



Review article

Overlapping sleep disturbances in persistent tic disorders and attention-deficit hyperactivity disorder: A systematic review and meta-analysis of polysomnographic findings

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ABSTRACT

Introduction: Persistent tic disorders (PTDs) and attention-deficit hyperactivity disorder (ADHD) are common neurodevelopmental conditions which tend to co-occur. Both diagnoses are associated with sleep problems. This systematic review and meta-analysis investigates overlaps and distinctions in objective sleep parameters based on diagnosis (PTD-only, PTD + ADHD, and ADHD-only).

Methods: Databases were searched to identify studies with objective sleep measures in each population. Meta-analyses were conducted using a random effects model.

Results: Polysomnography was the only measure included in all three groups. Twenty studies met final inclusion criteria, combining PTD-only ($N = 108$), PTD + ADHD ($N = 79$), and ADHD-only ($N = 316$). Compared to controls ($N = 336$), PTD-only and PTD + ADHD groups had significantly lower sleep efficiency and higher sleep onset latency. PTD + ADHD also had significantly increased time in bed and total sleep time. No significant differences were observed between ADHD-only groups and controls.

Discussion: Different sleep profiles appear to characterise each population. PTD + ADHD was associated with more pronounced differences. Further research is required to elucidate disorder-specific sleep problems, ensuring appropriate identification and monitoring of sleep in clinical settings.

1. Introduction

Sleep is a complex biobehavioural state essential for human functioning. Current conceptualisations organise sleep into a series of transitory stages, each mapping onto distinct neurophysiological changes (Tubbs et al., 2019). According to the most recent manual from the American Academy of Sleep Medicine (Berry et al., 2020), these stages can be grouped into wake, non-rapid eye movement sleep (NREM; sub-divided into stages N1, N2, and N3), and rapid eye movement sleep (REM). Our understanding of sleep stages continues to evolve in terms of underlying mechanisms (Hérick et al., 2019) and specific links to waking brain function (della Monica et al., 2018). Methods such as actigraphy and polysomnography (PSG) can offer insights into objective sleep behaviour.

Actigraphy is a non-invasive measure of sleep-wake cycles, which typically involves the participant wearing a wrist-worn device for

several days and nights in their own homes. The actiwatch monitors movement and activity, deriving data that can then be used to estimate sleep parameters including time in bed, total sleep time, sleep onset latency, wake after sleep onset, and sleep efficiency (Meltzer et al., 2012; Sadeh, 2011). PSG is often referred to as the ‘gold standard’ of sleep measurement, collecting overnight physiological data such as brain activity, eye movement, heart rate, and blood oxygen levels (Rundo and Downey, 2019). Traditionally, PSG takes place across one or two nights in a sleep lab or clinic, but at-home PSG protocols have also demonstrated high levels of accuracy (Bruyneel et al., 2015). Given the non-invasive nature of actigraphy compared to PSG, attempts have been made to ascertain levels of agreement between these two measures. A recent meta-analysis found that actigraphy slightly overestimates total sleep time and sleep efficiency, while underestimating sleep onset latency and wake after sleep onset (Conley et al., 2019). However, actigraphy remains a clinically useful tool for the assessment of sleep in

Abbreviations: PTD, persistent tic disorder; ADHD, attention deficit hyperactivity disorder.

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paediatric populations where PSG may not be feasible, such as in children with neurodevelopmental disorders (Yavuz-Kodat et al., 2019).

The need to effectively measure sleep in paediatric populations is underscored by the substantial literature base implicating high-quality sleep as a physiological necessity for healthy child development (Chaput et al., 2016; Matricciani et al., 2019; Mindell and Williamson, 2018). Poor sleep quality and quantity can have negative knock-on effects for the development of cognitive skills and socio-emotional behaviour (Spruyt, 2019). Sleep disturbances can also exacerbate cognitive and behavioural issues associated with various neurodevelopmental disorders (Cohen et al., 2014; Fershtman et al., 2019; Knight and Dimitriou, 2019). Due to the integral role of sleep in brain development, populations at a higher risk for sleep disturbances are important to flag. Two neurodevelopmental disorders where sleep appears to be impacted include attention-deficit hyperactivity disorder (ADHD; Viring et al., 2016) and Tourette syndrome (TS; Kirov et al., 2014).

ADHD is characterised by inattention, hyperactivity, and/or impulsivity (Thapar and Cooper, 2016) and has an estimated worldwide prevalence rate of approximately 5% (Polanczyk et al., 2007, 2014). The nature and prevalence of sleep disturbances have been investigated extensively in ADHD, but uncertainties remain regarding the complex relation between sleep and ADHD (Owens et al., 2013). Previous systematic reviews and meta-analyses have explored objective sleep disturbances in children (Díaz-Román et al., 2016; Sadeh et al., 2006), adolescents (Lunsford-Avery et al., 2016), and adults (Díaz-Román et al., 2018) with ADHD. Across these reviews, self- or parent-report measures of sleep highlighted significantly poorer sleep in ADHD compared to controls for each age group. However, meta-analyses of objective sleep measures did not support findings from subjective reports. Sadeh et al. (2006) found that children with ADHD ($N = 333$) differed significantly from controls on only one of 11 PSG variables, showing increased periodic limb movements during sleep. This finding was not replicated in the later meta-analysis from Díaz-Román et al. (2016), which found that children with ADHD spent significantly longer in stage 1 sleep than controls based on PSG ($N = 333$). No other PSG or actigraphy variables reached statistical significance. Finally, the meta-analysis from Díaz-Román et al. (2018) found that adults with ADHD had significantly longer sleep onset latency and poorer sleep efficiency based on actigraphy, but no PSG variables reached statistical significance. These mixed findings demonstrate the complexity of sleep functioning in ADHD and warrant further investigation into the reasons for the high discrepancy between subjective and objective measures, and between different age groups.

A neurodevelopmental disorder that has received comparably less attention in the sleep literature is Tourette syndrome (TS). TS is a type of persistent tic disorder (PTD) characterised by both motor and vocal tics, which vary in severity and complexity across the lifespan (Stern, 2014). It is estimated to affect up to 1% of children worldwide (Scharf et al., 2015) and is associated with a range of co-occurring conditions and symptoms, including sleep problems. Sleep is an important consideration in TS and PTDs more generally as increased tic severity has been linked to poorer sleep quality (Ricketts et al., 2018) and tiredness can increase tic severity (Conelea and Woods, 2008). Recently, a systematic review found that the prevalence rate of subjective sleep disturbances in children with PTDs ranged from under 10 % to over 80 %, but further research is needed to explain this wide range of estimate (Hibberd et al., 2020). A recent clinical review focusing on polysomnographic findings in TS identified some common objective sleep disturbances, including decreased sleep efficiency and increased periodic limb movements (Jiménez-Jiménez et al., 2020). The review also noted that the studies included tended to have low sample sizes. Given that TS is a highly heterogeneous condition, it is possible that these low-powered studies are not detecting the full range of objective sleep disturbances. Despite this, no meta-analysis has examined objective sleep differences between PTDs and controls.

While PTDs and ADHD are both associated with sleep disturbances,

conflicting evidence exists in regards to potential disorder-specific differences in these disturbances. This is complicated by the tendency for TS and ADHD to co-occur with one another. In clinic-based samples, TS has an estimated prevalence of 5%–15% in those diagnosed with ADHD (Hansen et al., 2018), while ADHD has an estimated prevalence of 55 % in TS (Freeman and the Tourette Syndrome International Database Consortium, 2007; Hirschtritt et al., 2015). These clinical estimates may be inflated due to referral bias, but population-based studies suggest a minimum prevalence rate of 17 % for ADHD co-occurring with TS (Scharf et al., 2012). Regardless of true prevalence, meta-analyses indicate a shared genetic basis for TS and ADHD (Tsetsos et al., 2016), demonstrating a need to conduct cross-disorder comparisons. While research on PTDs tends to focus more on TS, the two other types of PTDs (persistent vocal tic disorder and persistent motor tic disorder) likely share the same underlying aetiology as TS (Altun, 2017), suggesting research findings apply to other PTD diagnoses.

Subjective measures of sleep, such as questionnaires, have been used to investigate the prevalence of sleep disturbances in PTD *without* co-occurring ADHD ('PTD-only'), PTD *with* co-occurring with ADHD ('PTD + ADHD'), and ADHD *without* co-occurring PTD ('ADHD-only'). However, the results of these studies are mixed. Allen et al. (1992) administered parent-report questionnaires ($N = 313$) and identified sleep problems in 26 % of children with PTD-only, 41 % with PTD + ADHD, and 48 % with ADHD-only, suggesting sleep is impacted more frequently in ADHD. A later questionnaire study by Ghosh et al. (2014) found high and equal rates of sleep disorders in children with PTD-only and PTD + ADHD ($N = 123$): 65 % of children with PTD-only and 64 % of children with PTD + ADHD qualified for a DSM-V sleep disorder, suggesting that sleep problems are prevalent in PTD regardless of ADHD co-occurrence. These conflicting findings may highlight the heterogeneity in symptoms across populations, but they may also reflect the limitations of subjective measures of sleep. For example, discrepancies have been found between parent-report measures of children's sleep problems and actigraphy (Alfano et al., 2015) and PSG (Choi et al., 2010).

Despite the tendency for PTDs to co-occur with ADHD and the potential shared genetic basis (Tsetsos et al., 2016), reviews have not yet examined overlaps or distinctions in objective sleep parameters between PTD and ADHD populations. Previous systematic reviews have successfully synthesised findings from studies with different populations, allowing for cross-disorder comparisons of, for example, neurophysiological markers of ADHD and autism spectrum disorder (Lau-Zhu et al., 2019), and sleep across a range of psychiatric diagnoses (Baglioni et al., 2016). Synthesising findings from objective sleep studies in the ADHD and PTD literature will allow for comparisons between disorders and may identify sleep issues unique to each diagnosis. This is worthwhile from a scientific standpoint, but there is also a clinical need to understand sleep functioning in these populations. Primary symptoms of PTDs and ADHD may be exacerbated by sleep issues (Conelea and Woods, 2008; Hvolby, 2015) and symptoms common to each condition, such as executive dysfunction, share important links to sleep (Lowe et al., 2017; Taveras et al., 2017). Sleep interventions for children with ADHD can improve primary symptoms, quality of life, and family functioning (Hiscock et al., 2015), but the impact and efficacy of such interventions in PTDs appears unexplored. As these disorders are typically researched in different fields, synthesising this evidence will contribute towards a better understanding of the overlaps and distinctions between PTDs and ADHD.

1.1. Current review

This systematic review aimed to explore potential overlaps and distinctions in objective measures of sleep between PTDs and ADHD. We included any objective measures (i.e., polysomnography and actigraphy) used in both populations. Preliminary literature searches indicated that there would be insufficient actigraphy studies in PTD

populations to allow for meaningful comparisons with ADHD actigraphy studies. This was further supported by a recent systematic review that failed to identify any actigraphy studies in children with PTDs (Hibberd et al., 2020). Nevertheless, this review screened all objective sleep studies in both PTD and ADHD populations. The number of studies utilising various objective sleep measures in each population can therefore be clearly flagged. Inclusion criteria were refined following title and abstract screening to collate studies with comparable methodologies.

1.2. Specific objectives

- (i) To report the number of studies available in each population utilising objective measures of sleep, informing future research in this area.
- (ii) To compare and contrast findings of objective sleep studies with the following groups: PTD without ADHD (PTD-only), ADHD without PTD (ADHD-only), and PTD co-occurring with ADHD (PTD + ADHD). This will contribute towards our understanding of potential disorder-specific sleep disturbances.
- (iii) To conduct meta-analyses to explore the strength of the mean differences in standard sleep parameters between the populations of interest and typically developing controls.

2. Methods

2.1. Protocol

The protocol for this review was registered on PROSPERO and can be accessed at https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42020181933

2.2. Search methods

2.2.1. Databases

The following electronic databases were searched on 27/01/2020: PsycINFO, PubMed, EMBASE, and Scopus. Reference lists and citations of included studies and previous reviews were also manually searched for eligible studies that may not have appeared in the database search, ensuring research saturation. Databases were searched again on 08/09/2020 to identify any new studies published since the original search.

