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## Sleep disturbance in post-traumatic stress disorder (PTSD): a systematic review and meta-analysis of actigraphy studies

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### ABSTRACT

**Background:** Sleep disturbance has been described as a 'hallmark' symptom of posttraumatic stress disorder (PTSD). Although there are robust findings of self-reported sleep disturbance in PTSD, evidence of sleep disturbance measured using actigraphy is less certain.

**Objective:** To conduct a systematic review and meta-analysis to determine whether there are any significant differences between individuals with and without PTSD in actigraph-derived sleep measures.

**Method:** Case-control studies comparing participants with current PTSD to those without PTSD were eligible for inclusion. Sleep parameters of interest were: (1) total sleep time; (2) sleep onset latency; (3) wake after sleep onset (WASO); and (4) sleep efficiency. Data were meta-analysed as standardised mean differences (SMDs) and potential sources of heterogeneity were explored through meta-regression. Six actigraphy studies with 405 participants were included.

**Results:** There was no evidence of a statistically significant difference between those with and without PTSD in total sleep time (SMD 0.09, 95%CI -0.23 to 0.42); WASO (SMD 0.18, 95%CI -0.06 to 0.43); sleep latency (SMD 0.32, 95%CI -0.04 to 0.69); or sleep efficiency (SMD -0.28, 95%CI -0.78 to 0.21).

**Conclusions:** Further high-quality research is required to determine whether there is a true difference in sleep between those with and without PTSD.

### Perturbación del sueño en el Trastorno de Estrés Postraumático (TEPT): una revisión sistemática y metaanálisis de estudios de actigrafía

**Antecedentes:** La perturbación del sueño se ha descrito como un síntoma 'distintivo' del trastorno de estrés postraumático (TEPT). Aunque existen hallazgos sólidos de trastornos del sueño en el TEPT a través de auto-reportes, la evidencia de éstos medidos con el uso de actigrafía es más incierta.

**Objetivo:** Realizar una revisión sistemática y un metanálisis para determinar si hay diferencias significativas entre los individuos con y sin TEPT en medidas de sueño derivadas de la actigrafía.

**Método:** Los estudios de casos y controles incluidos como elegibles fueron aquéllos que compararon participantes con TEPT en curso con aquellos participantes sin TEPT. Los parámetros de sueño de interés fueron: (1) tiempo total del sueño; (2) latencia del inicio del sueño; (3) vigilia después del inicio de sueño (*wake after sleep onset*, WASO, en su sigla en inglés); y (4) eficiencia del sueño. Los datos fueron meta-analizados como diferencias de medias estandarizadas (DME) y se exploraron las posibles fuentes de heterogeneidad mediante metarregresión. Se incluyeron seis estudios de actigrafía con 405 participantes.

**Resultados:** No hubo evidencia de una diferencia estadísticamente significativa entre aquellos con y sin TEPT en el tiempo total del sueño (DME 0.09, IC 95%: -0,23 a 0,42); WASO (DME 0.18, IC 95% -0.06 a 0.43); latencia del sueño (SMD 0.32, IC 95% -0.04 a 0.69); o eficiencia del sueño (SMD -0.28, IC 95% -0.78 a 0.21).

**Conclusiones:** Se requieren futuras investigaciones de alta calidad para determinar si existe una verdadera diferencia en el sueño entre aquéllos con y sin TEPT.

### 创伤后应激障碍 ( PTSD ) 中的睡眠障碍 : 活动记录仪的系统综述和元分析

**背景:** 睡眠障碍被描述为创伤后应激障碍 (PTSD) 的'标志'症状。尽管在PTSD中有自我报告的睡眠障碍的强有力的发现, 但使用活动记录仪测量的睡眠障碍的证据尚不确定。

**目的:** 进行系统综述和元分析, 以确定在有或没有患有创伤后应激障碍的个体中, 从活动记录仪进行的睡眠测量之间是否存在显著差异。

### ARTICLE HISTORY

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Stress disorders; post-traumatic; sleep; review; actigraphy

### PALABRAS CLAVE

Sueño; TEPT; actigrafía; revisión sistemática; metaanálisis

### 关键词

睡眠; 创伤后应激障碍; 活动记录仪; 系统综述; 元分析

### HIGHLIGHTS

- We conducted a systematic review and meta-analysis to determine whether there are any differences between individuals with and without PTSD in actigraph-derived sleep of measures.
- There was no evidence of a difference between those with and without PTSD on any of the actigraph-derived measures of sleep considered by the review.

