Prevalence of insomnia and insomnia symptoms following mild-Traumatic Brain Injury: a systematic review and meta-analysis

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Summary

Sleep is commonly disrupted following mild traumatic brain injury (mTBI), however there is a lack of consensus in the existing literature regarding the prevalence of insomnia/insomnia symptoms after injury. The aim of this review was to conduct a systematic review and meta-analysis of insomnia and insomnia symptoms prevalence following mTBI.

Full-text articles published in English in peer-reviewed journals including adults with a clinical or self-reported mild traumatic brain injury diagnosis, were eligible for inclusion. Studies that assessed insomnia/insomnia symptoms after injury were included.

Of the 2091 records identified, 20 studies were included in the review. 19 of these were meta-analysed (n=95,195), indicating high heterogeneity among studies. Subgroup analyses indicated pooled prevalence estimates of post-mTBI insomnia disorder of 27.0% (95% CI 6.49-54.68) and insomnia symptoms of 71.7% (95% CI 60.31-81.85).

The prevalence of insomnia is significantly higher in individuals who have sustained mild traumatic brain injury compared to prevalence estimates reported in the general population but high heterogeneity and methodological differences among studies make it difficult to provide reliable prevalence estimates. Future research should continue to advance our understanding of the onset, progression and impact of post-mild traumatic brain injury insomnia to promote the recovery and wellbeing of affected individuals.

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Abbreviations

BAI Beck Anxiety Inventory

BDI Beck Depression Inventory

CBT-I Cognitive behavioural therapy for insomnia

CI confidence interval

DSM Diagnostic Statistical Manual

GABA Gamma-aminobutyric acid

GCS Glasgow Coma Scale

ICD International classification of disease

ICSD International Classification of Sleep Disorders

ISI Insomnia Severity Index

LOC Loss of consciousness

MeSH Medical subject heading

MOS Medical Outcomes Study

mTBI Mild traumatic brain injury

NREM Non-Rapid Eye Movement

NSI Neurobehavioral Symptom Inventory

OSA Obstructive Sleep Apnoea

PTA Post-traumatic amnesia

PCSC Post-Concussion Syndrome Checklist

PCL-C Post-traumatic disorder checklist- civilian

PTSD Post-traumatic stress disorder

PRISMA Preferred Reporting Items for Systematic Reviews and Meta-analysis

PROSPERO International prospective register of systematic reviews

PSG Polysomnography

PSQI The Pittsburgh Sleep Quality Index

REM Rapid eye movement

RLS Restless Legs Syndrome

SE Sleep Efficiency

SOL Sleep onset latency

SSD Subjective Sleep Disturbance

TBI Traumatic brain injury

TST Total sleep time

WASO Wake after sleep onset

Introduction

Mild Traumatic Brain Injury

Traumatic brain injury (TBI) is a major global public health concern, commonly referred to as the 'silent epidemic' as many TBI pathologies are not externally visible, causing many cases to go undiagnosed and untreated [1]. Every year at least 10 million TBIs will result in death or hospitalization, with mild traumatic brain injury (mTBI) constituting 70-90% of all treated brain injuries [2,3]. Despite few individuals visiting hospital or seeking medical consultation following mTBI, it is estimated that around 42 million people worldwide are affected by mTBI every year [2,4]. Most mTBIs are caused by a blunt force trauma to the head, largely a result of falls and road traffic accidents [1]. Mild TBI is also disproportionally common among teenagers and young adults, typically affecting more men than women [2]. Nevertheless, mTBI remains a diagnostic challenge and both its prevalence and impact are commonly underestimated [5]. Mild TBI is a highly heterogeneous and individualised condition for which no universal definition or diagnostic criteria currently exists [2,6]. However, following a comprehensive literature review, the World Health Organisation (WHO) Collaborating Centre for Neurotrauma Task Force on Mild Traumatic Brain Injury proposed the following definition and operational criteria:

"mTBI is an acute brain injury resulting from mechanical energy to the head from external physical forces. Operational criteria for clinical identification include: (i) 1 or more of the following: confusion or disorientation, loss of consciousness (LOC) for 30 minutes or less, post-traumatic amnesia (PTA) for less than 24 hours, and/or other transient neurological abnormalities such as focal signs, seizure, and intracranial lesion not requiring surgery; (ii) Glasgow Coma Scale (GCS) score of 13–15 after 30 minutes post-injury or later upon presentation for healthcare" [2].

Following mTBI, most individuals experience only temporary symptoms – such as headaches, dizziness, irritability and memory or attention deficits – and prove asymptomatic within 3-12 months [7,8]. In most circumstances, individuals should anticipate a full, or virtually full, recovery following an mTBI [6]. Losoi et al., [9] found that

nearly all previously healthy adults (96%) were able to return to work and to their normal pre-injury activities within one-year of sustaining a mTBI. However, conflicting research has reported that 15-30% of individuals with mTBI will likely endure some form of long-term physical, cognitive and/or emotional difficulties [10]. In addition, a large prospective cohort study conducted by McMahon et al., [11] discovered that 22.4% of individuals had not recovered full function when assessed at one-year post-mTBI. Masel & DeWitt [12] subsequently argued that TBI is not just an 'event' but a chronic disease process with sequalae, such as cognitive deficits, fatigue, low mood, chronic pain, post-traumatic stress and sleep disturbances, capable of long-term impact [9,13].

It is difficult to predict who will experience continuing symptoms following mTBI as symptom duration, severity and persistence are subject to an array of factors - including location of neural damage, underlying cognitive behavioural factors and both pre-injury characteristics and post-injury factors [14]. Different symptoms may also interact across varying functional domains to influence symptom expression and exacerbate long-term sequalae [14]. Repeated cases of mTBI can also increase the risk of developing persistent symptoms, such as cognitive, mood and sleep impairments [4,15]. In addition, recurrent mTBI may result in long-term regional and whole-brain volume reduction, as well as altered functional connectivity and plasticity in the brain [16]. Recurrent mTBI is especially common among military personnel and athletes engaged in contact and collision sports – both of which are populations commonly studied in TBI research [15,17].

TBI equates to significant brain injury which can be subdivided into 'primary' and 'secondary' damage [18]. Primary damage encompasses the structural and functional damage incurred upon impact [14]. This most commonly affects the frontal and temporal lobes of the brain and presents as contusions, haematomas, lacerations and/or diffuse axonal injury [6,18]. This primary damage can then trigger a pathophysiological cascade resulting in secondary brain damage such as inflammation, ischaemia, excitotoxicity, increased intracranial pressure and/or abnormal neurotransmitter or hormone release [6,18]. Neuronal damage following mTBI is therefore widespread in most cases and explains the array of potential symptoms that can develop [14].

Insomnia

Insomnia is defined as difficulty initiating/maintaining sleep, or early morning awakenings, experienced at least three nights per week for three months and equating to clinically significant distress and/or impaired functioning [19]. Recent advances in insomnia research and clinical perspectives on the condition have been reflected in changes in diagnostic criteria – namely the Diagnostic and Statistical Manual of Mental Disorder-V (DSM-V) [19] and International Classification of Sleep Disorders-3 (ICSD-3) [20]. Both the DSM-V and ICSD-3 have removed the previous distinction of 'primary' and 'secondary' insomnia and implemented the term "insomnia disorder" instead [21]. Therefore, insomnia is now acknowledged as an independent disorder that may present as comorbid, but not secondary, to other conditions [21]. This shift in insomnia diagnostic criteria is likely due to previous perceptions of insomnia as a 'secondary' disorder promoting inadequate insomnia treatment [22]. This review will utilise the terms insomnia and insomnia disorder interchangeably, in line with current literature.

Insomnia has been associated with decreased quality of life and poor mental and physical health [23]. It places a heavy burden on both individuals and health-care systems worldwide, as evidenced by its effects across many psychological, occupational, and economic domains [24]. Risk factors linked with onset and increased severity of insomnia and insomnia symptoms include a prior medical or psychiatric condition, older age, atypical employment hours and being female [25,26]. Within the general population, insomnia prevalence is relatively low (6.0%) when clinically diagnosed using the DSMI-IV criteria. However, within the general population the prevalence of insomnia symptoms is far higher (30-48%) when defined according to core insomnia symptoms [26]. Insomnia can be characterized according to both subjective and objective measures. However, diagnosis is typically based around subjective reports, with objective measures used to corroborate and validate subjective sleep complaints [27].

Sleep Problems Following mTBI

An abundance of scientific research has reported the occurrence of sleep problems following mTBI [28]. Sleep plays a critical role in recovery from mTBI by facilitating somatic growth, recovery and restoration [28]. It is also vital for synaptic plasticity and neural remodelling [27]. Whilst frequently perceived merely as a 'nuisance symptom', post-mTBI sleep disturbances can aggravate long-term sequalae and independently worsen morbidity by accelerating neurodegenerative processes and impairing recovery [29]. Among the cognitive domains most commonly affected are attention, memory and executive functioning [30]. Poor emotional outcomes have also been reported in individuals following chronic mTBI [31]. In addition, post-TBI sleep disruption can cause or amplify comorbid conditions, including depression, anxiety, fatigue, pain and irritability [32]. This will ultimately compromise recovery and prevent or defer a return to pre-injury activities, affecting quality of life [32].

An array of sleep disturbances may develop following mTBI. Individuals will typically experience reduced total sleep time (TST) and an increased proportion of sleep spent in light sleep stages - collectively termed "sleep fragmentation" – as well as reduced overall sleep quality [18,31]. Sleep disturbances may emerge soon after injury due to an initial disruption of sleep-wake patterns or during the subacute and chronic phases [33]. For example, attempting to return to pre-injury activities or employment after mTBI can result in increased sleep disruption or encourage relapse of sleep disorders experienced prior to injury [14]. Subjective sleep complaints, such as reduced sleep quality, extended sleep onset latency (SOL), poor sleep efficiency (SE), increased wake after sleep onset (WASO) and daytime sleepiness, have been identified at all stages succeeding mTBI [28]. Individuals with mTBI also report significantly greater sleep disturbance and sleep-related impairment, as well as more severe insomnia symptoms [34]. Objective sleep measures have also revealed occurrences of increased nocturnal wakefulness, increased beta power during non-rapid eye movement (NREM) sleep and less N2 and REM sleep post-TBI [28]. In addition, Mantua et al., [31] reported that individuals with chronic mTBI had more sleep complaints, less REM sleep and prolonged REM latency.

Post-mTBI sleep problems may also develop secondary to comorbid conditions as bidirectional relationships frequently link insomnia and various sequalae of mTBI, including

decreased neurocognitive performance, post-traumatic stress disorder (PTSD), depression and chronic pain [33]. For example, Paunio et al., [35] described an observable symbiotic relationship between depression and insomnia and insomnia symptoms.

Despite a growing body of research investigating sleep disturbances following TBI, the pathophysiology underlying post-mTBI sleep disturbances remains largely unknown [28]. However, complex associations between various physiological, environmental and physiological factors are commonly implicated [36]. Sleep and mTBI share many neurophysiological and neuroanatomical mechanisms [28]. Therefore, primary structural damage incurred by a traumatic insult to key brain regions, such as the retinohypothalamic tract, hypothalamus, brain stem and reticular activating system, have been implicated in the aetiology of TBI-induced sleep disturbance [37]. Secondary damage from mTBI may also sustain structural, genetic and biochemical alterations to mechanisms implicated in sleep-wake cycle control [18]. For example, mTBI can cause significant damage to long axons – key components of many neurotransmitter systems implicated in the modulation of sleep [27].

mTBI and Insomnia

A proposed aetiological model of insomnia defines two key components of the condition: a general predisposition to developing insomnia followed by an acute stressor [38]. mTBI may influence either component. Firstly, the mTBI could alter the neural anatomy or underlying biochemistry so that an individual has an increased risk of developing insomnia [27]. Either separately or in addition, mTBI may affect the second part of this model as many common mTBI sequalae could act as stressors, triggering onset of insomnia and insomnia symptoms [38]. Insomnia and insomnia symptoms are reported by individuals with TBI of all severities. A systematic review conducted by Mathias and Alvaro [32] discovered that approximately 53% of individuals with TBI suffer from a diagnosed sleep disorder, of which insomnia disorder was the most common (29%). However, the mTBI population appears more correlated with insomnia and insomnia symptoms than other TBI severities [28].

Limitations of Previous Research

The current literature on insomnia and insomnia symptoms following mTBI is subject to many limitations. Firstly, the current research is inundated by inconsistent definition and measurement of both mTBI and insomnia – with no universal operational criteria currently available for either condition [2,26]. There is also a distinct lack of agreement regarding standardised sleep assessments for evaluating sleep, sleep problems and sleep-related outcomes - especially those suitable for investigating mTBI [28]. Secondly, the majority of studies include a mixed TBI severity sample and aggregate the results from mild, moderate and severe forms of TBI [34]. This means studies specific to post-mTBI sleep disturbances are rare [28]. When combined with small sample sizes, it can therefore be difficult to detect subtler but key changes in underlying neurophysiological activity [33,39]. Many differing mTBI samples have also been studied by researchers, from hospital admissions to military veterans to athletes - amongst many other populations [32]. However, in some cases this may introduce a selection bias, especially when recruiting from rehabilitation or treatment settings, thus lowering the transferability of findings to the wider mTBI population [6]. Critically, few studies include participants who do not seek hospital treatment or other medical consultation following a sustained mTBI [33]. This must be considered by future researchers as many individuals who sustain a mTBI will not seek any form of medical assistance and subsequently be excluded from studies, even large epidemiological investigations [33].

Justification for the current Systematic Review & Meta-Analysis

Individual estimates of sleep disturbance prevalence following mTBI vary considerably, especially with regards to insomnia and insomnia symptoms. This has limited their clinical utility thus far and mirrors both the high intra-subject variability of mTBI, as well as variations in definitions, criteria and measures used to evaluate post-mTBI sleep disturbances [32]. This systematic review and meta-analysis will investigate the prevalence of insomnia and insomnia symptoms amongst individuals diagnosed with mTBI in peer-reviewed studies to date. No systematic review or meta-analysis has been published to date that focuses on post-mTBI insomnia and insomnia symptoms, and thus the current review is addressing a key gap in the literature and aims to consolidate existing research by reviewing the prevalence of insomnia following mTBI. It is hoped that the findings from this review

and meta-analysis will contribute to a greater understanding of post-mTBI insomnia and resolve prior inconsistencies in the literature, as well as inform future studies and treatment developments.

Methods

The review protocol was registered with the International Prospective Register of Systematic Reviews (PROSPERO), registration CRD42020168563. The research question was constructed using relevant PICOS terms for prevalence studies (population, outcomes, study type). Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) was utilised to navigate study selection and reporting. The database searches were conducted, and the titles and abstracts generated were independently screened by MM and MG. All full-text articles were then assessed by MM (and 20% by MG) for inclusion in the review. Hand searches were also carried out by MM on the reference lists of any full-text articles deemed eligible for inclusion from the database searches and the full-text articles of any studies appearing to meet the criteria were screened by MM, MG and SB. Quality ratings were then conducted independently by MM and MG with any disagreements in ratings resolved through discussion. The relevant data were extracted by MM and SB with the meta-analysis conducted by SB.

Literature Search

A concept-based search strategy centred on keywords and medical subject headings (MeSH) associated with mild traumatic brain injury (mTBI) and insomnia and insomnia symptoms, that was developed with assistance from a librarian, was used to search the following electronic databases: MEDLINE (OVID) including Epub ahead of print, In-process and other non-indexed citations, EMBASE (OVID), PsycINFO (EBSCO), Web of Science (Core Collection) and CINAHL (EBSCO) from inception to 2nd December 2019. Where possible by database, the searches were limited to publications in English and studies in humans. Further details of the search strategy can be found in Supplementary material. The searches were exported to EndNote Basic (Web) and duplicates removed. Two reviewers then used Rayyan QCRI [40] to remove any outstanding duplicates and screen the titles and abstracts generated

from the electronic database searches. The reviewers assessed the titles and abstracts independently for relevance. A 10% conflict rate was recorded and resolved through discussions between the reviewers, then irrelevant titles and abstracts were excluded and the full texts of articles potentially eligible for inclusion in the review were obtained. The same independent reviewers then assessed the eligibility of these full text articles and, as before, recorded and resolved any disagreements. Regarding full texts that could not be accessed, an attempt was made to request a copy directly from the authors.