2.2.2. Search strategy

A combination of MeSH terms and the following keywords were used in the searches: (Tourette* OR tics OR “tic disorder*” OR “chronic tic*” OR “persistent tic*” OR “chronic motor tic*” OR “chronic vocal tic*” OR ADHD OR “attention-deficit” OR “attention deficit*” OR “hyperactivity disorder”) AND (sleep* OR night* OR bedtime* OR polysomnograph* OR PSG OR actigraph* OR actimet* OR actograp* OR actomet* OR accelerometer* OR circadian OR insomnia* OR “wrist activit*”). Two searches (one for PTD, one for ADHD) were performed on each database simultaneously. See Appendix S1 for full search strings for each database. No filters (e.g., date, age, article type, etc.) were applied during database searching to avoid missing relevant articles that may have been mislabeled. This search strategy, including keywords and filter choice, was developed following a consultation with a librarian in UCD with expertise in systematic reviews. Results were uploaded as RIS files to Mendeley to identify and track duplicates. Files were then separated into two folders (PTD and ADHD) before uploading to Covidence systematic review software (Veritas Health Innovation, Melbourne, Australia. Available at www.covidence.org).

2.2.3. Inclusion criteria

Inclusion criteria were informed by previous systematic reviews with similar sleep measures (e.g., Baglioni et al., 2016) and populations (e.g., Díaz-Román et al., 2016; Hibberd et al., 2020). Study populations must

have included healthy controls and at least one of the following groups: (i) PTD-only, (ii) PTD + ADHD, or (iii) ADHD-only. All genders, ages, and ethnicities were included. Studies with an objective measure of sleep were included. Sufficient engagement must also have been given to the topic of sleep to allow relevant findings to be extracted in isolation of other data. Inclusion criteria were refined further during full-text screening to fulfil the aims of this review (see Screening procedures).

2.2.4. Exclusion criteria

Due to a lack of resources required for translation, studies published in non-English languages were excluded. Animal studies, reviews, commentaries, editorials, single-case studies, studies focused primarily on medication or drug efficacy (where baseline measures were not reported), and studies published as grey literature (e.g., conference abstracts, dissertations) were excluded. Studies where it was not possible to isolate the target population (PTD-only, PTD + ADHD, or ADHD-only) from a wider population were also excluded. Finally, studies including populations with unclear diagnoses or primary sleep disorders were excluded.

2.3. Study selection

2.3.1. Screening procedures

Results were uploaded to Covidence for screening, quality appraisal, and data extraction. Once duplicates were removed, two independent reviewers (LK & CS) conducted title/abstract screening, where papers were excluded if it was evident from the abstract alone that inclusion criteria were not met. Full-text screening was then conducted by the same independent reviewers with refined eligibility criteria. At this stage, actigraphy studies were excluded and PSG studies that did not utilise an adaptation night were also excluded. The rationale for these refined eligibility criteria is that the aim of this review was to compare objective sleep measures between populations, meaning that studies were only retained if the measure had been used in both populations of interest, ensuring balance. Consensus between reviewers regarding study eligibility must have been reached before proceeding to the next stage of screening. A third independent reviewer (MD) was consulted when uncertainties or disagreements arose. Authors were contacted for further information if eligibility was unclear. All eligible studies were collated in an Excel file and separated based on population included and objective sleep measure used (see Appendix S3). The PRISMA flow diagram (Moher et al., 2009) was updated throughout the screening process (see Appendix).

2.3.2. Appraisal of study quality

Study quality was assessed for each study by two independent reviewers (LK & CS) using the Newcastle-Ottawa scale (NOS) for case-control studies (Wells et al., 2000) and the 22-item STROBE (strengthening the reporting of observational studies in epidemiology) checklist (Von Elm et al., 2007). Prior to conducting quality appraisal, the reviewers performed practice assessments from previously published reviews, ensuring criteria were being followed in accordance to current standards and between the two reviewers. A third independent reviewer (MD) was consulted to resolve any inconsistencies or disagreements. NOS scores ranged from 0 to 9 stars and were interpreted as follows: 7 or more stars indicates high quality studies, 4–6 stars indicate medium quality, and fewer than 4 stars indicate poor quality (Li et al., 2020). STROBE scores ranged from 0 to 22, with a score of 11 or over indicating ‘good quality’ (Lu et al., 2019). In line with recent reviews, STROBE scores were transferred into a percentage to aid interpretation.

2.4. Data extraction

Means and standard deviations for the following standard sleep parameters were extracted into an Excel file: Time in bed (TIB; minutes recorded between ‘lights off’ and ‘lights on’); total sleep time (TST;

minutes recorded as ‘asleep’ across the night); sleep efficiency (ratio of TST to TIB, expressed as a percentage), sleep onset latency (minutes elapsed between ‘lights off’ and sleep onset); slow wave sleep (percentage of TST spent in slow wave sleep, a deep sleep characterised by low EEG frequency); and rapid eye movement sleep (percentage of TST spent in rapid eye movement sleep, characterised by mixed EEG frequency and increased brain activity). These variables were chosen as they were most consistently reported across studies (see Appendix S2 for a table outlining each variable reported in each study). Details on study design (country of publication, recruitment method, PSG methods) and sample characteristics (sample size, age, gender, medication status, tic severity, co-occurring disorders) were also extracted. This process was validated through a double extraction of papers by LK and CS, allowing any errors to be flagged and amended.

2.5. Data analysis

The qualitative synthesis involved basic tabulation and descriptives, recording characteristics of included studies and summarising main findings. Results were synthesised separately for PTD-only, PTD + ADHD, and ADHD-only populations. Meta-analyses were conducted to compare mean scores on standard sleep parameters between the target populations and control groups. Raw data (means and standard deviations) for core sleep parameters were inputted into Excel. Individual effect sizes for each variable in each study were calculated using the *esc* package in R. Hedges *g* was chosen due to its ability to better control for bias in studies with smaller sample sizes (Hedges and Olkin, 1985). Random-effects model meta-analyses were conducted using the *meta*, *metafor*, and *dmetar* packages in R to determine effect sizes, heterogeneity of effect sizes, confidence intervals, and to generate forest plots (Harrer et al., 2019).

The DerSimonian-Laird (DL; DerSimonian and Laird, 1986) approach, adjusted using the Hartung-Knapp-Sidik-Jonkman (HKSJ) method, was chosen as the estimator for τ^2 as we anticipated a relatively small number of studies for the PTD-only and PTD + ADHD meta-analyses, along with some heterogeneity within and between studies. The HKSJ method is less widely-used than the standard DL, but as DL can overestimate pooled effects of smaller meta-analyses (Veroniki et al., 2016) and inflate error rates (Int'Hout et al., 2014), the HKSJ method was considered most appropriate for the present meta-analysis.

Interpretation of effect sizes was based on standard rules of thumb ($g < 0.20$ is a small effect, 0.20 to 0.50 is moderate, and ≥ 0.80 is large). For the current analyses, positive effect sizes indicate higher scores in the clinical group compared to the control group, and vice versa. Heterogeneity of effect sizes were assessed using *Q* (where $p < 0.1$ indicates significant heterogeneity; Higgins et al., 2019) and I^2 statistics (where $I^2 < 25\%$ is low, $< 50\%$ is moderate, and $> 50\%$ is large; Higgins et al., 2003). Egger's regression intercept examined possible publication bias (Egger et al., 1997) when the number of included studies met the cut-off of $k = 10$ (Higgins et al., 2019). Mixed-effect model meta-regressions were conducted using the *metareg* package in R to examine the effect of tic severity on PSG variables in the PTD groups. We had originally planned to examine other potential moderating effects using weighted multiple regression analysis (Field and Gillett, 2010), but as the number of included studies in each subgroup was below the recommended cut-off of $k = 10$ (Borenstein et al., 2011; Borenstein and Higgins, 2013), this additional analysis was not conducted.

3. Results

3.1. Study selection

Database searches yielded 4899 publications (See Appendix for PRISMA flowchart). After duplicates were removed, 2627 titles/abstracts were screened, resulting in 221 publications eligible for full-text screening. The number of actigraphy studies identified with PTD

populations and controls ($n = 2$) was insufficient to allow for meaningful comparisons with the ADHD actigraphy studies ($n = 82$). Furthermore, these two PTD actigraphy studies existed only as grey literature, which was a pre-defined exclusion criterion. Actigraphy studies across both groups ($n = 84$) were therefore excluded at this stage. PSG was the only measure used in both populations. As adaptation nights were utilised in all eligible PTD studies retrieved, the additional criterion of a 2-night PSG protocol was added to the ADHD studies to ensure balance and meaningful comparison. This resulted in 20 studies meeting the final inclusion criteria for the qualitative synthesis, 19 of which were included in the meta-analysis.

3.2. Characteristics of included studies

Six of the 20 included studies had a population with PTD-only, four with PTD + ADHD, and 16 with ADHD-only. This resulted in 26 different pairings with controls, as three papers included more than one clinical population in the same study. The characteristics of included studies (Tables 1 and 2) and main PSG findings (Table 3) are described below.

3.2.1. Age, gender, and clinical characteristics of participants

Studies varied in terms of age, gender, and clinical characteristics of participants. The majority of study populations were comprised of children ($n = 14$). Two PTD-only studies and three ADHD-only studies had adult samples. In all but one study (Garbazza et al., 2018), samples were disproportionately male, and some ADHD studies had a male-only sample ($n = 3$). However, the majority of included studies had adequately gender-matched control groups. There was large variation in the medication status of participants both between and within studies. Most studies specified that any participants taking medication had a washout period before PSG recordings ($n = 12$), but this length of time varied from two days to four months. Some studies stated that all participants were either medication-naïve ($n = 5$) or continued taking medication throughout the study ($n = 2$), but three studies failed to report details on medication status. In terms of co-occurring disorders, ten studies described exclusion criteria that ensured the clinical group had no somatic, neurological, sleep, or psychiatric disorders other than the target condition (i.e., PTD-only, PTD + ADHD, or ADHD-only). Some ADHD-only studies excluded all conditions except oppositional defiant disorder ($n = 3$), restless leg syndrome ($n = 1$), or major depressive disorder ($n = 1$). One ADHD-only study did not exclude participants with co-occurring disorders (Miano et al., 2006), but no participant was reported as having a PTD diagnosis. The remaining four studies were less clear in their reporting of exclusion criteria, including participants with ‘symptoms’ of co-occurring psychiatric disorders ($n = 2$), a previous history of psychiatric disorders ($n = 1$), or failing to report co-occurring disorders ($n = 1$).

3.2.2. Setting

A large majority of studies took place in Germany ($n = 13$), followed by Italy ($n = 2$), the United States ($n = 2$), the Czech Republic ($n = 2$), and Canada ($n = 1$). Thirteen studies recruited participants from clinics, while three studies recruited participants from the local community in addition to clinic referrals. Four studies did not report on where or how participants were recruited.

3.2.3. PSG methods

Overnight PSG recordings typically took place in a sleep laboratory ($n = 16$), but two studies used an at-home protocol. Two studies did not report the setting in which PSG took place. All studies collected data from an electroencephalogram (EEG), electrooculogram (EOG), and electromyogram (EMG). Fifteen additionally collection electrocardiogram (ECG) data. Most studies scored PSG data according to Rechtschaffen & Kales criteria ($n = 18$), but two used American Academy of Sleep Medicine (AASM) criteria. More than half of the studies allowed participants to go to bed and wake ad libitum or according to

Table 1
Design characteristics of included studies.

