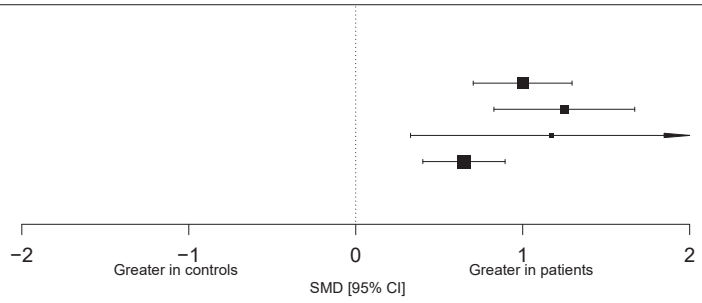


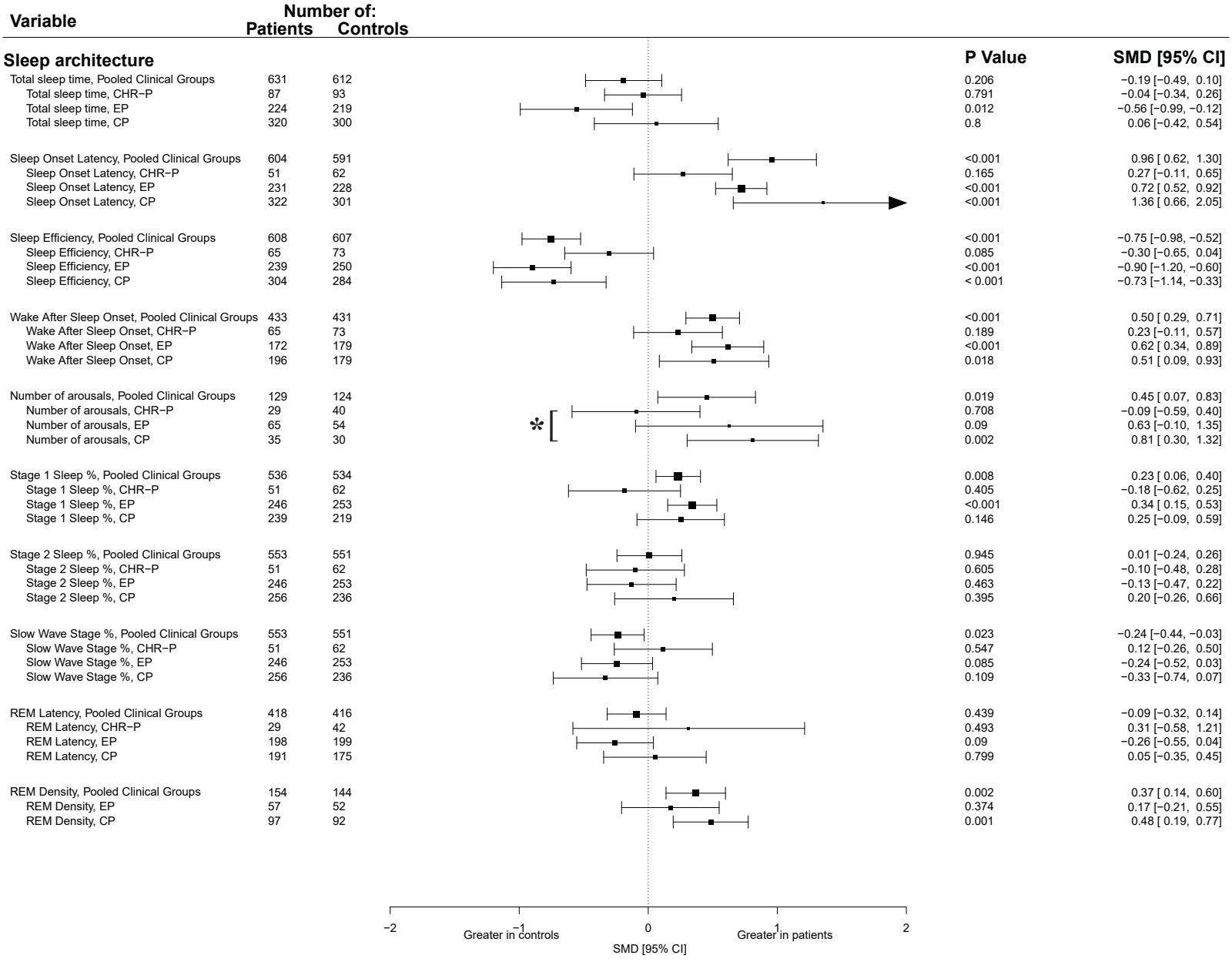
B)

Variable	Number of: Patients	Proportion [95% CI]
Prevalence		
Insomnia, Pooled Clinical Groups	2740	0.34 [0.24, 0.45]
Insomnia, EP	73	0.48 [0.37, 0.59]
Insomnia, CP	2656	0.27 [0.20, 0.35]



Variable	Number of: Patients	Controls	P Value	SMD [95% CI]
Sleep quality				
Total PSQI, Pooled Clinical Groups	972	389	<0.001	1.00 [0.70, 1.30]
Total PSQI, CHR−P	727	146	<0.001	1.25 [0.83, 1.67]
Total PSQI, EP	109	110	0.006	1.17 [0.33, 2.01]
Total PSQI, CP	136	133	<0.001	0.65 [0.40, 0.89]