**方法:** 将有患有PTSD与没有PTSD的参与者进行比较的病例-对照研究纳入。关注的睡眠参数为: (1) 总睡眠时间 (2) 睡眠潜伏期 (3) 入睡后醒来 (WASO) (4) 睡眠效率。对数据的标准均值差 (SMD) 进行元分析, 并通过探索潜在的异质性来源。共纳入包括405名参与者的六项活动记录仪研究。

**结果:** 没有证据表明有PTSD的人和没有PTSD的人的总睡眠时间与统计学差异 (SMD 0.09, 95%CI -0.23至0.42); WASO (SMD 0.18, 95%CI -0.06至0.43);睡眠潜伏期 (SMD 0.32, 95%CI -0.04至0.69);或睡眠效率 (SMD -0.28, 95%CI -0.78至0.21)。

**结论:** 需要进行进一步的高质量研究, 以确定是否患有PTSD的人在睡眠方面是否存在真正的差异。

## 1. Introduction

Post-traumatic stress disorder (PTSD) is a disabling psychiatric disorder that can develop after a serious traumatic event (American Psychiatric Association, 1994; World Health Organisation, 2018). The Diagnostic and Statistical Manual 5th Edition (DSM-5) outlines four clusters of symptoms: intrusion; avoidance; negative alterations in cognition and mood; and hyperarousal (American Psychiatric Association, 1994). The hyperarousal cluster references sleep disturbance as difficulty falling or staying asleep, and the intrusion cluster lists sleep disturbance in the form of recurrent or distressing dreams.

Given the apparent significance of disturbed sleep in the clinical presentation of PTSD, numerous assessment methods have aimed to determine the prevalence and nature of the problem (Kushida et al., 2005). A substantial body of evidence indicates a significant association between self-reported sleep disturbance and traumatic stress symptoms, with approximately 70–90% of those with PTSD reporting problems with the initiation or maintenance of sleep (Baird et al., 2018; Maher, Rego, & Asnis, 2006; Ohayon & Shapiro, 2000).

Compared with the robust findings of self-reported sleep disturbance in PTSD, the documented evidence of sleep disturbance using physical assessment methods is equivocal (Babson & Feldner, 2010; Harvey, Jones, & Schmidt, 2003; Khawaja, Hashmi, Aftab, Westermeyer, & Hurwitz, 2014; Kobayashi, Boarts, & Delahanty, 2007). Polysomnography (PSG) is the gold-standard physical measure of sleep (Jumabhoy et al., 2020; Kushida et al., 2005). Incorporating multiple physiological parameters, PSG assesses the critical components of sleep architecture, including sleep stages and rapid eye movement (REM) sleep, the frequency of eye movements during REM (REM density), and the ratio of time asleep to the time spent in bed (sleep efficiency) (Boulos et al., 2019; Kushida et al., 2005). A meta-analysis of 20 PSG studies found an elevated proportion of light sleep and greater REM density among participants with PTSD, compared to healthy controls (Kobayashi et al., 2007). However, the extent to which these abnormalities were specific to PTSD was unclear (Kobayashi et al., 2007). The pooled results of a more recent meta-analysis of PSG studies found evidence of decreased total sleep time, slow wave sleep and sleep efficiency,

as well as increased awakenings after sleep onset in participants with PTSD compared with healthy controls (Zhang et al., 2019). The review also indicated that REM sleep percentage was significantly decreased in participants with PTSD compared with healthy controls in studies including participants with mean age of less than 30, but not in studies with greater mean ages.

There are several limitations to the use of PSG in PTSD. Firstly, sleep in a laboratory setting may not be representative of sleep in the home environment (Sadeh, 2011). Those with PTSD may exhibit better sleep and fewer trauma-related dreams due to the perceived safety of the monitored environment (Domhoff & Kamiya, 1964; Hurwitz, Mahowald, Kuskowski, & Engdahl, 1998). Equally, it is plausible that sleep away from the home environment elicits a heightened sense of threat. Secondly, practical and ethical considerations prohibit monitoring for more than a night or two, which is problematic given the finding of variable sleep patterns among those with PTSD (Straus, Drummond, Nappi, Jenkins, & Norman, 2015). Additionally, the so-called ‘first night effect’, may have an impact (Agnew, Webb, & Williams, 1966). This describes a tendency for deviation from habitual patterns of sleep in a new environment, which is likely to dissipate over a longer period of monitoring (Browman & Cartwright, 1980).

Actigraphy is a method of measuring sleep in the home environment (Jean-Louis, Kripke, Cole, Assmus, & Langer, 2001). An actigraph is a small, minimally invasive, wrist-worn device that measures movement, which is used to provide a proxy of the sleep–wake cycle (Sadeh & Acebo, 2002). Although actigraphy does not allow for the investigation of sleep architecture (i.e. the cyclical pattern of sleep through different physiological stages), it can provide long-term measurements of several clinically important sleep-parameters, including total sleep time, sleep efficiency (the proportion of time asleep when in bed), sleep onset latency (the time taken to transition from full wakefulness to sleep), and awakenings after sleep onset (Ancoli-Israel et al., 2003). Estimates of sleep disturbance based on actigraphy have differentiated those with psychiatric disorders from healthy controls (Cox & Olatunji, 2016; Geoffroy et al., 2015). Meta-analyses of actigraphy studies of sleep in bipolar and other mood disorders have found

significant differences between the sleep of cases and unaffected controls (De Crescenzo, Economou, Sharpley, Gormez, & Queded, 2017; Fecteau & Nicki, 1999, Geoffroy et al., 2015; Tazawa et al., 2019)

