# Supplemental Online Content

Bagautdinova J, Mayeli A, Wilson JD, et al. Sleep abnormalities in different clinical stages of psychosis: a systematic review and meta-analysis. *JAMA Psychiatry*. Published online January 18, 2023. doi:10.1001/jamapsychiatry.2022.4599

This supplemental material has been provided by the authors to give readers additional information about their work.

## eMethods

### *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 had to be established using a recognized clinical assessment tool (see *Clinical Stages* section below). 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. For prevalence studies, the presence of clinically significant sleep disturbances was established using the Pittsburgh Sleep Quality Index (PQSI)[1] using a clinical threshold of > 5 to determine the proportion of "poor sleepers," the Insomnia Severity Index (ISI)[2], or DSM based questionnaires evaluating sleep disturbances. We also screened for papers reporting the prevalence of sleep disorders, including insomnia, obstructive sleep apnea (OSA), narcolepsy, periodic limb movement disorder (PLMD), nightmare disorder, delayed sleep phase disorder, and parasomnia. For PSG studies, sleep stages had to be established using conventional methods (e.g., Rechtschaffen and Kales, 1968[3]; American Academy of Sleep Medicine (AASM) criteria[4]) and measures had to be reported as a single (full or partial) night of recording (i.e., not averaged across multiple nights). Studies were excluded if they were unrelated to psychosis, case reports, comments, expert opinions, books, reviews, meta-analyses, animal studies, clinical trials, or intervention studies. Longitudinal studies were excluded when sleep and clinical assessments were not simultaneously obtained at baseline. Studies reporting quantitative measures of sleep disturbances without a control group were excluded. Similarly, studies were excluded when no demographic information was reported or when the patient group included psychiatric disorders unrelated to the schizophrenia spectrum and other psychotic disorders (e.g., bipolar disorder, major depressive disorder), and sleep data were not reported for schizophrenia and non-schizophrenia spectrum patients separately. Studies on veterans were excluded when participants had comorbid psychiatric disorders. When several studies were performed on the same cohort, we included the study with the largest sample and most appropriate data for the purpose of the meta-analysis.

Of note, the above defined inclusion and exclusion criteria led to the exclusion of a number of older studies, e.g., due to the absence of a standardized diagnostic tool for the diagnosis of mental

illness, a lack of sufficient information to establish clinical staging, and/or the absence of relevant sleep parameters that were considered in the current meta-analysis.

## *Search strategy*

The search was conducted from inception until June 15th, 2022. One author (JB) performed the literature search in Web of Science and PubMed. The following search string was used: ("psychosis risk" OR prodrom* OR "ultra-high risk" OR "clinical high risk" OR "genetic high risk" OR "at risk mental state" OR "CHR-P mental state" OR "basic symptoms" OR "ultra-high risk" OR psychosis OR schizo* OR "psychotic disorder" OR "first episode psychosis") AND (insomnia OR "sleep disturbances" OR "sleep problems" OR actigraph* OR actimet* OR polysomnograph* OR sleep EEG OR "sleep abnormalities" OR "sleep alterations" OR "sleep disorders"). JB, AM, and FD performed an additional manual search of the references of included articles and relevant prior reviews and meta-analyses.

## *Methodological quality appraisal*

Quality appraisal of included studies was assessed independently by two reviewers using the Agency for Healthcare Research and Quality (AHRQ) methodology checklist[5] for cross-sectional/prevalence studies. The checklist contains 11 items, each rated with “yes,” “no” or “unclear”. Articles were classified as "excellent" if they had ten or more items with a yes; "good" when their score was 7-9; "weak" with 4-6; and "poor" for scores from 1-3. In addition, given that some items were non-applicable to a majority of studies (e.g., item 9 regarding missing data and item 11 regarding follow-up), we computed the percentage of “yes” over the total number of answered questions and categorized studies as follows: excellent = 80-100% yes; good = 50-79%; weak = 30-49%; poor = 0-29%. The latter categorization was used to assess study quality so as to not penalize studies for which some questions were irrelevant.

## *Study selection*

After removal of duplicates, two authors (JB and AM) independently screened titles and abstracts and, where relevant, the full text of studies to assess their eligibility. The final study inclusion was reached through consensus and discussion with the last author (FF).

## *Clinical Stages*

**Clinical-High-Risk for Psychosis (CHR-P)**

The CHR-P state was established using Ultra-High Risk psychometric interviews, including the Comprehensive Assessment of CHR-P Mental States (CAARMS)[6] or the Structured Interview for Psychosis-risk Syndromes (SIPS)[7].

**Early Psychosis (EP)**

The EP stage comprised patients with first-episode or early-course schizophrenia spectrum and other psychotic disorders with a mean illness duration of ≤5 years. In the lack of a standard threshold for defining early psychosis, our 5-year cutoff was based on previous literature[8] and on the historical notion of a "critical period" of 5 years after the onset of the disorder[9].The diagnosis was assessed with III, IV, and 5 versions of the Diagnostic and Statistical Manual of Mental Disorders (DSM) or 9, 10 versions of the International Classification of Diseases (ICD).

**Chronic Psychosis (CP)**

The CP stage comprised patients diagnosed with schizophrenia spectrum and other psychotic disorders with a mean illness duration >5 years. The diagnosis was assessed as per the EP stage.

Of note, we included studies in both acute and remitted psychosis, and studying both unmedicated and medicated participants.

## *Data extraction*

Data extraction was performed independently by three different authors (JB, AM, FD). The following variables were extracted: publication year, geographical location, number of participants, age (mean, SD) of participants, sex, psychosis diagnostic tool, clinical stage, medication status, and illness duration. Eligible studies provided measures of either:

- The prevalence of individuals with sleep disturbances and/or insomnia related symptoms.
- A quantification of sleep architecture and sleep oscillatory parameters, including:
    - Total Sleep Time (TST, min), Sleep Onset Latency (SOL, min), Sleep Efficiency (SE, %), Wake After Sleep Onset (WASO, min), number of arousals (events/hour).
    - NREM sleep Stages 1-2 (S1, S2, %), Slow Wave Sleep (SWS, %) or S3 + S4 (%)
    - REM sleep (REM (%), REM latency (REML, min), REM sleep density (number/min), duration until first REM epoch (min)).
    - Sleep spindle (SS) density (number/hour), SS duration (sec), SS amplitude (μV), SS frequency (Hz))
    - Slow Wave density (SW, number/min) and Sigma power ($\mu V^2$ /Hz)

Where relevant, we extracted data on additional measures of interest, including psychotic symptoms severity and cognitive function. For PSG and EEG studies reporting multiple nights of recording, data from the main (e.g., second) night of sleep was extracted for the meta-analysis.

## *Statistical analysis*

**Missing summary statistics and data conversions**

For studies that reported the sleep staging in minutes, we divided sleep stage (minutes) by total sleep time (TST) to calculate the mean in percentage. For converting the standard deviation in minutes to percentage, we used a second-order Taylor approximation of the standard deviation, given by

$$SD_{stage\ x\%} = \sqrt{\left(\frac{m_{stage\ x}}{m_{TST}}\right)^2 \times \left(\left(\frac{SD_{stage\ x}{}^2}{m_{stage\ x}{}^2}\right) + \left(\frac{SD_{TST}{}^2}{m_{TST}{}^2}\right)\right)},$$

where SD is the standard deviation and m is the average.

Furthermore, prior to 2007, the American Academy of Sleep Medicine (AASM) guidelines divided slow-wave sleep into stages 3 and 4. However, the two stages have been combined as "Stage 3" since then. For studies that reported slow-wave sleep as stage 3 and stage 4, we calculated the average slow-wave sleep by summing up the two stages, and for the standard deviation, we used the following equation:

$$SD_{Slow-wave\ sleep} = \sqrt{SD_{Stage\ 3}{}^2 + SD_{Stage\ 4}{}^2}$$

In studies where outcome data were split into two subgroups (either for the clinical group or healthy controls, we calculated the average of each variable for the combined subgroups using weighted means as follows:

$$m_{combined} = \frac{n_{subgroup1} \times m_{subgroup1} + n_{subgroup2} \times m_{subgroup2}}{n_{subgroup1} + n_{subgroup2}}$$

in which n is the number of subjects. To calculate the SD of the combined subgroup, we calculated the pooled standard deviation, given by the following equation:

$$SD_{combined} = \sqrt{\frac{(n_{subgroup1} - 1) \times SD_{subgroup1}{}^2 + (n_{subgroup2} - 1) \times SD_{subgroup2}{}^2}{n_{subgroup1} + n_{subgroup2} - 1} + \frac{(n_{subgroup1} \times n_{subgroup2}) \times (m_{subgroup1} - m_{subgroup2})^2}{(n_{subgroup1} + n_{subgroup2}) \times (n_{subgroup1} + n_{subgroup2} - 1)}}$$

**Study heterogeneity**

Funnel plots were generated for each sleep parameter to visualize study heterogeneity. Hypothesis testing of the Cochran's Q statistic[10] was used to assess the heterogeneity of studies in each sleep parameter. The $I^2$ statistic[11] was utilized to assess the magnitude of heterogeneity. Egger's test[12] was used to assess funnel plot asymmetry.

## eResults

### *Meta-regression of medication, age, sex and psychotic symptoms*

Additional meta-regression analyses were conducted to examine the effects of age, sex, medication and psychotic symptoms severity. Calculation of chlorpromazine equivalents was not possible, given that only a few studies reported this information. Instead, we calculated the percentages of antipsychotic medicated patients in each study and included this as an approximate measure. Caution is therefore warranted when considering medication effects.

Meta-regressions for sex in pooled cases and controls showed that female patients have higher Stage 1 % ($z = 2.60$, uncorrected $p = 0.009$) and lower slow wave sleep ($z = -2.38$, uncorrected $p = 0.02$). Examining the sex effect on each clinical stage separately showed a lower PSQI total score ($z = -2.11$, uncorrected $p = 0.04$) in EP female patients.

Meta-regression of age in pooled cases and controls further showed that increasing age predicts a higher sleep onset latency ($z = 2.88$, $p < 0.001$), lower sleep spindle duration ($z = -3.79$, $p < 0.001$) and lower insomnia prevalence ($z = -2.64$ $p = 0.008$). Subgroup moderator analysis showed that older CHR-P individuals show higher total PSQI scores ($z = 2.23$, uncorrected $p = 0.03$), while older EP patients tend to have increased wake time after sleep onset ($z = 2.58$, $p = 0.01$).

Meta-regression of percent medicated showed that a greater proportion of medicated patients was associated with higher total sleep time ($z = 4.43$, $p < 0.001$), REM latency ($z = 3.54$, $p < 0.001$), sleep efficiency ($z = 3.85$, $p < 0.001$), and slow wave density ($z = 3.4$, $p < 0.001$), as well as lower wake time after sleep onset ($z = -2.82$, $p < 0.001$), number of arousals ($z = -3.01$, $p < 0.001$), spindle duration ($z = -2.13$, uncorrected $p = 0.03$), and spindle density ($z = -2.08$, uncorrected $p = 0.04$). Subgroup moderator analyses further showed that in EP and CP, a higher percentage of medicated patients was associated with higher total sleep time (EP $z = 2.07$, uncorrected $p = 0.04$; CP $z = 3.44$, $p = 0.001$), REM latency (EP $z = 2.06$, uncorrected $p = 0.04$; CP $z = 2.35$, uncorrected $p = 0.02$), sleep efficiency (EP $z = 3.15$, $p = 0.002$; CP $z = 4.77$, $p < 0.001$), and lower wake time after sleep onset (EP $z = -2.16$, uncorrected $p = 0.03$; CP $z = -2.75$, $p = 0.006$). Furthermore, CP was associated with lower Stage 1% ($z = -2.17$, uncorrected $p = 0.03$) and higher Stage 2% ($z = 2.09$, uncorrected $p = 0.04$). All other associations with age, sex, and medication were nonsignificant.

Meta-regression of PANSS positive symptoms severity in pooled clinical cases indicated that more severe positive symptoms were associated with increased total PSQI ($z = 4.84$, $p < 0.001$), reduced

total sleep time ($z = -2.94$, $p < 0.001$), reduced wake after sleep onset ($z = -3.23$, $p < 0.001$) and increased insomnia rates ($z = 1.97$, uncorrected $p = 0.04$). Meta-regression of PANSS negative symptoms in pooled cases showed that negative symptom severity was associated with reduced sleep efficiency ($z = -3.17$, $p < 0.001$), reduced Stage 2 NREM sleep ($z = -2.48$, $p = 0.01$) and reduced spindle duration ($z = -2.67$, $p = 0.01$). All other associations with psychotic symptoms were either nonsignificant or did not have sufficient available data to be analyzed. Subgroup moderator analyses were possible for early psychosis (EP) and chronic psychosis (CP), but only for a subset of sleep parameters. Specifically, out of 17 sleep variables only four (total sleep time, sleep onset latency, sleep efficiency and sleep disturbance prevalence) had enough studies available for positive symptoms in both EP and CP, and three sleep parameters (total sleep time, sleep onset latency and sleep efficiency) were available in both EP and CP for negative symptoms. For these sleep parameters, preliminary evidence suggests that in early stages of psychosis positive symptom severity may shorten total sleep time ($z = -2.9$, $p < 0.001$), while in chronic stages positive symptoms may increase sleep onset latency ($z = 3.36$, $p < 0.001$) and negative symptoms may reduce sleep efficiency ($z = -3.85$, $p < 0.001$). However, due to the limited amount of data currently available, analyses of symptoms severity in different clinical stages remain exploratory for the above-mentioned sleep variables, and unknown for other variables.
Detailed results are reported in eTables 3-8.

### *Study heterogeneity*

eFigure 18 illustrates funnel plots for each of the sleep parameters considered in the study. The figure also includes summaries of heterogeneity and asymmetry. Hypothesis testing of the Cochran's Q statistic was used to assess the heterogeneity of studies in each sleep parameter. Study heterogeneity was high for eleven of the fifteen sleep parameters considered in this analysis (evidenced with large $I^2$ and $p < 0.05$). Three parameters – SOL, prevalence of sleep disturbances, and prevalence of insomnia – had evidence of asymmetry according to Egger's test of asymmetry ($p\_sym < 0.05$).

### *Study quality appraisal*

Studies of sleep disturbance prevalence tended to be of higher quality, with more detailed reporting of population inclusion, assessment period, and patient response rates, resulting in four studies rated as "excellent," nine as "good," seven as "weak," and one as "poor" quality. Among objective sleep architecture and/or sleep oscillations studies, one study rated as excellent, 19 studies rated as "good," 20 studies rated as "weak," and one study rated as "poor" quality. The detailed results are presented in eTables 9 and 10.