Inclusion Criteria

The following criteria were applied throughout the screening process to determine eligibility of articles for inclusion in this review (further details located in the supplement). If the reviewers were unable to determine eligibility directly from the publication, an attempt was made to contact the study authors to clarify the methodological approach used or to obtain further data.

Types of Studies

Full-text articles published in English in peer-reviewed journals, and containing original research, were eligible for inclusion in this review. Studies that assessed insomnia and/or insomnia symptoms post-mTBI were included. All case studies or case series (defined as <10 participants) were excluded.

Population

Studies of adult humans (aged 18 years or older) with either clinical or self-reported diagnosis of mTBI in any location, and at any time post-mTBI, were included. Studies with a population comprising mixed TBI severity were included when there were more than 10 individuals with mTBI and their results were reported separately. For studies that included an intervention arm, included participants were drawn from baseline or the untreated arm.

Outcomes

The main outcome studied in this review was the prevalence of insomnia/insomnia symptoms post-mTBI. This was calculated by dividing the total number of individuals with mTBI and insomnia/insomnia symptoms at a particular time with the entire mTBI population at risk of having the condition at this time point.

Insomnia diagnosis was based on any recognised classification or clinical diagnostic criteria (e.g. ICD-9/10, ICSD-2 and DSM-V). Questionnaires and all other instruments [e.g. Pittsburgh Sleep Quality Index (PSQI), Insomnia Severity Index (ISI), Neurobehavioral Symptom Inventory (NSI), Medical Outcomes Study (MOS) Sleep Scale Revised, Post-Traumatic Disorder Checklist – Civilian (PCL-C)] or self-reported insomnia were classified as insomnia symptoms using author specific cut-offs and insomnia definitions. Therefore, studies utilizing both subjective and/or objective measurement of insomnia symptoms, such as actigraphy or polysomnography (PSG), were included. These symptoms typically reflected components of the diagnostic criteria proposed by the DSM and its insomnia symptom profile which encompasses problems with sleep onset, maintenance or frequent early morning awakenings, equating to daytime consequences as a result of poor sleep.

Secondary Outcomes

Data was collected on demographic, mTBI and sleep related factors and comorbidity, where available. In addition, information on lifetime TBI history, time since the mTBI and recurrence of mTBI was collected where available.

Data Extraction

A template was created and tailored to the study prior to data extraction by MM. Data extracted included: Reference details (authors, year, title, journal, volume pages); demographic characteristics (age, gender, employment, education, country); sample characteristics (numbers at baseline and again at follow-up); methods (sampling method, study design, setting, comparison group characteristics, statistical analysis method); mTBI characteristics (time since mTBI, mechanism of injury, lifetime TBI history, method of

diagnosis); insomnia/insomnia symptoms (definition, assessment method and instrument, prevalence, sleep quality before mTBI); and comorbidity (current or premorbid psychiatric, psychological, or physical health problems, medication use).

Study Quality

In order to examine the methodological quality of the studies included, this review utilised a critical appraisal tool by Munn et al., [41], which is the recommended and most commonly used validated critical appraisal tool of studies assessing prevalence in clinical conditions [42]. In addition, for assessment of valid methods, question number six was split into two parts to evaluate both methods used for the identification of 1. insomnia/insomnia symptoms (Y = use of clinical diagnostic instrument for insomnia e.g. ISI/validated questionnaires, e.g. PSQI, for insomnia symptoms, N = e.g. entirely self-report, U = unsure of method and/or its validity) and 2. mTBI (Y = clinical diagnosis of mTBI, N= self-report, U = assessment method not disclosed). Two reviewers independently assessed the quality of all the included papers. A 20% conflict rate was recorded and resolved by discussions between the reviewers. No studies were excluded from the review or meta-analysis based on the quality rating.

Data Analysis

The primary approach was to produce a narrative review of the results from the included studies, accompanied by tabulated displays of the details of the included studies; a summary of the findings, and the quality ratings for included studies. Meta-analysis techniques were also used to pool the data. The included studies were split by subgroup for analysis to allow investigation of the effects of Insomnia type (symptoms versus disorder), sample population (military versus non-military), study design (direct observation vs. records) and time since injury (acute versus chronic) with acute being defined as up to 6 months post mTBI and chronic as more than 6 months post mTBI.

The meta-analysis was conducted using the 'Metafor' [43] package with data visualised using the 'Meta' package [44] applied in R Statistical Software [45]. Double arcsine

transformation and random effects model were used as this accounts for both within- and between-study variability. The data was inspected for outliers and influential studies. Pooled prevalence estimates are reported using 95% confidence intervals (CIs) with the results and 95% CIs back-transformed for ease of interpretation. Heterogeneity was assessed using the I^2 statistic. An I^2 was classed to indicate low (25%), medium (50%) or large (75%) heterogeneity [46]. Subgroup analyses were performed to investigate potential sources of heterogeneity. Publication bias was assessed visually via Funnel plots and statistically using an Egger's regression test [47].

Results

2091 records were identified through electronic database searches and 10 additional records identified through hand searches. Following removal of duplicates, 1407 titles and abstracts were screened for relevance. 1229 were subsequently excluded, resulting in 178 full-text articles to be assessed for eligibility. Of these, 158 were excluded – leaving 20 studies to be included in the data synthesis (Figure 1) and 19 studies incorporated into the meta-analysis.

Study Characteristics

Details of the included studies can be found in Table 1. All of the studies included in this review were published between 1996 and 2019. Six studies were cross-sectional, eight were cohort based – five prospective (of which one was longitudinal) and three retrospective - three were case-control studies (one of which was longitudinal) and three clinical trials – one retrospective and two both prospective and longitudinal. Overall, the data was meta-analysed for 95,195 individuals with mTBI (mTBI sample size range n = 40-93,003).

[Insert Figure 1 – PRISMA Flow Diagram]

Study Setting

The studies included in this review collectively span a significant geographical area: North America (Canada, USA), n =14; Asia (Iraq, Taiwan, China, India), n =4; and Australia, n = 2. In addition, five studies were hospital based (including one rehabilitation hospital) and six were medical centre based (including army medical centres, university health centres and specialist neurosurgical and neuropsychological services). Six studies were conducted through rehabilitation programmes (four of which were specific for veterans or active-duty service members), one study was a cross-sectional survey of active-duty U.S. Army and one other cross-sectional study recruited participants from a university.

Insomnia Assessment

Insomnia was assessed by diagnostic tools in four of the 20 included studies (Table 2), one of which also evaluated insomnia symptom prevalence. In the remaining 16 studies investigating insomnia symptoms, the PSQI was the most commonly administered measure. Different cut-offs were applied to PSQI index scores by the included studies to distinguish between disturbed sleep/poor sleep quality (PSQI>5) and those with clinically significant insomnia symptoms (PSQI>8). Subjective sleep disturbance, poor sleep quality and sleep issues were amongst the sleep problems reported.

Prevalence of Post-mTBI Insomnia/Insomnia Symptoms Using Clinical Diagnostic Tools

The four studies that used diagnostic criteria and recognised classifications for insomnia are described in Table 2. Meares et al., [48] applied the 10th version of the International Classification of Disorders (ICD-10) diagnostic criteria for insomnia to a version of the 10 item Post-Concussion Syndrome Checklist (PCSC), which had been adapted to allow for equivalence with the ICD-10 PCS symptom criteria. Hou et al., [49] used the second version of the Internal Classification of Sleep Disorders (ICSD-2) to both evaluate and operationalise insomnia, and Pugh et al., [50] used the the ICD-9, with Clinical Modification, (ICD-9-CM) diagnosis codes from inpatient and outpatient obtained data. Mosti et al., [51] measured insomnia using the Brief Insomnia Questionnaire (BIQ) and utilised its psychometric properties to diagnose insomnia based on the DSM-V criteria. However, Mosti et al., [51] did not report their unweighted mTBI sample size. The mTBI sample sizes of the three other

studies examining insomnia prevalence combined was 93,134 [48–50]. Insomnia prevalence was measured longitudinally in just one of the studies, in which variations in prevalence were observed [48]. However, the overall insomnia prevalence in these four studies ranged between 10.0% to 51.1%.

[Insert Table 1- Study Characteristics]

Prevalence of Post-mTBI Insomnia/Insomnia Symptoms Using Non-Clinical Diagnosis Tools

16 studies (n = 2,130) investigated insomnia symptoms (Table 3). Insomnia symptoms prevalence was assessed by a number of questionnaire measures and, in one instance, according to medical records. Nine studies solely reported overall prevalence of poor sleep quality, sleep disturbance or other insomnia symptoms at one time point post-mTBI [52–60], with only two studies reporting prevalence of insomnia symptoms at different time points post-injury [61,62].

Five studies also reported prevalence according to different PSQI cut-off scores to distinguish between the severity of insomnia symptoms [62–66]. Kalmbach et al., [62] also separately reported sleep onset insomnia prevalence figures and three studies provided additional sleep data on their mTBI sample, as collected by the sleep measures they utilised [65–67].

Prevalence of insomnia symptoms varied considerably from 10.0% to 96.0%. Regarding the PSQI, prevalence of scores >5 (evidence of poor sleepers) ranged extensively from 10.0% to 96.0% whilst scores >8 (evidence of clinically significant symptoms) spanned 52.8% to 87.5%. The two studies utilizing the ISI reported two opposing prevalence rates for clinical insomnia symptoms: 19.7% to 69.2% [57,60].

mTBI Characteristics

Five studies reported mechanism of injury data for sustained mTBI, describing differing prevalence for each mode: blast (53.0% to 85.0%), motor vehicle accident (12.8% to 82.3%),

fall/jump/thrown (9.7% to 40.0%), being struck (19.1% to 36.0%), assault (3.0% to 10.5%), and other (3.2% to 23.0%) [48,54,56,60,65]. Three studies provided data on the prevalence or duration of PTA and one study disclosed whether participants were wearing a helmet at the time of injury (66.0% of mTBI with SSD were and 62.0% with no SSD were) [55].

Farrell-Carnahan et al., [54] determined TBI severity from the duration of PTA, Mosti et al., [51] classified mTBI according to reported LOC for 30 minutes or less and PTA lasting less than 24 hours, and Albicini et al., [53] defined mTBI when LOC lasting under 30 minutes was reported, or any PTA or feeling dazed was described following an injury. Lu et al., [58] classified mTBI using electronic medical record review and patient self-report based off semi-structured interviews conducted by health professionals. Towns et al., [63] based their TBI diagnosis of self-report and determined the injury to be of mild severity if LOC lasted 30 minutes or less, a GCS of 13-15 was recorded or PTA did not exceed 24 hours. The remaining 15 studies used GCS scores of 13-15 to determine mild severity of TBI. 10 studies did not report lifetime TBI history [50–52,54,55,58,61–64]. Seven studies provided data on previous TBI/mTBI [48,53,59,60,65–67], two studies included only first-time MTBI [49,56] and one included solely newly afflicted mTBI cases [57]. Nine studies did not report time since mTBI [49–51,53,54,61,65–67].

[Insert Table 2 – Studies Evaluating Insomnia Using Clinical Diagnostic Tools]

Impact of mTBI Characteristics on Insomnia/Insomnia Symptom Prevalence

Only two studies [61,62] investigated insomnia symptoms at different time points post-mTBI. Beetar et al., [61] reported a decline in insomnia symptom prevalence in the months, and years, succeeding an mTBI. Kalmbach et al., [62] described similar findings – a reduction in clinically significant insomnia symptoms and sleep onset insomnia over the first six months post-mTBI. However, prevalence of poor sleep (PSQI scores from 5-8) marginally increased between one and three months post-mTBI (72.2% to 75.1%) before decreasing by the time of the six-month follow-up assessments (69.3%). Three studies provided a further breakdown of GCS data in their mTBI sample, indicative of TBI severity. Hong et al., [56] found a mean GCS of 14.93 in their entire mTBI sample compared with 14.79 for those who

also experienced sleep disturbances and Al-Ameri et al., [52] reported lower initial GCS mean of 13.22, indicative of greater TBI severity in their mTBI sample.

One study also distinguished between complicated mTBI (mTBI with presence of intracranial abnormality - such as oedema, contusion or haemorrhage) and uncomplicated mTBI (mTBI with no intracranial abnormalities evident) [67]. A greater proportion of uncomplicated mTBI had lower scores on the MOS (58.0% scored <40), indicative of severe sleep problems, compared to those with complicated mTBI (33.3% scored <40). Similarly, the uncomplicated mTBI sub-group had a greater proportion of participants reporting sleeping for less than seven hours per night (48.5%) compared to the complicated sub-group (41.9%). Farrell-Carnahan et al., [55] also reported injury characteristics for individuals with mTBI who reported SSD compared to those who did not. A greater proportion of the SSD group had experienced LOC (72.0%) compared to those without SSD (46.0%). In addition, on average, those with SSD had experienced their injury before those without SSD – although the standard deviations around this data are notable. Regarding comparisons between individuals with mTBI with and without LOC, one study can be considered. Verfaellie et al., [64] found that compared with a control group of veterans subject to blast-exposure during deployment which did not result in TBI, ,individuals with mTBI without LOC had more severe PTSD symptoms, greater sleep disturbance and trend for worse manual dexterityIndividuals with mTBI with LOC also exhibited more severe symptoms, greater sleep disturbance and worse manual dexterity but also delayed processing speed.

Demographic Characteristics

Six studies [49,52,57,59,61,62] did not include the gender breakdown for the mTBI sample. Based on the 14 outstanding studies [48,50,51,53–56,58,60,63–67], on average 75.3% of the mTBI sample were male (unadjusted for study size). Only three studies [51,56,67] had mTBI samples of which less than half were male. Nine studies [49,51,52,56,57,59,61–63] failed to report the mean age for their mTBI sample. The average age across the remaining 11 studies [48,50,53–55,58,60,64–67] was 32.8 years (unadjusted for study size).

[Insert Table 3 – Studies assessing insomnia symptoms (mTBI sample only)]

Impact of Comorbidity on Prevalence of Insomnia/Insomnia Symptoms

Insomnia comorbidity was reported by nine of the 20 included studies. PTSD, depression and anxiety were among the most commonly reported comorbid conditions reported with insomnia and insomnia symptoms following mTBI. Significant increases in depression, nightmares, headaches and fatigue experienced by mTBI participants with SSD compared to those without SSD were noted by Farrell-Carnahan et al., [55]. Farrell-Carnahan et al., [54] also found depression and general anxiety to be significant predictors of sleep disturbance following mTBI. Julien et al., [67] also reported significant correlations between sleep problem scores and the following outcome measures: depression, anxiety and headaches. PTSD was also significantly more common in mTBI participants with SSD (91.0%) compared to those without (35.0%) [55]. Lu et al. [58] similarly reported comorbid diagnoses of PTSD (40.0%), major depressive disorder (30.0%), or both (20.0%) in their mTBI sample. In addition, Vuletic et al., [65] identified significant correlations between PSQI composite scores and symptoms of emotional distress, alcohol use disorders, pain, PTSD and depression.

Hong et al., [56] detected differences between individuals with mTBI with sleep disturbances versus those without sleep disturbances regarding the following outcome measures: headache (57.0% vs. 51.0%), mean scores on the Beck Anxiety Inventory (BAI) measure (12.5 vs. 10.4), mean scores on the Beck Depression Inventory (BDI) measure (12.1 vs. 10.3). Walker et al., [66] also reported that 74.0% of mTBI participants positive for insomnia were at increased risk of developing OSA, 31.0% were at higher risk for OSA and RLS. Finally, Martindale et al., [59] found that mTBI affected sleep beyond the effects of other behavioural issues, contributing to poorer sleep quality independently of PTSD, anxiety and depression.

Study Quality

The quality of the studies included in this review varied. A summary of the quality ratings can be found in Table 4. The overall scores ranged from 12-20, with four studies assessed as

having the highest possible rating [56,57,62,67]. The description of the study subjects and setting was the area that received the greatest proportion of low-quality ratings. We did not exclude studies from the review or meta-analysis based on study quality.

[Insert Table 4 - Study Quality]

Meta-analysis

Overall Prevalence

Of the 20 studies investigating mTBI prevalence, 19 were included in the meta-analysis (Figure 2). One study [51] was excluded due to unclear reporting of case numbers with overall prevalence percentage only reported for a weighted as opposed to an unweighted sample. The overall pooled prevalence of insomnia following mTBI was high 65.2% (95% CI 52.27- 77.07) with extremely high heterogeneity between studies (I^2 =100%). Publication bias was assessed using a funnel plot (Figure 3), which did not indicate asymmetry. Further, the Egger's regression test did not indicate significant publication bias (z= 0.151 p = 0.679).