Actigraphy studies in the field of PTSD have yielded inconsistent estimates of sleep disturbance across studies (Dagan, Zinger, & Lavie, 1997, Klein, Koren, Arnon, & Lavie, 2003). A recent narrative review of the evidence concluded that sleep disturbance measured by actigraphy did not differentiate participants with PTSD from those without (Khawaja et al., 2014). Given the lack of a significant difference in physical measures of sleep between those with and without PTSD, and discrepant patterns of self-reported and physically measured sleep, it has been suggested that people with PTSD may overestimate the magnitude of sleep disturbance, which has been described as ‘paradoxical insomnia’ or ‘sleep state misperception’ (Ghadami, Khaledi-Paveh, Nasouri, & Khazaie, 2015; Hurwitz et al., 1998; Rezaie, Fobian, McCall, & Khazaie, 2018). That is, PTSD may be associated with a negative cognitive bias towards the self-perception of sleep, rather than a true difference. It is also plausible that those with PTSD rate their sleep as subjectively poor due to the occurrence of nightmares. However, to date, there have been no meta-analyses of actigraphy studies in PTSD.

Given this backdrop, we aimed to contribute to a refined understanding of sleep disturbance in PTSD by conducting a comprehensive systematic review and meta-analysis to determine whether sleep parameters measured using actigraphy differentiate those with PTSD from those without. We also aimed to explore potential sources of heterogeneity among the included studies. It was hypothesised that the following potential confounders would account for heterogeneity between studies: mean age of study participants (due to varying patterns of sleep across the lifespan (Ohayon, Carskadon, Guilleminault, & Vitiello, 2004)); the number of nights of sleep monitoring due to a tendency to deviate from habitual sleep patterns over a shorter period of monitoring (Agnew et al., 1966; Browman & Cartwright, 1980); presence of psychiatric comorbidities in the control group due to a likely influence on sleep (Benca, Obermeyer, Thisted, & Gillin, 1992); and whether or not the participants were selected from military/veteran populations (due a greater likelihood of complex or severe PTSD, which may result in more significant sleep disturbance).

## 2. Method

The review followed the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) recommendations (Moher, Liberati, Tetzlaff, & Altman, 2009). Guidance set out by the Cochrane Collaboration informed methods for data extraction and synthesis (Higgins & Green, 2011).

### 2.1. Selection criteria

The review included case-control studies that compared participants with and without current PTSD on actigraphic measures of sleep. To be considered eligible for inclusion, studies were required to monitor sleep for a minimum duration of one night in the home environment. Studies were required to include a group of participants who were currently symptomatic and met diagnostic criteria for PTSD according to DSM or ICD (all relevant iterations), and a control group of participants who did not. Diagnostic status was determined by a clinical interview or validated questionnaire. Studies were excluded if participants in either group were selected on the basis of a known history of a sleep disturbance. Studies were not excluded on the basis of participants taking sleep-affecting medication, but this information was extracted and recorded. Studies were excluded if they failed to report sufficient data to be included in a meta-analysis. There were no other exclusions based on co-morbidity, the severity of PTSD, trauma-type, or whether or not participants in the control group had been exposed to trauma. This review considered studies of adults aged 18 or over. Only English language studies were eligible.

### 2.2. Search strategy

The databases Embase, Pubmed and PTSDpubs were searched from inception to 17 February 2019 using the search terms PTSD, post-traumatic stress disorder, and trauma; combined with actigraph\*, accelerometer, sleep duration, sleep time, sleep efficiency, sleep quality, sleep onset, sleep latency or sleep awakening. The reference lists of all included studies were scrutinised for additional eligible studies. Experts in the field were contacted with the aim of identifying unpublished data. Potentially eligible studies were reviewed by two researchers independently and in duplicate.

### 2.3. Assessment of methodological quality

The quality of studies was assessed using the Newcastle-Ottawa Scale (NOS) for case-control studies (Wells et al., 2012). The NOS uses a star rating system to judge the quality of studies in three domains: selection of study groups, comparability of study groups and assessment of the outcome of interest. The maximum number of stars a study may receive in each of the three categories is 4, 2 and 3, respectively. The scale has been shown to be valid and reliable (Wells et al., 2012). Two reviewers assessed the methodological quality of studies. Any disagreements were discussed with a third reviewer and final decisions were made by consensus.

## 2.4. Data extraction

Using a form that had been piloted on one of the included studies, two reviewers extracted study characteristics and outcome data. Extracted data included the number of participants; the country in which the study was conducted; the type of trauma experienced by participants; the diagnostic criteria for PTSD and measurement tool that was used for inclusion; the presence of psychiatric co-morbidities in cases or controls; whether cases or controls were using sleep-affecting medications; the proportion of the control group that had been exposed to trauma; the number of consecutive nights of sleep monitoring; the mean age of participants; and the proportion of female participants. Sleep parameters of interest were: (1) total sleep time; (2) sleep onset latency; (3) wake after sleep onset (WASO) and (4) sleep efficiency. Means and standard deviations (SDs) were extracted for each parameter. Subjective measures of sleep were not universally available or measured uniformly across studies and it was not therefore possible to extract or meta-analyse this data.