**eTable 1: Study characteristics for papers included in the sleep disturbance prevalence analysis.**

| Clinical stage | 1st author, year, country | Diagnostic tool | Illness duration (mean ± SD) | N participants | Age (mean ± SD) | Sex (M/F) | Sleep disturbance prevalence (N, %) | Sleep assessment | Medication status (% medicated) |
|---|---|---|---|---|---|---|---|---|---|
| At-risk | Goines, 2019[13], United States | SIPS | | 740 | 18.5 ± 4.3 | 424/316 | 386 (52.2%) | SIPS G1 item | medicated |
| At-risk | Miller, 2003[14], United States + Canada | SIPS | | 60 | 17.8 ± 4.8 | 39/21 | 22 (36.7%) | SIPS G1 item | medicated (12%) |
| At-risk | Poe, 2017[15], USA | SIPS | | 194 | 20 ± 3.8 | 142/52 | 117 (60.3%) | SIPS G1 item | medicated (32%) |
| At-risk | Waite, 2018[16], United Kingdom | CAARMS | | 11 | 18.3 ± 2 | 5/6 | 9 (81.8%) | Insomnia Severity Index (ISI) | NA |

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|---|---|---|---|---|---|---|---|---|---|
| Early Psychosis | Fekih-Romdhane, 2020[17], Tunisia | DSM-5 | 1.8 ± 1.7 | 54 | 26.8 ± 6.1 | 35/19 | 52 (96.3%) | PSQI | medicated (100%) |
| Early Psychosis | Huang, 2014[18], Taiwan | DSM-IV-TR | | 13 | 18.4 ± 3.6 | 6/7 | 5 (38.5%) | DSM-IV-TR | medicated |
| Early Psychosis | Ong, 2020[19], Singapore | DSM-IV | | 280 | NA ± NA | 142/138 | 176 (62.9%) | PSQI | medicated |
| Early Psychosis | Reeve, 2019[20], UK | DSM-5, ICSD-2 and ICSD-3 | | 60 | 23.7 ± 3.2 | 39/21 | 30 (50%) | Diagnostic Interview for Sleep Patterns and Disorders (DISP) | medicated (81.7%) |
| Chronic Psychosis | Chen, 2020[21], United States | DSM-IV-TR, DSM-5 | 16.4 ± 14 | 75 | 36.1 ± 14.3 | 47/28 | 47 (62.7%) | PSQI | medicated (88%) |
| Chronic Psychosis | Hou, 2015[22], China | ICD-10 | 22 ± 11.1 | 623 | 47.7 ± 10.3 | 341/282 | 180 (28.9%) | In-house questionnaire | medicated |

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|---|---|---|---|---|---|---|---|---|---|
| Chronic Psychosis | Johansson, 2016[23], Sweden | DSM-IV | | 11 | 44.4 ± 11.9 | 5/6 | 7 (63.6%) | Minimal Insomnia Symptom Scale (MISS) | medicated (100%) |
| Chronic Psychosis | Lee, 2019[24], United States | DSM-IV-TR | 25.3 ± 11.8 | 138 | 48.2 ± 10.6 | 78/66 | 89 (64.5%) | Four Likert-scale ratings evaluating the frequency of problems with falling asleep, overnight awakening, waking too early, and waking feeling unrefreshed. | medicated (100%) |
| Chronic Psychosis | Li, 2016[25], Hong Kong | ICD-10 | 11.1 ± 8.6 | 388 | 41 ± 11.4 | 175/213 | 75 (19.3%) | In-house questionnaire | medicated (97.2%) |
| Chronic Psychosis | Ma, 2018[26], China | DSM-5, ICD-10 | | 104 | 43.4 ± 15.2 | 47/57 | 82 (78.8%) | PSQI | medicated |
| Chronic Psychosis | Miller, 2020[27], China | ICD-10 | 19.1 ± 10.4 | 328 | 45.1 ± 11.8 | 196/132 | 58 (17.7%) | Insomnia Severity Index (ISI) | medicated |
| Chronic Psychosis | Ritsner, 2004[28], Israel | DSM-IV | 15 ± 9.1 | 145 | 38.2 ± 9.6 | 118/27 | 66 (45.4%) | PSQI | medicated (100%) |

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|---|---|---|---|---|---|---|---|---|---|
| Chronic Psychosis | Sunhary de Verville[29], 2021, France | DSM-5 | 10.8 ± 7.4 | 562 | 31.3 ± 9 | 417/145 | 327 (58.2%) | PSQI | medicated |
| Chronic Psychosis | Xiang, 2009[30], China | DSM-IV | | 505 | 43 ± 8.4 | 243/262 | 182 (36%) | Three questions based on DSM-IV sleep disturbances | medicated |
| Chronic Psychosis | Hacimusalar, 2022[31], Turkey | DSM-5 | 19.2 | 43 | 42.6 ± 9.8 | 28/15 | 28 (65.1%) | PSQI | NA |
| Chronic Psychosis | Zhu, 2022[32], China | DSM-IV | 16 | 718 | 45.9 ± 12.5 | 480/238 | 149 (20.8%) | Insomnia Severity Index (ISI) | medicated (100%) |
| Chronic Psychosis | Zhang, 2021[33], China | DSM-IV | 14.6 ± 7.9 | 83 | 39.7 ± 9.7 | 45/38 | 27 (0.3%) | Insomnia Severity Index (ISI) | NA |

**eTable 2: Study characteristics for papers included in the case-control comparisons of sleep quality, sleep architecture and sleep oscillations.**

| Clinical stage | 1st author, year, country | Diagnostic tool | Illness duration (mean ± SD) | N patients/ controls | Age (mean ± SD) | Sex (M/F) | Sleep assessment | PSG scoring system | Medication status (% medicated) |
|---|---|---|---|---|---|---|---|---|---|
| At-risk | Lederman, 2017[34], Australia | CAARMS | | 10/10 | Patients: 19.5 ± 0.6, Controls: 22 ± 0.9 | Patients: 8/2, Controls: 7/3 | self-reported (PSQI) | | medicated (100%) |
| At-risk | Lunsford-Avery, 2015[35], United States | SIPS | | 36/31 | Patients: 18.7 ± 1.9, Controls: 17.9 ± 2.6 | Patients: 19/17, Controls: 16/15 | Actigraphy, self-reported (PSQI) | | medicated (5.6%) |
| At-risk | Mayeli, 2021[36], United States | DSM-IV | | 22/20 | Patients: 20.3 ± 4.6, Controls: 20.6 ± 4.2 | Patients: 10/12, Controls: 9/11 | PSG | AASM | medicated (40.9%) |
| At-risk | Purple, 2020[37], United Kingdom | CAARMS | | 22/22 | Patients: 22 ± 3, Controls: 22 ± 3 | Patients: 6/16, Controls: 7/15 | PSG, self-reported (PSQI) | AASM | unmedicated (0%) |
| At-risk | Zanini, 2015[38], Brazil | DSM-IV | | 7/20 | Patients: 18.3 ± 3.9, Controls: 19.1 ± 4 | Patients: 5/2, Controls: 13/7 | PSG, self-reported (PSQI) | AASM | medicated (40%) |
| At-risk | Zaks, 2022[39], United States | SIPS | | 688/94 | Patients: 18.2 ± 4.1, Controls: 18.6 ± 4.2 | Patients: 372/316, Controls: 48/46 | self-reported (PSQI) | | NR, Psychotropic medication reported |

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|---|---|---|---|---|---|---|---|---|---|
| Early Psychosis | Das, 2005[40], India | DSM-III-R | 4.6 ± 4.1 | 15/15 | Patients: 32.1 ± 6.7, Controls: 31 ± 8.1 | Patients: 8/7, Controls: 8/7 | PSG | R&K | unmedicated (0%) |
| Early Psychosis | Fekih-Romdhane, 2020[17], Tunisia | DSM-5 | 1.8 ± 1.8 | 54/61 | Patients: 26.8 ± 6.1, Controls: 28.6 ± 4.8 | Patients: 35/19, Controls: 44/17 | self-reported | | medicated (100%) |
| Early Psychosis | Gerstenberg, 2020[41], Switzerland | DSM-IV | | 12/24 | Patients: 16.6 ± 1.4, Controls: 16.5 ± 1.4 | Patients: 7/5, Controls: 13/11 | PSG | AASM | medicated (83.3%) |
| Early Psychosis | Hoffmann, 2000[42], United States | DSM-III-R | 0.9 ± 0.6 | 13/13 | Patients: 33.5 ± 8.8, Controls: 31.3 ± 5.1 | Patients: 13/0, Controls: 13/0 | PSG | R&K | unmedicated (0%) |
| Early Psychosis | Kaskie, 2019[43], United States | DSM-IV | | 20/20 | Patients: 22.9 ± 5.4, Controls: 24.7 ± 5.7 | Patients: 12/8, Controls: 16/4 | PSG | AASM | medicated (40%) |
| Early Psychosis | Kaskie, 2019[44], United States | DSM-IV | | 27/23 | Patients: 23.2 ± 5.8, Controls: 24.7 ± 5.7 | Patients: 17/10, Controls: 16/7 | PSG | AASM | medicated (44.4%) |
| Early Psychosis | Lauer, 1997[45], Germany | DSM-III-R | 2.8 ± 3.4 | 22/22 | Patients: 32.7 ± 8.6, Controls: 30.7 ± 6.7 | Patients: 14/8, Controls: 13/7 | PSG | R&K | unmedicated (0%) |
| Early Psychosis | Lederman, 2017[34], Australia | CAARMS | | 10/10 | Patients: 21.6 ± 1.8, Controls: 22 ± 0.9 | Patients: 8/2, Controls: 7/3 | self-reported (PSQI) | | medicated (100%) |
| Early Psychosis | Manoach, 2014[46], United States | DSM-IV | | 15/25 | Patients: 28 ± 8, Controls: 27 ± 7 | Patients: 11/4, Controls: 16/9 | PSG | R&K | unmedicated (0%) |
| Early Psychosis | Poulin, 2003[47], Canada | DSM-IV | | 11/11 | Patients: 29.6 ± 15.8, Controls: 25.3 ± 11.3 | Patients: 6/5, Controls: 8/3 | PSG | R&K | unmedicated (0%) |

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|---|---|---|---|---|---|---|---|---|---|
| Early Psychosis | Riemann, 1995[48], Germany | DSM-III-R | 0.8 ± 1 | 10/10 | Patients: 15.8 ± 1.8, Controls: 16.6 ± 1.9 | Patients: 4/6, Controls: 7/3 | PSG | R&K | unmedicated (0%) |
| Early Psychosis | Sarkar, 2010[49], India | ICD-10-DCR | 2.9 ± 1.5 | 20/20 | Patients: 26.6 ± 5.3, Controls: 29.2 ± 10.1 | Patients: 20/0, Controls: 20/0 | PSG | R&K | unmedicated (0%) |
| Early Psychosis | Sasidharan[50], 2017, India | DSM-IV | 2.6 ± 2.4 | 45/39 | Patients: 27.8 ± 6.8, Controls: 27.3 ± 4.6 | Patients: 32/13, Controls: 28/11 | PSG, self-reported (PSQI) | AASM | medicated (31.1%) |
| Early Psychosis | Schilling, 2017[51], Germany | DSM-IV-TR | 5 ± 5.4 | 17/17 | Patients: 29.9 ± 10.6, Controls: 26.5 ± 8.8 | Patients: 10/7, Controls: 11/6 | PSG | AASM | medicated (94.1%) |
| Early Psychosis | Tandon, 1992[52], United States | DSM-III-R | 3.5 ± 2.2 | 20/15 | Patients: 26.8 ± 7.1, Controls: 25.6 ± 5.3 | Patients: 12/8, Controls: 10/5 | PSG | R&K | unmedicated (0%) |
| Early Psychosis | Yazıhan, 2020[53], Turkey | DSM-IV | | 21/21 | Patients: 22.7 ± 2.4, Controls: 22.7 ± 3.5 | Patients: 21/0, Controls: | PSG | AASM | unmedicated (0%) |
| Early Psychosis | Yetkin, 2011[54], Turkey | DSM-IV | 4.6 ± 5.2 | 13/13 | Patients: 24.4 ± 5.9, Controls: 25.3 ± 5 | Patients: 13/0, Controls: 13/0 | PSG | R&K | unmedicated (0%) |
| Chronic Psychosis | Afonso, 2014[55], Portugal | DSM-IV | 11.8 ± 8.5 | 34/34 | Patients: 33.8 ± 8.6, Controls: 34.7 ± 8.3 | Patients: 22/12, Controls: 19/15 | PSQI, actigraphy | | medicated (100%) |
| Chronic Psychosis | Buchmann, 2014[56], United States | DSM-IV | 13 ± 7 | 21/21 | Patients: 36 ± 10.2, Controls: 36.2 ± 8.5 | Patients: 13/8, Controls: 17/4 | PSG | AASM | medicated (100%) |

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|---|---|---|---|---|---|---|---|---|---|
| Chronic Psychosis | Ferrarelli, 2007[57], United States | DSM-IV-TR | 16.7 ± 7.7 | 18/17 | Patients: 39.6 ± 9.5, Controls: 37 ± 10.1 | Patients: 13/5, Controls: 12/5 | PSG | | medicated (100%) |
| Chronic Psychosis | Ferrarelli, 2010[58], United States | DSM-IV | 15 ± 8 | 49/44 | Patients: 38.2 ± 10.6, Controls: 36.7 ± 7.8 | Patients: 33/16, Controls: 29/15 | PSG | AASM | medicated (100%) |
| Chronic Psychosis | Genzel, 2015[59], Germany | DSM-IV, ICD- 10 | 7.8 ± 6.4 | 16/16 | Patients: 39.1 ± 8.7, Controls: 41.8 ± 10.1 | Patients: 8/8, Controls: 8/8 | PSG, self-reported (PSQI) | AASM | medicated (100%) |
| Chronic Psychosis | Göder, 2015[60], Germany | ICD-10 | 6 ± 4 | 16/16 | Patients: 29.4 ± 6.4, Controls: 28.3 ± 6.1 | Patients: 9/7, Controls: 7/9 | PSG, self-reported (PSQI) | AASM | medicated (100%) |
| Chronic Psychosis | Keshavan, 1998[61], United States | DSM-III-R | 7.8 ± 10 | 30/30 | Patients: 30.9 ± 8.5, Controls: 30.9 ± 8.2 | Patients: 17/13, Controls: 17/13 | PSG | R&K | unmedicated (0%) |
| Chronic Psychosis | Korenic, 2020[62], United States | DSM-IV | 13.8 ± 12 | 19/22 | Patients: 33 ± 11.6, Controls: 26.9 ± 9.8 | Patients: 12/7, Controls: 14/8 | self-reported (PSQI) | | medicated |
| Chronic Psychosis | Manoach, 2010[63], United States | DSM-IV | 16 ± 8 | 14/15 | Patients: 41 ± 7, Controls: 42 ± 6 | Patients: 11/3, Controls: 11/4 | PSG | R&K | medicated (100%) |
| Chronic Psychosis | Markovic, 2020[64], United States | DSM-III-R, DSM-IV | 6.7 ± 3.6 | 17/17 | Patients: 16 ± 3.6, Controls: | Patients: 5/12, Controls: 5/12 | PSG | R&K | medicated (100%) |
| Chronic Psychosis | Oh, 2017[65], Korea | ICD-10 | 9 ± 13.4 | 9/10 | Patients: 30 ± 13.6, Controls: 30.3 ± 8.4 | Patients: 6/3, Controls: 7/3 | PSG | AASM | medicated (88.9%) |