[Insert Figure 2 - Forest plot of overall insomnia prevalence]

[Insert Figure 3 – Funnel plot of publication bias]

Insomnia Disorder vs. Insomnia Symptoms

Subgroup analyses were conducted to investigate whether heterogeneity among studies would be reduced by assessing prevalence in studies reporting prevalence of insomnia disorder and insomnia symptoms separately (Figure 4). There was a marked difference in pooled prevalence estimates between studies reporting prevalence for insomnia disorder, 27.0% (95% CI 6.49-54.68) compared to studies reporting prevalence for insomnia symptoms, 71.7% (95% CI 60.39-81.85) with an effect of moderator ($p < 0.003$) indicating that insomnia assessment type moderates estimated prevalence. Due to heterogeneity

remaining high (I^2 =97% and I^2 =96% respectively) the reported prevalence estimates should be interpreted with caution.

[Insert Figure 4 - Forest plot for subgroup analysis of prevalence estimates of insomnia disorder and insomnia symptoms]

Military vs. Non-Military Studies

Comparing studies assessing prevalence in military and non-military samples (Figure 5), those with military samples reported higher pooled prevalence estimates 77.2% (CI 60.40-90.50) compared to non-military studies 54.4% (CI 37.82-70.452) with a moderating effect of subgroup border-lining significance (p= 0.05). Due to high heterogeneity in both groups (I^2=100 and I^2=95 respectively) and the subgroup estimates including both studies assessing insomnia disorder and insomnia symptoms, prevalence the estimates should be interpreted with caution.

[Insert Figure 5 - Forest plot for subgroup analysis]

Studies Utilising Direct Observations vs. Medical Records

Subgroup analysis of studies comparing different data collection methods (Figure 6) indicated small difference in pooled prevalence estimates between the studies using direct observations 62.6% (CI 44.50-78.99) compared to studies using record-based approaches 68.3% (48.78-84.98) with heterogeneity remaining high with no significant effect of subgroup (p=0.66).

[Insert Figure 6 - Forest plot for subgroup analysis of prevalence estimates in studies using direct observation and medical records]

Prevalence Estimates in Acute vs. Chronic Phase Post-mTBI

For assessing the impact of time post-injury on prevalence, the studies were divided into those that reported prevalence, on average, up to six months post-injury (acute) and those that reported prevalence more than six months post-injury (chronic). Six studies did not report how long post mTBI, the prevalence of insomnia was assessed (Figure 7). These studies formed a third group (NR; not reported). The pooled prevalence estimate for studies assessing insomnia within the first six months post mTBI was 60.8% (CI 36.49-82.68) compared to studies assessing a more chronic presentation 68.6% (CI 49.10-85.30) and studies that did not report an assessment time window 67.1% (CI 42.85-88.33). No moderator effect was present (p= 0.87) and the heterogeneity remained high within all subgroups ($I^{2=}$96%, $I^{2=}$ 96% and $I^{2=}$ 100% respectively).

[Insert Figure 7 - Forest plot for subgroup analysis of studies reporting prevalence estimates for early (acute) and late (chronic) after mild TBI]

Discussion

There has been a recent surge in research investigating post-mTBI insomnia and insomnia symptoms, with all but two of the 20 studies included in this review published within the last 10 years, and 11 published since 2016. Four of the included prevalence studies utilised diagnostic tools for insomnia assessment, whilst the remaining 16 used non-diagnostic instruments. All but one of the included studies contributed to the meta-analysis, which indicated high overall pooled prevalence - with approximately six in ten estimated to experience either insomnia or insomnia symptoms following mTBI. However, high heterogeneity among studies was indicated. Further exploration revealed that prevalence of insomnia was lower in studies employing diagnostic criteria (approximately one in three) compared to studies using insomnia symptom assessment (approximately seven in ten). The pooled prevalence estimate for insomnia disorder aligns with previous research suggesting that insomnia prevalence in mTBI populations is around four to five-times higher than in the general population (6.0%) [26] and similar to that reported following TBI (29.0%) [32]. The prevalence of insomnia symptoms, also mirrors previous findings that difficulty

falling asleep and/or difficulty staying asleep (with associated daytime consequence) is the most common sleep disorder (30-65%) experienced post mTBI [28].

Measurement of Insomnia Symptoms

A number of subjective sleep measures were used by the included studies to evaluate insomnia symptoms. This array of non-diagnostic tools is very likely to account somewhat for the notable variance in the reported prevalence estimates. Whilst objective assessments were conducted in some instances, these findings could not be mapped on to insomnia symptoms. Notably, six studies used measures other than the PSQI and ISI to investigate the proportion of individuals with mTBI experienced difficulty falling asleep, staying asleep and/or early morning awakenings. These studies reported insomnia symptoms in 43.0% to 84.1% of their mTBI samples – generally far higher than is found in the general population and consistent with existing literature [28].

The PSQI, a measure of insomnia symptoms and currently one of only two validated sleep measures in individuals with TBI [68], was used by almost half of the included studies - revealing significant variation in the prevalence based on cut-off for sleep disturbance/poor sleep quality (PSQI>5) (10.0% to 96.0%) in comparison to clinically significant insomnia symptoms (PSQI>8) (52.8% to 87.5%). Fichtenberg et al., [69] discovered that a PSQI cut-off of 8, compared to 5, more accurately discriminated between individuals with mTBI with and without clinically significant insomnia. Therefore, clinically significant symptoms appear consistently and highly prevalent following mTBI, based on the findings of this review.

Interestingly, the six highest prevalence estimates of post-mTBI insomnia symptoms were all derived from studies utilising the PSQI [58,59,63–66]. Whilst studies that used the ISI [57,60] – a measure specifically designed to detect insomnia symptoms – or NSI [54] - a measure tailored towards use in mTBI populations – all reported more conservative prevalence estimates for insomnia symptoms. Nevertheless, four of the six lowest prevalence estimates for insomnia symptoms also used the PSQI, suggesting that the type of insomnia symptom measure used is one of many factors influencing prevalence of post-mTBI insomnia symptoms.

Prevalence estimates in the two hospital-based studies that used the ISI to measure insomnia symptoms (19.7% [57] and 69.2% [60]) indicated a notable disparity, which may be accreditable to the ISI measure and/or differences in study characteristics. However, the results from Kaufmann et al., [70] found that the ISI demonstrated good validity and internal consistency when used to measure insomnia symptoms in TBI populations. They concluded, based on the findings from their study population of military veterans with a history of TBI, that a cut-off score alike that used in non-TBI populations would be applicable [70]. Therefore, the difference in these two estimates may instead be due to differences in the study characteristics - particularly time since injury. For example, Jain et al., [57] prospectively recruited participants in the acute stages of mTBI recovery – with the initial assessment conducted within two-weeks of the mTBI and follow-up assessments conducted over the following year. Whereas Mollayeva et al., [60] recruited participants in the chronic stages of mTBI recovery – a median of 197 days post-injury.

Post-mTBI Sleep Profile

More detailed information on post-mTBI sleep was provided by a minority of the included studies. Julien et al., [67] revealed that nearly half of their mTBI participants slept for less than seven hours, mirroring actigraphy findings from Walker et al., [66] who found the average TST among those with mTBI was 6.7 hours. This is a key indicator of poor sleep as less than seven hours per night is termed as short sleep duration [66]. SOL was also extended in the mTBI samples of two included studies [65,66], with Walker et al., [66] also reporting an average actigraphy-measured WASO of 42.9 minutes – indicative of frequent night-time or early morning awakenings. Vuletic et al., [65] indicated that more than nine in ten also described early morning and/or night-time awakenings, consistent with previous literature suggesting WASO is the primary sleep complaint after mTBI and roughly twice as long as experienced by members of the general population [34]. A recent meta-analysis also corroborates the view that individuals with TBI experience widespread objective sleep deficits, namely increased WASO, reduced TST and poorer SE [39].

Longitudinal Studies

Only three of the included studies employed longitudinal measurements of post-mTBI insomnia. This reflects the mTBI literature overall, where follow-up of individuals is either too limited (and therefore unable to capture the progression of symptoms) or too broad (lacking intermediary assessment capable of detecting emerging factors with the potential to impact post-mTBI insomnia associations and outcomes) (10). As previously described Meares et al., [48] reported a decrease in post-mTBI insomnia prevalence during the acute recovery phase. This aligns with previous research suggesting that mTBI symptoms typically resolve within 3-12 months [9]. However, Meares et al., [48] also found evidence of insomnia development out-with the acute recovery phase. Whilst these insomnia cases may have resolved out-with the scope of this study, prior research has shown that sleep disturbances and other mTBI sequalae may persist or even escalate by twelve-months post-injury [71]. Cross sectional prevalence estimates from the subgroup analysis, however, do not indicate lower prevalence in the in the first part of the first year post-mTBI in comparison to the second part [61,62]. This highlights the importance of conducting further longitudinal studies assessing the progression and emergence of insomnia symptoms post-mTBI.

Two included longitudinal studies evaluating insomnia symptoms reported an overall decline in insomnia symptoms over the months [62], and years [61], following mTBI. However, both reported a higher prevalence of insomnia symptoms in their mTBI sample during the acute recovery phase than is typically observed in the general population. Beetar et al., [61] also reported that a quarter of individuals with mTBI were still experiencing insomnia symptoms over 60 months after injury – suggesting that insomnia symptoms can become chronic and persist for years post-mTBI. These findings correlate with those of previous studies, such as Theadom et al., [33] who found that more than half of those with mTBI had sleep difficulties that became chronic and 39.0% experienced further deterioration in sleep quality.

Recurrent mTBI

As supported by the findings from this review, recurrent cases of mTBI are frequently associated with insomnia and insomnia symptoms [18]. In addition, insomnia and other sleep disturbances are risk factors for sustaining repeated TBI, highlighting the reciprocal nature of the relationship between mTBI and insomnia [18]. Extremely high prevalence of clinically significant insomnia symptoms ranging from 69-88% in samples containing individuals with repeated mTBI exposure were reported by the included studies - most of which investigated military personnel. Schwab et al., [72] reported that sleep problems were in fact the most frequently reported symptoms in approximately a third of soldiers with mTBI returning from Afghanistan and Iraq. Compared with individuals with no prior TBIs, Bryan [17] previously highlighted that approximately four times as many individuals with a single TBI (22.4%), and ten times as many individuals with multiple TBIs (47.6%), exceeded the threshold for clinical insomnia in a military population – as supported by the findings of this review.

Military Studies

Subgroup analyses indicated higher prevalence of insomnia/insomnia symptoms in studies with military populations compared to studies of non-military samples. TBI, especially in its mildest form, has been labelled a signature injury and invisible wound of military conflict due to its systematic under-documentation and array of potential effects [17,73]. Blast injury is thought to make up roughly 60% of military related TBIs, of which 80% are mild [18]. Of the three US military studies included in this review describing mechanism of injury, blast was identified as the main cause of mTBI. Unlike blunt trauma, blast injury produces shockwaves which generate propagating changes in intracranial pressure, resulting in extensive brain damage such as contusions, oedemas, axonal injury and haemorrhages [18].

Comorbid Conditions

Post-mTBI insomnia has been linked to a number of comorbid conditions, with depression, anxiety and PTSD among those most commonly reported in the current review. These results mirror those from previous research linking post-mTBI insomnia with comorbidities such as anxiety, irritability, fatigue, pain and depression [74]. The presence of comorbid

conditions following mTBI can complicate efforts to infer insomnia causality, as many reciprocal connections link insomnia with some of the most frequently reported mTBI symptoms [28]. As a result, previous literature has frequently misidentified insomnia as a symptom of other post-mTBI comorbidities – and not as a primary condition [28]. In the current review, depression was identified as a comorbid condition that both paralleled increased reports of sleep disturbance [54] and predicted sleep disturbance following mTBI [55] – supporting the symbiotic nature of the association between post-mTBI insomnia and comorbid conditions such as depression [35]. However, less than half of the included studies provided data on the comorbid conditions of mTBI participants. Therefore, more consistent and diverse outcome measurement would benefit future research around the bidirectional associations between insomnia/insomnia symptoms and other common post-mTBI sequalae [6].

The development of sleep problems following mTBI may also be influenced by additional factors. For example, pharmacological treatments, such as hypnotic drugs, may exacerbate sleep problems and cause 'rebound' sleep complaints once the medication course is completed [75]. Changes to health-related habits, including caffeine consumption, diet and alcohol intake, may also further disrupt sleep-wake cycles and contribute to insomnia and insomnia symptom development following mTBI [14]. Neither the health-related habits or potential pharmacological treatment of individuals with mTBI were reported in detail by any of the included studies.

Strengths, Limitations and Recommendations for Future Research

This review is the first to provide a systematic overview of post-mTBI insomnia and insomnia symptom prevalence estimates. The papers included in this review span many countries, settings and populations to provide a comprehensive overview of the current research on post-mTBI insomnia and insomnia symptoms. It is the first systematic review and meta-analysis published to date focusing exclusively on post-mTBI insomnia and as such addresses a critical gap in the current literature. However, some limitations were identified that are worthy of consideration as they highlight potential research avenues for future studies to

ensure that they support the continuous refinement and enhancement of scientific knowledge in this key research area.

Firstly, the review included almost 100,000 individuals with mTBI - 98% of those included in the meta-analysis from studies using diagnostic criteria. However, roughly 93% of the total mTBI population included in this review originate from a single study – Pugh et al., [50]. The contribution of this single study to the meta-analysis is also notable as it was one of only four studies included that used diagnostic criteria. It was also the only study that used ICD-9-CM codes to diagnose insomnia disorder - used officially in the United States to classify operations and diagnoses linked with hospital utilisation [76]. This may explain their low prevalence estimate, as many people do not seek medical assistance following mTBI and only those seeking treatment are likely to have been accounted for [33]. Nevertheless, further investigation revealed that excluding this study from the meta-analysis would have little impact on the overall pooled prevalence estimate.

Secondly, the vast majority of the included studies failed to provide data on the demographic characteristics of individuals with mTBI experiencing insomnia and insomnia symptoms. Only six of the included studies had a total sample comprised solely of individuals with mTBI, and in the outstanding studies reporting of the demographic information on the mTBI group was limited. This is reflective of the mTBI literature as a whole, where insufficient measurement and inadequate reporting of demographic and clinical data are common [28]. Future studies should provide more detailed demographic and clinical data on individuals with mTBI and clearly distinguish between the different TBI severities in their reporting.

Although the meta-analysis did not reveal significant differences in prevalence estimates between studies which collected data using medical records, rather than through direct observation, a combination of other factors such as sampling bias, the effects of research participation and differences in study characteristics, methods and operational definitions of mTBI and insomnia may be associated with the high heterogeneity observed, limiting the certainty with which conclusions can be drawn from the findings. This is supported by the observation that all military studies assessing insomnia symptoms using direct observation

methods reported prevalence estimates of over 90%. This could be due to selection bias, such as targeted selection of cohorts carrying a heightened risk of mTBI – for instance, those returning from combat zones).

Despite studies having only been included if their participants were not known to have a history of pre-existing sleep disorders, many of the included studies did not report this information. Therefore, it is possible that some participants were included who had prior history of unreported or undiagnosed sleep problems. As a result, it is essential that future studies either solely include participants with no pre-existing sleep complaints, or report prevalence separately for those with and without pre-existing complaints to prevent the reporting of only a continuation of pre-existing sleep impairments [32]. Clinically, medical practitioners should be alert to the development of insomnia and insomnia symptoms to ensure they diagnose and treat these sleep problems as soon as possible [26].

In addition, it was not possible to account for the potential effects of other variables, such as medication use and chronic pain, on the prevalence of post-mTBI insomnia in this review. Only Beetar et al., [61] presented separate insomnia symptom prevalence rates for individuals with mTBI with and without pain, with just over half without pain experiencing symptoms with a ten percent higher prevalence in those with pain. Therefore, post-injury pain may have impacted on the results of other included studies and would be a factor to consider as part of clinical management of insomnia symptoms. Individuals recovering from TBI also tend to use more medications than the general population, which can alter the quantity and quality of their sleep independently from the effects of mTBI [14,39]. Future research should therefore account for potential confounding variables by assessing factors such as psychiatric disorders, chronic pain and medication use within their mTBI samples [77].