## 2.5. Data synthesis

Meta-analyses were conducted using the Cochrane Collaboration's Review Manager 5 software (RevMan, 2014). Data were analysed as standardised mean differences (SMDs). All outcomes were presented using 95% confidence intervals. Heterogeneity was assessed using both the  $I^2$  statistic and the chi-squared test of heterogeneity, as well as visual inspection of the forest plots. An  $I^2$  of less than 30% was taken to indicate mild heterogeneity and a fixed effects model was used. When the  $I^2$  was greater or equal to 30%, a random-effects model based on the DerSimonian and Laird method was used (DerSimonian & Laird, 1986). To explore potential sources of heterogeneity, meta-regression was performed using the *metareg* function of STATA version 13.1 (StataCorp, 2013).

## 2.6. Publication bias

In accordance with guidance set out by the Cochrane collaboration (Higgins & Green, 2011), we planned to explore the possibility of publication bias for any comparison that contained 10 or more studies. With fewer studies, there is insufficient power to distinguish the influence of publication bias from chance.

## 3. Results

The initial search identified 1422 potentially eligible studies. Abstracts were reviewed and full text copies obtained for 63 studies that appeared to be relevant. Six case-control studies of 405 participants met inclusion criteria for the review (Bertram et al., 2014;

Calhoun et al., 2007; Dagan et al., 1997; Klein et al., 2003; Kobayashi, Huntley, Lavela, & Mellman, 2012, Kobayashi, Lavela, & Mellman, 2014). Figure 1 presents a flow diagram for study selection.

## 3.1. Study characteristics

Study characteristics are summarised in Table 1. Studies were conducted in the USA (three studies); Israel (two studies); and Germany (one study). The number of participants included as PTSD cases (i.e. participants who currently met diagnostic criteria for PTSD) or controls ranged from 27 to 110 (median 65.5). Studies included individuals exposed to military trauma (two studies); road traffic accidents (one study); or a variety of different traumatic events (three studies). The duration of sleep monitoring ranged from one to five nights (median two nights). The mean age of participants ranged from 22.7 to 53.4 years. Four of the studies included participants with psychiatric comorbidities as cases and two allowed controls with psychiatric diagnoses other than PTSD. One study allowed participants to take sleep-affecting medication. The proportion of control participants exposed to trauma ranged from 43% to 100%.

## 3.2. Outcomes

### 3.2.1. Methodological quality of studies

Quality assessments for the included studies are summarised in Table 1. All but one study defined cases in an acceptable way (i.e. via a diagnostic interview); however, the representativeness of cases was only judged to be adequate in a single study (Klein et al., 2003). The definition of control participants was adequate across all studies, but none used an adequate method of selecting these participants, often recruiting participants from the general public via advertisements or analysing data from larger studies without a satisfactory outline of the inclusion criteria. None of the studies were optimal in terms of the comparability of cases and controls. Ascertainment of the outcomes of interest was sufficient in all studies. None of the included studies reported non-response rates. Four of the included studies were awarded a total of four stars on the NOS (Bertram et al., 2014; Calhoun et al., 2007; Kobayashi et al., 2012, 2014); and two were awarded five stars (Dagan et al., 1997; Klein et al., 2003).

## 3.3. Meta-analysis

### 3.3.1. Total sleep time

here was no evidence of a statistically significant difference in total sleep time between the PTSD and control groups (SMD 0.09, 95% CI -0.23 to 0.42;