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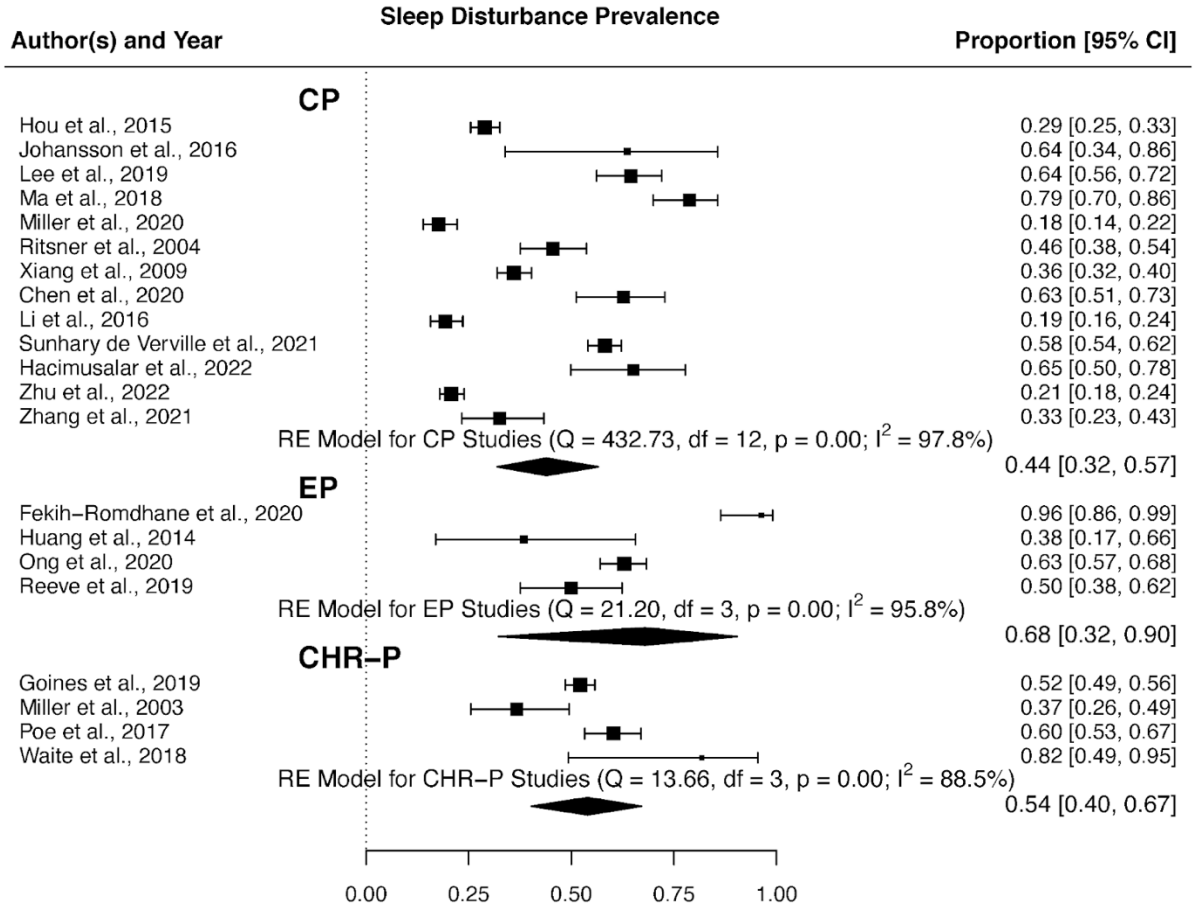
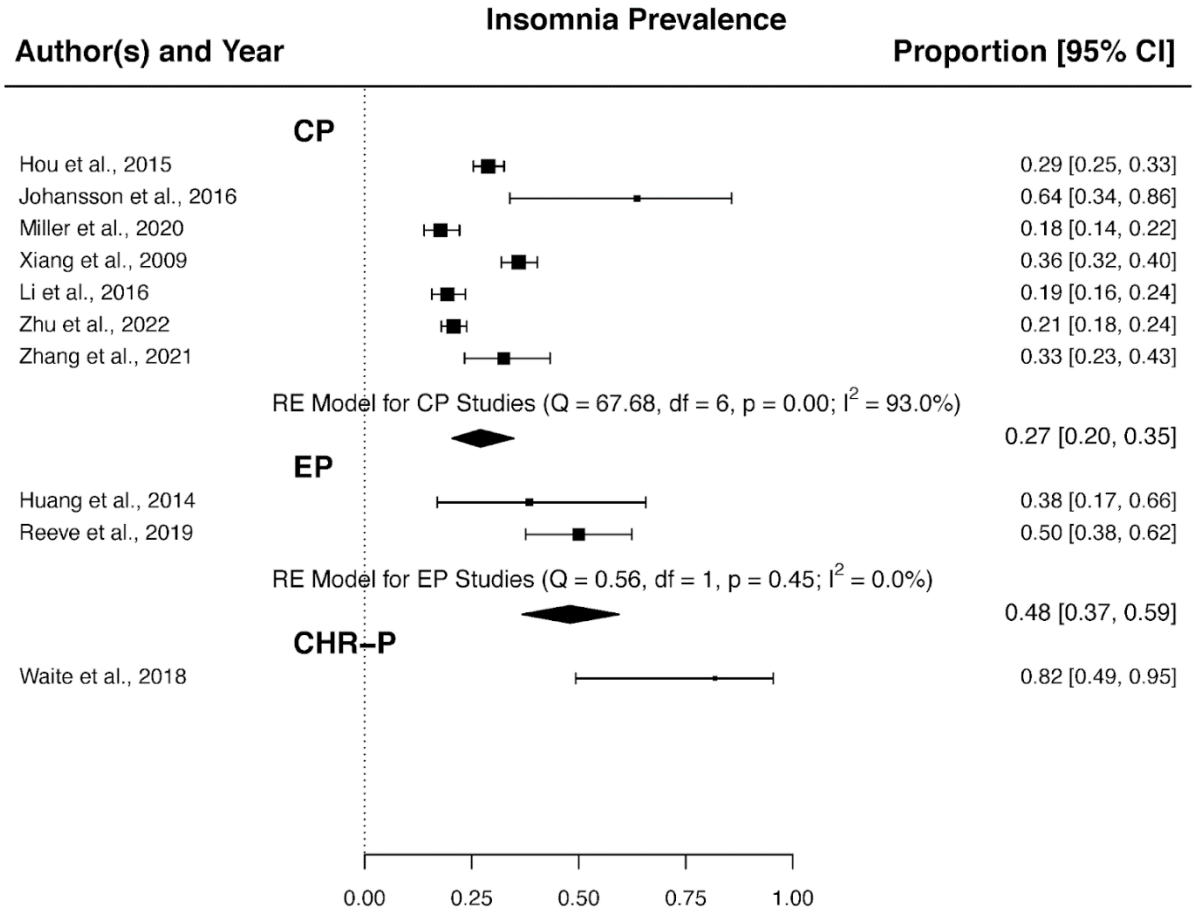
|---|---|---|---|---|---|---|---|---|---|
| Chronic Psychosis | Sahbaz, 2019[66], Turkey | DSM-IV | 18.6 ± 9.7 | 47/40 | Patients: 42.1 ± 10.7, Controls: 39.3 ± 11 | Patients: 30/17, Controls: 21/19 | self-reported (PSQI) | | medicated (100%) |
| Chronic Psychosis | Sekimoto, 2011[67], Japan | DSM-IV | 11.4 ± 6.3 | 17/18 | Patients: 30.4 ± 7.2, Controls: 28.5 ± 7.3 | Patients: 17/0, Controls: 18/0 | PSG | R&K | medicated (70.6%) |
| Chronic Psychosis | Sekimoto, 2007[68], Japan | DSM-IV | 10.7 ± 6.3 | 11/12 | Patients: 30.6 ± 7.8, Controls: 30.3 ± 7.4 | Patients: 11/0, Controls: 12/0 | PSG | R&K | medicated (72.7%) |
| Chronic Psychosis | Tandon, 1992[52], United States | DSM-III-R | 6.9 ± 4.4 | 20/15 | Patients: 29.8 ± 7.7, Controls: 25.6 ± 5.3 | Patients: 14/6, Controls: 10/5 | PSG | R&K | unmedicated (0%) |
| Chronic Psychosis | Wulff, 2012[69], United Kingdom | DSM-IV | 12 ± 8.7 | 20/21 | Patients: 38.8 ± 8.6, Controls: 37.5 ± 9.6 | Patients: 15/5, Controls: 13/8 | Actigraphy | | medicated (100%) |
| Chronic Psychosis | Yang, 2006[70], Korea | DSM-IV | 17.3 ± 3.7 | 15/15 | Patients: 40.6 ± 3.7, Controls: 40.2 ± 4.1 | Patients: , Controls: 15/0 | PSG | R&K | unmedicated (0%) |
| Chronic Psychosis | Kozhemiako, 2022[71], China/United States | DSM-5 | 11 ± 6.9 | 72/58 | Patients: 35 ± 7, Controls: 32 ± 6.3 | Patients: 47/25, Controls: 36/22 | PSG | AASM | medicated |




**eFigure 1: Sleep disturbance prevalence forest plot of individual studies**

Prevalence estimates were logit transformed for analysis and back-transformed to proportions for ease of interpretation of the forest plot. Heterogeneity estimates are provided for each subgroup (Cochran's Q; p-values; $I^2$ statistic).




**eFigure 2: Insomnia prevalence forest plot of individual studies**

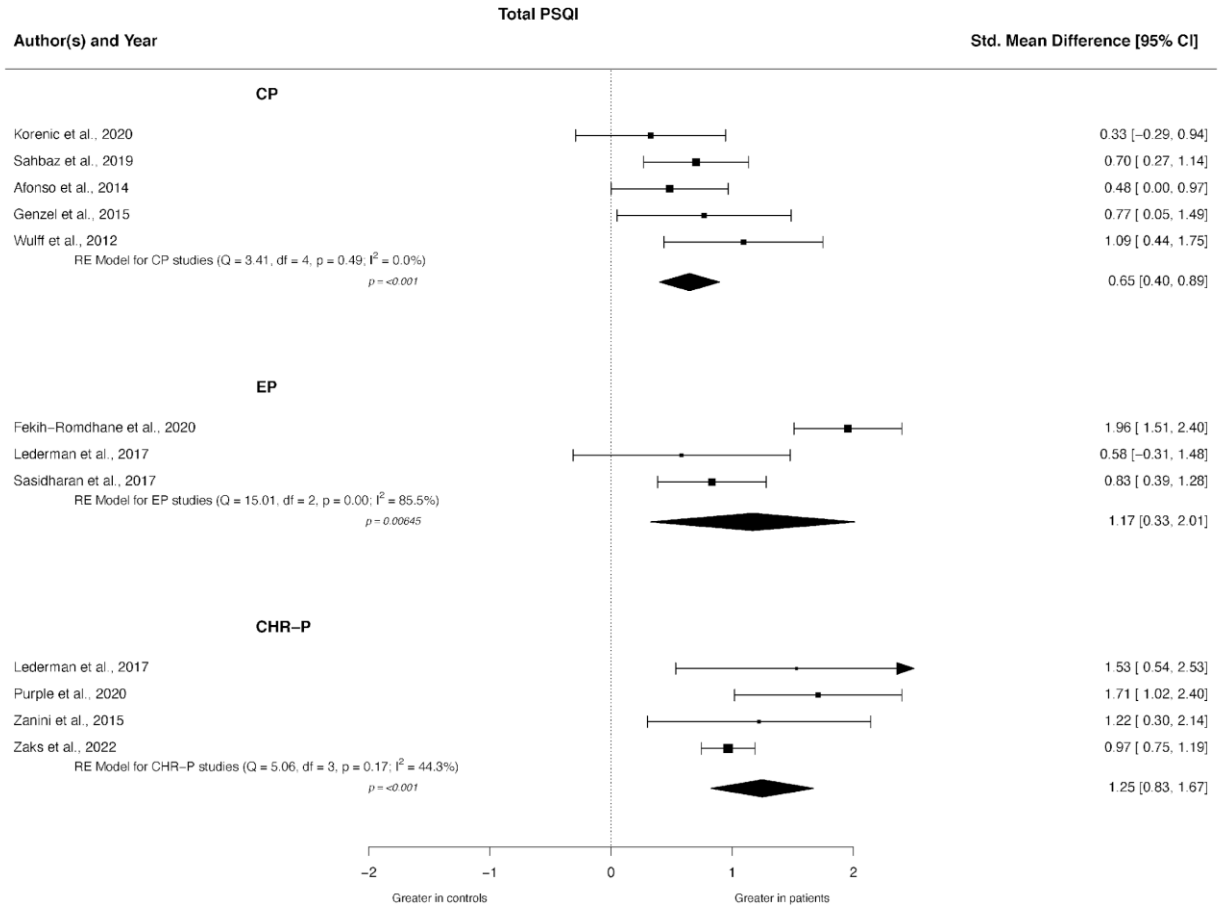
Prevalence estimates were logit transformed for analysis and back-transformed to proportions for ease of interpretation of the forest plot. Heterogeneity estimates are provided for each subgroup (Cochran's Q; p-values; $I^2$ statistic).