As mTBI results from head trauma, researchers and clinicians should also consider the emotional impact of the trauma and where relevant PTSD, as potential confounding factors, which may inflate estimated insomnia and insomnia symptom prevalence values [78]. This is especially true for military studies where comorbidities arising from trauma exposure, such as PTSD, are likely to be significant confounding factors in the development and progression

of sleep problems [78,79]. Only nine of the studies included in this review reported insomnia comorbidities. Therefore, future research should endeavour to better report this information, in order to enhance the scientific understanding of how insomnia and other common comorbid conditions interact.

The high insomnia symptom prevalence indicated by this review, coupled with previous research in this area, highlight the need for a standardized sleep assessment battery following mTBI [28]. As has been identified in the existing literature, a frame of reference issue currently encompasses insomnia research due to the array of instruments, namely different questionnaires, administered for diagnosis and symptom identification [27]. Wickwire et al., [77] have encouraged a multi-method approach when evaluating sleep and sleep disturbances following mTBI. Whilst insomnia is primarily a subjective sleep complaint, individuals with mTBI experiencing insomnia usually underestimate the time they spend asleep [18]. For example, Walker et al., [66] reported actigraphy, sleep diary and PSQI results for a variety of sleep components – highlighting the degree to which results can vary for the same sleep component when different measures are used. Therefore, post-TBI sleep research would greatly benefit from self-report instruments validated against objective measurements to increase measurement consistency and allow for greater cross-study comparison.

Furthermore, studies were only included if all participants were aged 18 years or older, limiting the transferability of the findings from the current review to child and adolescent mTBI populations. Limited data currently exists on post-mTBI sleep problems in young people, however age at the time of injury is believed to influence post-mTBI insomnia development [18,80]. Whilst it has generally been accepted that young people recover quickly following mTBI, post-injury effects can greatly impact young people given the significance of the late-childhood and teenage years as key developmental periods [18,80]. Negative sequalae following mTBI sustained during adolescence, such as cognitive impairments, and any comorbid conditions developed, may compound and reverberate through to adulthood [80]. Therefore, more research is needed to investigate post-mTBI insomnia/insomnia symptoms in paediatric and adolescent populations and the impact of paediatric mTBI on the development of sleep difficulties in adulthood.

Chronic mTBI may be associated with slightly higher prevalence of insomnia and insomnia symptoms, however many of the studies did not report time since injury making it difficult to draw conclusions in the presence of limited data from longitudinal studies assessing insomnia and insomnia symptoms. Therefore, future research should endeavour to include time since injury in their reporting – especially considering the wealth of research demonstrating the impact of time since mTBI on the onset and severity of sleep problems [31,33]. Comprehensive serial-assessment throughout the various recovery phases following mTBI would allow capturing of the potential trajectories of symptoms – including the onset, progression and remission of sleep and non-sleep related sequalae. Long-term future research may also help delineate the course of sleep and sleep disturbances following mTBI and potentially uncover the underlying neuropathological processes [14,28]. In addition, as the number of studies increases, future reviews should investigate the potential sources of heterogeneity in greater detail to develop a better understanding of factors contributing to prevalence estimates following mTBI.

Treatment of Post-mTBI Insomnia

This review highlights the high prevalence of insomnia and insomnia symptoms following mTBI and the subsequent requirement for effective and accessible treatment methods. Cognitive behavioural treatment for insomnia (CBTI) is currently considered the first line of treatment for post-mTBI insomnia [21]. This behaviourally focused and time-limited treatment has proven beneficial for not only improving sleep but comorbid conditions too, such as obstructive sleep apnoea (OSA) [28]. It is also highly suited to telehealth methods, lending itself to remote therapy provision following mTBI as part of follow-up treatment [28]. The studies included in this review span various continents and contexts across the globe, from US military rehabilitation programmes to neurosurgery clinics in India and Iraq. Therefore, the ability to provide effective treatment for post-mTBI insomnia via telehealth could be beneficial for many following mTBI worldwide.

Whilst there are many medications available for insomnia that may prove effective over a short-term period, current TBI treatment guidelines recommend avoiding these due to their

many potential side-effects [81]. A literature review concerning the available pharmacotherapy for post-TBI insomnia concluded that benzodiazepine use for treatment of post-TBI insomnia should be discouraged as it may result in cognitive deficits [81]. The use of atypical gamma-aminobutyric acid (GABA) agonists has also been discouraged as they may impair neuroplasticity – a key component of mTBI recovery – and instead therapies centred on functional recovery and promotion of neural plasticity should be prescribed where possible [81].

If treated as a negligible consequence following mTBI, sleep disorders such as insomnia and insomnia symptoms will continually go undiagnosed and untreated to the detriment of the individual's rehabilitation, recovery and quality of life [32]. For example, Mollayeva et al., [74] identified insomnia as the sole predictor of work disability amongst a mTBI sample of workers – highlighting the potential devastating impact untreated post-mTBI insomnia can have on an individual's quality of life. It is therefore essential that healthcare professionals screen for and tackle post-mTBI sleep disturbances early on, especially in those with repeated injury, to prevent potential long-term impact and help identify those potentially at risk of poor outcomes [17,33]. Treatments focused on improving sleep through functional recovery and promotion of neural plasticity are likely to prove more efficacious and effective at treating insomnia and insomnia symptoms within the mTBI population. Non-pharmacological treatments, such as CBTI, should therefore be prescribed where possible as they are not subject to the potential side effects of pharmacological drugs, have an existing evidence base [21,24,82] and can be provided remotely [81].

Conclusion

Insomnia and insomnia symptoms have a negative impact on individuals with mTBI. They can prove detrimental to an individuals' recovery, preventing or deferring return to pre-injury activities and normal functioning – resulting in reduced quality of life [18]. Sleep is therefore a key modifiable risk factor and treatment target following mTBI [28]. Researchers and clinicians alike must be alert to the frequency and potential significance of post-mTBI insomnia in order to guide clinical practice as well as treatment guidelines and research advances [28,32]. The findings highlight high (and variable) prevalence rates of

insomnia and insomnia symptoms within the mTBI population, with an estimated one in three people suffering from insomnia, as assessed by diagnostic tools, and seven in eight from insomnia symptoms, as evaluated by non-diagnostic sleep measures. Both insomnia and insomnia symptoms appear to be significantly higher in the mTBI population compared with the general population. However, due to the high heterogeneity among studies, the findings from the meta-analysis should be interpreted with care.

Practice points

- The presence of insomnia or insomnia symptoms should be routinely assessed following mTBI in clinical practice particularly in military settings.
- Due to the high prevalence of insomnia and insomnia symptoms in this population, treatment should be considered to reduce and manage insomnia and insomnia symptoms.
- Due to lack of available data on comorbidities, clinicians should carefully evaluate the potential impact of comorbidities such as PTSD or affective disorders on the development, maintenance and treatment of insomnia and insomnia symptoms post mTBI.

Research Agenda

- Studies should include a measure of both pre-TBI insomnia and current insomnia symptoms whenever possible.
- More studies providing longitudinal assessment of insomnia symptoms should be undertaken to understand symptom progression during recovery from mTBI, including repeated mTBI.
- Future studies should assess comorbid conditions such as PTSD, anxiety and depression and report these in relation to mTBI cases, along with the cause of injury.

References

[1] Peeters W, van den Brande R, Polinder S, Brazinova A, Steyerberg EW, Lingsma HF, et al. Epidemiology of traumatic brain injury in Europe. Acta Neurochir (Wien) 2015;157:1683–96. https://doi.org/10.1007/s00701-015-2512-7.

[2] Cassidy JD, Carroll L, Peloso P, Borg J, von Holst H, Holm L, et al. Incidence, risk factors and prevention of mild traumatic brain injury: results of the who collaborating centre task force on mild traumatic brain injury. J Rehabil Med 2004;36:28–60. https://doi.org/10.1080/16501960410023732.

[3] Langlois JA, Rutland-Brown W, Wald MM. The Epidemiology and Impact of Traumatic Brain Injury: A Brief Overview. J Head Trauma Rehabil 2006;21:375–8. https://doi.org/10.1097/00001199-200609000-00001.

[4] Gardner RC, Yaffe K. Epidemiology of mild traumatic brain injury and neurodegenerative disease. Mol Cell Neurosci 2015;66:75–80. https://doi.org/10.1016/j.mcn.2015.03.001.

[5] Ponsford J, Willmott C, Rothwell A, Cameron P, Kelly A-M, Nelms R, et al. Factors influencing outcome following mild traumatic brain injury in adults. J Int Neuropsychol Soc 2000;6:568–79. https://doi.org/10.1017/S1355617700655066.

[6] Iverson GL. Outcome from mild traumatic brain injury: Curr Opin Psychiatry 2005;18:301–17. https://doi.org/10.1097/01.yco.0000165601.29047.ae.

[7] Belanger HG, Curtiss G, Demery JA, Lebowitz BK, Vanderploeg RD. Factors moderating neuropsychological outcomes following mild traumatic brain injury: A meta-analysis. J Int Neuropsychol Soc 2005;11:215–27. https://doi.org/10.1017/S1355617705050277.

[8] Boake C, McCauley SR, Levin HS, Pedroza C, Contant CF, Song JX, et al. Diagnostic Criteria for Postconcussional Syndrome After Mild to Moderate Traumatic Brain Injury. J Neuropsychiatry Clin Neurosci 2005;17:350–6. https://doi.org/10.1176/jnp.17.3.350.

[9] Losoi H, Silverberg ND, Wäljas M, Turunen S, Rosti-Otajärvi E, Helminen M, et al. Recovery from Mild Traumatic Brain Injury in Previously Healthy Adults. J Neurotrauma 2016;33:766–76. https://doi.org/10.1089/neu.2015.4070.

[10] Carroll LJ, Cassidy JD, Cancelliere C, Côté P, Hincapié CA, Kristman VL, et al. Systematic Review of the Prognosis After Mild Traumatic Brain Injury in Adults: Cognitive, Psychiatric, and Mortality Outcomes: Results of the International Collaboration on Mild Traumatic Brain Injury Prognosis. Arch Phys Med Rehabil 2014;95:S152–73. https://doi.org/10.1016/j.apmr.2013.08.300.

[11] McMahon PJ, Hricik A, Yue JK, Puccio AM, Inoue T, Lingsma HF, et al. Symptomatology and Functional Outcome in Mild Traumatic Brain Injury: Results from the Prospective TRACK-TBI Study. J Neurotrauma 2014;31:26–33. https://doi.org/10.1089/neu.2013.2984.

[12] Masel BE, DeWitt DS. Traumatic Brain Injury: A Disease Process, Not an Event. J Neurotrauma 2010;27:1529–40. https://doi.org/10.1089/neu.2010.1358.

[13] Lundin A, de Boussard C, Edman G, Borg J. Symptoms and disability until 3 months after mild TBI. Brain Inj 2006;20:799–806. https://doi.org/10.1080/02699050600744327.

[14] Ouellet M, Beaulieu-Bonneau S, Savard J, Morin CM. Insomnia and Fatigue Following Traumatic Brain Injury: Prevalence, Correlates Evolution, and Treatment Options. Insomnia Fatigue Trauma. Brain Inj., Elsevier; 2020, p. 3–59. https://doi.org/10.1016/B978-0-12-811316-5.00001-X.

[15] Fehily B, Fitzgerald M. Repeated Mild Traumatic Brain Injury: Potential Mechanisms of Damage. Cell Transplant 2017;26:1131–55. https://doi.org/10.1177/0963689717714092.
[16] Wilke S, Prehn K, Taud B, List J, Flöel A. Multimodal Assessment of Recurrent mTBI across the Lifespan. J Clin Med 2018;7:95. https://doi.org/10.3390/jcm7050095.
[17] Bryan CJ. Repetitive Traumatic Brain Injury (or Concussion) Increases Severity of Sleep Disturbance among Deployed Military Personnel. Sleep 2013;36:941–6. https://doi.org/10.5665/sleep.2730.
*[18] Zhou Y, Greenwald B. Update on Insomnia after Mild Traumatic Brain Injury. Brain Sci 2018;8:223. https://doi.org/10.3390/brainsci8120223.
[19] American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. 5th ed. Arlington, VA: 2013.
[20] American Academy of Sleep Medicine. International Classification of Sleep Disorders. 3rd ed. Darien, IL: 2014.
[21] Riemann D, Baglioni C, Bassetti C, Bjorvatn B, Dolenc Groselj L, Ellis JG, et al. European guideline for the diagnosis and treatment of insomnia. J Sleep Res 2017;26:675–700. https://doi.org/10.1111/jsr.12594.
[22] Sateia MJ. International Classification of Sleep Disorders-Third Edition. Chest 2014;146:1387–94. https://doi.org/10.1378/chest.14-0970.
[23] Sasai T, Inoue Y, Komada Y, Nomura T, Matsuura M, Matsushima E. Effects of insomnia and sleep medication on health-related quality of life. Sleep Med 2010;11:452–7. https://doi.org/10.1016/j.sleep.2009.09.011.
[24] Morin CM, Benca R. Chronic insomnia. The Lancet 2012;379:1129–41. https://doi.org/10.1016/S0140-6736(11)60750-2.
[25] Fogelberg DJ, Hoffman JM, Dikmen S, Temkin NR, Bell KR. Association of Sleep and Co-Occurring Psychological Conditions at 1 Year After Traumatic Brain Injury. Arch Phys Med Rehabil 2012;93:1313–8. https://doi.org/10.1016/j.apmr.2012.04.031.
[26] Ohayon MM. Epidemiology of insomnia: what we know and what we still need to learn. Sleep Med Rev 2002;6:97–111. https://doi.org/10.1053/smrv.2002.0186.
[27] Zeitzer JM, Friedman L, OHara R. Insomnia in the context of traumatic brain injury. J Rehabil Res Dev 2009;46:827. https://doi.org/10.1682/JRRD.2008.08.0099.
*[28] Wickwire EM, Schnyer DM, Germain A, Smith MT, Williams SG, Lettieri CJ, et al. Sleep, Sleep Disorders, and Circadian Health following Mild Traumatic Brain Injury in Adults: Review and Research Agenda. J Neurotrauma 2018;35:2615–31. https://doi.org/10.1089/neu.2017.5243.
[29] Worthington AD, Melia Y. Rehabilitation is compromised by arousal and sleep disorders: Results of a survey of rehabilitation centres. Brain Inj 2006;20:327–32. https://doi.org/10.1080/02699050500488249.
[30] Duclos C, Beauregard M-P, Bottari C, Ouellet M-C, Gosselin N. The impact of poor sleep on cognition and activities of daily living after traumatic brain injury: A review. Aust Occup Ther J 2015;62:2–12. https://doi.org/10.1111/1440-1630.12164.
[31] Mantua J, Henry OS, Garskovas NF, Spencer RMC. Mild Traumatic Brain Injury Chronically Impairs Sleep- and Wake-Dependent Emotional Processing. Sleep 2017;40. https://doi.org/10.1093/sleep/zsx062.
*[32] Mathias JL, Alvaro PK. Prevalence of sleep disturbances, disorders, and problems following traumatic brain injury: A meta-analysis. Sleep Med 2012;13:898–905. https://doi.org/10.1016/j.sleep.2012.04.006.