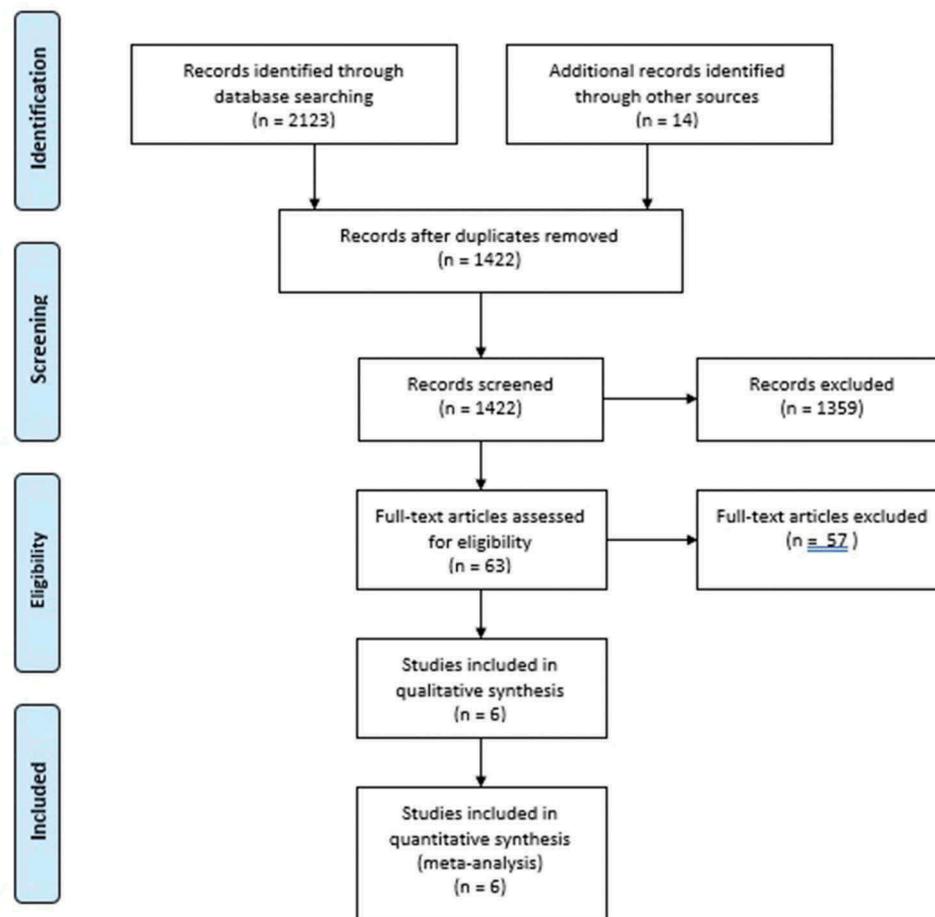


Figure 1. Flow diagram for study selection.

participants = 329; studies = 6;  $I^2 = 49%$ ; random-effects model). See Figure 2(a).

### 3.3.2. WASO

There was no evidence of a statistically significant difference in WASO between the PTSD and control groups (SMD 0.18, 95% CI  $-0.06$  to  $0.43$ ; participants = 271; studies = 4;  $I^2 = 0%$ ; fixed effects model). See Figure 2(b).

### 3.3.3. Sleep onset latency

There was no evidence of a statistically significant difference in sleep onset latency between the PTSD and control groups (SMD 0.32, 95% CI  $-0.04$  to  $0.69$ ; participants = 267; studies = 4;  $I^2 = 50%$ ; random-effects model). See Figure 2(c).

### 3.3.4. Sleep efficiency

There was no evidence of a statistically significant difference in sleep efficiency between the PTSD and control groups (SMD  $-0.28$ , 95% CI  $-0.78$  to  $0.21$ ; participants = 161; studies = 4;  $I^2 = 58%$ ; random-effects model). See Figure 2(d).

## 3.4. Heterogeneity

There was considerable heterogeneity across studies, which varied in terms of the population from which

participants were drawn; the type of trauma; the proportions of male and female participants; the number of participants in the PTSD and control groups with psychiatric co-morbidities; the extent to which control participants had been exposed to trauma; and the duration of sleep monitoring. Considerable statistical heterogeneity was evident in many of the pooled comparisons resulting in use of a random-effects model in three of the four comparisons. There was no evidence that mean age; the number of nights of sleep monitoring; or whether or not the sample was drawn from a military population were associated with the observed effect size for any of the sleep parameters considered by the review (see Table 2 for full results).

## 3.5. Publication bias

There were an insufficient number of studies to investigate publication bias.

## 4. Discussion

### 4.1. Main findings

We did not find evidence of significant differences between those with and without PTSD on any sleep-parameter measured by actigraphy. This contrasts with findings from meta-analyses of a similar number of

**Table 1.** Study characteristics.

Study ID	Country	n PTSD	n Healthy controls	Trauma type	PTSD measurement	PTSD diagnostic criteria	Actigraph	PTSD group psychiatric comorbidities	Control group psychiatric comorbidities	PTSD group sleep affecting medication	Control group sleep-affecting medication	Control group trauma exposed (%)	Participants with sleep apnoea	No. nights consecutive objective sleep monitoring	Female	Age – mean (SD)	PTSD group sleep-affecting medication (%)	Control group sleep-affecting medication (%)
Bertram et al. (2014)/ Slightam et al. (2018)	Germany	56	54	Military	CAPS	DSM-IV	Affectiva Q (Affectiva Inc., Waltham, MA)	Yes	No	Yes	Yes	43%	Yes (30.4% PTSD group; 18.5% control group)	1	0%	53.93 (10.39)	Unclear	Unclear
Calhoun et al. (2007)	USA	30	22	Various	CAPS	DSM-IV	Mini-Mitter Actwatch (Mini-Mitter Co., Inc., Bend, OR)	Yes	No	No	No	77%	Unclear	3	100%	39.12 (13.66)	0%	0%
Dagan et al. (1997)	Israel	16	11	Military	Unclear	DSM-III-R	Actigraph (Ambulatory Monitoring, Ardsley, NY)	Unclear	No	No	No	100	No	5	0%	31.35 (5.92)	0%	0%
Klein et al. (2003)	Israel	26	76	RTA	SCID	DSM-IV	Actigraph (Ambulatory Monitoring, Ardsley, NY)	No	No	No	No	Unclear	Unclear	2	31%	27.6 (10.5)	0%	0%
Kobayashi et al. (2012)	USA	25	54	Various	CAPS	DSM-IV	Actigraph (Ambulatory Monitoring, Ardsley, NY)	Yes	Yes	Unclear	Unclear	57%	Yes (but apnoea-hypopnoea index > 10 excluded)	2	42%	22.62 (4.60)	Unclear	Unclear
Kobayashi et al. (2014)	USA	19	16	Various	CAPS	DSM-IV-TR	Motionlogger (AMI, Ardsley, NY)	Yes	Yes	No	No	100	Yes (but apnoea-hypopnoea index > 10 excluded)	1	75%	22.71 (4.72)	0%	0%