**eTable 3: Sleep parameters differences in effect size (p-value) across different clinical stages of psychosis**

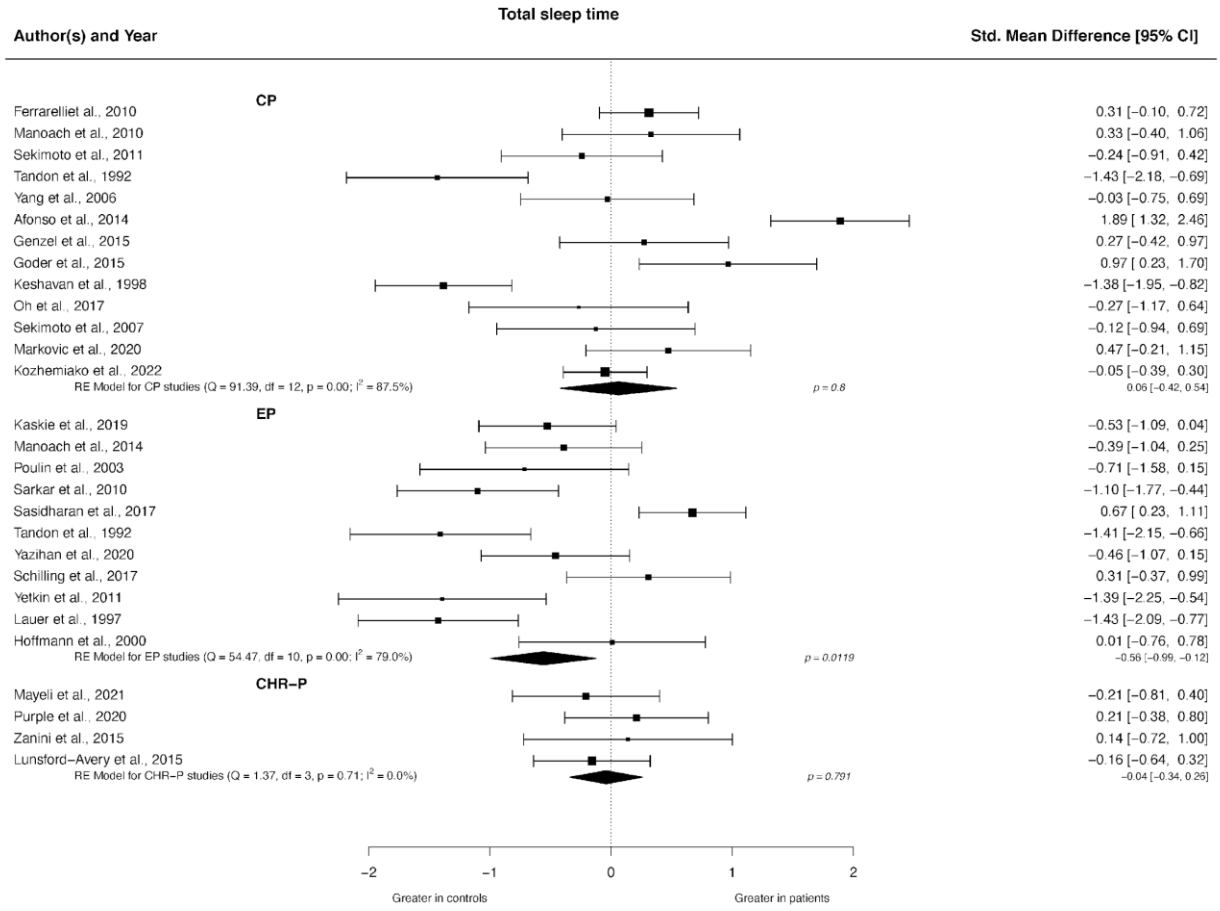
For each subgroup comparison, we report the number of studies in each group and effect sizes, shown here as Z-scores (p-values). Of note, for total sleep disturbances and insomnia, Z-scores quantify the additive effect of each variable on the logit transformed prevalence values. Bold black values are moderating effects that are significant, whereas italic values reflect a trend to significant difference. CHR-P: Clinical High Risk for Psychosis; EP: Early Psychosis; CP: Chronic Psychosis.

| **Parameter** | **EP vs CHR-P** | | | **CP vs CHR-P** | | | **CP vs EP** | | |
|---|---|---|---|---|---|---|---|---|---|
| | # EP studies | #CHR-P studies | z-score (p-value) | # CP studies | #CHR-P studies | z-score (p-value) | # CP studies | #EP studies | z-score (p-value) |
| **Total PSQI** | 3 | 4 | -0.15 (0.878) | *5* | *4* | *-1.91 (0.056)* | 5 | 3 | -1.65 (0.098) |
| **TST** | 11 | 4 | -1.23 (0.220) | 13 | 4 | 0.17 (0.864) | *13* | *11* | *1.97 (0.049)* |
| **SOL** | 12 | 3 | 0.77 (0.440) | *13* | *3* | *1.83 (0.067)* | *13* | *12* | *1.68 (0.093)* |
| **SE** | 13 | 3 | -1.64 (0.102) | 12 | 3 | -1.16 (0.248) | 12 | 13 | 0.75 (0.453) |
| **WASO** | 8 | 3 | 1.32 (0.187) | 8 | 3 | 0.96 (0.337) | 8 | 8 | -0.48 (0.632) |
| **Number of arousals** | *2* | *2* | *1.78 (0.076)* | 2 | 2 | **2.24 (0.025)** | 2 | 2 | 0.69 (0.488) |
| **S1** | *13* | *3* | *1.82 (0.068)* | 10 | 3 | 1.44 (0.150) | 10 | 13 | -0.54 (0.589) |
| **S2** | 13 | 3 | -0.08 (0.934) | 11 | 3 | 0.66 (0.509) | 11 | 13 | 1.18 (0.238) |

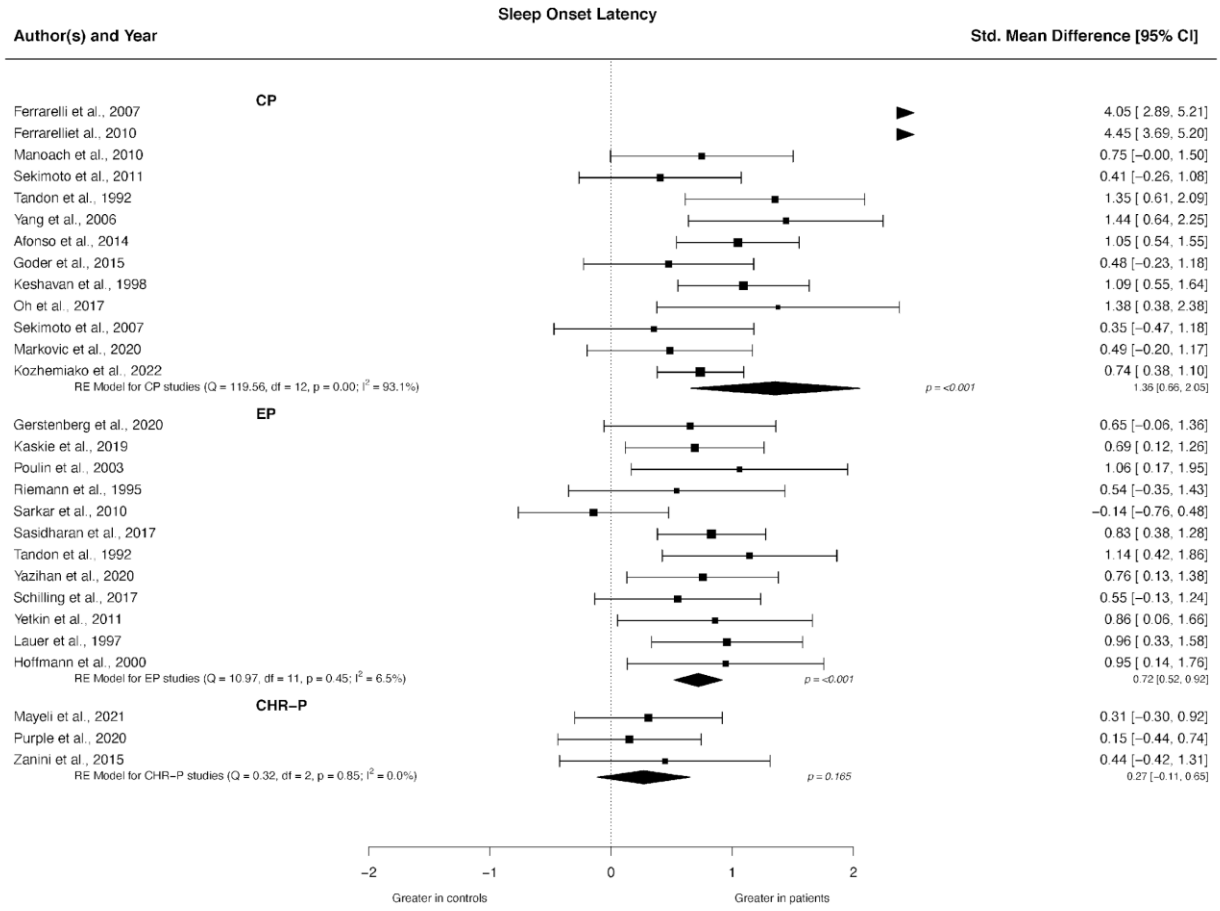
| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **SWS** | 13 | 3 | -1.02 (0.307) | 11 | 3 | -1.21 (0.226) | 11 | 13 | -0.33 (0.741) |
| **REML** | 11 | 2 | -1.31 (0.189) | 8 | 2 | -0.56 (0.576) | 8 | 11 | 1.26 (0.208) |
| **REMD** | 4 | 0 | NA | 5 | 0 | NA | 5 | 4 | 1.29 (0.199) |
| **Sleep Spindle Density** | 5 | 1 | NA | 7 | 1 | NA | 7 | 5 | -1.39 (0.166) |
| **Sleep Spindle Amplitude** | 3 | 0 | NA | 3 | 0 | NA | 3 | 3 | -1.5 (0.135) |
| **Sleep Spindle Duration** | 3 | 0 | NA | 3 | 0 | NA | 3 | 3 | **-3.91 (<0.001)** |
| **Slow Wave density** | 2 | 0 | NA | 2 | 0 | NA | 2 | 2 | 0.61 (0.545) |
| **Insomnia Prevalence** | 2 | 1 | NA | 7 | 1 | NA | 7 | 2 | **-1.89 (0.059)** |
| **Sleep Disturbance Prevalence** | 4 | 4 | 0.59 (0.553) | 13 | 4 | -0.87 (0.384) | 13 | 4 | -1.58 (0.114) |