First author (Year)	Country	Recruitment	PSG setting	PSG timing	PSG methods	PSG scoring criteria	STROBE score (%)	NOS
Bestmann et al. (2019)	Germany	Clinic / community	At home	Ad-lib	EEG, EOG, EMG	R&K	18 (82 %)	7
Garbazza et al. (2018)	US	Clinic	Sleep lab	NR	EEG, EOG, EMG, ECG	AASM	21 (95 %)	8
Kirov et al. (2017)	Germany	Clinic	Sleep lab	Ad-lib	EEG, EOG, EMG	R&K	21 (95 %)	8
Saletin et al. (2017)	US	NR	Sleep lab	Ad-lib	EEG, EOG, EMG, ECG	R&K	19 (86 %)	6
Ferri et al. (2013)	Italy	NR	NR	NR	EEG, EOG, EMG, ECG	R&K	19 (86 %)	7
Prehn-Kristensen et al. (2013)	Germany	Clinic	At home	NR	EEG, EOG, EMG	R&K	19 (86 %)	8
Stephens et al. (2013)	Canada	Clinic	Sleep lab	Ad-lib	EEG, EOG, EMG	AASM	20 (91 %)	9
Kirov et al. (2012)	Germany	Clinic	Sleep lab	Ad-lib	EEG, EOG, EMG, ECG	R&K	20 (91 %)	8
Průhová et al. (2012)	Czech Republic	NR	Sleep lab	NR	EEG, EOG, EMG, ECG	R&K	17 (77 %)	6
Prehn-Kristensen et al. (2011)	Germany	Clinic / community	Sleep lab	NR	EEG, EOG, EMG	R&K	20 (91 %)	8
Průhová et al. (2010)	Czech Republic	Clinic	Sleep lab	Ad-lib	EEG, EOG, EMG, ECG	R&K	21 (95 %)	8
Sobanski et al. (2008)	Germany	Clinic	Sleep lab	Fixed	EEG, EOG, EMG, ECG	R&K	18 (82 %)	7
Kirov et al. (2007b)	Germany	Clinic	Sleep lab	Ad-lib	EEG, EOG, EMG, ECG	R&K	19 (86 %)	8
Kirov et al. (2007a)	Germany	Clinic	Sleep lab	Ad-lib	EEG, EOG, EMG, ECG	R&K	20 (91 %)	8
Miano et al. (2006)	Italy	Clinic	Sleep lab	Ad-lib	EEG, EOG, EMG, ECG	R&K	19 (86 %)	6
Philipsen et al. (2005)	Germany	Clinic	Sleep lab	Fixed	EEG, EOG, EMG, ECG	R&K	18 (82 %)	7
Kirov et al. (2004)	Germany	Clinic	Sleep lab	Ad-lib	EEG, EOG, EMG, ECG	R&K	17 (77 %)	7
Kostanecka-Endress et al. (2003)	Germany	Clinic	Sleep lab	Ad-lib	EEG, EOG, EMG, ECG	R&K	19 (86 %)	8
Cohrs et al. (2001)	Germany	Clinic / community	Sleep lab	Ad-lib	EEG, EOG, EMG, ECG	R&K	18 (82 %)	6
Voderholzer et al. (1997)	Germany	NR	NR	NR	EEG, EOG, EMG, ECG	R&K	16 (73 %)	5

Note. PSG timing refers to the sleep-wake protocol used in the study (Fixed = participants had a fixed bedtime protocol, Ad-lib = participants were allowed to sleep ad-libitum); EEG = electroencephalogram; EOG = electrooculogram; EMG = electromyogram; AASM = American Academy of Sleep Medicine; R&K = Rechtschaffen & Kales criteria; Higher STROBE percentages and higher NOS values (maximum of 9 points) indicate higher quality. See supplementary materials for completed STROBE and NOS tables for each study (including rationale for scoring); NR = Not reported.

their own sleep schedule preferences ($n = 12$), while two employed a fixed bedtime routine. Six studies did not report this detail.

3.2.4. Quality appraisal

Methodological quality was relatively high across the included studies according to the Newcastle-Ottawa scale. Fifteen of the 20 studies scored 7 or more stars out of 9, indicating high methodological quality. The remaining studies scored either 5 stars ($n = 1$) or 6 stars ($n = 4$), indicating medium methodological quality (Li et al., 2020). In terms of reporting quality, STROBE ranged from 73 % (score of 16/22) to 95 % (score of 21/22). As 50 % (score of 11/22) concordance with the STROBE checklist is commonly considered 'good' quality (Lu et al., 2019), the range of scores found here demonstrates high-quality reporting of research. The most common item that was not met by included studies was Item 10 (study size), as no study provided a clear rationale for the chosen sample size based on previous studies or power analyses. This was followed by Item 19 (limitations), as 8 of the 20 studies failed to adequately discuss study limitations. See Appendix S4 and S5 for completed checklists for each study.

3.2.5. Publication bias

It was not possible to conduct Egger's test of the intercept for the PTD-only and PTD + ADHD groups as the number of included studies was lower than the recommended cut-off (Higgins et al., 2019). There was a sufficient number of studies in the ADHD-only group for the variables of time in bed ($n = 11$), sleep onset latency ($n = 13$), and REM

sleep percentage ($n = 13$). No publication bias was found for these variables.

3.3. Qualitative synthesis of included studies

3.3.1. PTD-only

Six studies included a population with PTD-only. In all but one study (Stephens et al., 2013), significant differences were found between PTD-only participants and controls. The most common sleep parameters impacted were sleep efficiency and sleep onset latency. PTD-only groups had lower sleep efficiency and longer sleep onset latency than controls in three of the five studies reporting significant between-group PSG differences (Cohrs et al., 2001; Kostanecka-Endress et al., 2003; Kirov et al., 2007a). REM sleep percentage was increased in PTD-only compared to controls in two studies (Kirov et al., 2007a, 2017). Other sleep parameters were impacted less consistently. Voderholzer et al. (1997) reported significantly lower sleep period and total sleep time in adults with PTD-only, but Kostanecka-Endress et al. (2003) found that these parameters were significantly higher in children with PTD-only compared to controls.

3.3.2. PTD + ADHD

Four studies included a population with PTD + ADHD. Three of these also included groups with PTD-only and ADHD-only. Kirov et al. (2007a) found sleep disturbances in each population: Increased REM sleep in ADHD-only; increased arousal during sleep and reduced sleep

Table 2
Sample characteristics of included studies.

First author (Year)	Sample (n)	Age range	M age (SD)	Gender (M:F)	n on medication	TSSS score	Co-occurring disorders	Conditions excluded	Diagnostic criteria ²
Bestmann et al. (2019)	ADHD (17) Controls (16)	9–12	10.7 (1.1) 10.9 (1.1)	All male	12 (ceased 2 days prior)	n/a	ODD (n = 6)	All but ODD	NR
Garbazza et al. (2018)	ADHD (15) Controls (18)	NR	33.9 (7.9) 35.8 (7.5)	6:9 8:10	7 (not ceased)	n/a	MDD (n = 2)	Somatic / Neurological diseases, substance abuse	DSM-IV
Kirov et al. (2017)	PTD (21) PTD + ADHD (21) ADHD (24) Controls (22)	8–16	11.8 (1.8) 11.0 (2.3) 11.2 (2.1) 11.4 (2.3)	19:2 19:2 10:14 19:3	26 (ceased 5–14 days prior)	3.41 (1.47) 4.17 (1.72)	None	All	DSM-IV
Saletin et al. (2017)	ADHD (7) Controls (14)	10–12	11.9 (0.9) 11.7 (0.9)	5:2 10:4	NR	n/a	None	Sleep / Learning disorders, PDDs	DSM-IV
Ferri et al. (2013)	ADHD (18) Controls (17)	7–12	8.9 (1.4) 9.4 (2.0)	11:7 9:8	0	n/a	RLS (n = 8)	All but RLS	DSM-IV
Prehn-Kristensen et al. (2013)	ADHD (16) Controls (16)	9–12	10.6 (.95) 11.1 (.95)	16:0 16:0	12 (ceased 2 days prior)	n/a	ODD (n = 4)	All but ODD	DSM-IV
Stephens et al. (2013)	PTD (20) PTD + ADHD (21) ADHD (33) Controls (16)	6–16	10.8 (NR)	75:15	0	NR	None	All, IQ < 80	DSM-3-R
Kirov et al. (2012)	ADHD (20) Controls (19)	8–15	11.2 (2.3) 11.3 (2.5)	19:1 17:2	11 (ceased 7 days prior)	n/a	None	All, IQ < 80	DSM-IV
Průhová et al. (2012)	ADHD (14) Controls (12)	7–12	9.6 (1.6) 9.0 (1.6)	12:2 8:4	0	n/a	None	All	DSM-IV
Prehn-Kristensen et al. (2011)	ADHD (12) Controls (12)	10–16	13.0 (0.5) 12.6 (0.2)	12:0 12:0	5 (ceased 2 days prior)	n/a	ODD (n = 3)	All but ODD, IQ < 85	DSM-IV
Průhová et al. (2010)	ADHD (31) Controls (26)	6–12	9.3 (1.7) 9.2 (1.5)	26:5 22:4	0	n/a	None	All	DSM-IV
Sobanski et al. (2008) ¹	ADHD (24) Controls (24)	NR	36.2 (8.9)	16:8	NR (ceased 4 weeks prior)	n/a	None	All	DSM-IV
Kirov et al. (2007b)	PTD (18) PTD + ADHD (18) ADHD (18) Controls (18)	8–16	11.7 (2.3) 11.1 (2.3) 10.9 (2.0) 11.6 (2.3)	16:2 17:1 17:1 16:2	37 (ceased 5–14 days prior)	NR	None	All, IQ < 80	DSM-IV & ICD-10
Kirov et al. (2007a)	PTD + ADHD (19) Controls (19)	8–16	11.1 (2.3) 11.1 (2.2)	18:1 17:2	12 (ceased 7 days prior)	4.17 (1.77)	None	All, IQ < 80	DSM-IV & ICD-10
Miano et al. (2006)	ADHD (20) Controls (20)	6–13	9.3 (NR) 8.4 (NR)	18:2 9:11	0	n/a	Learning disabilities (n = 10), ODD (n = 2), GAD (n = 2), conduct disorder (n = 1)	Neurological diseases / seizure disorders, sleep apnoea & IQ < 70	DSM-IV
Philipsen et al. (2005)	ADHD (20) Controls (20)	22–55	33.5 (8.9) 33.3 (8.8)	11:9	NR (ceased 2 weeks prior)	n/a	Previous substance abuse (n = 4) / depressive disorder (n = 10) / agoraphobia (n = 1) / bulimia nervosa (n = 1)	Current depressive disorder / substance abuse	DSM-IV & ICD-10

(continued on next page)

Table 2 (continued)

First author (Year)	Sample (n)	Age range	M age (SD)	Gender (M:F)	n on medication	TSSS score	Co-occurring disorders	Conditions excluded	Diagnostic criteria ²
Kirov et al. (2004)	ADHD (17)	8–14	11.2 (2.0)	17:0	14 (ceased 2 days to 4 months prior)	n/a	Nocturnal enuresis ($n = 1$), Symptoms of dyslexia ($n = 12$) / conduct disorder ($n = 3$) / panic disorder ($n = 1$)	Somatic diseases, axis-II disorders, IQ < 80	DSM-IV & ICD-10
	Controls (17)		11.2 (2.3)	17:0					
Kostanecka-Endress et al. (2003)	PTD (17)	7–15	11.8 (2.2)	12:5	10 (ceased 14 days prior)	3.40 (1.80)	None	All, IQ < 80	DSM-IV & ICD-10
	Controls (16)		11.8 (2.3)	12:4					
Cohrs et al. (2001)	PTD (25)	16–44	29.0 (6.8)	16:9	12 (not ceased)	5.68 (1.80)	NR	NR	DSM-IV & ICD-10
	Controls (14)		28.7 (5.0)	8:6					
Voderholzer et al. (1997)	PTD (7)	18–52	31 (11)	6:1	1 (ceased 7 days prior)	NR	OCD symptoms ($n = 2$)	Chronic diseases associated with RLS or PLMS	DSM-III-R
	Controls (7)		31 (10)	6:1					

M = mean; SD = standard deviation; NR = not reported in study; TSSS = mean score Tourette syndrome severity scale (only applicable to studies with PTD-only or PTD + ADHD groups); RLS = restless leg syndrome; PLMS = periodic limb movements in sleep. Conditions excluded refers to the clinical groups (All = somatic diseases, neurological disorders, sleep disorders, and co-occurring psychiatric disorders).

¹ This study provided two sets of PSG data based on presence of co-occurring disorders; only data from the ADHD-only group were included here.