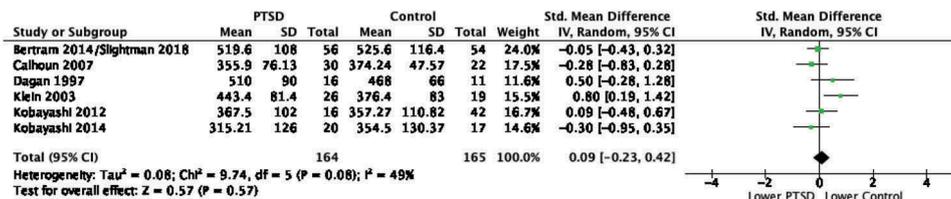
CAPS – Clinician Administered PTSD Scale (CAPS); DSM-III – Diagnostic and Statistical Manual of Mental Disorders, third edition; DSM-IV – Diagnostic and Statistical Manual of Mental Disorders, fourth edition; DSM-IV-TR – Diagnostic and Statistical Manual of Mental Disorders, fourth edition text revision; RTA – Road Traffic Accident; SCID – Structured Clinical.

studies that have found a difference between healthy controls and participants diagnosed with bipolar disorder (De Crescenzo et al., 2017; Geoffroy et al., 2015). Although this may appear to challenge the view that sleep disturbance is a ‘hallmark’ symptom of PTSD (Ross, Ball, & Morrison, 1989), there are several possible explanations for the findings.

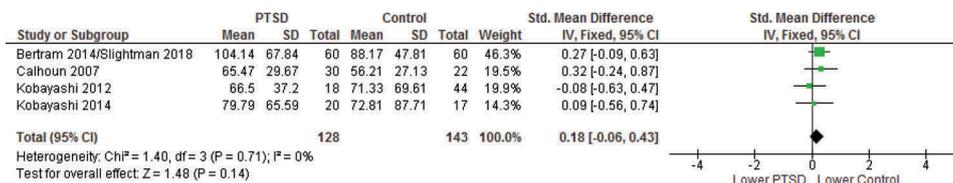
Firstly, the collective actigraphy findings may indicate the absence of a physical difference in sleep between those with and without PTSD. Taken alongside previous robust findings of self-reported sleep disturbance (Spoormaker & Montgomery, 2008), the results may indicate a negative cognitive bias towards the self-perception of sleep in PTSD (Ghadami et al., 2015; Hurwitz et al., 1998). The discrepancy between self-report and physical measurement of sleep disturbance may suggest that those with PTSD are prone to ‘paradoxical insomnia’ or ‘sleep state misperception’ (Harvey

et al., 2003). In support of this explanation, retrospective self-report measures of sleep such as the Pittsburgh Sleep Quality Index (PSQI) were largely uncorrelated with sleep parameters measured using actigraphy among studies that included the measure alongside actigraphy (Calhoun et al., 2007; Klein et al., 2003; Kobayashi et al., 2012). Although this suggests that sleep complaints are subjective, one study found a moderate correlation between actigraphy and daily sleep-logs which included items that assessed the previous night’s bedtime, rising time, sleep latency, and wake after sleep onset, despite the absence of a correlation with the PSQI (Calhoun et al., 2007). This may suggest that retrospective measures spanning a longer period of time may be more prone to bias than measures collected soon after waking. A bias may exist towards recall of nights that sleep was poor, distorting measures that cover multiple nights. Another

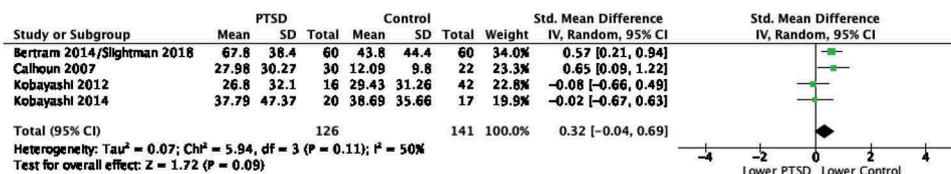
1. Total sleep time



2. Wake after sleep onset



3. Sleep onset latency



4. Sleep efficiency

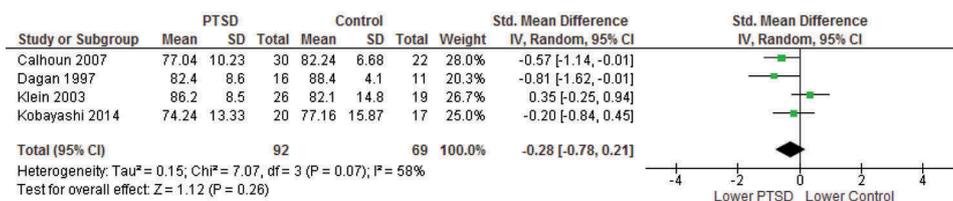


Figure 2. Forest plots of meta-analyses comparing groups of participants with PTSD to groups of participants without PTSD on the following actigraphically measures sleep parameters: (a) Total sleep time; (b) wake after sleep onset; (c) sleep onset latency; and (d) sleep efficiency.