[33] Theadom A, Cropley M, Parmar P, Barker-Collo S, Starkey N, Jones K, et al. Sleep difficulties one year following mild traumatic brain injury in a population-based study. Sleep Med 2015;16:926–32. https://doi.org/10.1016/j.sleep.2015.04.013.
[34] Sullivan KA, Edmed SL, Allan AC, Karlsson LJE, Smith SS. Characterizing Self-Reported Sleep Disturbance after Mild Traumatic Brain Injury. J Neurotrauma 2015;32:474–86. https://doi.org/10.1089/neu.2013.3284.
[35] Paunio T, Korhonen T, Hublin C, Partinen M, Koskenvuo K, Koskenvuo M, et al. Poor sleep predicts symptoms of depression and disability retirement due to depression. J Affect Disord 2015;172:381–9. https://doi.org/10.1016/j.jad.2014.10.002.
[36] Duclos C, Dumont M, Wiseman-Hakes C, Arbour C, Mongrain V, Gaudreault P-O, et al. Sleep and wake disturbances following traumatic brain injury. Pathol Biol 2014;62:252–61. https://doi.org/10.1016/j.patbio.2014.05.014.
[37] Mayer G, Jennum P, Riemann D, Dauvilliers Y. Insomnia in central neurologic diseases – Occurrence and management. Sleep Med Rev 2011;15:369–78. https://doi.org/10.1016/j.smrv.2011.01.005.
[38] Roth T, Drake C. Evolution of insomnia: current status and future direction. Sleep Med 2004;5:S23–30. https://doi.org/10.1016/S1389-9457(04)90004-4.
[39] Grima N, Ponsford J, Rajaratnam SM, Mansfield D, Pase MP. Sleep Disturbances in Traumatic Brain Injury: A Meta-Analysis. J Clin Sleep Med 2016;12:419–28. https://doi.org/10.5664/jcsm.5598.
[40] Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan—a web and mobile app for systematic reviews. Syst Rev 2016;5:210. https://doi.org/10.1186/s13643-016-0384-4.
[41] Munn Z, Moola S, Riitano D, Lisy K. The development of a critical appraisal tool for use in systematic reviews addressing questions of prevalence. Int J Health Policy Manag 2014;3:123–8. https://doi.org/10.15171/ijhpm.2014.71.
[42] Migliavaca CB, Stein C, Colpani V, Barker TH, Munn Z, Falavigna M. How are systematic reviews of prevalence conducted? A methodological study. BMC Med Res Methodol 2020;20:96. https://doi.org/10.1186/s12874-020-00975-3.
[43] Viechtbauer W. Conducting Meta-Analyses in *R* with the **metafor** Package. J Stat Softw 2010;36. https://doi.org/10.18637/jss.v036.i03.
[44] Schwarzer G, Carpenter JR, Rücker G. Meta-Analysis with R. Cham: Springer International Publishing; 2015. https://doi.org/10.1007/978-3-319-21416-0.
[45] R Core Team. R: A language and environment for statistical computing. Vienna, Austria: R Foundation for Statistical Computing; 2019.
[46] Higgins JPT. Measuring inconsistency in meta-analyses. BMJ 2003;327:557–60. https://doi.org/10.1136/bmj.327.7414.557.
[47] Egger M, Smith GD, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. BMJ 1997;315:629–34. https://doi.org/10.1136/bmj.315.7109.629.
[48] Meares S, Shores EA, Taylor AJ, Batchelor J, Bryant RA, Baguley IJ, et al. The prospective course of postconcussion syndrome: The role of mild traumatic brain injury. Neuropsychology 2011;25:454–65. https://doi.org/10.1037/a0022580.
*[49] Hou L, Han X, Sheng P, Tong W, Li Z, Xu D, et al. Risk Factors Associated with Sleep Disturbance following Traumatic Brain Injury: Clinical Findings and Questionnaire Based Study. PLoS ONE 2013;8:e76087. https://doi.org/10.1371/journal.pone.0076087.

*[50] Pugh MJ, Swan AA, Amuan ME, Eapen BC, Jaramillo CA, Delgado R, et al. Deployment, suicide, and overdose among comorbidity phenotypes following mild traumatic brain injury: A retrospective cohort study from the Chronic Effects of Neurotrauma Consortium. PLOS ONE 2019;14:e0222674. https://doi.org/10.1371/journal.pone.0222674.
[51] Mosti CB, Klingaman EA, Brownlow JA, Gehrman PR. Insomnia prevalence among U.S. Army soldiers with history of TBI. Rehabil Psychol 2019;64:475–81. https://doi.org/10.1037/rep0000283.
[52] Al-Ameri L, Mohsin T, Abdul Wahid A. Sleep Disorders Following Mild and Moderate Traumatic Brain Injury. Brain Sci 2019;9:10. https://doi.org/10.3390/brainsci9010010.
[53] Albicini MS, Lee J, McKinlay A. Ongoing daytime behavioural problems in university students following childhood mild traumatic brain injury. Int J Rehabil Res 2016;39:77–83. https://doi.org/10.1097/MRR.0000000000000149.
[54] Farrell-Carnahan L, Barnett S, Lamberty G, Hammond FM, Kretzmer TS, Franke LM, et al. Insomnia symptoms and behavioural health symptoms in veterans 1 year after traumatic brain injury. Brain Inj 2015;29:1400–8. https://doi.org/10.3109/02699052.2015.1063161.
[55] Farrell-Carnahan L, Franke L, Graham C, McNamee S. Subjective Sleep Disturbance in Veterans Receiving Care in the Veterans Affairs Polytrauma System Following Blast-Related Mild Traumatic Brain Injury. Mil Med 2013;178:951–6. https://doi.org/10.7205/MILMED-D-13-00037.
*[56] Hong C-T, Wong C-S, Ma H-P, Wu D, Huang Y-H, Wu C-C, et al. PERIOD3 polymorphism is associated with sleep quality recovery after a mild traumatic brain injury. J Neurol Sci 2015;358:385–9. https://doi.org/10.1016/j.jns.2015.09.376.
*[57] Jain A, Mittal RS, Sharma A, Sharma A, Gupta ID. Study of insomnia and associated factors in traumatic brain injury. Asian J Psychiatry 2014;8:99–103. https://doi.org/10.1016/j.ajp.2013.12.017.
[58] Lu LH, Reid MW, Cooper DB, Kennedy JE. Sleep problems contribute to post-concussive symptoms in service members with a history of mild traumatic brain injury without posttraumatic stress disorder or major depressive disorder. NeuroRehabilitation 2019;44:511–21. https://doi.org/10.3233/NRE-192702.
[59] Martindale SL, Farrell-Carnahan LV, Ulmer CS, Kimbrel NA, McDonald SD, Rowland JA, et al. Sleep quality in returning veterans: The influence of mild traumatic brain injury. Rehabil Psychol 2017;62:563–70. https://doi.org/10.1037/rep0000159.
[60] Mollayeva T, Shapiro CM, Mollayeva S, Cassidy JD, Colantonio A. Modeling community integration in workers with delayed recovery from mild traumatic brain injury. BMC Neurol 2015;15:194. https://doi.org/10.1186/s12883-015-0432-z.
[61] Beetar JT, Guilmette TJ, Sparadeo FR. Sleep and pain complaints in symptomatic traumatic brain injury and neurologic populations. Arch Phys Med Rehabil 1996;77:1298–302. https://doi.org/10.1016/S0003-9993(96)90196-3.
*[62] Kalmbach DA, Conroy DA, Falk H, Rao V, Roy D, Peters ME, et al. Poor sleep is linked to impeded recovery from traumatic brain injury. Sleep 2018;41:zsy147. https://doi.org/10.1093/sleep/zsy147.
[63] Towns SJ, Silva MA, Belanger HG. Subjective sleep quality and postconcussion symptoms following mild traumatic brain injury. Brain Inj 2015;29:1337–41. https://doi.org/10.3109/02699052.2015.1045030.

[64] Verfaellie M, Lee LO, Lafleche G, Spiro A. Self-Reported Sleep Disturbance Mediates the Relationship Between PTSD and Cognitive Outcome in Blast-Exposed OEF/OIF Veterans. J Head Trauma Rehabil 2016;31:309–19. https://doi.org/10.1097/HTR.0000000000000197.
[65] Vuletic S, Bell KR, Jain S, Bush N, Temkin N, Fann JR, et al. Telephone Problem-Solving Treatment Improves Sleep Quality in Service Members With Combat-Related Mild Traumatic Brain Injury: Results From a Randomized Clinical Trial. J Head Trauma Rehabil 2016;31:147–57. https://doi.org/10.1097/HTR.0000000000000221.
[66] Walker JM, Mulatya C, Hebert D, Wilson SH, Lindblad AS, Weaver LK. Sleep assessment in a randomized trial of hyperbaric oxygen in U.S. service members with post concussive mild traumatic brain injury compared to normal controls. Sleep Med 2018;51:66–79. https://doi.org/10.1016/j.sleep.2018.06.006.
*[67] Julien J, Tinawi S, Anderson K, Frenette LC, Audrit H, Ferland MC, et al. Highlighting the differences in post-traumatic symptoms between patients with complicated and uncomplicated mild traumatic brain injury and injured controls. Brain Inj 2017;31:1846–55. https://doi.org/10.1080/02699052.2017.1346289.
[68] Buysse DJ, Reynolds CF, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh sleep quality index: A new instrument for psychiatric practice and research. Psychiatry Res 1989;28:193–213. https://doi.org/10.1016/0165-1781(89)90047-4.
[69] Fichtenberg N, Millis S, Mann N, Zafonte R, Millard A. Factors associated with insomnia among post-acute traumatic brain injury survivors. Brain Inj 2000;14:659–67. https://doi.org/10.1080/02699050050044015.
[70] Kaufmann CN, Orff HJ, Moore RC, Delano-Wood L, Depp CA, Schiehser DM. Psychometric Characteristics of the Insomnia Severity Index in Veterans With History of Traumatic Brain Injury. Behav Sleep Med 2019;17:12–8. https://doi.org/10.1080/15402002.2016.1266490.
[71] Barker-Collo S, Jones K, Theadom A, Starkey N, Dowell A, McPherson K, et al. Neuropsychological outcome and its correlates in the first year after adult mild traumatic brain injury: A population-based New Zealand study. Brain Inj 2015;29:1604–16. https://doi.org/10.3109/02699052.2015.1075143.
[72] Schwab K, Terrio HP, Brenner LA, Pazdan RM, McMillan HP, MacDonald M, et al. Epidemiology and prognosis of mild traumatic brain injury in returning soldiers: A cohort study. Neurology 2017;88:1571–9. https://doi.org/10.1212/WNL.0000000000003839.
[73] Chase RP, Nevin RL. Population Estimates of Undocumented Incident Traumatic Brain Injuries Among Combat-Deployed US Military Personnel: J Head Trauma Rehabil 2015;30:E57–64. https://doi.org/10.1097/HTR.0000000000000061.
[74] Mollayeva T, Pratt B, Mollayeva S, Shapiro CM, Cassidy JD, Colantonio A. The relationship between insomnia and disability in workers with mild traumatic brain injury/concussion. Sleep Med 2016;20:157–66. https://doi.org/10.1016/j.sleep.2015.09.008.
[75] Wang M-Y, Wang S-Y, Tsai P-S. Cognitive behavioural therapy for primary insomnia: a systematic review. J Adv Nurs 2005;50:553–64. https://doi.org/10.1111/j.1365-2648.2005.03433.x.
[76] Cartwright DJ. ICD-9-CM to ICD-10-CM Codes: What? Why? How? Adv Wound Care 2013;2:588–92. https://doi.org/10.1089/wound.2013.0478.

*[77] Wickwire EM, Williams SG, Roth T, Capaldi VF, Jaffe M, Moline M, et al. Sleep, Sleep Disorders, and Mild Traumatic Brain Injury. What We Know and What We Need to Know: Findings from a National Working Group. Neurotherapeutics 2016;13:403–17. https://doi.org/10.1007/s13311-016-0429-3.
[78] Sinha SS. Trauma-induced insomnia: A novel model for trauma and sleep research. Sleep Med Rev 2016;25:74–83. https://doi.org/10.1016/j.smrv.2015.01.008.
[79] Gilbert KS, Kark SM, Gehrman P, Bogdanova Y. Sleep disturbances, TBI and PTSD: Implications for treatment and recovery. Clin Psychol Rev 2015;40:195–212. https://doi.org/10.1016/j.cpr.2015.05.008.
[80] Tham SW, Fales J, Palermo TM. Subjective and Objective Assessment of Sleep in Adolescents with Mild Traumatic Brain Injury. J Neurotrauma 2015;32:847–52. https://doi.org/10.1089/neu.2014.3559.
[81] Larson EB, Zollman FS. The Effect of Sleep Medications on Cognitive Recovery From Traumatic Brain Injury: J Head Trauma Rehabil 2010;25:61–7. https://doi.org/10.1097/HTR.0b013e3181c1d1e1.
[82] Mitchell MD, Gehrman P, Perlis M, Umscheid CA. Comparative effectiveness of cognitive behavioral therapy for insomnia: a systematic review. BMC Fam Pract 2012;13:40. https://doi.org/10.1186/1471-2296-13-40.

Figure Legends

Figure 1. PRISMA flow diagram

Figure 2. Forest plot of overall insomnia prevalence

Figure 3. Funnel plot of publication bias

Figure 4. Forest plot for subgroup analysis of prevalence estimates of insomnia disorder and insomnia symptoms

Figure 5. Forest plot for subgroup analysis of prevalence estimates in military and non-military studies

Figure 6. Forest plot for subgroup analysis of prevalence estimates in studies using direct observation and medical records

Figure 7. Forest plot for subgroup analysis of studies reporting prevalence estimates for early (acute) and late (chronic) after mild TBI

Table 1
Study Characteristics

Study Details					**Sample Characteristics (mTBI sample)**				
Study Details	**Country**	**Total N (%, n of mTBI)**	**Design**	**Sampling**	**Mean Age (years, SD)**	**Gender (% male)**	**Setting**	**Lifetime TBI History**	**Time since TBI (mean, SD)**
Al-Ameri et al. 2019 [52]	Iraq	220 (19.1%, n = 42)	Case-control	NR	NR	NR	Tertiary Neurosurgical Centre	NR	3 months
Albicini et al., 2016 [53]	Australia	247 (19%, n = 47)	Cross-sectional	Recruited through flyers placed around Monash University	20.36 (2.09)	38.30%	University	TBI with LOC = 32 (68.10%) TBI with LOC >30mins = 2 (4.26%) Multiple TBI = 8 (17.02%)	NR
Beetar et al. 1996 [61]	USA	325 (39.1%, n = 127)	Case-control	Consecutive	NR	NR	Medical Centre Neuropsychology Service	NR	NR
Farrell-Carnahan et al. 2015 [54]	USA	112 (35.7%, n = 40)	Cross-sectional	Retrospective sub-study of the VA PRC TBIMS programme	29 (13)	93%	Rehabilitation Programme	NR	NR

Farrell-Carnahan et al. 2013 [55]	USA	114 (100%)	Cross-sectional	Retrospective sub-study of the Defense and Veterans Brain Injury Centre: Prospective TBI Tracking Protocol study	31 (8)	96%	Rehabilitation Programme	NR	1,044 (538) days
Hong et al. 2015 [56]	Taiwan	96 (100%)	Longitudinal prospective cohort study	NR	NR	44%	Hospital	First-time mTBI	Baseline assessment conducted within 1 week of injury
Hou et al. 2013 [49]	China	98 (70.4%, n = 69)	Prospective questionnaire and clinical findings-based cohort study	NR	NR	NR	Hospital	First-time mTBI	NR
Jain et al. 2014 [57]	India	204 (59.8%, n =122)	Longitudinal prospective cohort study	Recruited through follow-up from neurosurgery ward, medical college and group of hospitals	NR	NR	Hospital	Newly afflicted TBI	Initial evaluations at 2 weeks post-injury
Julien et al. 2017 [67]	Canada	198 (79.3%, n =157)	Medical chart review and interview-based cohort study	Retrospective	UC-mTBI: 40.15 (16.885) C-mTBI: 42.81 (19.527)	43%	University Health Centre	Previous TBI: UC-mTBI: 71.9% N, 28.1% Y C-mTBI: 67.4% N, 44.2% Y	NR