² Diagnostic criteria for ADHD and/or PTD.

efficiency in PTD-only; and a combination of these sleep disturbances in PTD + ADHD. Similarly, Kirov et al. (2007b) found that, compared to controls, children with PTD + ADHD had increased REM sleep and shorter latency to REM sleep. Children with PTD + ADHD also showed a longer sleep period time and increased time in bed. Like Kirov et al. (2007b), 2017 found differences between populations. Children with PTD-only had significantly longer sleep onset latency and slow wave sleep latency compared to ADHD-only and controls. REM sleep parameters significantly differed between all clinical groups and controls, but there were no significant differences in REM sleep between PTD-only, PTD + ADHD, and ADHD-only groups. Unlike Kirov et al. (2007a, 2007b, 2017), Stephens et al. (2013) found no significant differences in REM sleep duration between groups. However, there was a significantly greater number of periodic limb movements during sleep in children with PTD + ADHD compared to PTD-only, ADHD-only, and control groups.

3.3.3. ADHD-only

Sixteen studies included a population with ADHD-only. There was large heterogeneity in specific findings, and four studies found no significant differences in standard sleep or movement parameters between ADHD-only and control groups. In the 12 studies where differences were found, the most common PSG variables to be impacted were REM sleep (6/12), time in bed (5/12), total sleep time (4/12), and sleep onset latency (4/12). However, the way in which these sleep parameters were impacted varied between studies. Reduced time in REM sleep was reported in ADHD-only groups in two studies (Kirov et al., 2017; Sobanski et al., 2008), but increased time in REM sleep was also found in two studies (Kirov et al., 2007a, 2012). ADHD-only groups had significantly lower time in bed compared to controls in two studies (Saletin et al., 2017; Miano et al., 2006), while others found increased time in bed (Kirov et al., 2012, 2007a; 2004). Compared to control groups, sleep onset latency was increased in ADHD-only groups in all studies reporting differences in this measure (Garbaza et al., 2018; Ferri et al., 2013; Prehn-Kristensen et al., 2011; Sobanski et al., 2008).

3.4. Meta-analysis

Nineteen of the 20 studies were included in the meta-analysis. Kirov et al. (2007b) was excluded as it was not possible to extract relevant group-level data. The most commonly-reported major PSG variables were included: Time in bed (Fig. 1), total sleep time (Fig. 2), sleep efficiency (Fig. 3), sleep onset latency (Fig. 4), rapid eye movement sleep

(Fig. 5), and slow wave sleep (Fig. 6). Individual effect sizes (Hedges g) were calculated for each variable in each study before conducting the meta-analyses (Appendix S3). See Table 4 for a summary.

3.4.1. Time in bed

Compared to controls, no significant effect was found for time in bed in PTD-only ($k = 4$; SMD = 0.34, 95 % CI = -0.49 to 1.17, $p = 0.279$) or ADHD-only populations ($k = 11$; SMD = 0.14, 95 % CI = -0.38 to 0.66, $p = 0.565$). A moderate-large effect size was found for PTD + ADHD populations ($k = 2$), with significantly increased time in bed compared to controls (SMD = 0.77, 95 % CI = 0.31–1.22, $p = 0.030$). No significant heterogeneity between studies was found for PTD-only ($I^2 = 40\%$, $\tau^2 = 0.09$, $p = 0.169$) or PTD + ADHD ($I^2 = 0\%$, $\tau^2 = 0$, $p = 0.878$), but heterogeneity between ADHD-only studies was substantial and significant ($I^2 = 77\%$, $\tau^2 = 0.40$, $p < 0.0001$).

3.4.2. Total sleep time

Compared to controls, no significant effect was found for time in bed in PTD-only ($k = 5$; SMD = -0.06, 95 % CI = -0.69 to 0.57, $p = 0.806$) or ADHD-only populations ($k = 14$; SMD = 0.11, 95 % CI = -0.24 to 0.46, $p = 0.499$). A moderate effect size was found for total sleep time in PTD + ADHD populations ($k = 3$), with significantly increased total sleep time compared to controls (SMD = 0.60, 95 % CI = 0.42 to 0.78, $p = 0.005$). No significant heterogeneity between studies was found for PTD-only ($I^2 = 38\%$, $\tau^2 = 0.08$, $p = 0.166$) or PTD + ADHD ($I^2 = 0\%$, $\tau^2 = 0$, $p = 0.953$). Heterogeneity between ADHD-only studies was substantial and significant ($I^2 = 64\%$, $\tau^2 = 0.21$, $p = 0.001$).

3.4.3. Sleep efficiency

A large effect size was found for sleep efficiency in PTD-only populations ($k = 5$), with significantly lower sleep efficiency compared to controls (SMD = -0.75, 95 % CI = -1.13 to -0.37, $p = 0.005$). A small effect size was found in PTD + ADHD populations ($k = 3$), with significantly lower sleep efficiency compared to controls (SMD = -0.25, 95 % CI = -0.46 to -0.04, $p = 0.037$). No significant effect was found for sleep efficiency in ADHD-only populations ($k = 15$; SMD = -0.14, 95 % CI = -0.39 to 0.11, $p = 0.258$). No significant heterogeneity between studies was found for PTD-only ($I^2 = 0\%$, $\tau^2 = 0$, $p = 0.596$) or PTD + ADHD ($I^2 = 0\%$, $\tau^2 = 0$, $p = 0.933$). Heterogeneity between ADHD-only studies was moderate and significant ($I^2 = 42\%$, $\tau^2 = 0.08$, $p = 0.045$).

3.4.4. Sleep onset latency

A medium-large effect size was found for sleep onset latency in PTD-

Table 3
Main PSG findings of included studies by diagnostic group.

PTD-only	
First author (year)	Main PSG findings (95% CI)
Kirov et al. (2017)*	↑REM sleep % in PTD than controls. ↓REM sleep latency in PTD than controls. ↑SOL in PTD than controls or ADHD. ↑SWS latency in PTD than controls or ADHD.
Stephens et al. (2013)*	No significant differences between PTD and controls, ADHD, or PTD + ADHD.
Kirov et al. (2007a)*	↑REM sleep % in PTD than controls. ↓SE in PTD than controls. ↓SE in PTD than controls. ↑SOL in PTD than controls. ↑SPT in PTD than controls. ↑TIB in PTD than controls. ↑WASO in PTD than controls. ↓SE in PTD than controls
Kostanecka-Endress et al. (2003)	↑SOL in PTD than controls. ↓SWS % in PTD than controls. ↑Wake % in PTD than controls.
Cohrs et al. (2001)	↓SPT in PTD than controls. ↓TST in PTD than controls.
Voderholzer et al. (1997)	
PTD + ADHD	
First author (year)	Main PSG findings (95% CI)
Kirov et al. (2017)*	↑REM sleep % in PTD + ADHD than controls. ↓REM sleep latency in PTD + ADHD than controls.
Stephens et al. (2013)*	↑Arousals from sleep in PTD + ADHD than controls or PTD. ↑PLMI in PTD + ADHD than controls, ADHD, and PTD. ↑REM sleep % in PTD + ADHD than controls.
Kirov et al. (2007a)*	↑SPT in PTD + ADHD than controls. ↑TIB in PTD + ADHD than controls. ↑TST in PTD + ADHD than controls. ↑REM sleep % in PTD + ADHD than controls.
Kirov et al. (2007b)	↓REM sleep latency in PTD + ADHD than controls. ↑SPT in PTD + ADHD than controls. ↑TIB in PTD + ADHD than controls.
ADHD-only	
First author	Main PSG findings (95% CI)
Bestmann et al. (2019)	No significant differences between ADHD and controls.
Garbazza et al. (2018)	↑SOL in ADHD than controls.
Kirov et al. (2017)*	↓REM sleep latency in ADHD than controls. ↑REM sleep % in ADHD than controls.
Saletin et al. (2017)	↓TIB in ADHD than controls.
Stephens et al. (2013)*	↑Arousals from sleep in ADHD than controls or PTD. ↑Total number of leg movements during sleep in ADHD than controls or PTD.
Prehn-Kristensen et al. (2013)	No significant differences between ADHD and controls. ↑Night-time awakenings in ADHD than controls. ↑PLMI in ADHD than controls.
Ferri et al. (2013)	↑SOL in ADHD than controls. ↑Stage shifts in ADHD than controls. ↑Stage 1 sleep % in ADHD than controls.
Příhodová et al. (2012)	No significant differences between ADHD and controls. ↑REM sleep % in ADHD than controls.
Kirov et al. (2012)	↓REM sleep latency in ADHD than controls. ↑TST in ADHD than controls. ↑TIB in ADHD than controls. ↑REM sleep (minutes) in ADHD than controls.
Prehn-Kristensen et al. (2011)	↓SE in ADHD than controls. ↑SOL in ADHD than controls. ↓SWS latency in ADHD than controls.
Příhodová et al. (2010)	No significant differences between ADHD and controls. ↓SE in ADHD than controls.
Sobanski et al. (2008)	↑SOL in ADHD than controls. ↓REM (total density) in ADHD than controls. ↑WASO in ADHD than controls. ↑REM sleep % in ADHD than controls.
Kirov et al. (2007a)*	↑SPT in ADHD than controls. ↑TIB in ADHD than controls. ↑TST in ADHD than controls. ↓SPT in ADHD than controls. ↓TIB in ADHD than controls. ↓TST in ADHD than controls.
Miano et al. (2006)	↑TST in ADHD than controls.
Philipsen et al. (2005)	↑TST in ADHD than controls.
Kirov et al. (2004)	↑REM sleep (minutes) in ADHD than controls.

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Table 3 (continued)

ADHD-only	
First author	Main PSG findings (95% CI)
	↑SPT in ADHD than controls.
	↑TIB in ADHD than controls.

SOL = sleep onset latency; SWS = slow wave sleep; REM = rapid eye movement; SE = sleep efficiency; TIB = time in bed; TST = total sleep time; SPT = sleep period time; PLMI = periodic leg movement index; *These studies included groups with PTD-only, PTD + ADHD, and ADHD-only, so are included in each diagnostic category.

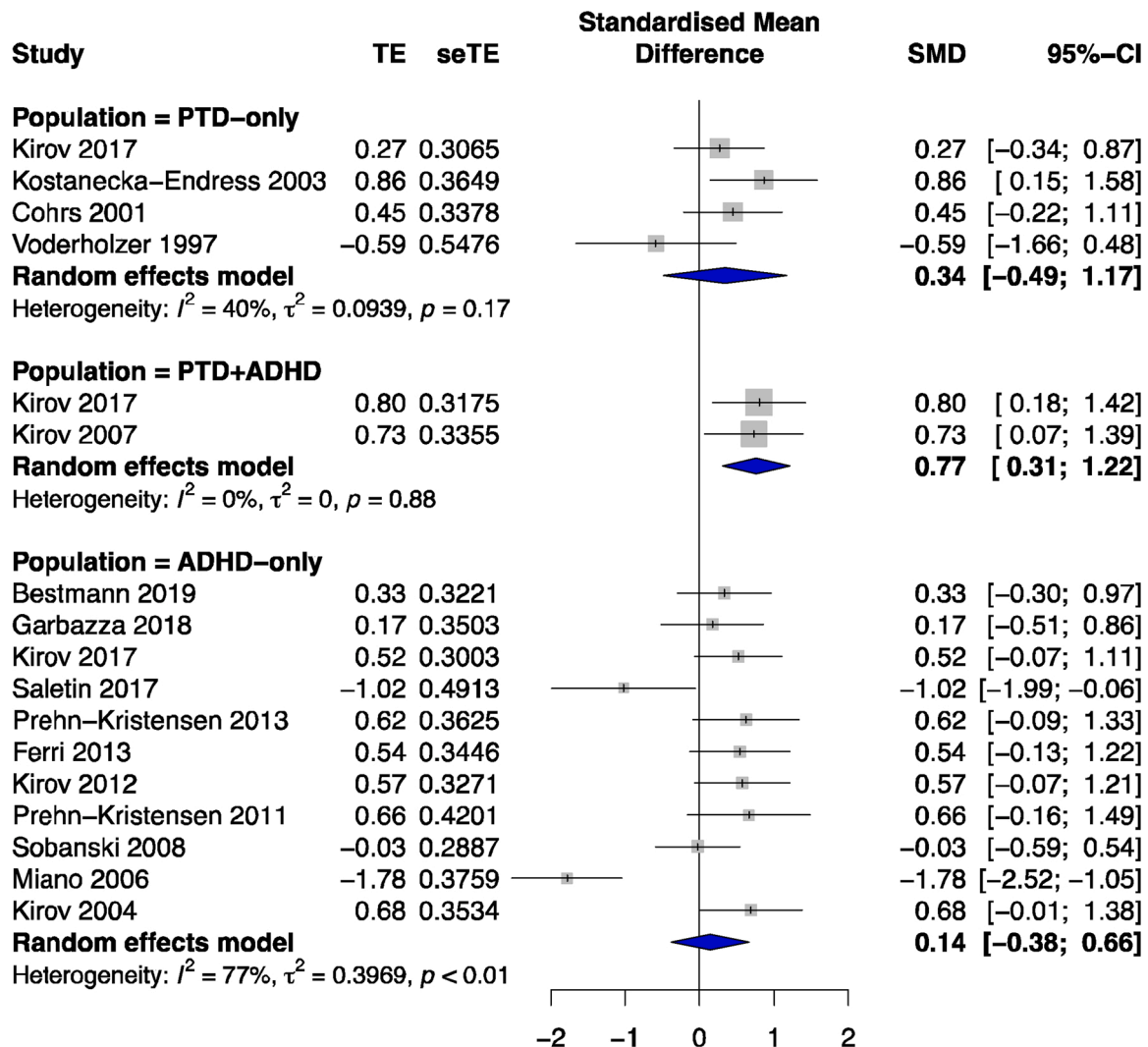


Fig. 1. Forest plot for time in bed across populations.