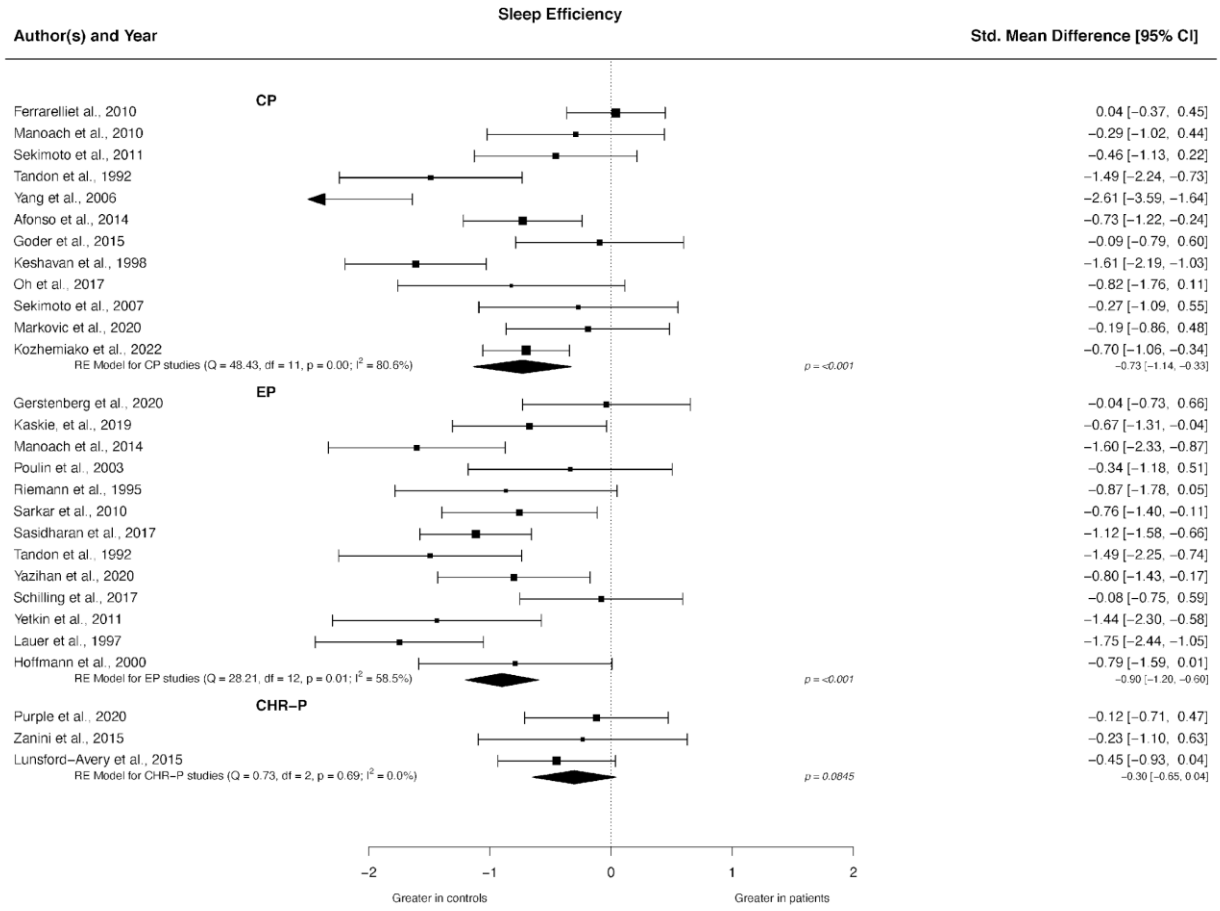

**eFigure 3: Total PSQI forest plot of individual studies**



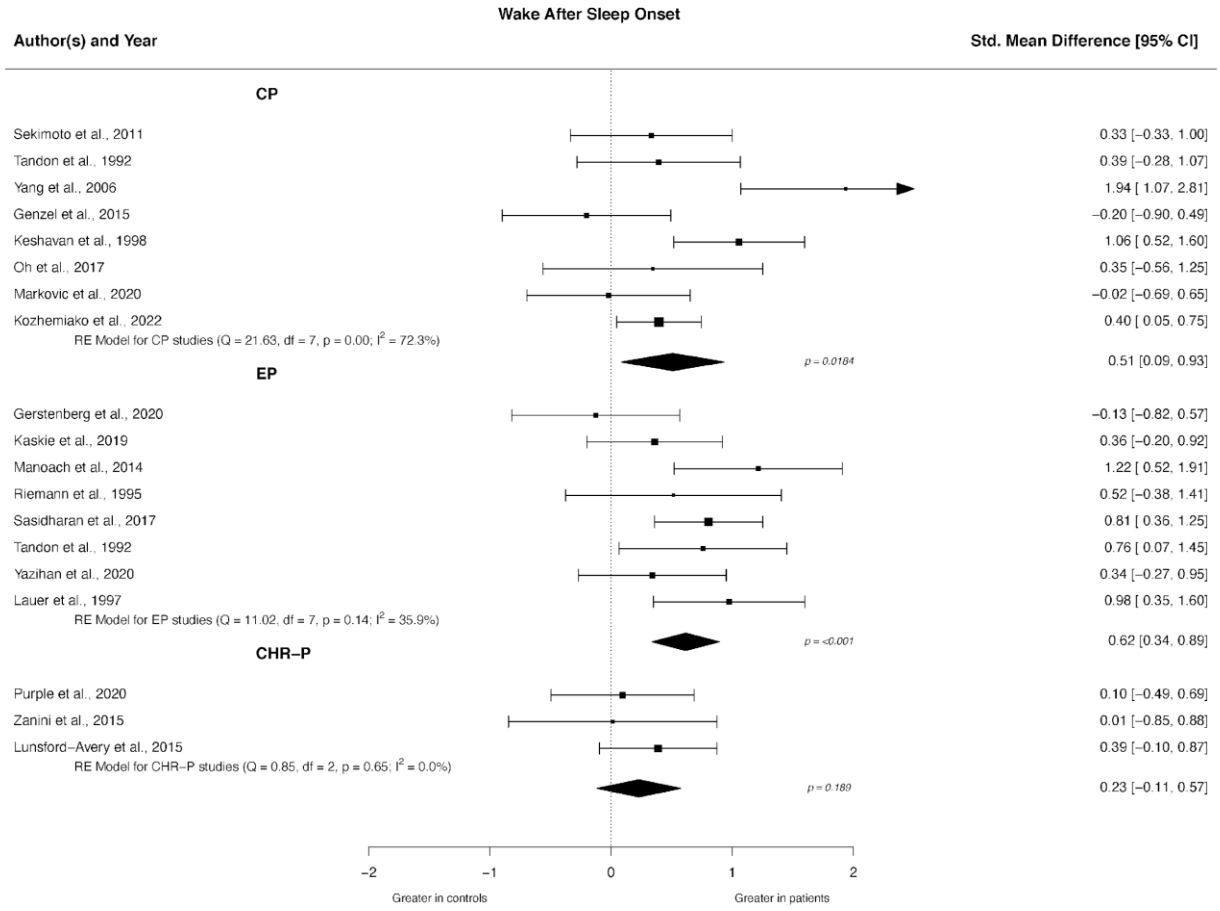

**eFigure 4: Total sleep time forest plot of individual studies**



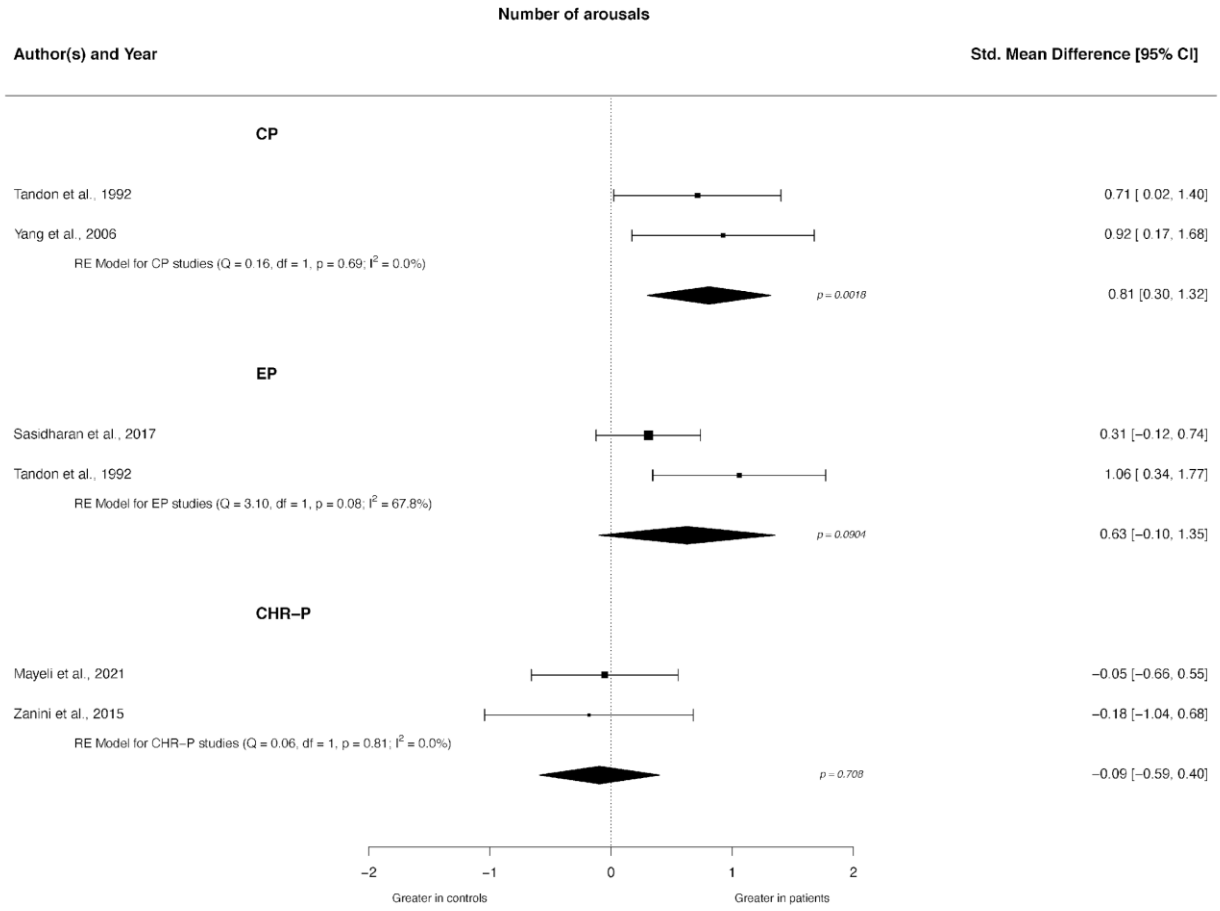

**eFigure 5: Sleep onset latency forest plot of individual studies**



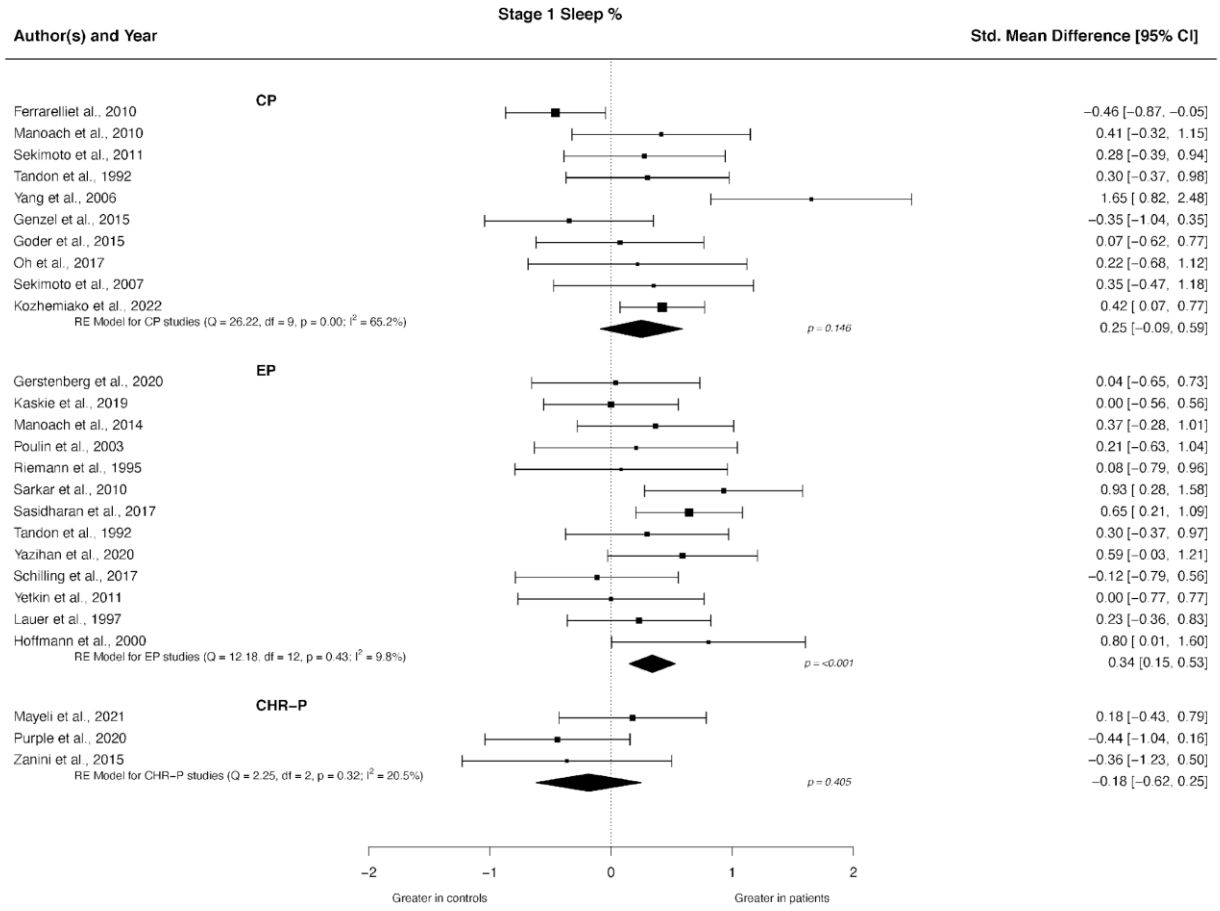

**eFigure 6: Sleep efficiency forest plot of individual studies**



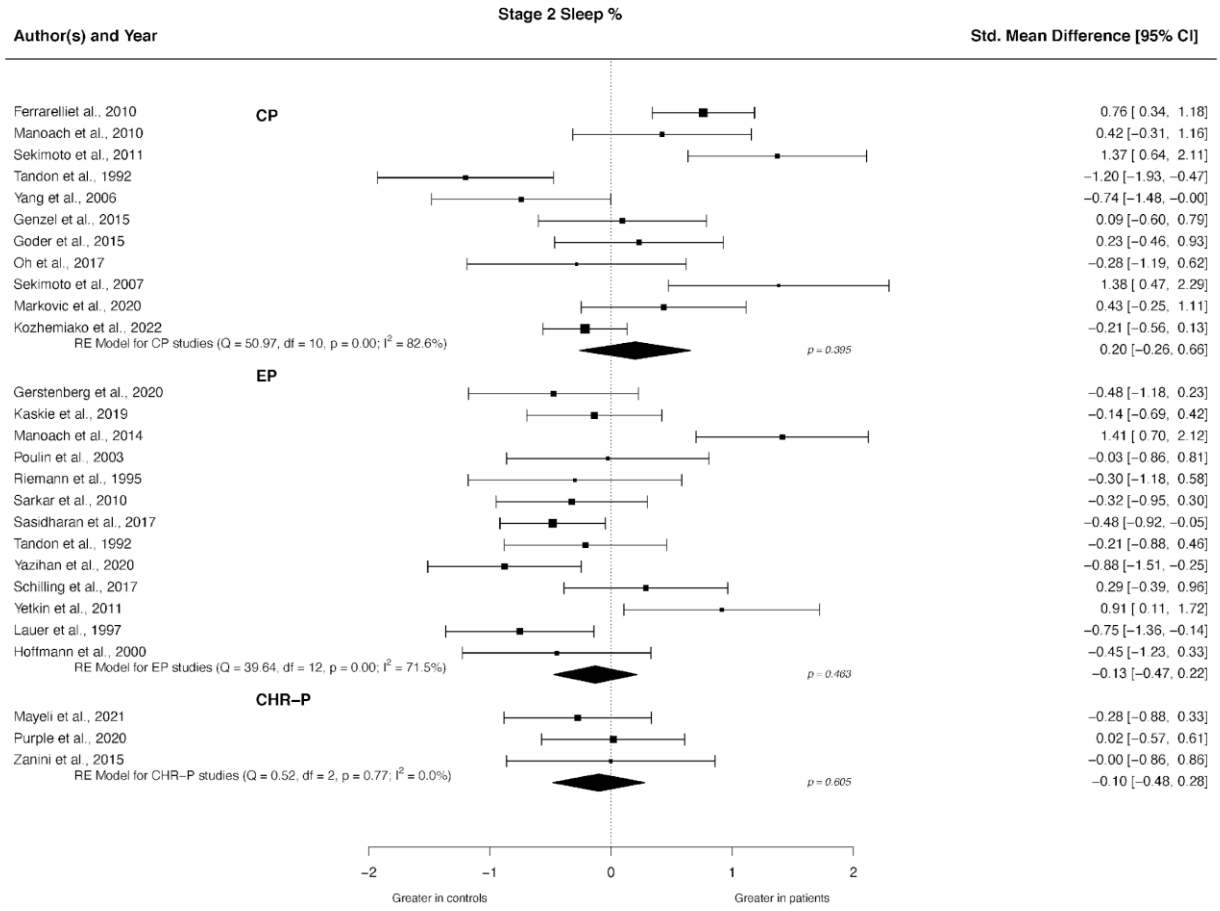

**eFigure 7: Wake after sleep onset forest plot of individual studies**



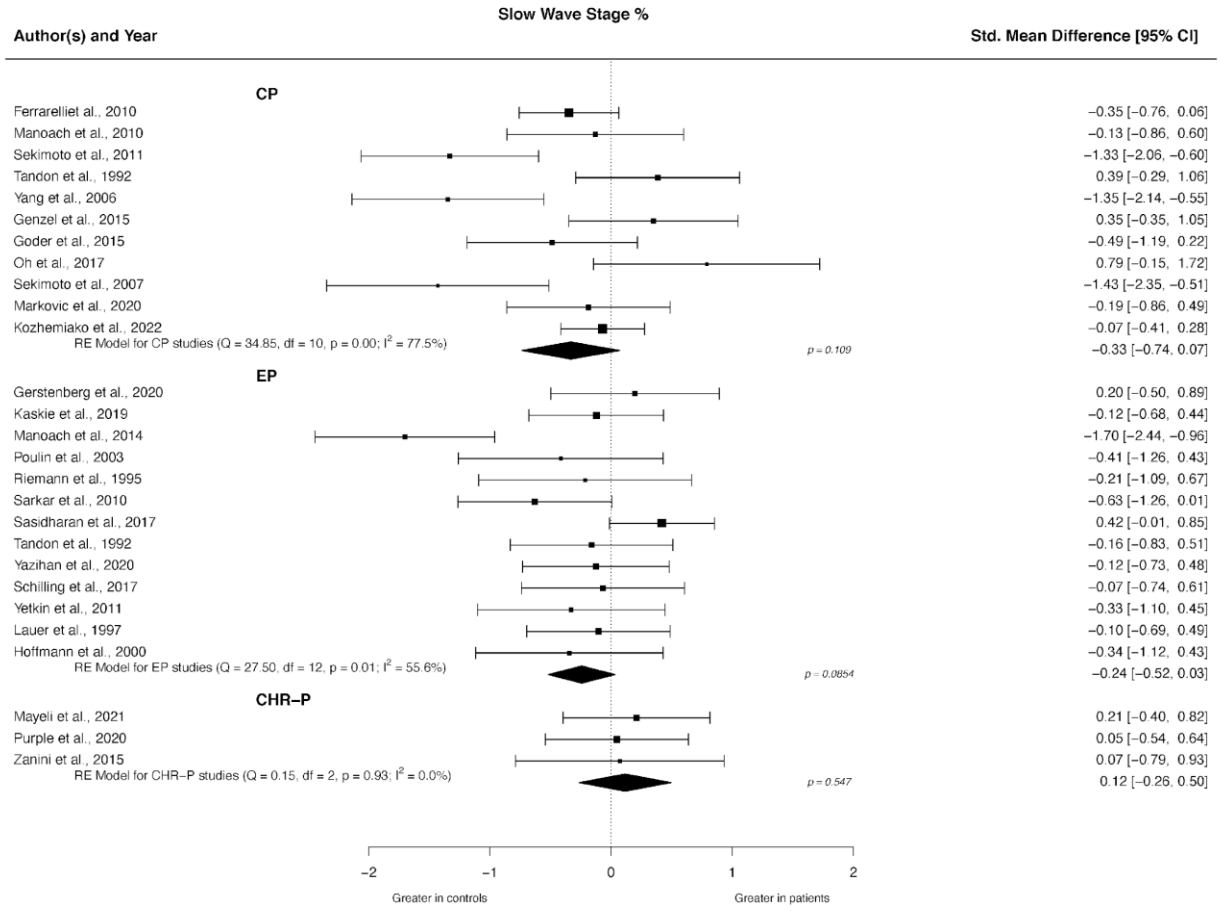

**eFigure 8: Number of arousals forest plot of individual studies**



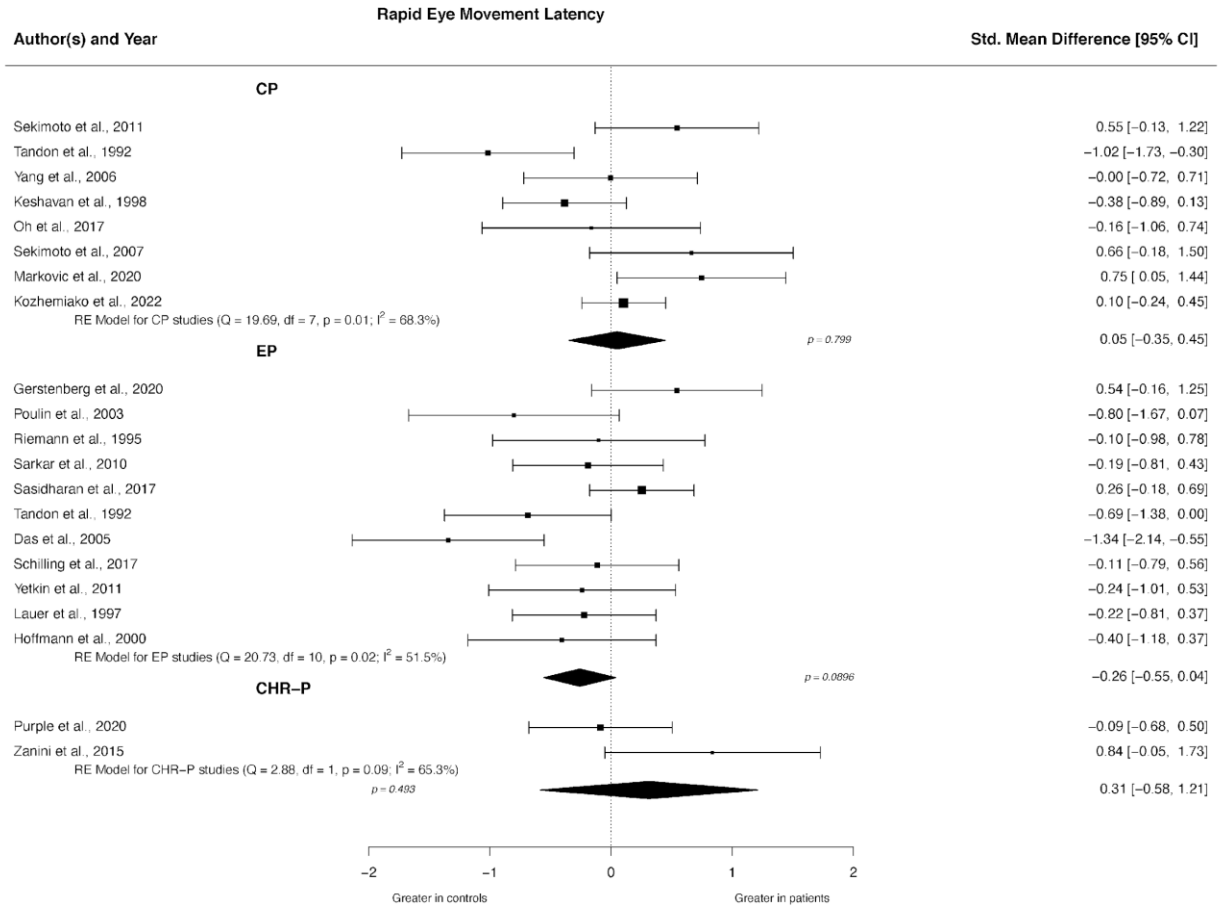

**eFigure 9: Stage 1 sleep % forest plot of individual studies**



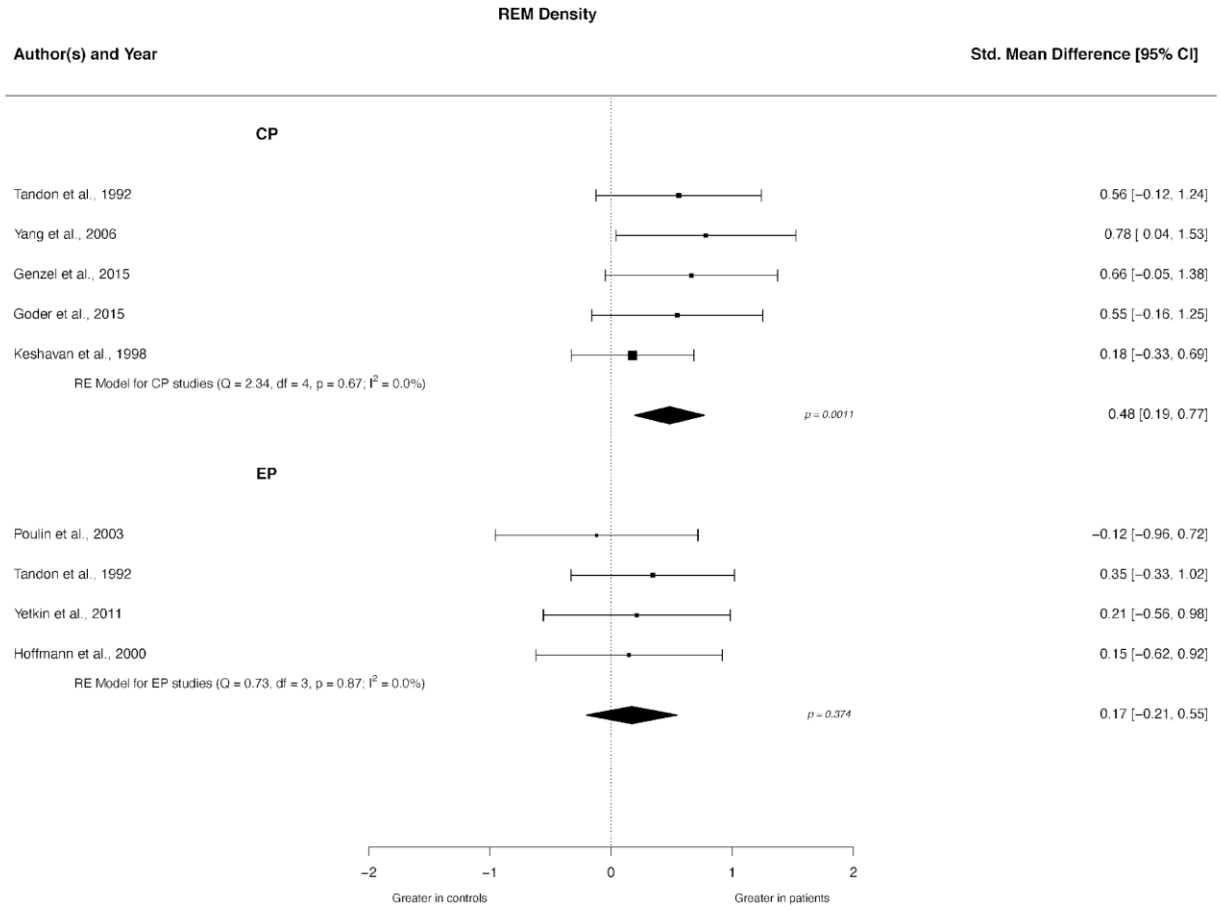

**eFigure 10: Stage 2 sleep % forest plot of individual studies**



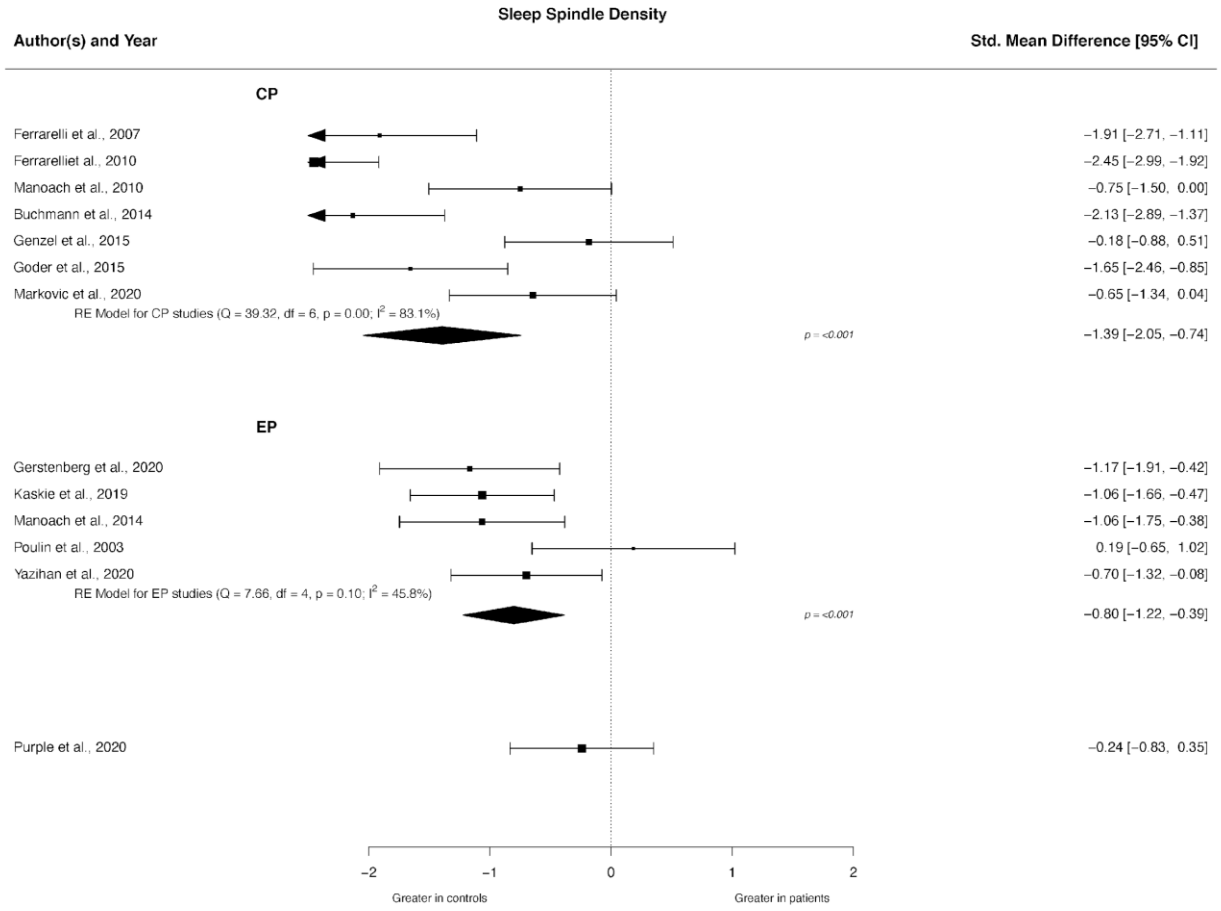

**eFigure 11: Slow wave stage % forest plot of individual studies**



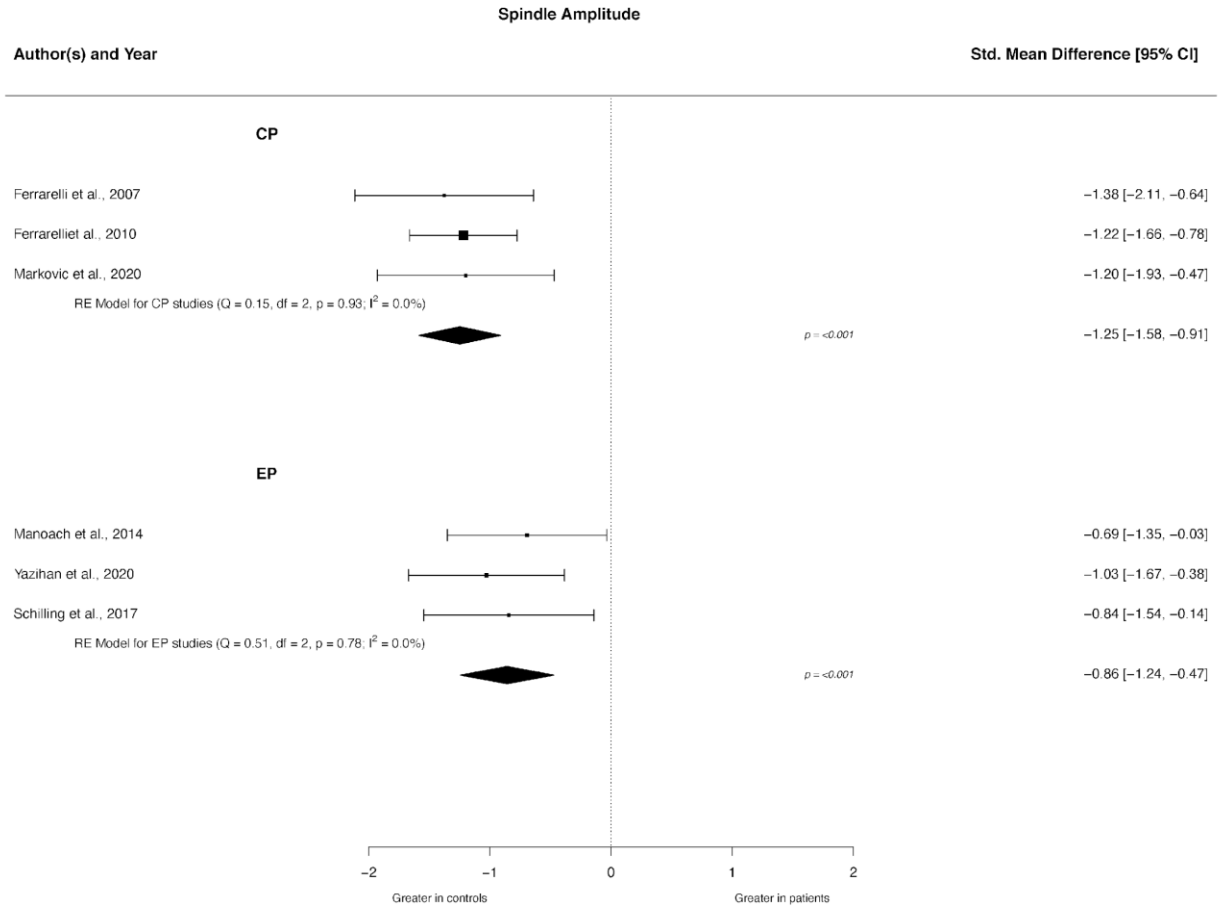

**eFigure 12: Rapid eye movement latency forest plot of individual studies**



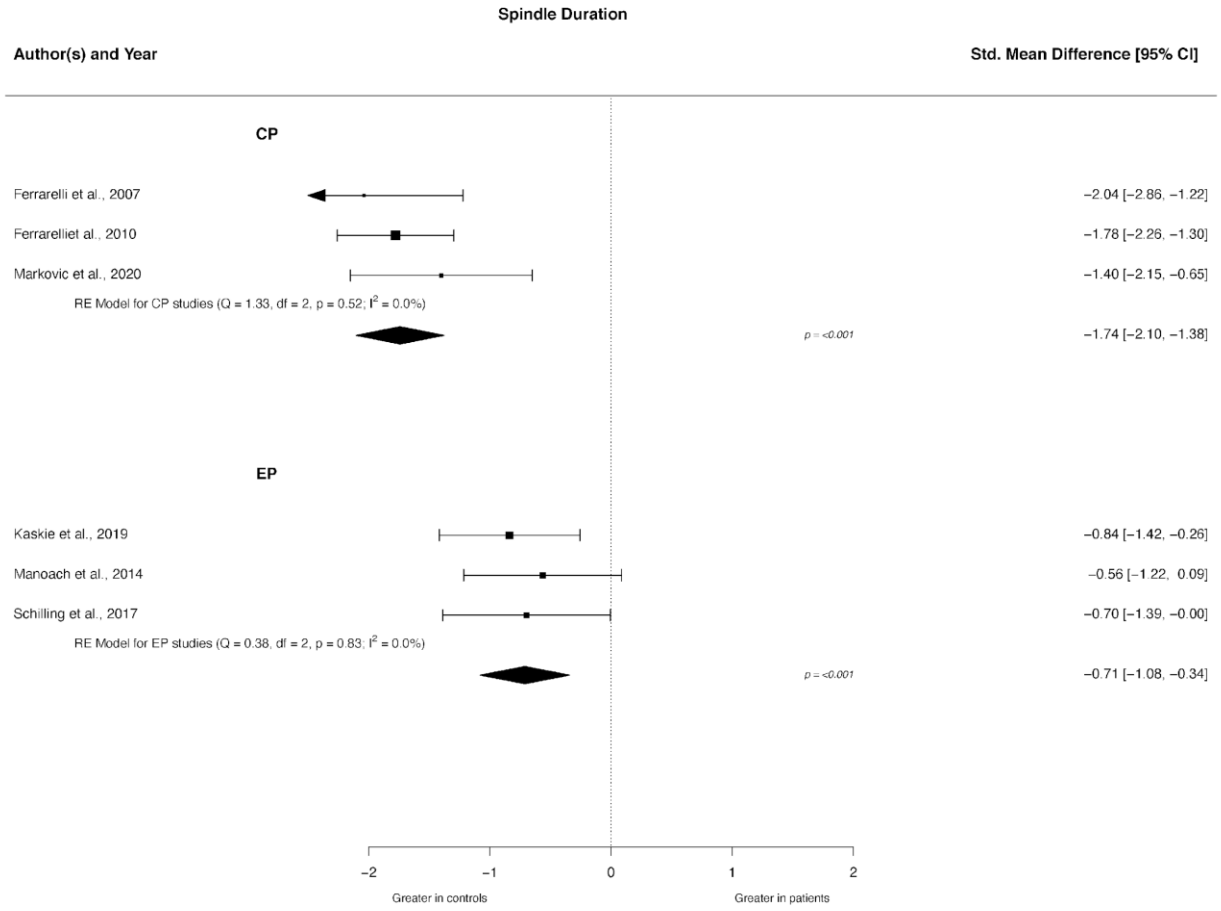

**eFigure 13: Rapid eye movement density forest plot of individual studies**



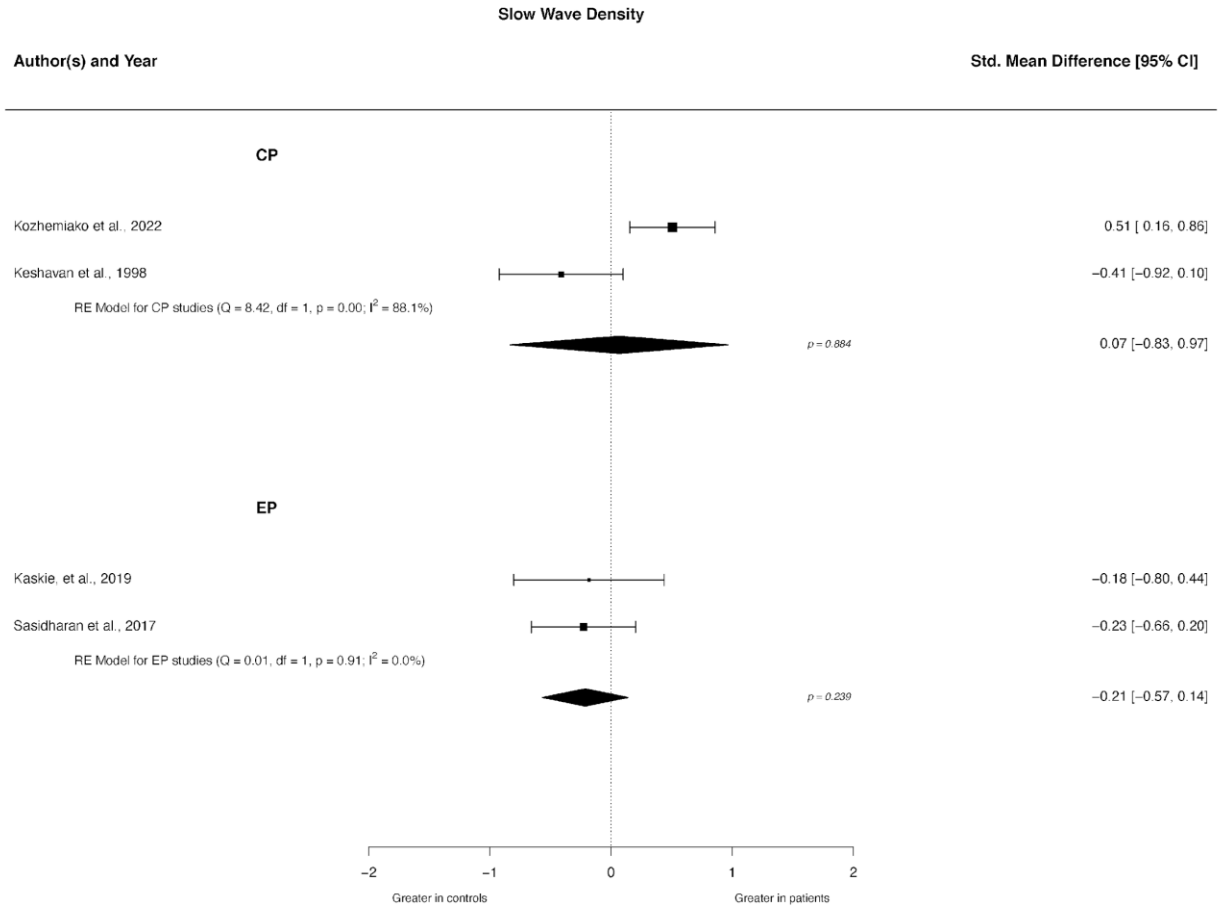

**eFigure 14: Sleep spindle density forest plot of individual studies**




**eFigure 15: Sleep spindle amplitude forest plot of individual studies**




**eFigure 16: Sleep spindle duration forest plot of individual studies**




**eFigure 17: Slow wave density forest plot of individual studies**

**eTable 4: Meta-regressions of sex, age, and proportion of sample on antipsychotic medication**

Meta-regressions were performed using random-effects model, comparing three explanatory variables (sex, age, and proportion of sample on antipsychotic medication) versus the null model on sleep parameters in the pooled clinical groups. The first column shows the standardized mean difference between cases - controls; the other columns report the effects of moderating variables. Values are shown as Z-scores (p-values). Of note, for total sleep disturbances and insomnia, Z-scores quantify the additive effect of each variable on the logit transformed prevalence values. Bonferroni corrected P threshold for three explanatory variables is 0.017. Bold black values are moderating effects that are significant before Bonferroni correction, whereas bold red values reflect significant moderating effects after Bonferroni correction.

| Parameter | Group difference (cases – controls)_ | sex | Age | Proportion Medicated |
|---|---|---|---|---|
| **Total PSQI** | **6.62 (<0.001)** | -0.43 (0.666) | -1.17 (0.242) | -1.04 (0.300) |
| **TST** | -1.27 (0.206) | -1.44 (0.150) | 1.17 (0.244) | **4.43 (<0.001)** |