**Table 2.** Meta-regression of variables on the following actigraphically measures sleep parameters: (1) Total sleep time; (2) wake after sleep onset; (3) sleep onset latency; and (4) sleep efficiency.

Variable	Total sleep time		Wake after sleep onset		Sleep onset latency		Sleep efficiency	
	$\beta$ (95% confidence intervals)	P						
Mean age	-0.08 (-0.54-0.37)	0.636	0.009 (-0.03-0.05)	0.448	0.02 (-0.2-0.6)	0.165	-0.39 (-0.23-0.14)	0.468
Number of nights of sleep monitoring	0.11 (-0.29-0.52)	0.482	0.01 (-0.66-0.68)	0.979	0.11 (-1.10-1.33)	0.734	-0.23 (-0.93-0.48)	0.302
Presence of control group psychiatric comorbidities	-0.29 (-1.45-0.86)	0.391	-0.29 (-1.46-0.84)	0.380	-0.66 (-1.82-0.50)	0.134	-0.13 (-2.99-3.25)	0.875
Sample drawn from military population	0.82 (-1.08-1.25)	0.854	0.15 (-0.94-1.25)	0.606	0.38 (-1.47-2.24)	0.471	-0.69 (-3.37-1.98)	0.382

Presence of control group psychiatric comorbidities coded as 0 = absent; 1 = present. Sample drawn from military population coded 0 = not from a military population; 1 = from a military population.

explanation is that participants deviated from their usual patterns of sleep on the nights of monitoring using actigraphy and the lack of temporal concordance between measures partly explains the discrepancy. It is also worth noting that disagreement between self-reported and physical measures of sleep is sometimes evident among healthy volunteers and it may not therefore be unique to PTSD. A large-scale study of a healthy elderly sample found that participants with poor self-reported sleep quality tended to report shorter sleep durations than were measured through actigraphy, whereas participants without sleep complaints generally reported longer sleep durations (Van Den Berg et al., 2008). These results were interpreted as reflecting either (1) an underestimation of sleep duration in those with sleep disturbance; (2) an overestimation of sleep duration by actigraphy; or (3) a combination of the two.

Secondly, actigraphy may fail to capture the specific sleep-parameters that are disturbed in PTSD. Although actigraphy is highly correlated with the gold-standard measure of sleep, PSG, it has higher sensitivity than specificity (Marino et al., 2013). It accurately establishes periods when a participant is asleep but does not optimally identify when a participant is awake in bed. This is problematic given that awakenings after sleep onset are a common source of complaint in PTSD (van Liempt et al., 2013). It may also fail to capture sleep onset latency, which is another subjectively reported problem among those with PTSD (Baird et al., 2018; Maher et al., 2006; Ohayon & Shapiro, 2000). Additionally, actigraphy does not capture key sleep-parameters like the percentage of time in light, deep or REM sleep, REM density, and nightmares, which might differentiate the two groups (Kobayashi et al., 2007). Focusing on night-time sleep may also be inappropriate in this population, who may be inclined to nap during the daytime. One of the included studies compared PSG-derived sleep measures in people with and without PTSD (Klein et al., 2003) but this study had a total sample size of 14 participants. Therefore, sufficiently powered studies using ambulatory PSG are needed before any meaningful conclusions can be made. The pooled results of a recent meta-analysis of PSG studies found evidence of decreased total sleep time, slow wave sleep and sleep

efficiency, as well as increased wake time after sleep onset in participants with PTSD compared with healthy controls, indicating the presence of differences that are not evident in the pooled results of actigraphy studies (Zhang et al., 2019).

Lastly, methodological flaws among the included studies may have precluded the detection of a difference between the two groups. The small number of studies with limited sample sizes may not have generated sufficient statistical power to detect a difference between those with and without PTSD. This explanation is supported by the observation of non-significant tendency towards more disturbed sleep in the PTSD groups for all comparisons. Equally, the short duration of monitoring, often relying on a night or two of observation, may have failed to account for the variable patterns of sleep that are characteristic of PTSD (Straus et al., 2015). The short periods of monitoring may have measured sleep that deviated from normal due to the 'first night effect' (Browman & Cartwright, 1980). In addition, most of the studies excluded participants who were taking sleep-affecting medication, which may have omitted participants with more pronounced sleep disturbance, leading to an underestimation of sleep disturbances associated with PTSD. The inclusion of participants with other psychiatric disorders as both cases and controls may also have attenuated any differences.