only populations ($k = 5$), with significantly increased sleep onset latency compared to controls (SMD = 0.67, 95 % CI = 0.28–1.07, $p = 0.009$). A small-medium effect size was found in PTD + ADHD populations ($k = 3$), with significantly increased sleep onset latency (SMD = 0.33, 95 % CI = 0.01 to 0.66, $p = 0.048$). No significant effect was found in ADHD-only populations ($k = 13$; SMD = 0.24, 95 % CI = -0.08 to 0.55, $p = 0.124$). No significant heterogeneity between studies was found for PTD-only ($I^2 = 0\%$, $\tau^2 = 0$, $p = 0.554$) or PTD + ADHD ($I^2 = 0\%$, $\tau^2 = 0$, $p = 0.847$). Heterogeneity between ADHD-only studies was substantial and significant ($I^2 = 56\%$, $\tau^2 = 0.14$, $p = 0.007$).

3.4.5. Rapid eye movement (REM) sleep percentage

Compared to controls, no significant effect was found for time in bed in PTD-only ($k = 5$; SMD = -0.01, 95 % CI = -0.88 to 0.86, $p = 0.973$), PTD + ADHD ($k = 3$; SMD = 0.63, 95 % CI = -1.24 to 2.49, $p = 0.285$), or

ADHD-only ($k = 13$; SMD = -0.11, 95 % CI = -0.54 to 0.31, $p = 0.57$). Heterogeneity between studies was substantial and significant for PTD-only ($I^2 = 74\%$, $\tau^2 = 0.37$, $p = 0.004$), PTD + ADHD ($I^2 = 80\%$, $\tau^2 = 0.46$, $p = 0.007$), and ADHD-only ($I^2 = 76\%$, $\tau^2 = 0.36$, $p < 0.0001$).

3.4.6. Slow wave sleep

Compared to controls, no significant effect was found for slow wave sleep in PTD-only ($k = 5$; SMD = 0.16, 95 % CI = -0.64 to 0.95, $p = 0.613$), PTD + ADHD ($k = 3$; SMD = -0.02, 95 % CI = -1.67 to 1.63, $p = 0.961$), or ADHD-only ($k = 13$; SMD = 0.12, 95 % CI = -0.08 to 0.31, $p = 0.216$). Heterogeneity between studies was substantial and significant for PTD-only ($I^2 = 66\%$, $\tau^2 = 0.25$, $p = 0.020$) and PTD + ADHD ($I^2 = 75\%$, $\tau^2 = 0.32$, $p = 0.019$), but not for ADHD-only ($I^2 = 0\%$, $\tau^2 = 0$, $p = 0.479$).

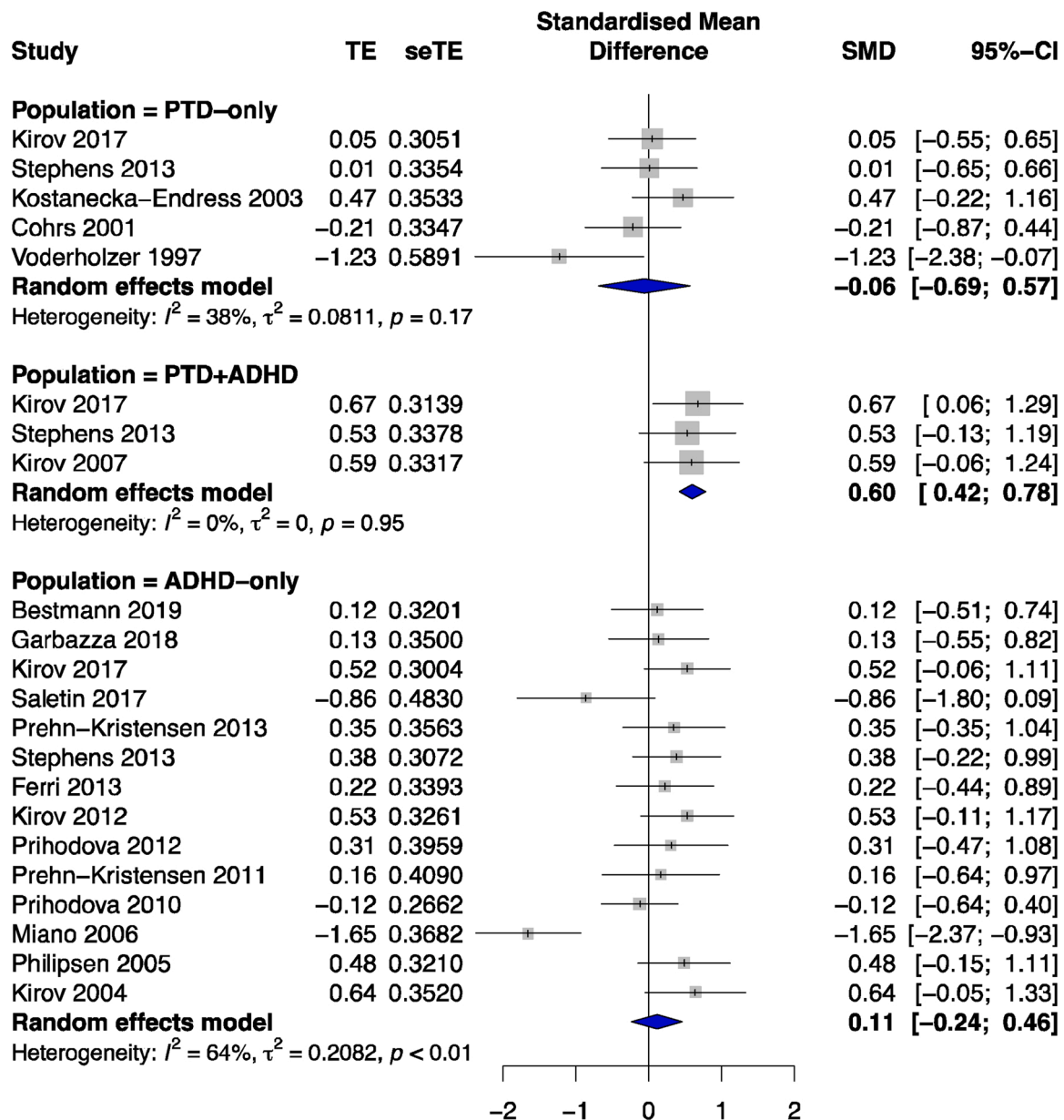


Fig. 2. Forest plot for total sleep time across populations.

3.5. Meta-regressions: Impact of tic severity on PSG effect sizes

Mixed-effect model meta-regressions were conducted to examine the effect of tic severity on observed effect sizes for each PSG variable. Studies with PTD-only groups and studies with PTD + ADHD groups were merged to increase power. Five out of the eight datasets with either PTD-only or PTD + ADHD groups provided mean scores on the Tourette syndrome severity scale. Random effects model meta-analyses were conducted for each variable before running the meta-regressions (see Table 5).

3.5.1. Time in bed

Compared to controls, PTD groups had significantly increased time in bed ($k = 5$; SMD = 0.60, 95 % CI = 0.28 to 0.92, $p = 0.006$). Heterogeneity between studies was not significant ($I^2 = 0\%$, $\tau^2 = 0$, $p = 0.654$). Tic severity was not significantly related to the time in bed effect size, $F(1, 3) = 0.03$, $p = 0.878$ ($R^2 = 0.00\%$).

3.5.2. Total sleep time

Compared to controls, PTD groups did not have significantly increased total sleep time ($k = 5$; SMD = 0.31, 95 % CI = -0.16 to 0.78, $p = 0.141$). Heterogeneity between studies was not significant ($I^2 = 26\%$, $\tau^2 = 0.037$, $p = 0.249$). Tic severity was not significantly related to the total sleep time effect size, $F(1, 3) = 0.84$, $p = 0.425$ ($R^2 = 0.00\%$).

3.5.3. Sleep efficiency

Compared to controls, PTD groups had significantly poorer sleep efficiency ($k = 5$; SMD = -0.50, 95 % CI = -0.86 to -0.15, $p = 0.017$). Heterogeneity between studies was not significant ($I^2 = 0\%$, $\tau^2 = 0$, $p = 0.613$). Tic severity was not significantly related to the sleep efficiency effect size, $F(1, 3) = 0.04$, $p = 0.847$ ($R^2 = 0.00\%$).

3.5.4. Sleep onset latency

Compared to controls, PTD groups had significantly increased sleep onset latency ($k = 5$; SMD = 0.627, 95 % CI = 0.29 to 0.97, $p = 0.007$). Heterogeneity between studies was not significant ($I^2 = 0\%$, $\tau^2 = 0$, $p = 0.609$). Tic severity was not significantly related to the sleep onset