| **SOL** | **5.51 (<0.001)** | 0.11 (0.911) | **2.88 (0.004)** | 1.32 (0.188) |
| **SE** | **-6.49 (<0.001)** | -1.05 (0.293) | -0.22 (0.827) | **3.85 (<0.001)** |
| **WASO** | **4.71 (<0.001)** | 1.49 (0.135) | 0.68 (0.497) | **-2.82 (0.005)** |
| **Number of arousals** | **2.34 (0.019)** | 0.67 (0.505) | 1.77 (0.077) | **-3.01 (0.003)** |
| **S1** | **2.64 (0.008)** | **2.6 (0.009)** | 0.19 (0.846) | -1.92 (0.055) |
| **S2** | 0.07 (0.945) | 1.23 (0.219) | 1.05 (0.291) | 1.98 (0.047) |
| **SWS** | **-2.27 (0.023)** | **-2.38 (0.017)** | -0.38 (0.700) | 0.83 (0.409) |
| **REML** | -0.78 (0.439) | 0.19 (0.853) | -1.37 (0.172) | **3.54 (<0.001)** |
| **REMD** | **3.13 (0.002)** | -0.71 (0.478) | 0.72 (0.469) | 1.04 (0.296) |
| **Sleep Spindle Density** | **-4.81 (<0.001)** | -1.64 (0.101) | -0.82 (0.410) | **-2.08 (0.038)** |

| | | | | |
|---|---|---|---|---|
| **Sleep Spindle Amplitude** | **-8.33 (<0.001)** | 0.15 (0.883) | -1.63 (0.104) | -1.14 (0.255) |
| **Sleep Spindle Duration** | **-4.92 (<0.001)** | 0.04 (0.968) | **-3.79 (<0.001)** | **-2.13 (0.033)** |
| **Slow Wave density** | **-0.22 (<0.001)** | 0.08 (0.939) | -1.08 (0.278) | **3.4 (<0.001)** |
| **Insomnia Prevalence** | NA | -0.99 (0.321) | **-2.64 (0.008)** | -0.63 (0.53) |
| **Sleep Disturbance Prevalence** | NA | 0.11 (0.911) | -1.3 (0.192) | 0.29 (0.769) |

**eTable 5: Meta-regressions of sex, age, and proportion of sample on antipsychotic medication in CHR-P**

Meta-regressions using random-effects model, comparing three explanatory variables (sex, age, and proportion of sample on antipsychotic medication) versus the null model on sleep parameters in CHR-P: Clinical High Risk for Psychosis. For each meta-regression, effect sizes are shown as Z-scores (p-values). Of note, for total sleep disturbances and insomnia, Z-scores quantify the additive effect of each variable on the logit transformed prevalence values. Bonferroni corrected P threshold is 0.017. Bold black values are moderating effects that are significant before Bonferroni correction.

| | **Sex-CHR-P** | **Age-CHR-P** | **Proportion Medicated-CHR-P** |
|---|---|---|---|
| **Total PSQI** | -0.51 (0.612) | **2.23 (0.026)** | -0.78 (0.438) |
| **TST** | -0.48 (0.632) | 0.7 (0.484) | -0.37 (0.708) |
| **SOL** | 0.56 (0.574) | -0.57 (0.571) | 0.5 (0.614) |
| **SE** | -0.53 (0.597) | 0.79 (0.431) | 0.02 (0.986) |
| **WASO** | 0.23 (0.820) | -0.63 (0.529) | -0.39 (0.697) |
| **Number of arousals** | NA | NA | NA |
| **S1** | 0.13 (0.897) | -0.23 (0.816) | 1.13 (0.259) |
| **S2** | -0.14 (0.890) | 0.21 (0.834) | -0.53 (0.600) |
| **SWS** | 0.1 (0.923) | -0.13 (0.893) | 0.3 (0.765) |
| **REML** | NA | NA | NA |
| **REMD** | NA | NA | NA |

| | | | |
|---|---|---|---|
| **Sleep Spindle Density** | NA | NA | NA |
| **Sleep Spindle Amplitude** | NA | NA | NA |
| **Sleep Spindle Duration** | NA | NA | NA |