#### 4.2. Strengths and limitations

The review followed PRISMA recommendations and the Cochrane Collaboration guidance for the identification of relevant studies; data extraction and synthesis; and interpretation of findings (Higgins & Green, 2011; Moher et al., 2009). This was the first meta-analysis of actigraphy case-control studies in the field of PTSD. Despite the many strengths of the review, there were limitations. The methodological quality of included studies varied considerably and risk of bias was identified for several domains of the NOS (Wells et al., 2012). The representativeness of PTSD cases was questionable in many studies, often relying on convenience samples of participants who responded

to adverts, or sub-groups of participants from larger trials with eligibility criteria that were not described. Control groups were not always comparable to the PTSD groups. Actigraphy scoring rules differed across studies; however, this is unlikely to have influenced the pooled estimates on the basis that individual studies applied their rules consistently across the PTSD and control groups. Most of the participants were relatively young, with only one study having a mean age of over 50. As a consequence, the findings may not inform us about the needs of older people with PTSD, for example, Vietnam-era veterans. The studies focused on night-time sleep and did not explore daytime napping, which may be a factor that differentiates cases and controls. The studies did not explore the possible impact of Obstructive Sleep Apnoea (OSA). OSA is highly prevalent among Veterans and it may offer an explanation for the finding of normal actigraph measurements, combined with poor self-reported sleep, and daytime fatigue. Although insomnia may seem to be 'paradoxical', another possible explanation is that the sleep is fragmented. It was not possible to explore the influence of publication bias due to the small number of included studies. However, many of the studies reported negative findings. Sample sizes were often small and the duration of sleep monitoring was usually short.

#### 4.3. Research implications

The use of actigraphy in research has many advantages compared to the use of PSG (Martin & Hakim, 2011). It holds the potential to provide a more ecologically valid measure of sleep disturbance in the home environment over a longer period than PSG in order to better understand the nature of sleep disturbance in PTSD, which is complex and poorly understood (Bertram et al., 2014; Calhoun et al., 2007; Dagan et al., 1997; Klein et al., 2003; Kobayashi et al., 2012, 2014; Slightam et al., 2018). To advance the field and draw more robust conclusions, further well-designed studies, with larger sample sizes and an increased duration of sleep monitoring, are indicated. Specifically, it is recommended that researchers monitor sleep for a minimum of seven consecutive nights and determine minimum sample sizes with a priori power calculations. Future research should seek to determine whether actigraphy can accurately capture the specific sleep disturbances that may be characteristic of PTSD, or whether the methodological limitations of the studies to date have precluded the detection of a difference. It is recommended that representative cases are recruited rather than using a methodology that relies on convenience samples. It is also necessary for controls to be more carefully matched to cases. Further work using ambulatory PSG is needed to explore the hypothesis that PTSD is associated with a negative

cognitive bias towards the self-perception of sleep, by determining whether similar tendencies exist for other symptom domains. Studies that concurrently monitor self-reported and physical measures of sleep with temporal concordance, with comparison between those with and without PTSD, would move the field forward in terms of being able to determine whether the current clinical significance of sleep disturbance as a core symptom of PTSD is warranted.

#### 4.4. Clinical implications

There is a clear need for a more detailed characterisation of sleep-disturbance in PTSD to inform effective treatment strategies. If sleep disturbance in PTSD is a subjective phenomenon, it has implications for the way in which it is addressed clinically. If problems relate to a misperception of the quality and quantity of sleep, this suggests that psychological therapies may be a particularly appropriate treatment option. Sleep disturbance is not specifically addressed by current first-line treatments for PTSD and formal treatment guidelines for PTSD do not address evidence-based treatment strategies for sleep (National Institute for Health and Care Excellence [NICE], 2018). If there is a true difference in sleep in those with PTSD, there is a need to determine whether this is primarily due to recurrent nightmares. If so, sleep therapies that target nightmare disorders might be the most effective option (Zak et al., 2010), with Imagery Rescripting Therapy (IRT) currently being the preferred psychological treatment option (Germain, McKeon, & Campbell, 2017; Waltman, Shearer, & Moore, 2018). Sleep disturbance has also been found to remain residual to therapy for PTSD (Australian Centre for Posttraumatic Mental Health, 2007; International Society of Traumatic Stress Studies [ISTSS], 2018; Pruiksma et al., 2016). There is preliminary evidence for the efficacy of cognitive behavioural therapy for insomnia (CBT-I) as an effective intervention in psychiatric populations (Wu, Appleman, Salazar, & Ong, 2015). It is currently recommended as the best treatment option for sleep disturbance in PTSD (Colvonen et al., 2018; Miller, Brownlow, & Gehrman, 2020); however, it has not received significant attention in this context (Taylor & Pruiksma, 2014) and the optimal ordering with treatment for the waking symptoms of PTSD, is unknown (Colvonen et al., 2018). Preliminary studies of integrated treatment approaches that target both sleep and other symptoms of PTSD have shown promise (Colvonen, Drummond, Angkaw, & Norman, 2019; Miller et al., 2020). However, the efficacy of CBT-I in terms of objective improvements in sleep is less certain than that of subjective improvements (Mitchell, Bisdounis, Balleisio, Omlin, & Kyle, 2019). Evaluating treatment strategies for sleep disturbance

relies on the ability to accurately measure sleep and there is no current consensus on the optimal method of doing so in the context of PTSD.

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This work was unfunded. We conducted a systematic review and meta-analysis to determine whether there are any differences between individuals with and without PTSD in actigraph-derived sleep of measures. There was no evidence of a difference between those with and without PTSD on any of the actigraph-derived measures of sleep considered by the review.

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