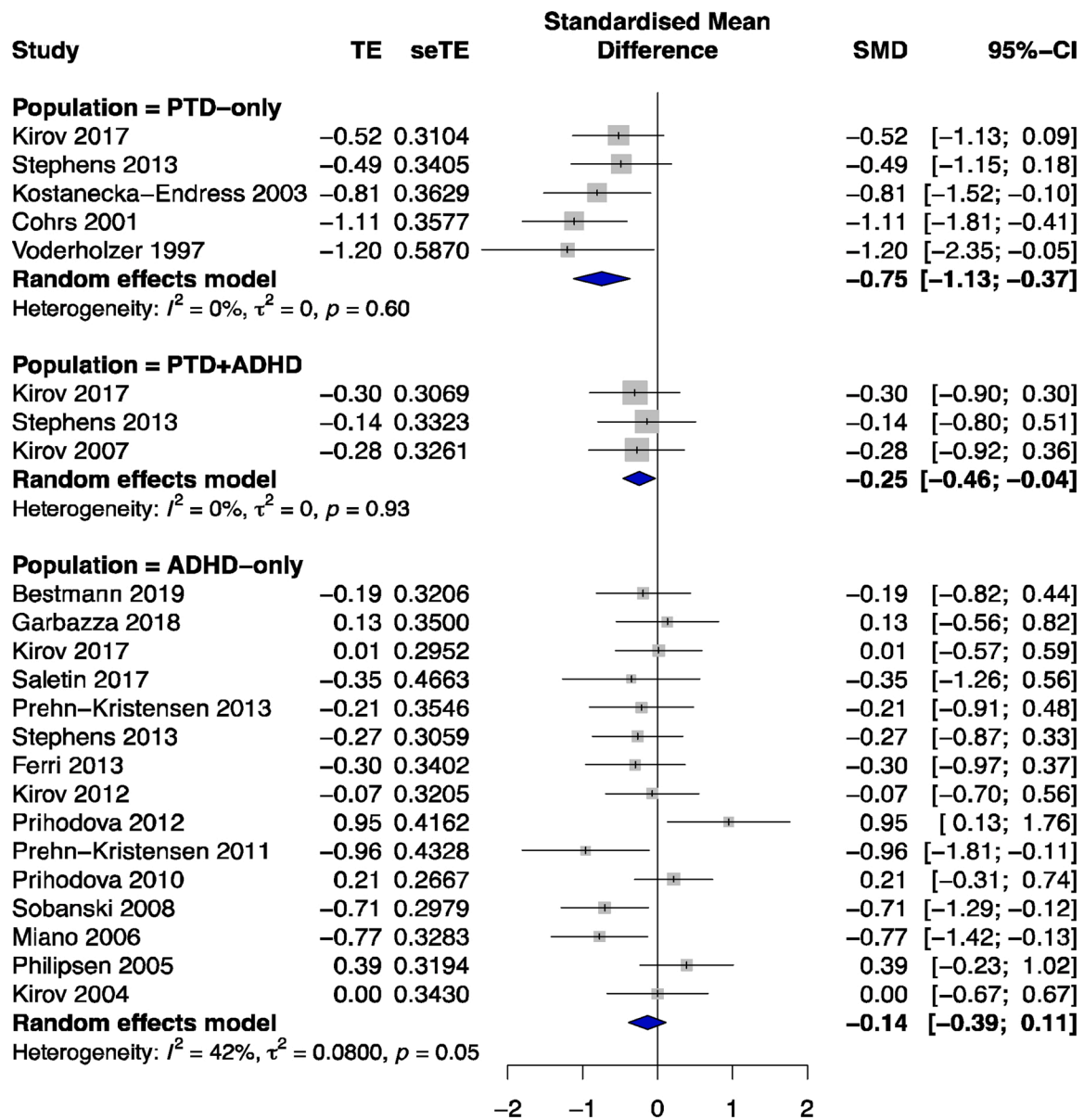


Fig. 3. Forest plot for sleep efficiency across populations.

latency effect size, $F(1, 3) = 1.06$, $p = 0.380$ ($R^2 = 0.00\%$).

3.5.5. Rapid eye movement

Compared to controls, PTD groups had significantly increased rapid eye movement sleep percentage ($k = 5$; $SMD = 0.657$, $95\% CI = 0.01-1.31$, $p = 0.049$). Heterogeneity between studies was significant ($I^2 = 59\%$, $\tau^2 = 0.16$, $p = 0.044$). Tic severity was not significantly related to the rapid eye movement effect size, $F(1, 3) = 1.92$, $p = 0.260$ ($R^2 = 34.14\%$).

3.5.6. Slow wave sleep

Compared to controls, PTD groups had significantly reduced slow wave sleep percentage ($k = 5$; $SMD = -0.300$, $95\% CI = -0.59$ to -0.01 , $p = 0.044$). Heterogeneity between studies was not significant ($I^2 = 0\%$, $\tau^2 = 0$, $p = 0.733$). Tic severity was significantly related to the slow wave sleep effect size, but did not explain any of the variation, $F(1, 3) = 12.75$, $p = 0.038$ ($R^2 = 0.00\%$).

4. Discussion

4.1. Summary of findings

The primary aim of this systematic review and meta-analysis was to compare and contrast objective sleep disturbances in PTD without co-occurring ADHD (PTD-only), PTD with co-occurring ADHD (PTD + ADHD), and ADHD without co-occurring PTD (ADHD-only). As no actigraphy studies with PTD populations were eligible for inclusion, the review focused exclusively on PSG. This limits our understanding of objective sleep disturbances across these populations in naturalistic settings as the majority of included studies took place in lab-based environments. However, a key strength of this review is that the eligibility criteria were refined throughout the review process, allowing for an inductive process. This has allowed the state of the literature to be assessed, identifying a clear disparity in the number of objective sleep studies in ADHD and PTD populations. In particular, it highlights the need for high-quality actigraphy studies in PTD groups.

Compared to typically developing controls, the majority of studies revealed differences in standard sleep parameters in each clinical

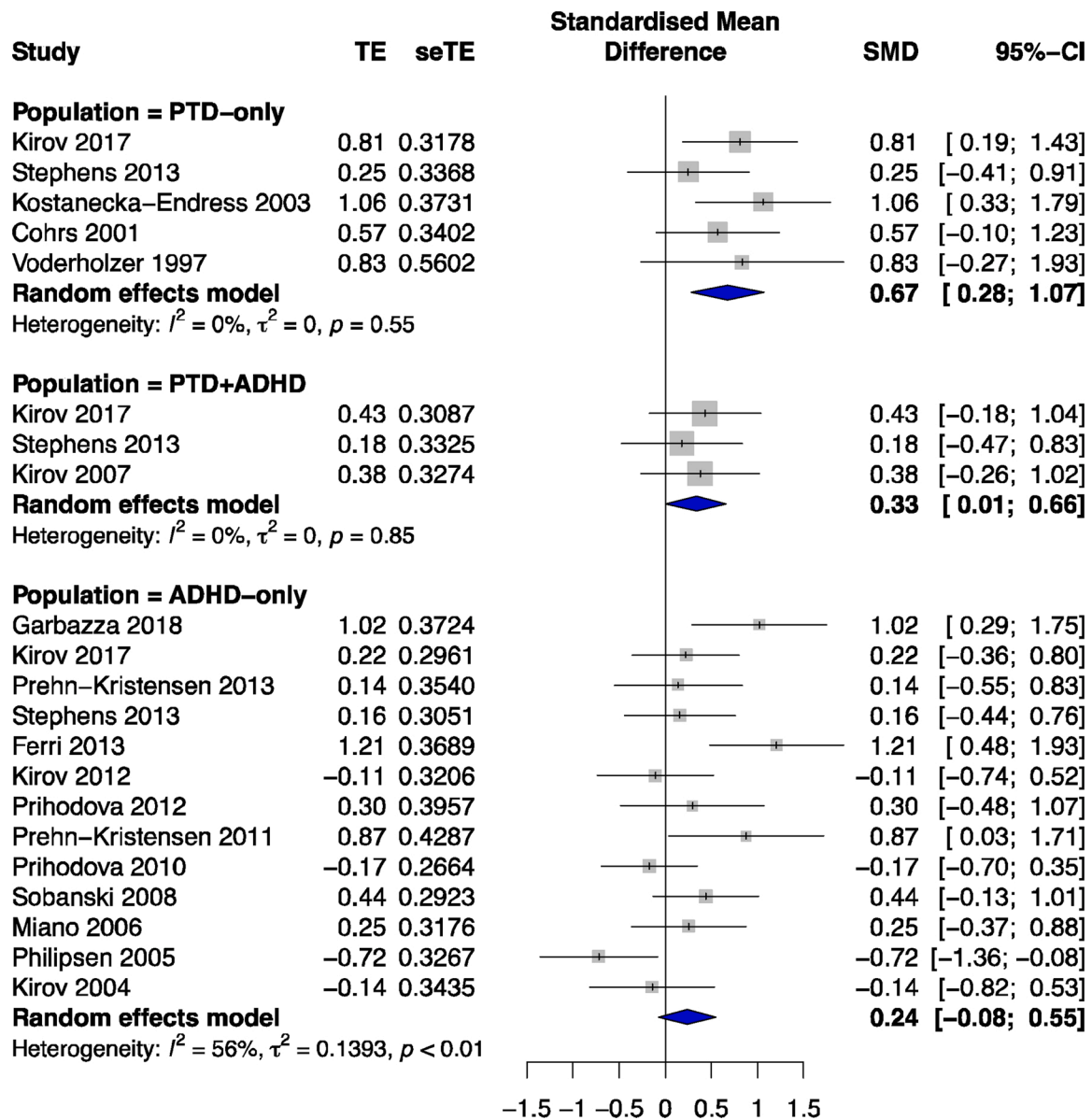


Fig. 4. Forest plot for sleep onset latency across populations.

population relative to controls. Meta-analytic findings indicate that PTD + ADHD populations are most significantly impacted in terms of the number of sleep parameters impacted, followed by PTD-only populations. While the qualitative synthesis suggested that ADHD-only populations display objective sleep disturbances, this group did not significantly differ from controls on any PSG variable in the random effects model. Findings suggest that, despite a potential underlying neurophysiological link between disorders (Tsetsos et al., 2016), there are different sleep parameters impacted to varying degrees in each population.

4.2. Sleep in PTD-only populations

In PTD-only groups, sleep efficiency was lower and sleep onset latency was higher than controls in the majority of included studies. The magnitude of the pooled mean difference found for sleep efficiency (SMD = -0.75) is considerably higher than effect sizes previously

reported for other neurodevelopmental conditions, including ADHD (SMD = -0.12; Díaz-Román et al., 2016) and autism spectrum disorder (SMD = -0.40; Morgan et al., 2020). The effect size found here is more comparable to sleep efficiency in patients with primary insomnia relative to controls (SMD = -0.70; Baglioni et al., 2013). Previous reviews have identified sleep efficiency as one of the most common PSG variables to be impacted in PTD populations (Hibberd et al., 2020; Jiménez-Jiménez et al., 2020), but the magnitude of this effect was previously unknown.

The finding that PTD-only groups have significantly increased sleep onset latency or difficulty initiating sleep was not specifically flagged in these previous reviews with PTD populations. However, the magnitude of the pooled mean difference for sleep onset latency in PTD-only populations relative to controls found here is large (SMD = 0.65), suggesting significant difficulties with sleep initiation. It is possible that differences in sleep onset latency between PTD-only and control groups did not reach statistical significance in individual studies due to low power. This

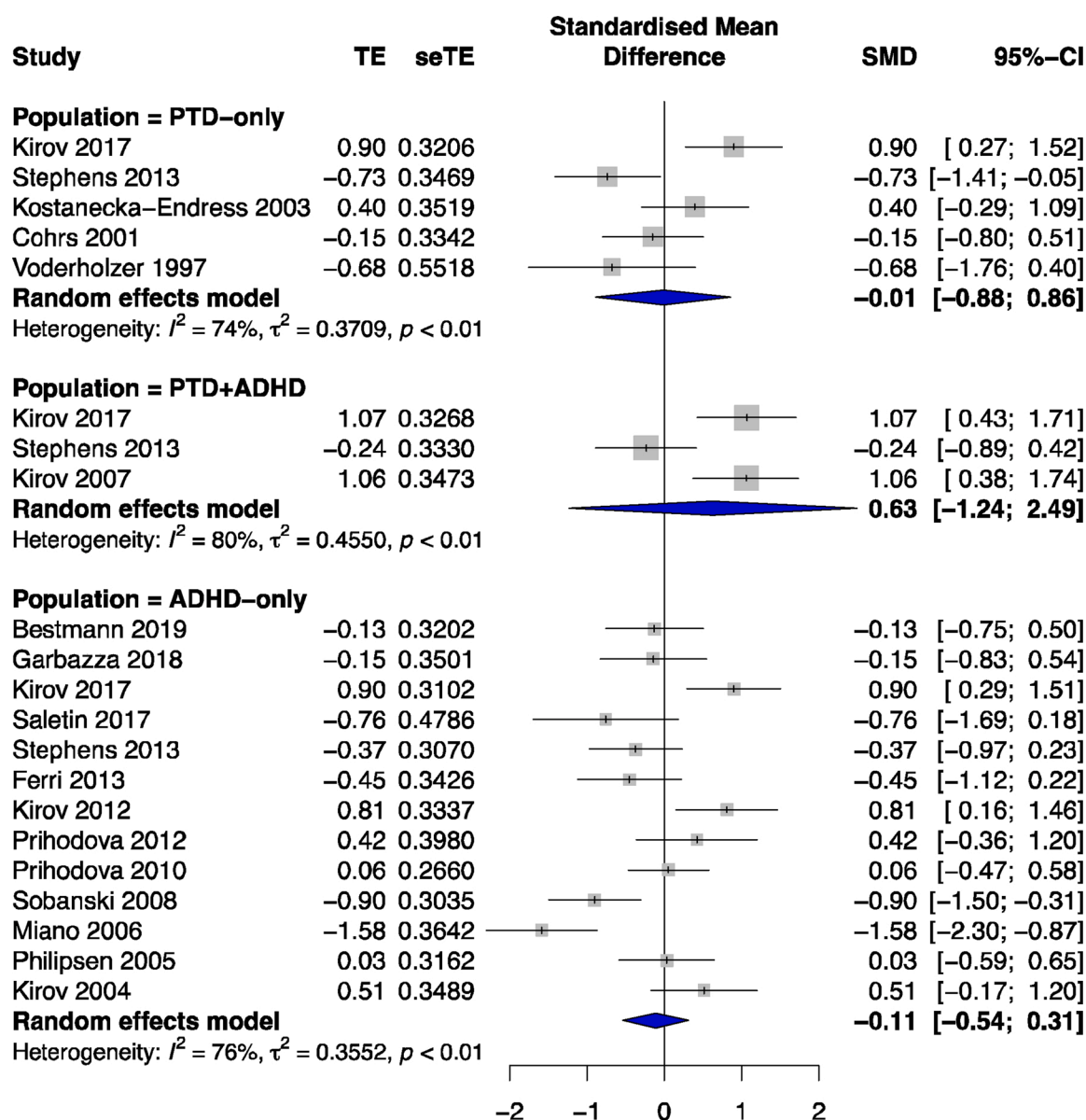


Fig. 5. Forest plot for REM sleep percentage across populations.