| **Slow Wave density** | NA | NA | NA |
| **Insomnia Prevalence** | NA | NA | NA |
| **Sleep Disturbance Prevalence** | -0.75 (0.451) | 0.41 (0.682) | NA |

**eTable 6: Meta-regressions of sex, age, and proportion of sample on antipsychotic medication in EP**

Meta-regressions using random-effects model, comparing three explanatory variables (sex, age, and proportion of sample on antipsychotic medication) versus the null model on sleep parameters in EP: Early Psychosis. For each meta-regression, effect sizes are shown as Z-scores (p-values). Of note, for total sleep disturbances and insomnia, Z-scores quantify the additive effect of each variable on the logit transformed prevalence values. Bonferroni corrected P threshold is 0.017. Bold black values are moderating effects that are significant before Bonferroni correction, whereas bold red values reflect significant moderating effects after Bonferroni correction.

| | **Sex-EP** | **Age-EP** | **Proportion Medicated-EP** |
|---|---|---|---|
| **Total PSQI** | **-2.11 (0.035)** | 0.83 (0.409) | 0.43 (0.669) |
| **TST** | -0.4 (0.691) | 0.35 (0.724) | **2.07 (0.038)** |
| **SOL** | -1.33 (0.183) | 0.46 (0.644) | -0.38 (0.703) |
| **SE** | -0.56 (0.572) | -1.29 (0.196) | **3.15 (0.002)** |
| **WASO** | 1.71 (0.086) | **2.58 (0.010)** | **-2.16 (0.031)** |
| **Number of arousals** | NA | NA | NA |
| **S1** | 1.98 (0.048) | 1.48 (0.138) | -1.68 (0.092) |
| **S2** | 0.4 (0.69) | -0.01 (0.995) | -0.04 (0.97) |
| **SWS** | -0.71 (0.477) | -0.6 (0.547) | 1.54 (0.124) |
| **REML** | 0.23 (0.82) | -1.75 (0.081) | **2.06 (0.040)** |
| **REMD** | 0.04 (0.972) | -0.22 (0.829) | NA |

| | | | |
|---|---|---|---|
| **Sleep Spindle Density** | 0.17 (0.862) | 0.87 (0.383) | -1.22 (0.222) |
| **Sleep Spindle Amplitude** | NA | NA | 0.05 (0.962) |
| **Sleep Spindle Duration** | 0.12 (0.901) | 0.49 (0.621) | -0.28 (0.783) |
| **Slow Wave density** | NA | NA | NA |
| **Insomnia Prevalence** | NA | NA | NA |
| **Sleep Disturbance Prevalence** | 0.94 (0.346) | 1.5 (0.133) | NA |

**eTable 7: Meta-regressions of sex, age, and proportion of sample on antipsychotic medication in CP**

Meta-regressions using random-effects model, comparing three explanatory variables (sex, age, and proportion of sample on antipsychotic medication) versus the null model on sleep parameters in CP: Chronic Psychosis. For each meta-regression, effect sizes are shown as Z-scores (p-values). Of note, for total sleep disturbances and insomnia, Z-scores quantify the additive effect of each variable on the logit transformed prevalence values. Bonferroni corrected P threshold is 0.017. Bold black values are moderating effects that are significant before Bonferroni correction, whereas bold red values reflect significant moderating effects after Bonferroni correction.