Kalmbach et al. 2018 [62]	USA	238 (98.7%, n = 235)	Longitudinal interview and survey based prospective cohort study	Consecutive	NR	NR	Hospital	NR	Presented to ED within 24 hours of head injury
Lu et al., 2019 [58]	USA	279 (100%)	Questionnaire -based cohort study	Retrospective	36.5 (7.5)	86%	Rehabilitation	NR	61.5 months
Martindale et al. 2017 [59]	USA	527 (13.7%, n = 72)	Interview and questionnaire based cross-sectional study	Retrospective	NR	NR	Veteran Medical Centres	Participants with deployment-related mTBI history reported an average of 1.57 injury events during cumulative deployments (SD = 0.77, range = 1–3).	Time since most recent mTBI: M 72.15 months (35.37, range = 0-183)
Meares et al. 2011 [48]	Australia	120 (51.7%, n = 62)	Longitudinal prospective case-control study	Consecutive	35.7 (14.5)	67.70%	Hospital	Number of prior mTBI: None = 61.3% One = 32.3% More than one = 6.5%	4.8 (3.1) days
Mollayeva et al. 2015 [60]	Canada	94 (100%)	Cross-sectional study	Initial contact made with potential participants at orientation sessions, where they were informed of the	45.2 (9.94)	62%	Rehabilitation Hospital	Previous head trauma: 23 Y and 67 N. 21 had PTA, 56 did not. 29 experienced LOC and 56 did not. 0 showed trauma-related head MRI findings, 84 did not.	Time since mTBI (median, interquartile range) = 197 days, 139-416

				ongoing study and invited to participate					
Mosti et al., 2019 [51]	USA	Unweighted 21,499; weighted 674,335 (63.3% of weighted sample reported mTBI)	Retrospective cross-sectional study	Data obtained from the All Army Study (AAS)	NR	65.6% - (based off weighted sample)	Military	NR	NR
Pugh et al. 2019 [50]	USA	527,381 (17.6%, n = 93,003)	Retrospective cohort study	Part of the CENC epidemiology study - acquired data from the VHA and DoD	29.79 (7.8)	94%	Veteran Rehabilitation Care (VHA Care)	NR	NR
Towns et al., 2015 [63]	USA	158 (100%)	Retrospective study of data from randomised controlled trial	Recruited for original study either in person at Veterans' Hospital clinics or online through web-based Veteran and injured groups	NR	74.7%	Veteran Rehabilitation	NR	36.7% <1 month; 31.6% 1 month to 1 year; 31.6% >1 year
Verfaellie et al. 2016 [64]	USA	160 (65.6%, n = 105)	Prospective questionnaire and interview-	Recruited through VA Boston Polytrauma Network and through community flyers and outreach events	mTBI-LOC: 30.57 (8.39); mTBI+LOC: 28.88 (6.80)	97%	Veteran Rehabilitation Care (VA Boston Polytrauma Network)	NR	Months since blast exposure: mTBI-LOC:

			based cohort study						43.59 (26.85); mTBI+LOC: 52.40 (24.87)
Vuletic et al. 2016 [65]	USA	356 (100%)	Longitudinal randomized clinical trial	IN-TRuST study "CONcussion Treatment After Combat Trauma"	29.35 (7.23)	93.3%	Army Medical Centres	No. of TBIs, M (SD) = 5.88 (5.58) No. of mTBIs in most recent deployment, M (SD) = 1.86 ± 2.04, in previous deployments = 1.14 ± 2.51, and non-deployment related = 2.99 ± 4.29.	NR
Walker et al. 2018 [66]	USA	146 (48.6%, n = 71)	Longitudinal clinical trial	Opportunity	32.8 (7.3)	99%	Military Bases	Most recent injury <1-year: 28% More than one injury: 28% Lifetime TBI history: Blast injuries only: 32% Blunt force head injuries only: 20% Blast and blunt force head injuries: 48%	NR

Note: M, mean; SD, standard deviation; %, percentage; NR, not reported; VA PRC TBIMS: Veterans Affairs Polytrauma Rehabilitation Centres Traumatic Brain Injury Model Systems; UC-mTBI, uncomplicated mTBI; C-mTBI, complicated mTBI; ED, emergency department; Y, yes; N, no; MRI, magnetic resonance

imaging; CENC, Chronic Effects of Neurotrauma Consortium; VHA, Veteran Health Administration; DoD, Department of Defence; VA, Veterans Administration; mTBI-LOC, mTBI without LOC; mTBI+LOC, mTBI with LOC

Table 2

Studies Evaluating Insomnia Using Clinical Diagnostic Tools

First Author, Year	Insomnia Assessment	mTBI Assessment	Overall Prevalence %	Insomnia mTBI/Clinical Characteristics
Hou 2013 [49]	ICSD-2	Acute TBI with positive findings on cranial computerised tomography (CT) scans. Initial evaluation of severity during hospitalization, based on GCS (13-15) and LOC.	26.1% insomnia; 30% sleep disturbance (PSQI)	NR
Meares 2011 [48]	ICD-10	Criteria for mild, uncomplicated mTBI based on WHO definition.	16.1% insomnia within 14 days of injury but recovered by 3-month assessment; 16.1% insomnia within 14 days of injury and still at 3-month assessment; 19.4% developed insomnia by 3-month assessment	mTBI Population: **Injury severity score**, M (SD) = 6.2 (6.6) **GCS**: 13 = 3.2%; 14 = 11.3%; 15 = 85.5% **Mode of injury:** Motor vehicle accident (82.3%), fall/jump (9.7%), assault (4.8%), other (3.2%) **Duration of PTA:** <5 mins = 40.3%; 6-60 mins = 21%; 61 mins-12 hrs = 24.2%; >12-24 hrs = 14.5%
Mosti 2019 [51]	DSM-5	Participants deemed to have suffered a probable TBI if they provided a positive response to any of the following AAS questions: "(C1) How many times in your life did you have a head, neck or blast injury that a) knocked you out for less than 30 min b) knocked you out for between 30min and 24 hr c) knocked you out for more than 24 hr or d) didn't knock you out, but caused you to be dazed, confused, or 'see stars'?" and "(C2) How many times in your life did you have ahead,	51.1% met diagnostic criteria for clinically elevated insomnia (based on weighted mTBI sample)	Prevalence of symptoms meeting clinically elevated insomnia threshold in mTBI participants: 44.1% sleep latency 40.4% night-time awakenings 26.3% WASO 35.9% early morning awakenings 49.2% non-restorative sleep.

		neck, or blast injury that caused you to have a lapse in memory of events before, during, or after injury lasting a) less than 30 min b) between 30 min and 24 hr or c) more than 24 hr?" Participants who indicated only a history of injury with LOC<30 min and PTA lasting<24 hr were classified as “mild.”		
Pugh 2019 [50]	ICD-9-CM	Participants diagnosed with mTBI following mandatory TBI screening by VHA. TBI severity determined by an algorithm incorporating DoD and VHA data sources.	9.96% insomnia	GCS range = 13-15

Note: details of insomnia demographic characteristics and insomnia comorbidity are not included in the above table as these were not reported for any of the five studies described above.

Table 3
Studies assessing insomnia symptoms (mTBI sample only)

First Author, Year	Insomnia Symptoms Assessment	Classification	mTBI Assessment	Prevalence %	Insomnia Demographic Characteristics %, mean (SD), Age/Education (years), Gender (% male)	Insomnia mTBI/Clinical Characteristics (%), mean (SD)	Insomnia Comorbidity % significant interactions
Al-Ameri 2019 [52]	PSQI (Translated to Arabic)	PSQI>5 = poor sleep quality	Diagnosed by on-call neurosurgical team on admission as having mTBI. Severity determination based on GCS 13-15.	46.28% poor sleep quality	NR	Mild TBI Subgroup: Initial GCS = 13.22 ± 1.76	NR
Albicini 2016 [53]	PSQI	PSQI≥5 = poor sleep	The Ohio State University TBI Identification Method Short Form (OSU TBI-ID SF) was used as a self-report measure to screen lifetime TBI exposure.	55.30% sleep disturbance	NR	NR	NR
Beetar 1996 [61]	A sleep problem was deemed present if it was mentioned in	Problems with difficulty falling asleep, sleep maintenance, and early morning awakening were	Applied diagnostic criteria established by the Mild Traumatic Brain Injury Committee of the Head Injury Interdisciplinary Special	65.3% insomnia. By time (months) post-injury: 47.4% (1-12), 28.9% at (13-59), and 23.7% (≥60).	NR	GCS: 13-15	NR

	medical records as a concern reported by the patient.	grouped as one variable - “insomnia”.	Interest Group of the American Congress of Rehabilitation Medicine.	55.3% insomnia in mTBI subjects without pain (n = 38).			
Farrell-Carnahan 2015 [54]	NSI item #18 asks how much participants were disturbed by 'difficulty falling or staying asleep' in the past 2 weeks.	Insomnia symptoms: answer 3 (severe) and 4 (very severe).	Diagnosed by VA PRC TBIMS, supported by self-report/medical records of symptoms following mTBI. Injury severity classified by duration of PTA.	43% insomnia symptoms	NR	**Cause of mTBI:** Motor-vehicle (25%), blast (53%), other (23%) **Duration of PTA** = 0 **mTBI during deployment** = 65%	Univariable logistic regression for predicting sleep disturbance, unadjusted effect (95% confidence interval (CI)): **Depression** = 1.33 (1.12-1.58) p<0.001; **General Anxiety** = 1.38 (1.12-1.71) p<0.003
Farrell-Carnahan 2013 [55]	Item #13 on PCL-C: "Please indicate how much you have been bothered by trouble falling and staying	Subjective Sleep Disturbance (SSD): answer 4 (quite a bit) or 5 (extremely)	Physician-diagnosed mTBI.	77% SSD	Gender SSD: 94% No SSD: 100%	**Days Since Injury** SSD: 1076 ± 533 No SSD: 935 ± 551 **Experienced LOC:** (p<0.05) SSD: 72%; No SSD: 46% **Wearing Helmet at Injury**: SSD: 66% Y, 25% N, 9% U; No SSD: 62% Y, 35% N, 4% U	**Positive PTSD Screen** (p<0.05) SSD: 91%; No SSD: 35% **Nightmares** (p<0.05) SSD: 4.00; No SSD: 2.00 **Depression** (p<0.05) SSD: 2.00; No SSD: 0.00 **Headaches** (p<0.05) SSD: 3.00; No SSD: 2.00

	asleep in the past month".					**Primary cause of mTBI**: blast	**Fatigue** (p<0.05) SSD: 3.00; No SSD: 1.00
Hong 2015 [56]	PSQI (Chinese Version)	PSQI>5 = sleep disturbance	Patients who visited hospital A&E with GCS of 13-15 at the time of triage; LOC for less than 30 mins; and trauma to the head.	74% sleep disturbance	Age: MTBI with PSQI>5 = 42,21 ± 14.15 Education: All MTBI = 13.59 MTBI with PSQI>5 = 13.21 ± 2.99 Gender: All MTBI = 44% MTBI with PSQI>5 = 46%	**GCS:** MTBI = 14.93 MTBI+PSQI>5 =14.79 ± 0.40 **Mechanism of Injury:** Traffic accident: MTBI = 51%; MTBI+PSQI>5 = 51% Falls: MTBI = 32%; MTBI+PSQI>5 = 32% Other MTBI = 17%; MTBI+PSQI>5 = 17%	**Headache:** All MTBI = 51%; MTBI with PSQI>5 = 57% **BAI Scores:** All MTBI = 10.37 ± 10.37; MTBI with PSQI>5 = 12.46 ± 10.97 **BDI Scores:** All MTBI = 10.32 ± 9.75; MTBI with PSQI>5 = 12.1 ± 10.34
Jain 2014 [57]	ISI (Hindi Version)	ISI scores: 0-7 = no insomnia; 8-14 = sub-threshold insomnia; 15-21 = moderate insomnia; 22-28 clinically severe insomnia	History of TBI with a documented LOC or other evidence of TBI (i.e. pathology on neuroimaging). Severity assessed by GCS.	19.7% insomnia	NR	NR	NR
Julien 2017 [67]	MOS Sleep Scale Revised	MOS Total Scores: <45 sleep problems; >45 no sleep problems	History of recent head trauma; mTBI identification based on	84.06% UC-mTBI and 62.96% C-mTBI had sleep issues.	NR	**MOS Q1 + Q3 to 12 (total score)** UC-mTBI: 58.0% <40; 26.1% 40-44; 16.0% >44	Correlations for outcome measures: MOS index 1 + Rivermead

			WHO Task Force criteria and physician confirmed.			C-mTBI: 33.3% <40; 29.6% 40-44; 37.0% >44 Controls: 46.7% <40; 26.7% 40-44; 26.7% >44 **MOS Q2 (total no. of hours of sleep at night)** UC-mTBI: 48.5% <7; 25% 7-8; 26.5% >8 C-mTBI: 41.9% <7; 29.0% 7-8; 29.0% >8 Controls: 36.8% <7; 36.8% 7-8; 26.3% >8 **PTS related to mTBI:** None: UC-mTBI = 87.0%, C-mTBI = 90.2% Acute stress disorder: UC-mTBI = 5.6%, C-mTBI = 5.0% Adjustment disorder: UC-mTBI = 5.6%, C-mTBI = 2.4% PTSD: UC-mTBI = 1.9%, C-mTBI = 2.4%	total = -0.342 (p<0.001) MOS index 1 + Beck anxiety = -0.347 (p<0.01) MOS index 1 + BDI = -0.450 (p<0.001) MOS index 1 + HIT-6-TOTAL = -0.292 (p<0.01)

Kalmbach 2018 [62]	PSQI	PSQI>5 = poor sleeper. PSQI>8 = clinically poor sleepers	TBI diagnosed according to the definition proposed by the Demographics and Clinical Assessment Working Group of the International and Interagency. Severity rated using revised GCS.	PSQI>5: 1m: 72.2%; 3m: 75.1%; 6m: 69.3% PSQI>8: 1m: 66.9%; 3m: 63.0%; 6m: 52.8% PSQI - SOI 1m: 44.0%; 3m: 36.5%; 6m: 33.3%	NR	NR	NR
Lu 2019 [58]	Self-Report	Semi-structured study-specific questionnaire	TBI diagnosis based on electronic medical record review and patient self-report based off semi-structured interviews with trained research nurses. mTBI defined using the VA/DoD criteria.	45 individuals (16.1%) self-reported that they don't have sleep disturbances. The remainder endorsed sleep disturbances.	NR	NR	133 (47%) had comorbid diagnoses of PTSD (n=112; 40%), MDD (n=78; 30%), or both (n=57; 20%)
Martindale 2017 [59]	PSQI	PSQI>8 = clinically significant poor sleep quality	Structured clinical TBI interview. Participants asked about cause of event, medical care, other injuries, LOC, PTA, and other post-	87.5% clinically significant poor sleep quality	NR	NR	MTBI contributed to poorer sleep quality independently of PTSD, anxiety and depression. It affected sleep beyond effects of behavioural issues but effect of mTBI on sleep

			concussive symptoms. TBI severity assigned as mild per the ACRM definition.				quality was approx. 50% of the effect of PTSD/mood disorders, which were more strongly associated with sleep quality – comparable to effect of combat exposure.
Mollayeva 2015 [60]	ISI	ISI scores (0-29): 0-7: no insomnia, 8-14: sub-threshold, 15-21: clinical insomnia (moderate), 22-28: clinical insomnia (severe).	Multidisciplinary team of specialists established a TBI diagnosis based on the initial LOC, GCS score, post-traumatic amnesia, MRI, and clinical assessment.	69.2% insomnia	NR	Mechanisms of mTBI: falls (19.1%), being struck by (19.1%) or against (17%) an object, motor vehicle accidents (12.8%), and assault (10.5%). Of 86 mTBI with data available, 31% = LOC, 24.7% = PTA, 0 = trauma-related brain changes.	NR
Towns 2015 [63]	PSQI	PSQI>5 = poor sleep quality; PSQI>8/9 = more conservative cut-off	TBI diagnosis based on self-report questionnaires.	92% poor sleep quality (PSQI>5); 60% (PSQI>8/9)	NR	NR	NR

Verfaellie 2016 [64]	PSQI	PSQI>5 = poor sleep; PSQI>8 = clinically significant symptoms	TBI diagnosis based on extensive clinical interview.	mTBI-LOC: 17% poor sleepers and 76% had clinically significant symptoms. mTBI+LOC: 7% poor sleepers and 86% had clinically significant symptoms.	NR	NR	Compared with controls, mTBI-LOC had more severe PTSD symptoms, greater sleep disturbance and a trend for worse manual dexterity; mTBI+LOC had more severe PTSD symptoms, greater sleep disturbance, slower processing speed, and worse manual dexterity. Proportion of mTBI participants with PSQI>8 positively associated with TBI severity.
Vuletic 2016 [65]	PSQI and Brief Demographic Questionnaire	PSQI: 6-8 mild poor sleep quality, 9-11 moderate poor sleep quality, ≥12 severely reduced sleep quality.	Positive mTBI screen at post-deployment examination and positive response to questions 1, 2, or 6 on the "2 + 10 TBI Screening Questionnaire," or positive response to questions 1c, 4, 5, or 6 on the Military Acute	Brief demographic questionnaire administered at baseline: 77.1% evaluated sleep quality as fairly bad/very bad. PSQI scores: 10% reported mild, 16%	NR	**PSQI** (n = 352), M (SD): Composite: 12±4.30 Sleep quality: 2.13±0.82 Sleep latency: 2.19±0.97 Sleep duration: 2.23±1.00 Sleep efficiency: 1.61±1.23 Sleep disturbances: 1.51±0.58 Sleep medications: 1.43±1.34 Day dysfunction = 1.43 ± 0.92 **Early morning/night-time**	Correlations (rho values) between PSQI composite score and other variables: Rivermead total = 0.42**** RIvermead cognitive = 0.28**** BSI GSI = 0.43**** AUDIT-C total = -0.02 LEC = 0.21*** Pain (EuroQOL4) = 0.29****

			Concussion Evaluation, MACE. Criteria correspond to sections of the CDC operational definition of mTBI.	reported moderate and 64% reported severe sleep dysfunction.		**awakenings** = 93.47% **Cannot get to sleep within 30 mins** = 89.77% **Circumstances of mTBI**: blast = 85%; vehicular = 23%; fragment = 8%; struck = 36%; fall = 27%; thrown = 40%; training = 9%; assault = 3%	PCL-M = 0.45**** PHQ-9 = 0.47**** Days lost = 0.24**** Days unproductive = 0.29**** **** P<.0001 ***P<0.005
Walker 2018 [66]	PSQI	PSQI>5 = poor sleeper; PSQI>8 = insomnia symptoms.	mTBI diagnosis based on structured interview and medical records.	96% = poor sleepers (PSQI score >5). 87% met criteria for insomnia (global PSQI score >8).	NR	**Sleep Duration (min), M (SD)** Actigraphy = 400.2 (64.1) PSQI = 288.2 (73.6) Sleep Diary = 301.7 (115.0) **WASO (min), M (SD)** Actigraphy = 42.9 (17.7) PSQI = 69.5 (59.2) Sleep Diary = 52.4 (55.2) **Sleep Maintenance Efficiency** Actigraphy = 90.4% (4.1) PSQI = 79.1% (13.9) Sleep Diary = 82.7% (16.6) **Sleep Latency (min), M (SD)** PSQI = 57.3 (49.9) Sleep Diary = 58.9 (53.9) **PSQI, M (SD)**	74% of mTBI participants positive for insomnia at higher risk for OSA, and 31% at higher risk for OSA and RLS.