may explain why significantly increased sleep onset latency in PTD-only groups is evident from the meta-analysis, but not from the qualitative synthesis of PSG studies. A similar effect size was found in a recent meta-analysis examining sleep in adults with autism spectrum disorder ($SMD = 0.68$; Morgan et al., 2020), but reviews with other neurodevelopmental populations have found substantially smaller effect sizes for sleep onset latency (e.g., Baglioni et al., 2016; Díaz-Román et al., 2016, 2018).

4.3. Sleep in PTD + ADHD populations

Like PTD-only groups, sleep efficiency was significantly lower and sleep onset latency was significantly higher in PTD + ADHD, though to a lesser magnitude than PTD-only. Unlike PTD-only groups, the additional variables of time in bed and total sleep time were significantly higher than controls in PTD + ADHD groups. In contrast to studies that have assessed sleep using questionnaires in PTD-only, PTD + ADHD, and

ADHD-only populations (Allen et al., 1992; Ghosh et al., 2014), these findings suggest that sleep is most impacted when ADHD co-occurs with PTD. However, results should be interpreted with caution as only three studies were available for the meta-analysis in this population. These three studies (Kirov et al., 2007a, 2017; Stephens et al., 2013) also included groups with PTD-only and ADHD-only and found significant between-group differences, providing some support for the present findings.

There are a number of possible explanations for this finding that PTD + ADHD groups experience more sleep disturbances than populations with PTD-only or ADHD-only. One hypothesis relates to the tendency for children with PTD + ADHD to display higher rates of co-occurring psychiatric disorders than children with PTD-only, including anxiety and mood disorders (Roessner et al., 2007). Anxiety has been flagged as a risk factor for sleep problems in children with PTDs (Hibberd et al., 2020), so it is possible that the increased prevalence of psychiatric disorders in PTD + ADHD could explain the greater levels of sleep

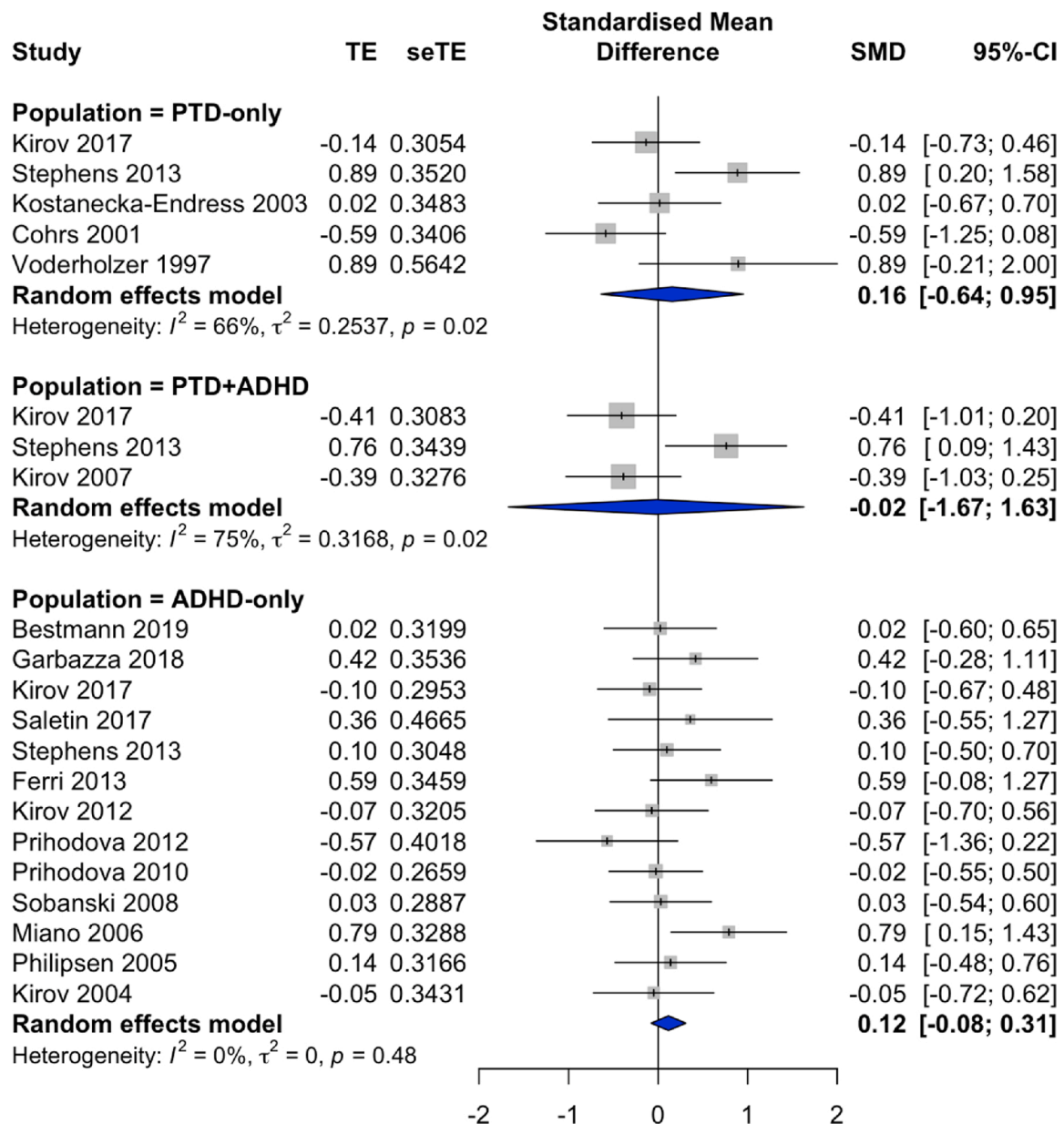


Fig. 6. Forest plot for slow wave sleep percentage across populations.

disturbances in this population. While most of the studies reviewed here excluded participants with diagnoses other than PTD or ADHD, future studies should aim to have more rigorous screening and assessment procedures to control for psychiatric symptoms. ADHD rating scales should also be incorporated in PTD studies to account for the potential impact of sub-clinical ADHD symptoms, which have been associated with sleep disturbances (Floros et al., 2020; Merikanto et al., 2019).

In studies with PTD-only and PTD + ADHD groups, tic severity was not significantly related to any sleep parameter. This is in contrast to previous studies reporting a link between increased tic severity and poorer sleep based on self- or parent-report measures (Ricketts et al., 2018), but corroborates findings from a recent actigraphy study that similarly reported no significant relation between tic severity and objective sleep parameters (Pringsheim et al., 2020). This may reflect the well-documented discrepancies between subjective and objective

sleep measures (Alfano et al., 2015; Choi et al., 2010), but an alternative explanation is that the timeframe of the tic severity scales used in previous studies is not appropriate for capturing the impact of tics on sleep. Specifically, as tics can rapidly change in frequency and intensity (Barnea et al., 2016), assessing tic severity in the more immediate window of time prior to sleep may elucidate the link. It remains unexplored if increased tic severity immediately before bedtime could explain the subjective reports of increased tics impacting sleep. Future studies using PSG or actigraphy should aim to acknowledge the changing nature of tics throughout the day and examine tic severity prior to bedtime. Direct observation through the Rush video-based tic rating scale may be used for this purpose if resources permit (Martino et al., 2017), but a less invasive measure of tic severity within the specified temporal window would be a worthwhile new development.

Table 4

Meta-analysis summary per PSG variable between each group and controls.

PTD-only											
PSG variable	k	PTD-only			Controls			SMD	95 % CI	p-value	I ²
		Mean	SD	N	Mean	SD	N				
Time in bed, mins	4	541.68	64.74	70	519.99	37.28	59	0.34	−0.49 to 1.17	0.279	40 %
Total sleep time, mins	5	472.64	72.39	90	483.16	40.24	75	−0.06	−0.69 to 0.57	0.806	38 %
Sleep efficiency, %	5	87.24	7.34	90	93.24	3.91	75	−0.75	−1.13 to −0.37	0.005	0%
Sleep onset latency, mins	5	29.03	27.74	90	13.30	8.16	75	0.67	0.28 to 1.07	0.009	0%
REM sleep, %	5	21.72	4.27	90	22.15	4.65	75	−0.01	−0.88 to 0.86	0.973	74 %**
Slow wave sleep, %	5	20.38	6.47	90	19.04	5.21	90	0.16	−0.64 to 0.95	0.613	66 %*
PTD + ADHD											
PSG variable	k	PTD + ADHD			Controls			SMD	95 % CI	p-value	I ²
		Mean	SD	N	Mean	SD	N				
Time in bed, mins	2	604.22	53.39	40	565.92	44.53	41	0.77	0.31 to 1.22	0.030	0%
Total sleep time, mins	3	538.70	43.38	61	513.42	38.39	57	0.60	0.42 to 0.78	0.005	0%
Sleep efficiency, %	3	92.94	3.80	61	93.81	2.54	57	−0.25	−0.46 to −0.04	0.037	0%
Sleep onset latency, mins	3	17.56	14.52	61	13.01	9.56	57	0.33	0.01 to 0.66	0.048	0%
REM sleep, %	3	24.35	4.01	61	21.85	3.96	57	0.63	−1.24 to 2.49	0.285	80 %**
Slow wave sleep, %	3	23.85	5.40	61	24.60	4.76	57	−0.02	−1.67 to 1.63	0.961	75 %*
ADHD-only											
PSG variable	k	ADHD-only			Controls			SMD	95 % CI	p-value	I ²
		Mean	SD	N	Mean	SD	N				
Time in bed, mins	11	560.01	41.03	190	547.97	35.88	202	0.14	−0.38 to 0.66	0.565	77 %***
Total sleep time, mins	14	509.03	45.50	264	502.54	39.90	252	0.11	−0.24 to 0.46	0.499	64 %**
Sleep efficiency, %	15	90.87	5.01	288	91.67	4.80	276	−0.14	−0.39 to 0.11	0.258	42 %*
Sleep onset latency, mins	13	23.42	17.55	264	18.21	13.08	239	0.24	−0.08 to 0.55	0.124	56 %**
REM sleep, %	13	21.31	4.15	260	21.97	4.03	248	−0.11	−0.54 to 0.31	0.574	76 %***
Slow wave sleep, %	13	23.92	6.12	260	22.98	5.59	248	0.12	−0.08 to 0.31	0.216	0%

k = number of included studies; SMD = Standardised mean difference; Higher I² percentages indicate greater heterogeneity.

* p < 0.05.

** p < 0.01.

*** p < 0.001.

Table 5

Meta-analysis and meta-regression summaries per PSG variable for PTD-only and PTD + ADHD groups combined, with tic severity as a predictor.