| | **Sex-CP** | **Age-CP** | **Proportion Medicated-CP** |
|---|---|---|---|
| **Total PSQI** | 0.27 (0.786) | 1.32 (0.188) | NA |
| **TST** | -0.76 (0.447) | 1.19 (0.234) | **3.44 (0.001)** |
| **SOL** | -0.05 (0.959) | 1.75 (0.080) | 0.39 (0.698) |
| **SE** | 0.11 (0.914) | 1.36 (0.174) | **4.77 (<0.001)** |
| **WASO** | 0.56 (0.575) | -1.42 (0.155) | **-2.75 (0.006)** |
| **Number of arousals** | NA | NA | NA |
| **S1** | 0.96 (0.340) | -1.17 (0.242) | **-2.17 (0.030)** |
| **S2** | 1.39 (0.165) | 0.36 (0.721) | **2.09 (0.036)** |
| **SWS** | **-2.06 (0.039)** | 0.64 (0.524) | 0.74 (0.458) |
| **REML** | 0.27 (0.783) | 0.75 (0.451) | **2.35 (0.019)** |
| **REMD** | -0.12 (0.905) | 0.43 (0.666) | 0.58 (0.561) |
| **Sleep Spindle Density** | -1.31 (0.189) | 0.99 (0.324) | NA |
| **Sleep Spindle Amplitude** | -0.19 (0.853) | NA | NA |
| **Sleep Spindle Duration** | -1.07 (0.284) | NA | NA |
| **Slow Wave density** | NA | NA | NA |
| **Insomnia Prevalence** | -1.26 (0.207) | -0.21 (0.835) | 0.59 (0.554) |

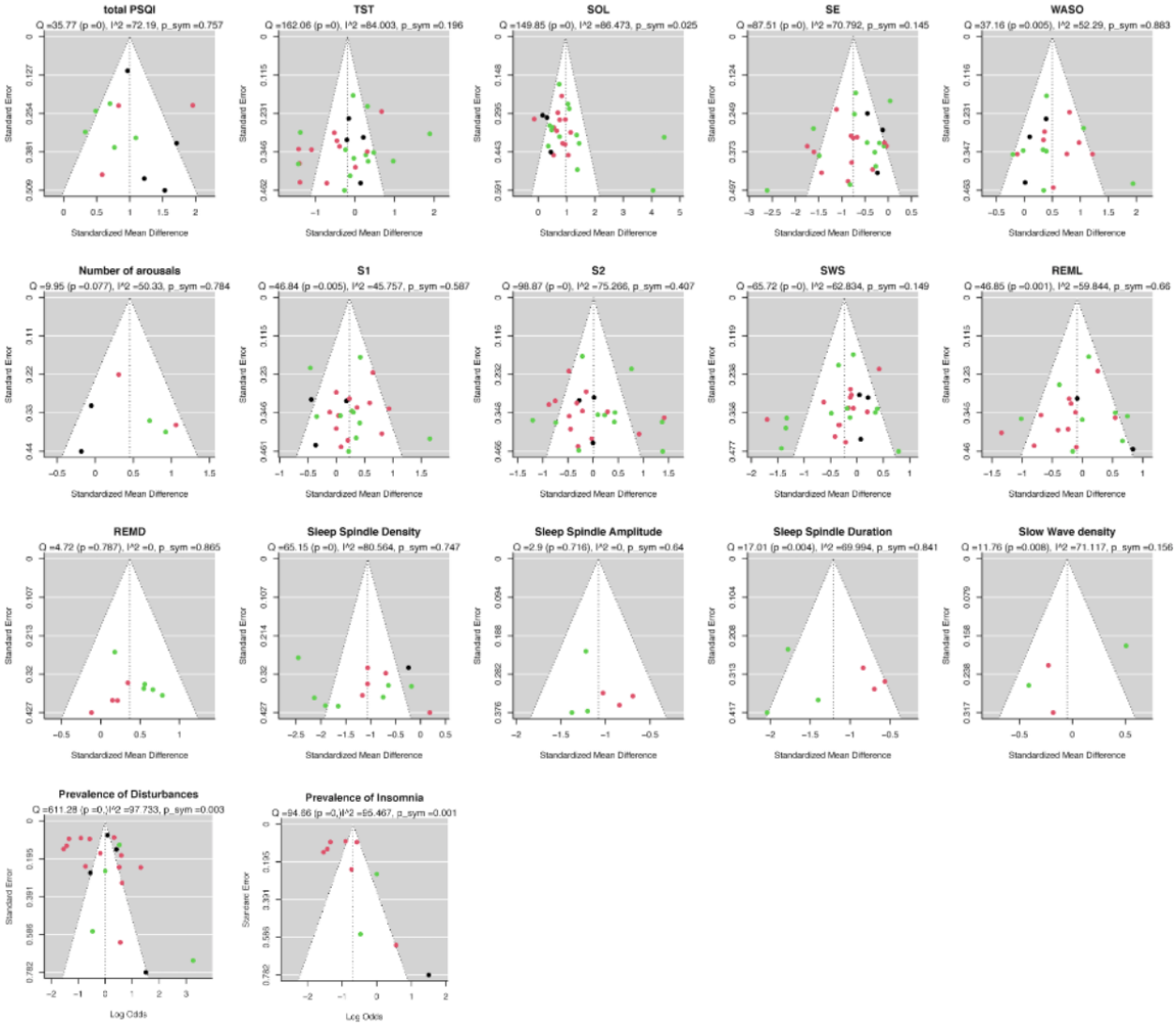
| | | | |
|---|---|---|---|
| **Sleep Disturbance Prevalence** | 0.02 (0.981) | -0.78 (0.438) | -0.53 (0.594) |

**eTable 8: Meta-regressions of psychotic symptoms**

Meta-regressions using random-effects model, comparing the Positive and Negative Syndrome Scale (PANSS) versus the null model on sleep parameters in EP: Early Psychosis; CP: Chronic Psychosis and pooled EP and CP groups. For each meta-regression, effect sizes are shown as Z-scores (p-values). Of note, for total sleep disturbances and insomnia, Z-scores quantify the additive effect of each variable on the logit transformed prevalence values. Bonferroni corrected P threshold is 0.025 (corrected for positive and negative symptoms). Bold black values are moderating effects that are significant before Bonferroni correction, whereas bold red values reflect significant moderating effects after Bonferroni correction.

| | **PANSS-Positive-CP** | **PANSS-Positive-EP** | **PANSS-Positive-Pooled** | **PANSS-Negative-CP** | **PANSS-Negative-EP** | **PANSS-Negative-Pooled** |
|---|---|---|---|---|---|---|
| **Total PSQI** | NA | NA | **4.84 (<0.001)** | NA | NA | 0.92 (0.359) |
| **TST** | -0.53 (0.6) | **-2.9 (<0.001)** | **-2.94 (<0.001)** | -0.67 (0.5) | 0.11 (0.92) | -0.2 (0.842) |
| **SOL** | **3.36 (<0.001)** | -1.43 (0.15) | -0.28 (0.781) | 0.22 (0.82) | 0.97 (0.33) | 0.9 (0.370) |
| **SE** | 0.62 (0.53) | -1.41 (0.16) | 0.34 (0.731) | **-3.85 (<0.001)** | -0.61 (0.54) | **-3.17 (0.002)** |
| **WASO** | NA | NA | **-3.23 (<0.001)** | NA | NA | 1.36 (0.175) |
| **Number of arousals** | NA | NA | NA | NA | NA | NA |
| **S1** | NA | **2.19 (0.03)** | 0.00 (0.999) | NA | 0.32 (0.75) | 1.93 (0.054) |
| **S2** | NA | -0.86 (0.39) | -0.63 (0.529) | NA | **-2.03 (0.04)** | **-2.48 (0.013)** |
| **SWS** | NA | -1.23 (0.22) | 0.21 (0.830) | NA | 0.55 (0.58) | -1.58 (0.115) |
| **REML** | NA | 0.1 (0.92) | -0.24 (0.813) | NA | **-2.52 (0.01)** | -0.31 (0.754) |
| **REMD** | NA | NA | NA | NA | NA | NA |
| **Sleep Spindle Density** | **-2.7 (0.01)** | NA | -0.97 (0.333) | **-2.65 (0.01)** | NA | -0.19 (0.851) |
| **Sleep Spindle Amplitude** | NA | NA | -0.76 (0.445) | NA | NA | -0.37 (0.715) |

| | | | | | | |
|---|---|---|---|---|---|---|
| **Sleep Spindle Duration** | NA | NA | -0.73 (0.47) | NA | NA | **-2.67 (0.008)** |
| **Slow Wave density** | NA | NA | NA | NA | NA | NA |
| **Insomnia Prevalence** | NA | NA | **1.97 (0.049)** | NA | NA | 0.24 (0.81) |
| **Sleep Disturbance Prevalence** | -1.28 (0.199) | -0.79 (0.431) | 0.1 (0.918) | -0.53 (0.595) | -0.02 (0.983) | -1 (0.316) |




**eFigure 18. Funnel plots for each sleep parameter considered in the meta-analysis**

Plots are shown for the residuals of the meta-analysis model fitted with clinical staging as a moderator. Points are colored according to clinical staging (black = CHR-P, green = EP, red = CP). Also shown for each funnel plot is Cochran's Q-value and its associated p-value based on a Chi-squared test that tests for heterogeneity in the studies, as well as Egger's test results assessing funnel plot asymmetry (p_sym). CHR-P: Clinical High Risk for Psychosis; EP: Early Psychosis; CP: Chronic Psychosis.

**eTable 9: AHRQ based study quality for sleep disturbance prevalence studies (N=21)**

Study ratings are shown for both the original categorization (>10 “yes” = excellent; 7-9 = good; 4-6 = weak; 1-3 = poor) as well as the adapted percentage “yes” over the total number of answered questions categorization (excellent = 80-100% yes; good = 50-79%; weak = 30-49%; poor = 0-29%). The latter categorization was used to assess study quality to not penalize studies for which some questions were irrelevant.

| Study Rating | N (absolute number of "yes") | N (based on percent) |
|---|---|---|
| Excellent | 0 | 4 |
| Good | 7 | 9 |
| Weak | 11 | 7 |
| Poor | 3 | 1 |

**eTable 10: AHRQ based study quality for sleep architecture studies (N=39)**

Study ratings are shown for both the original categorization (>10 “yes” = excellent; 7-9 = good; 4-6 = weak; 1-3 = poor) as well as the adapted percentage “yes” over the total number of answered questions categorization (excellent = 80-100% yes; good = 50-79%; weak = 30-49%; poor = 0-29%). The latter categorization was used to assess study quality so as to not penalize studies for which some questions were irrelevant.

| Study Rating | N (absolute number of "yes") | N (based on percent) |
|---|---|---|
| Excellent | 0 | 1 |
| Good | 4 | 18 |
| Weak | 34 | 19 |
| Poor | 3 | 1 |

**eTable 11: PRISMA 2020 Checklist[72]**

| Section and Topic | Item # | Checklist item | Location where item is reported |
|---|---|---|---|
| **TITLE** | | | |
| Title | 1 | Identify the report as a systematic review. | 1 |
| **ABSTRACT** | | | |
| Abstract | 2 | See the PRISMA 2020 for Abstracts checklist. | 3-4 |
| **INTRODUCTION** | | | |
| Rationale | 3 | Describe the rationale for the review in the context of existing knowledge. | 5-6 |
| Objectives | 4 | Provide an explicit statement of the objective(s) or question(s) the review addresses. | 6 |
| **METHODS** | | | |
| Eligibility criteria | 5 | Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses. | 7, s2 |
| Information sources | 6 | Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted. | 7, s2 |
| Search strategy | 7 | Present the full search strategies for all databases, registers and websites, including any filters and limits used. | s2-3 |
| Selection process | 8 | Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process. | 7 |
| Data collection process | 9 | Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process. | s3-4 |

| | | | |
|---|---|---|---|
| Data items | 10a | List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect. | s4 |
| | 10b | List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information. | s4 |
| Study risk of bias assessment | 11 | Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process. | 8, s3 |
| Effect measures | 12 | Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results. | 8 |
| Synthesis methods | 13a | Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)). | s3-4 |
| | 13b | Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions. | s5-6 |
| | 13c | Describe any methods used to tabulate or visually display results of individual studies and syntheses. | NA |
| | 13d | Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used. | 8 |
| | 13e | Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression). | 9 |
| | 13f | Describe any sensitivity analyses conducted to assess robustness of the synthesized results. | NA |
| Reporting bias assessment | 14 | Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases). | 8 |
| Certainty assessment | 15 | Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome. | NA |
| **RESULTS** | | | |

| | | | |
|---|---|---|---|
| Study selection | 16a | Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram. | 10 |
| | 16b | Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded. | 11, Fig. 1 |
| Study characteristics | 17 | Cite each included study and present its characteristics. | s26-34 |
| Risk of bias in studies | 18 | Present assessments of risk of bias for each included study. | s43 (tables S8 and S9) |
| Results of individual studies | 19 | For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots. | s9-25 |
| Results of syntheses | 20a | For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies. | 12-16, s7-8 |
| | 20b | Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect. | 12-16 |
| | 20c | Present results of all investigations of possible causes of heterogeneity among study results. | s7, s35-41 |
| | 20d | Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results. | NA |
| Reporting biases | 21 | Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed. | s42 |
| Certainty of evidence | 22 | Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed. | NA |
| **DISCUSSION** | | | |
| Discussion | 23a | Provide a general interpretation of the results in the context of other evidence. | 17-20 |
| | 23b | Discuss any limitations of the evidence included in the review. | 20-21 |
| | 23c | Discuss any limitations of the review processes used. | 20-21 |

| | | | |
|---|---|---|---|
| | 23d | Discuss implications of the results for practice, policy, and future research. | 21-22 |
| **OTHER INFORMATION** | | | |
| Registration and protocol | 24a | Provide registration information for the review, including register name and registration number, or state that the review was not registered. | 3, 7 |
| | 24b | Indicate where the review protocol can be accessed, or state that a protocol was not prepared. | 3, 7 |
| | 24c | Describe and explain any amendments to information provided at registration or in the protocol. | NA |
| Support | 25 | Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review. | 23 |
| Competing interests | 26 | Declare any competing interests of review authors. | 23 |
| Availability of data, code and other materials | 27 | Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review. | NA |

## eDiscussion

Results of the current meta-analysis highlighted the presence of decreased spindle density, spindle amplitude, and duration in both EP and CP, suggesting that spindle deficits may represent a neurophysiological biomarker that could be used to monitor the course of psychotic disorders. While the available meta-analytic data only allowed for the analysis of spindle oscillations as a whole (ranging from 7-16Hz in included studies), increasing evidence suggests that sleep spindles can be subdivided into “slow” (<12Hz) and “fast” (>12Hz) spindles, as each subtype has distinct topographic organizations, with slow spindles occurring mostly in frontal/prefrontal areas and fast spindles occurring primarily in centroparietal areas[73–75]. Moreover, fast and slow spindles tend to occur at different moments of the slow wave cycle, and the timing of fast spindles is thought to play a role in sleep-dependent memory processes[76]. Also, evidence suggests that fast, rather than slow spindles are found in first-degree relatives, suggesting that genetic risk may be involved in psychosis-related spindle deficits[51]. Therefore, future work should examine spindle properties in distinct CHR-P, EP and CP stages while also differentiating between fast and slow spindles to accurately delineate psychosis-related sleep alterations.

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