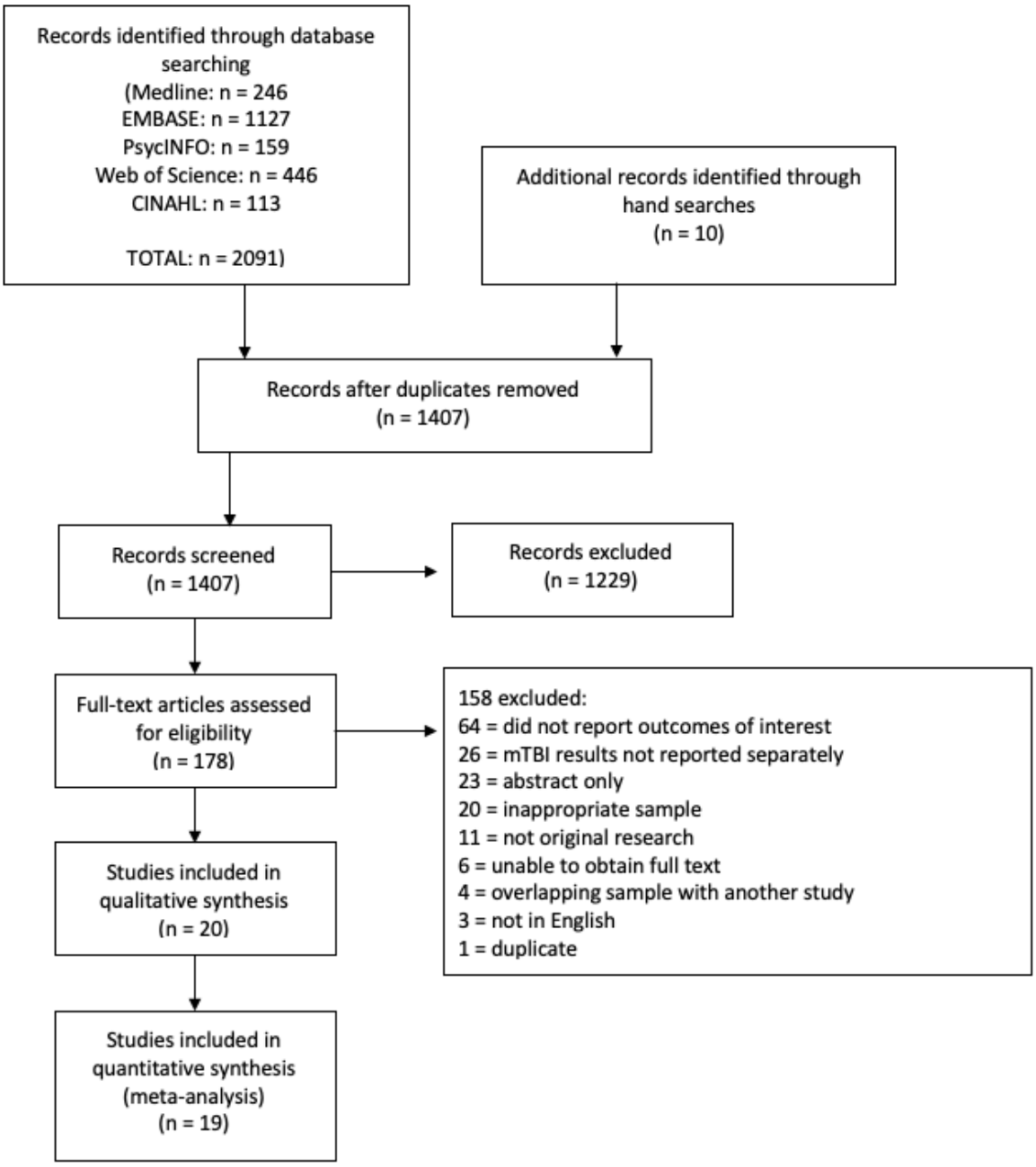
						Global Score = 13.5 (3.8) Sleep Quality = 2.0 (0.7) Sleep Latency = 2.3 (0.9) Sleep Duration = 2.2 (0.9) Sleep Efficiency: 1.8 (1.1) Sleep Disturbances: 1.8 (0.5) Sleep Medication: 1.6 (1.4) Daytime Dysfunction: 1.7 (0.9)	

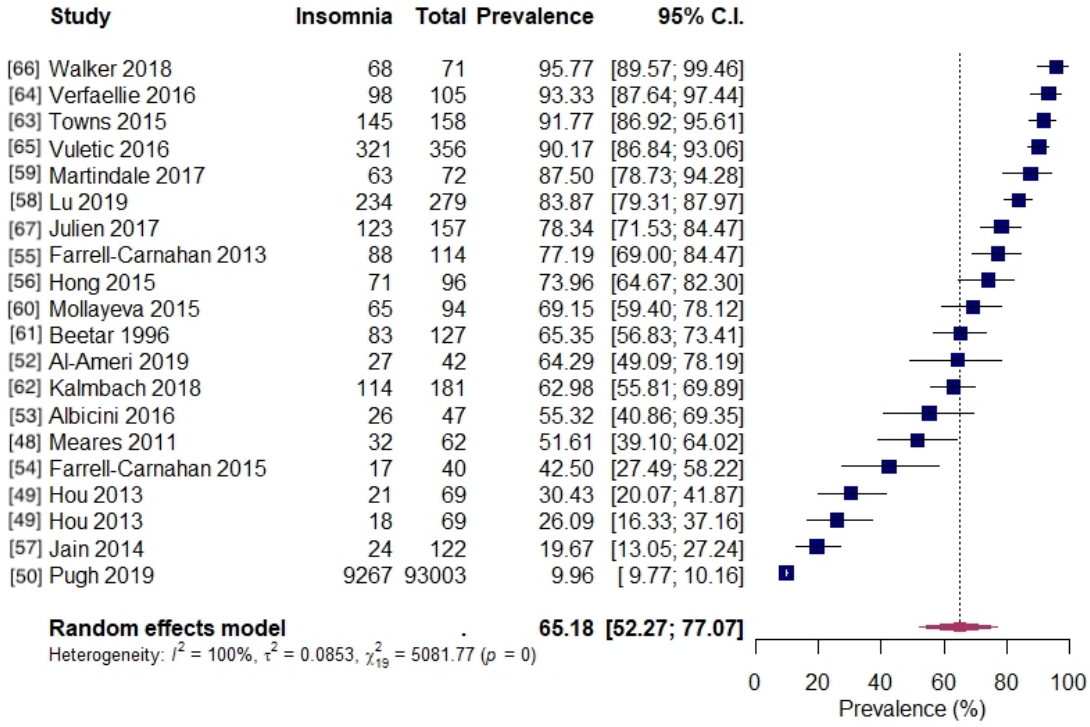
Note: MDD, Major Depressive Disorder; HIT-6, Headache Impact Test – 6th edition; BDI, Beck Depression Inventory; CDC, Centres for Disease Control and Prevention; BSI GSI, Behavioural Symptoms Inventory Global Severity Index; AUDIT-C, Alcohol Use Disorders Identification Test; EuroQOL, European Quality of Life questionnaire; PCL-M, PTSD Checklist—Military Version; PHQ-9, Patient Health Questionnaire; Department of Veterans Affairs/Department of Defence, VA/DoD

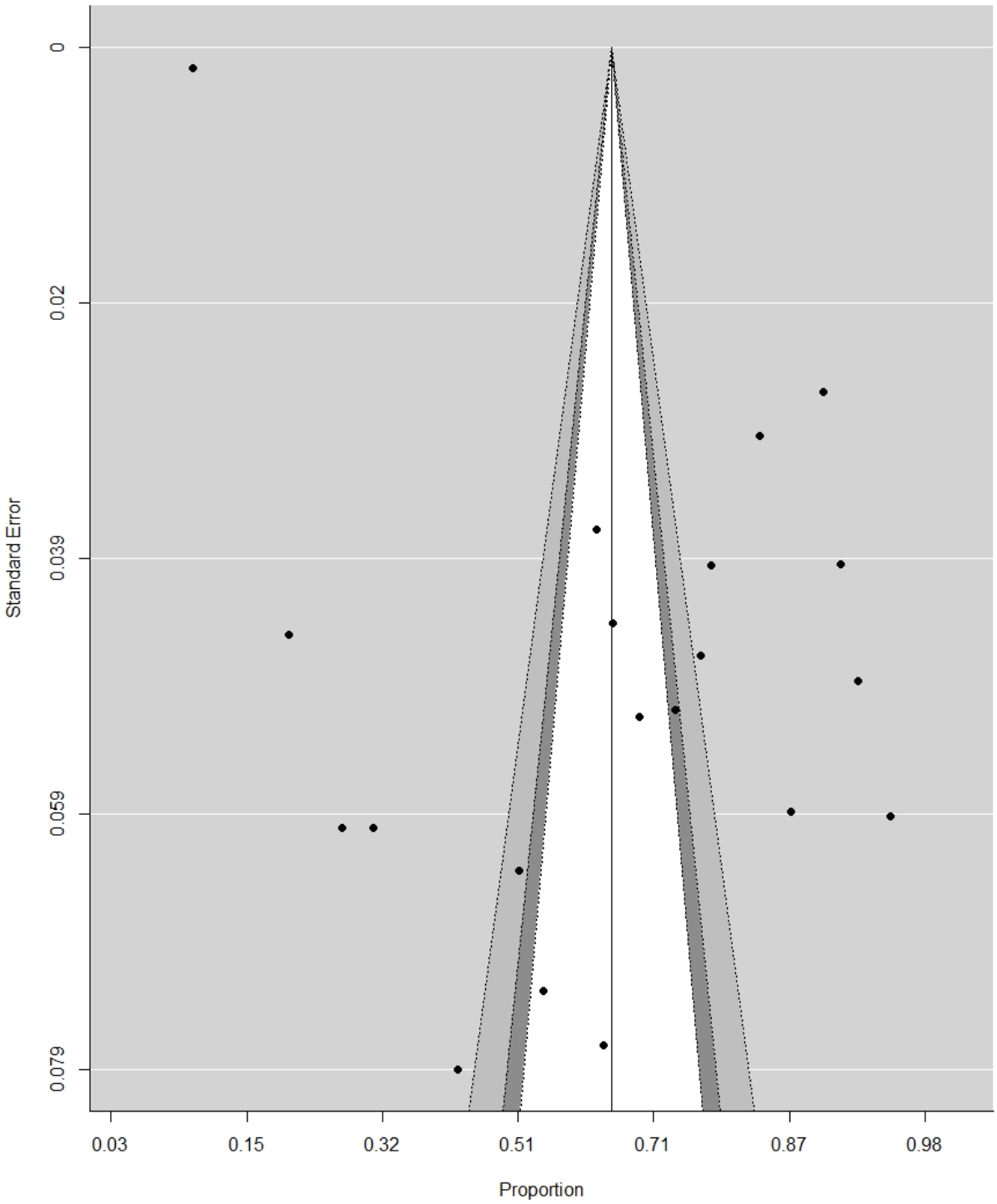
Table 4
Study Quality

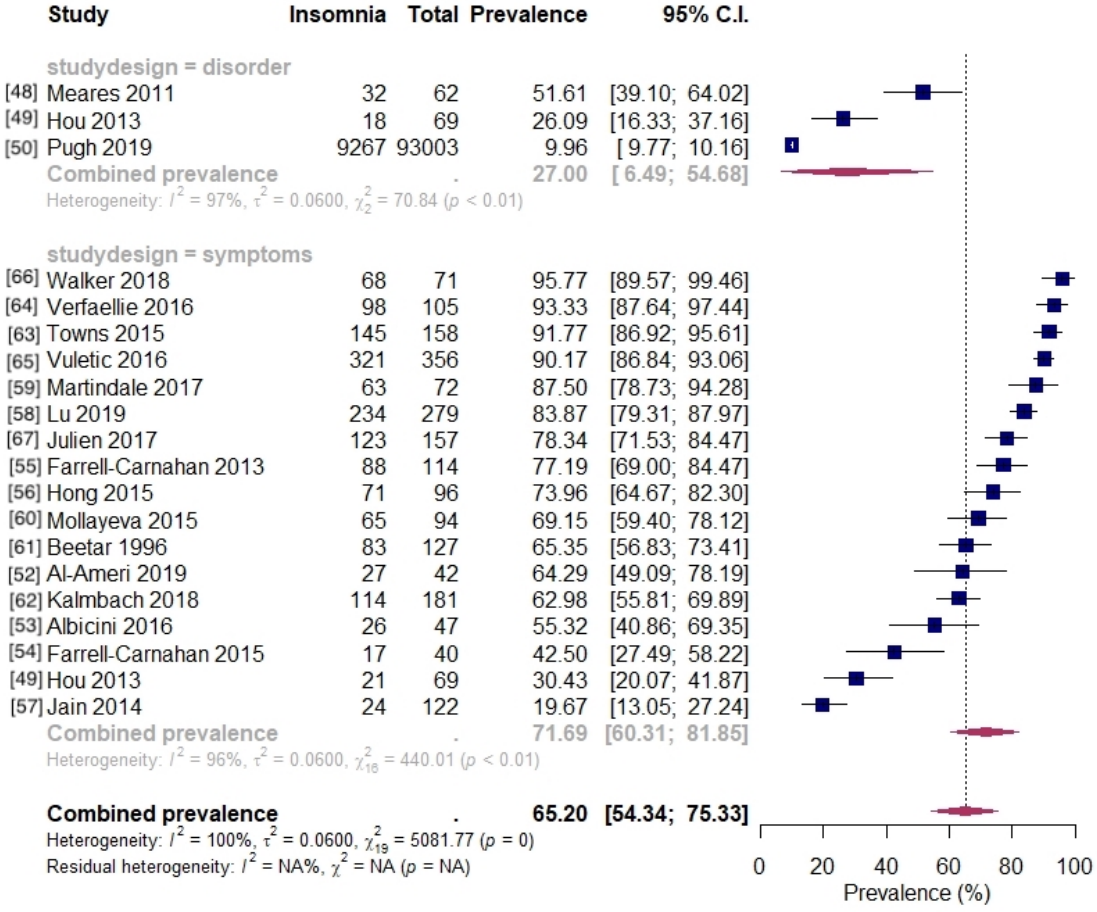
Author	Was the sample frame appropriate to address the target population?	Were study participants recruited in an appropriate way?	Was the sample size adequate?	Were the study subjects and the setting described in detail?	Was the data analysis conducted with sufficient coverage of the identified sample?	Were valid methods used for the identification of insomnia or insomnia symptoms (= the condition)?	Were valid methods used for the identification of mTBI (= the condition)?	Was the condition measured in a standard, reliable way for all participants?	Was there appropriate statistical analysis?	Was the response rate adequate, and if not, was the low response rate managed appropriately?	Overall Score
(Al-Ameri et al., 2019) [52]	Y	U	U	N	Y	Y	Y	U	U	U	13
(Albicini et al., 2016) [53]	U	Y	U	N	Y	Y	N	U	Y	U	12
(Beetar et al., 1996) [61]	Y	Y	Y	Y	Y	N	Y	U	Y	U	16
(Farrell-Carnahan et al., 2015) [54]	Y	Y	U	Y	Y	U	U	Y	Y	U	16
(Farrell-Carnahan et al., 2013) [55]	U	Y	Y	N	Y	Y	Y	Y	Y	Y	17
(Hong et al., 2015) [56]	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	20
(Hou et al., 2013) [49]	Y	Y	N	Y	Y	Y	Y	Y	Y	Y	18
(Jain et al., 2014) [57]	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	20
(Julien et al., 2017) [67]	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	20
(Kalmbach et al., 2018) [62]	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	20
(Lu et al., 2019) [58]	Y	Y	Y	Y	Y	Y	Y	Y	U	Y	19
(Martindale et al., 2017) [59]	Y	Y	Y	U	Y	Y	Y	U	Y	Y	18
(Meares et al., 2011) [48]	Y	Y	U	Y	Y	N	Y	Y	U	Y	16
(Mollayeva et al., 2015) [60]	Y	U	U	Y	Y	Y	Y	Y	Y	U	17
(Mosti et al., 2019) [51]	U	Y	Y	U	Y	Y	N	U	Y	Y	15
(Pugh et al., 2019) [50]	U	Y	Y	Y	Y	Y	Y	Y	Y	Y	19
(Towns et al., 2015) [63]	Y	Y	U	Y	U	Y	N	Y	U	U	14
(Verfaellie et al., 2016) [64]	U	Y	U	U	Y	Y	Y	Y	Y	Y	17
(Vuletic et al., 2016) [65]	U	U	Y	Y	Y	Y	Y	Y	U	U	16
(Walker et al., 2018) [66]	U	Y	U	U	Y	Y	Y	Y	Y	Y	17