PSG variable	k	Meta-analysis				Meta-regression				
		SMD	95 % CI	p-value	I ²	tau ²	I ²	H ²	R ²	p-value
TIB	5	0.6034	0.2823; 0.9245	0.0064	0.0%	0.00	0.0%	1.00	0.00 %	0.878
TST	5	0.3106	−0.1605; 0.7817	0.1411	26.0%	0.05	30.1%	1.43	0.00 %	0.425
SE	5	−0.5043	−0.8594; 0.1491	0.0169	0.0%	0.00	0.0%	1.00	0.00 %	0.849
SOL	5	0.6267	0.2886; 0.9649	0.0068	0.0%	0.00	0.0%	1.00	0.00 %	0.380
REM	5	0.6565	0.0047; 1.3082	0.0490	59.2%	0.11	48.8%	1.95	34.14 %	0.260
SWS	5	−0.3002	−0.5862; 0.0142	0.0435	0.0%	0.00	0.0%	1.00	0.00 %	0.0375

Note. Values in bold font indicate statistical significance.

4.4. Sleep in ADHD-only populations

While the majority of included studies reported poorer sleep based on PSG in ADHD-only populations, the present meta-analysis found no significant differences in sleep parameters between ADHD-only and control groups. Effect sizes tended to be small and heterogeneity between studies was high. These findings are consistent with previous meta-analyses of PSG sleep parameters in child (Sadeh et al., 2006; Díaz-Román et al., 2016), adult (Díaz-Román et al., 2018), and mixed age groups (Baglioni et al., 2016) with ADHD. The large and significant heterogeneity between ADHD-only studies for each PSG variable reported here reflects findings from the qualitative synthesis, as similar sleep parameters were impacted, but the direction of impact differed between studies. This may be due to variability in terms of age, gender, co-occurring diagnoses, or medication status. In particular, the effect of

both stimulant and non-stimulant medication on sleep in ADHD is highly complex (Stein et al., 2012). Subgroup analyses were not appropriate for the current review to explore this possibility, and while previous meta-analyses found no significant differences based on gender or medication status (Sadeh et al., 2006), these mixed findings require further investigation.

Given that studies with ADHD-only groups failed to reach statistical significance on any PSG parameter, it is somewhat puzzling that ADHD would serve as an additive factor in PTD + ADHD populations, leading to additional sleep disturbances. However, it is important to note that these findings do not discount the existence of significant objective sleep disturbances in ADHD. Rather, they may be due to the heterogeneity across studies in terms of age, methodological protocols, and clinical factors. There were only three included studies with PTD + ADHD groups, each of which had paediatric samples (Kirov et al., 2007a, 2017;

Stephens et al., 2013). This resulted in less scope for heterogeneity compared to the 16 ADHD-only studies with different age groups. A meta-analysis from Sadeh et al. (2006) found that children aged under 9 had significantly shorter sleep durations relative to controls, while children aged over 9 had significantly longer sleep durations. However, a later meta-analysis from Lee et al. (2019) performed subgroup analyses by age and not only found similar effect sizes across children and adults for sleep duration, but also found that the high heterogeneity remained for these analyses. This may be due to other moderating factors, such as medication status or ADHD sub-type. Untangling these factors is beyond the scope of this review, but discussion is ongoing regarding how to best approach sleep research in ADHD. Some recommendations include adopting a more holistic methodological approach and developing standardised inclusion and exclusion criteria in future studies (Yoon et al., 2012), which may elucidate the complex ADHD-sleep relation.

4.5. Limitations

The current findings must be interpreted with caution in light of some limitations. Studies were included regardless of the age of participants and subgroup analyses were not possible due to an insufficient number of studies. This is important to highlight as sleep functioning changes significantly during adolescence and into adulthood (Colrain and Baker, 2011). The decision to include mixed age groups was primarily due to the very limited number of studies with PTD-only populations ($n = 6$): Four of these studies had paediatric populations (Kirov et al., 2007a, 2017; Stephens et al., 2013; Kostanecka-Endress et al., 2003) while two had adult populations (Cohrs et al., 2001; Voderholzer et al., 1997). As this appears to be the first meta-analysis conducted on PSG in groups with PTDs, we sought to capitalise on the minimal number of studies currently available by merging child and adult populations. Our use of a random-effects model meta-analysis may have limited any inaccurate findings due to the varied populations between and within studies. Additionally, previous meta-analyses exploring PSG variables in children (Díaz-Román et al., 2016) and adults (Díaz-Román et al., 2018) with ADHD reported similar effect sizes. However, PSG differences by age in PTD populations remain unexplored. Given that tics tend to improve with age (Bloch & Leckman, 2009) and greater tic severity may negatively impact sleep (Hibberd et al., 2020), future meta-analyses should aim to conduct subgroup analyses by age once a sufficient number of studies have been conducted.

Another limitation to note is that a number of variables, including periodic limb movement index (PLMI) and apnoea-hypopnea index (AHI), were not included in the present meta-analysis due to inconsistent reporting across included studies. Our qualitative synthesis suggests that children with ADHD or PTD + ADHD have increased PLMI compared to controls (Ferri et al., 2013; Stephens et al., 2013), a finding also reported in the meta-analysis on sleep in children with ADHD from Sadeh et al. (2006). Researchers should therefore aim to report this variable more consistently in PSG studies, allowing for further investigation and clarity.

4.6. Clinical relevance

This review highlights the issue of sleep functioning in neurodevelopmental conditions, particularly in PTDs with and without co-occurring ADHD. This may be no surprise to clinicians and families who have recognised longstanding difficulties with children's sleep quality as it is an area where parents can feel very helpless and struggle the most (Martin et al., 2019; Meltzer and Mindell, 2007). In clinical

settings, there can be an underappreciation of the burden of sleep disturbances in children with chronic health conditions and their families (Hulst et al., 2020). It is important for clinicians to raise awareness of this issue in the context of PTDs and make recommendations regarding how to improve sleep where possible, including sleep hygiene strategies and behavioural management. While sleep interventions have been developed specifically for both children and adults with ADHD (e.g., Arns et al., 2014; Hiscock et al., 2019; Sciberras et al., 2020), none appear to be available for children or adults with PTDs, with the exception of an ongoing clinical trial using short wavelength light therapy in adolescents with PTDs (ClinicalTrials.gov, NCT03508245). Nevertheless, further research needs to be conducted to develop targeted sleep interventions and examine the efficacy of these interventions in terms of symptoms and overall family functioning.

4.7. Future research

This review highlights the need to address the disparity in research focus between disorders. In particular, further PSG studies are required in PTD populations to add to this literature base and elucidate the present findings. Actigraphy should also be incorporated in future studies to provide a more naturalistic measure of sleep in PTD populations. This may permit future reviews to compare actigraphic findings between PTD and ADHD. The lack of significant PSG differences between ADHD populations and controls in the present meta-analysis and in previous meta-analyses also needs to be elucidated. Greater emphasis should be placed on confounding variables including treatment, symptom severity, co-occurring disorders, and age. In particular, more highly controlled studies with unmedicated ADHD populations are warranted. Finally, further studies are required that include participants with PTD-only, PTD + ADHD, and ADHD-only, allowing the differences in sleep parameters between groups identified here to be better understood. This may also lead to investigations exploring the underlying causes of these differences.

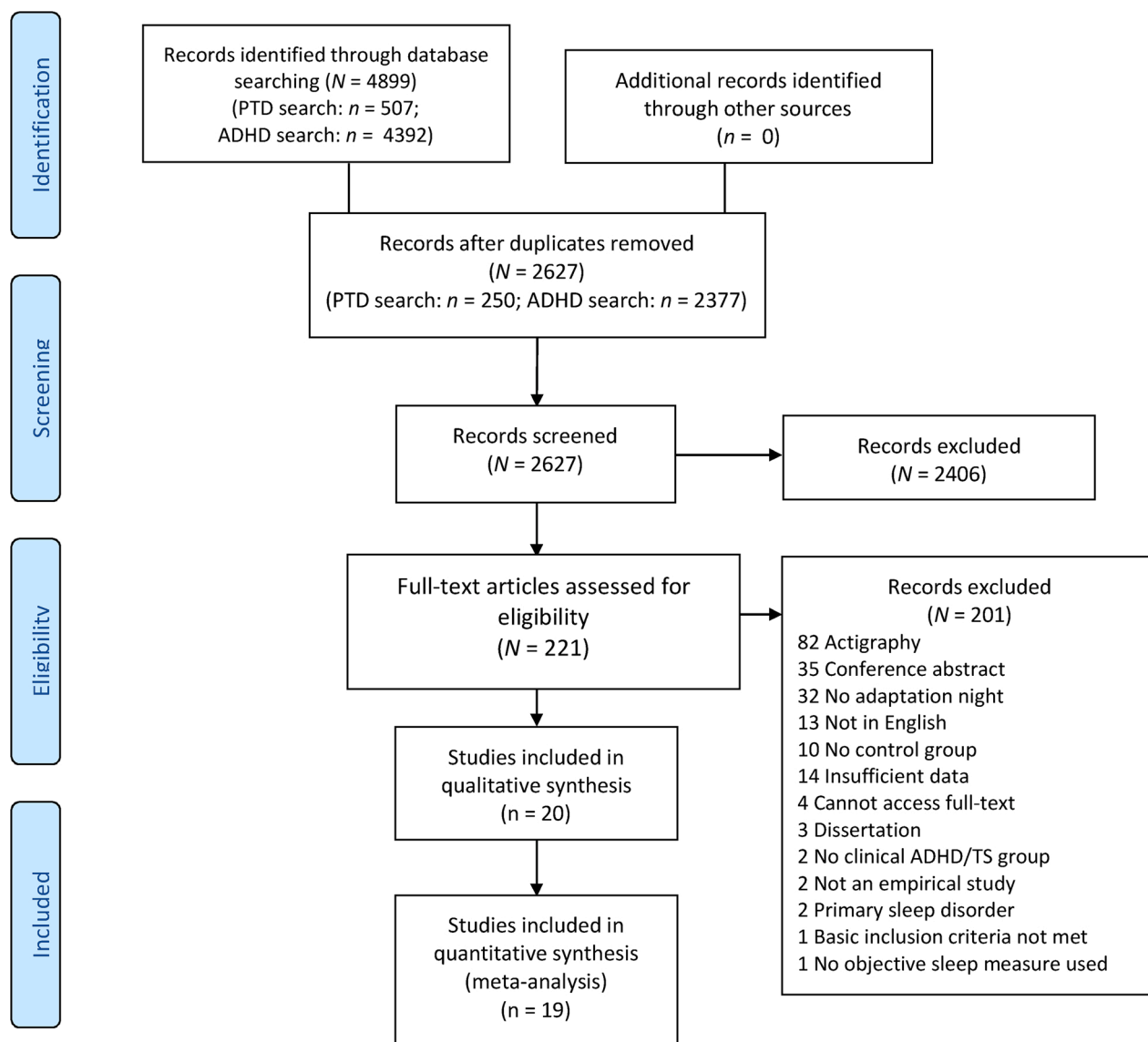
4.8. Conclusion

This systematic review and meta-analysis has identified specific differences in objective sleep parameters in populations with PTD-only, PTD + ADHD, and ADHD-only. Results should be interpreted with caution, as sample sizes tended to be low and the number of studies available in each group varied. This is the first meta-analysis to be conducted on PSG in populations with PTD. It is also the first review with the explicit aim of comparing objective sleep disturbances across these three populations. Based on PSG evidence, sleep is significantly impacted in PTDs regardless of ADHD co-occurrence. This review adds to the complex clinical picture of these neurodevelopmental populations, calling for an increased focus on sleep in clinical settings. From a scientific standpoint, the review highlights both the substantial literature base examining sleep in ADHD and the highly limited attention sleep has received in PTD research. Future efforts should address the disparity in research focus between disorders, ensuring actigraphy is incorporated to allow for more naturalistic comparisons. Additional studies with PTD-only, ADHD-only, and PTD + ADHD are also required to further elucidate disorder-specific sleep problems.

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Appendix A. PRISMA flowchart



Appendix B. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:<https://doi.org/10.1016/j.neubiorev.2021.03.018>.

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¹ References marked with an asterisk are included in the systematic review.

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