Variable
Number of:
Patients
Controls
Sleep architecture
P Value
SMD [95% CI]
Total sleep time, Pooled Clinical Groups 631 612 0.206 −0.19 [−0.49, 0.10]
Total sleep time, CHR−P 87 93 0.791 −0.04 [−0.34, 0.26]
Total sleep time, EP 224 219 0.012 −0.56 [−0.99, −0.12]
Total sleep time, CP 320 300 0.8 0.06 [−0.42, 0.54]
Sleep Onset Latency, Pooled Clinical Groups 604 591 <0.001 0.96 [0.62, 1.30]
Sleep Onset Latency, CHR−P 51 62 0.165 0.27 [−0.11, 0.65]
Sleep Onset Latency, EP 231 228 <0.001 0.72 [0.52, 0.92]
Sleep Onset Latency, CP 322 301 <0.001 1.36 [0.66, 2.05]
Sleep Efficiency, Pooled Clinical Groups 608 607 <0.001 −0.75 [−0.98, −0.52]
Sleep Efficiency, CHR−P 65 73 0.085 −0.30 [−0.65, 0.04]
Sleep Efficiency, EP 239 250 <0.001 −0.90 [−1.20, −0.60]
Sleep Efficiency, CP 304 284 < 0.001 −0.73 [−1.14, −0.33]
Wake After Sleep Onset, Pooled Clinical Groups 433 431 <0.001 0.50 [0.29, 0.71]
Wake After Sleep Onset, CHR−P 65 73 0.189 0.23 [−0.11, 0.57]
Wake After Sleep Onset, EP 172 179 <0.001 0.62 [0.34, 0.89]
Wake After Sleep Onset, CP 196 179 0.018 0.51 [0.09, 0.93]
Number of arousals, Pooled Clinical Groups 129 124 0.019 0.45 [0.07, 0.83]
Number of arousals, CHR−P 29 40 0.708 −0.09 [−0.59, 0.40]
Number of arousals, EP 65 54 0.09 0.63 [−0.10, 1.35]
Number of arousals, CP 35 30 0.002 0.81 [0.30, 1.32]
Stage 1 Sleep %, Pooled Clinical Groups 536 534 0.008 0.23 [0.06, 0.40]
Stage 1 Sleep %, CHR−P 51 62 0.405 −0.18 [−0.62, 0.25]
Stage 1 Sleep %, EP 246 253 <0.001 0.34 [0.15, 0.53]
Stage 1 Sleep %, CP 239 219 0.146 0.25 [−0.09, 0.59]
Stage 2 Sleep %, Pooled Clinical Groups 553 551 0.945 0.01 [−0.24, 0.26]
Stage 2 Sleep %, CHR−P 51 62 0.605 −0.10 [−0.48, 0.28]
Stage 2 Sleep %, EP 246 253 0.463 −0.13 [−0.47, 0.22]
Stage 2 Sleep %, CP 256 236 0.395 0.20 [−0.26, 0.66]
Slow Wave Stage %, Pooled Clinical Groups 553 551 0.023 −0.24 [−0.44, −0.03]
Slow Wave Stage %, CHR−P 51 62 0.547 0.12 [−0.26, 0.50]
Slow Wave Stage %, EP 246 253 0.085 −0.24 [−0.52, 0.03]
Slow Wave Stage %, CP 256 236 0.109 −0.33 [−0.74, 0.07]
REM Latency, Pooled Clinical Groups 418 416 0.439 −0.09 [−0.32, 0.14]
REM Latency, CHR−P 29 42 0.493 0.31 [−0.58, 1.21]
REM Latency, EP 198 199 0.09 −0.26 [−0.55, 0.04]
REM Latency, CP 191 175 0.799 0.05 [−0.35, 0.45]
REM Density, Pooled Clinical Groups 154 144 0.002 0.37 [0.14, 0.60]
REM Density, EP 57 52 0.374 0.17 [−0.21, 0.55]
REM Density, CP 97 92 0.001 0.48 [0.19, 0.77]
−2
−1
0
1
2
Greater in controls
Greater in patients
SMD [95% CI]

Variable	Number of: Patients	Controls	P Value	SMD [95% CI]
Sleep spindle and slow wave				
Spindle Density, Pooled Clinical Groups	259	272	<0.001	−1.06 [−1.50, −0.63]
Spindle Density, EP	86	104	<0.001	−0.80 [−1.22, −0.39]
Spindle Density, CP	151	146	<0.001	−1.39 [−2.05, −0.74]
Spindle Amplitude, Pooled Clinical Groups	137	141	<0.001	−1.08 [−1.33, −0.82]
Spindle Amplitude, EP	53	63	<0.001	−0.86 [−1.24, −0.47]
Spindle Amplitude, CP	84	78	<0.001	−1.25 [−1.58, −0.91]
Spindle Duration, Pooled Clinical Groups	143	143	<0.001	−1.21 [−1.69, −0.73]
Spindle Duration, EP	59	65	<0.001	−0.71 [−1.08, −0.34]
Spindle Duration, CP	84	78	<0.001	−1.74 [−2.10, −1.38]
Sleep slow wave				
Slow Wave density, Pooled Clinical Groups	167	147	0.825	−0.05 [−0.48, 0.38]
Slow Wave density, EP	65	59	0.239	−0.21 [−0.57, 0.14]
Slow Wave density, CP	102	88	0.884	0.07 [−0.83, 0.97]