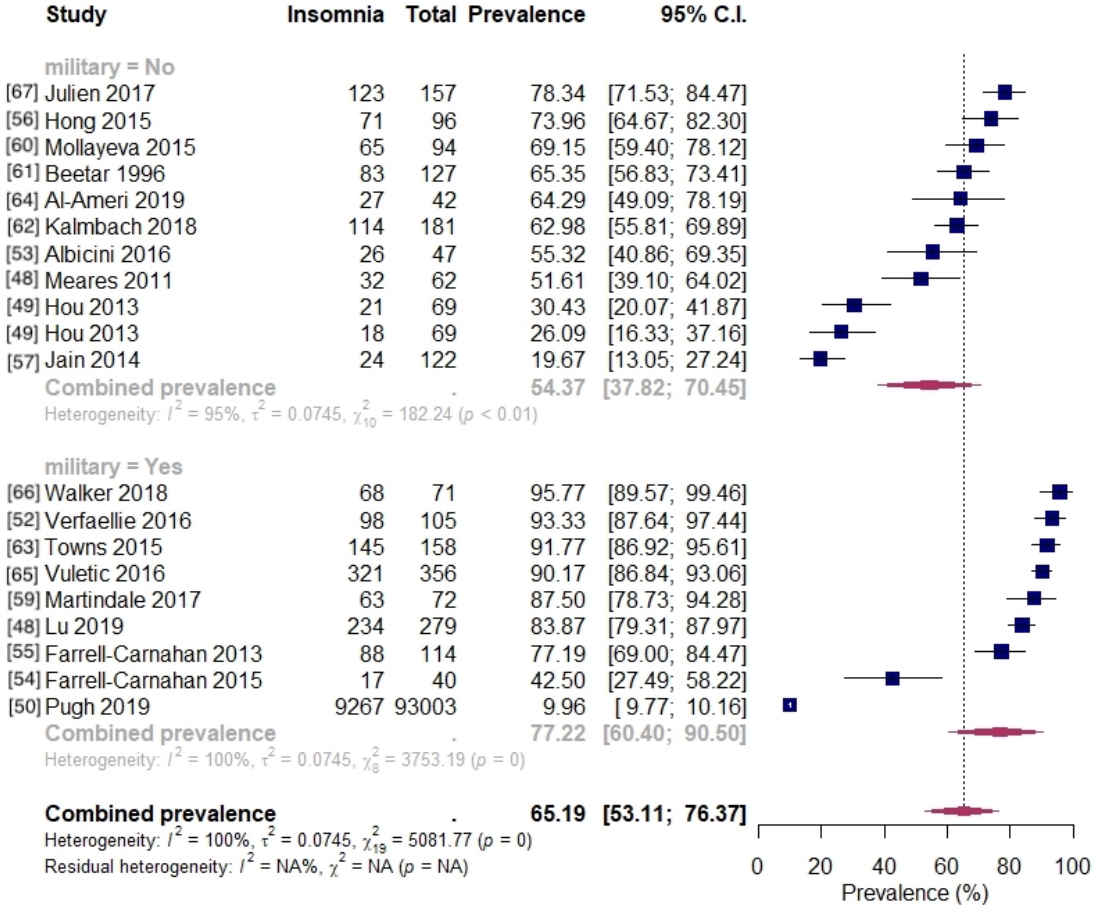
Note: 2 point for yes (Y); 0 points for no (N); 1 point for unsure (U)

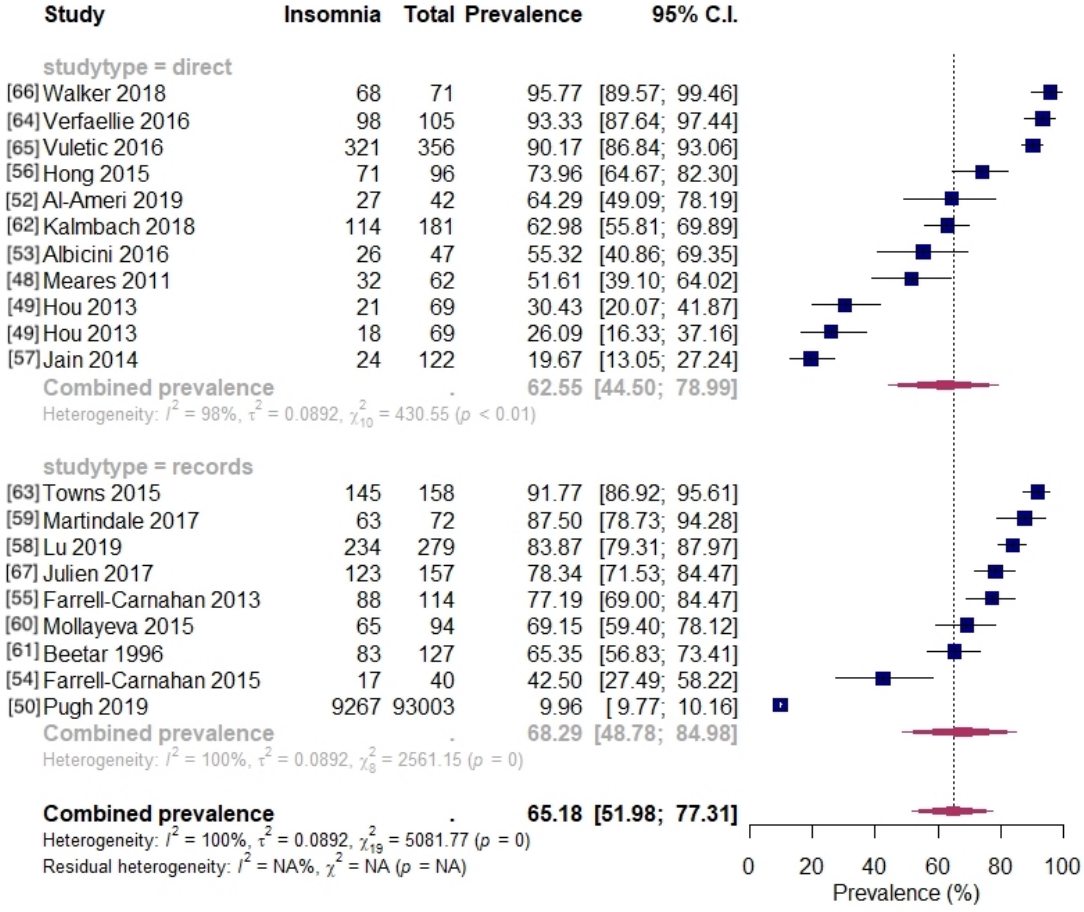

Records identified through database searching
(Medline: n = 246
EMBASE: n = 1127
PsycINFO: n = 159
Web of Science: n = 446
CINAHL: n = 113
TOTAL: n = 2091)
Additional records identified through hand searches
(n = 10)
Records after duplicates removed
(n = 1407)
Records screened
(n = 1407)
Records excluded
(n = 1229)
Full-text articles assessed for eligibility
(n = 178)
158 excluded:
64 = did not report outcomes of interest
26 = mTBI results not reported separately
23 = abstract only
20 = inappropriate sample
11 = not original research
6 = unable to obtain full text
4 = overlapping sample with another study
3 = not in English
1 = duplicate
Studies included in qualitative synthesis
(n = 20)
Studies included in quantitative synthesis
(meta-analysis)
(n = 19)


Study
Insomnia
Total
Prevalence
95% C.I.
[66] Walker 2018 68 71 95.77 [89.57; 99.46]
[64] Verfaellie 2016 98 105 93.33 [87.64; 97.44]
[63] Towns 2015 145 158 91.77 [86.92; 95.61]
[65] Vuletic 2016 321 356 90.17 [86.84; 93.06]
[59] Martindale 2017 63 72 87.50 [78.73; 94.28]
[58] Lu 2019 234 279 83.87 [79.31; 87.97]
[67] Julien 2017 123 157 78.34 [71.53; 84.47]
[55] Farrell-Carnahan 2013 88 114 77.19 [69.00; 84.47]
[56] Hong 2015 71 96 73.96 [64.67; 82.30]
[60] Mollayeva 2015 65 94 69.15 [59.40; 78.12]
[61] Beetar 1996 83 127 65.35 [56.83; 73.41]
[52] Al-Ameri 2019 27 42 64.29 [49.09; 78.19]
[62] Kalmbach 2018 114 181 62.98 [55.81; 69.89]
[53] Albicini 2016 26 47 55.32 [40.86; 69.35]
[48] Meares 2011 32 62 51.61 [39.10; 64.02]
[54] Farrell-Carnahan 2015 17 40 42.50 [27.49; 58.22]
[49] Hou 2013 21 69 30.43 [20.07; 41.87]
[49] Hou 2013 18 69 26.09 [16.33; 37.16]
[57] Jain 2014 24 122 19.67 [13.05; 27.24]
[50] Pugh 2019 9267 93003 9.96 [9.77; 10.16]
Random effects model . 65.18 [52.27; 77.07]
Heterogeneity: I^2 = 100%, τ^2 = 0.0853, χ^2_{19} = 5081.77 (p = 0)
0
20
40
60
80
100
Prevalence (%)


Standard Error
0
0.02
0.039
0.059
0.079
0.03
0.15
0.32
0.51
0.71
0.87
0.98
Proportion


Study
Insomnia
Total
Prevalence
95% C.I.
studydesign = disorder
[48] Meares 2011 32 62 51.61 [39.10; 64.02]
[49] Hou 2013 18 69 26.09 [16.33; 37.16]
[50] Pugh 2019 9267 93003 9.96 [9.77; 10.16]
Combined prevalence . 27.00 [6.49; 54.68]
Heterogeneity: I^2 = 97%, τ^2 = 0.0600, χ^2_2 = 70.84 (p < 0.01)
studydesign = symptoms
[66] Walker 2018 68 71 95.77 [89.57; 99.46]
[64] Verfaellie 2016 98 105 93.33 [87.64; 97.44]
[63] Towns 2015 145 158 91.77 [86.92; 95.61]
[65] Vuletic 2016 321 356 90.17 [86.84; 93.06]
[59] Martindale 2017 63 72 87.50 [78.73; 94.28]
[58] Lu 2019 234 279 83.87 [79.31; 87.97]
[67] Julien 2017 123 157 78.34 [71.53; 84.47]
[55] Farrell-Carnahan 2013 88 114 77.19 [69.00; 84.47]
[56] Hong 2015 71 96 73.96 [64.67; 82.30]
[60] Mollayeva 2015 65 94 69.15 [59.40; 78.12]
[61] Beetar 1996 83 127 65.35 [56.83; 73.41]
[52] Al-Ameri 2019 27 42 64.29 [49.09; 78.19]
[62] Kalmbach 2018 114 181 62.98 [55.81; 69.89]
[53] Albicini 2016 26 47 55.32 [40.86; 69.35]
[54] Farrell-Carnahan 2015 17 40 42.50 [27.49; 58.22]
[49] Hou 2013 21 69 30.43 [20.07; 41.87]
[57] Jain 2014 24 122 19.67 [13.05; 27.24]
Combined prevalence . 71.69 [60.31; 81.85]
Heterogeneity: I^2 = 96%, τ^2 = 0.0600, χ^2_{18} = 440.01 (p < 0.01)
Combined prevalence . 65.20 [54.34; 75.33]
Heterogeneity: I^2 = 100%, τ^2 = 0.0600, χ^2_{19} = 5081.77 (p = 0)
Residual heterogeneity: I^2 = NA%, τ^2 = NA (p = NA)
0
20
40
60
80
100
Prevalence (%)


Study
Insomnia
Total
Prevalence
95% C.I.
military = No
[67] Julien 2017 123 157 78.34 [71.53; 84.47]
[56] Hong 2015 71 96 73.96 [64.67; 82.30]
[60] Mollayeva 2015 65 94 69.15 [59.40; 78.12]
[61] Beetar 1996 83 127 65.35 [56.83; 73.41]
[64] Al-Ameri 2019 27 42 64.29 [49.09; 78.19]
[62] Kalmbach 2018 114 181 62.98 [55.81; 69.89]
[53] Albicini 2016 26 47 55.32 [40.86; 69.35]
[48] Meares 2011 32 62 51.61 [39.10; 64.02]
[49] Hou 2013 21 69 30.43 [20.07; 41.87]
[49] Hou 2013 18 69 26.09 [16.33; 37.16]
[57] Jain 2014 24 122 19.67 [13.05; 27.24]
Combined prevalence . 54.37 [37.82; 70.45]
Heterogeneity: I^2 = 95%, τ^2 = 0.0745, χ^2_{10} = 182.24 (p < 0.01)
military = Yes
[66] Walker 2018 68 71 95.77 [89.57; 99.46]
[52] Verfaellie 2016 98 105 93.33 [87.64; 97.44]
[63] Towns 2015 145 158 91.77 [86.92; 95.61]
[65] Vuletic 2016 321 356 90.17 [86.84; 93.06]
[59] Martindale 2017 63 72 87.50 [78.73; 94.28]
[48] Lu 2019 234 279 83.87 [79.31; 87.97]
[55] Farrell-Carnahan 2013 88 114 77.19 [69.00; 84.47]
[54] Farrell-Carnahan 2015 17 40 42.50 [27.49; 58.22]
[50] Pugh 2019 9267 93003 9.96 [9.77; 10.16]
Combined prevalence . 77.22 [60.40; 90.50]
Heterogeneity: I^2 = 100%, τ^2 = 0.0745, χ^2_8 = 3753.19 (p = 0)
Combined prevalence . 65.19 [53.11; 76.37]
Heterogeneity: I^2 = 100%, τ^2 = 0.0745, χ^2_{19} = 5081.77 (p = 0)
Residual heterogeneity: I^2 = NA%, χ^2 = NA (p = NA)
0
20
40
60
80
100
Prevalence (%)


Study
Insomnia
Total
Prevalence
95% C.I.
studytype = direct
[66] Walker 2018 68 71 95.77 [89.57; 99.46]
[64] Verfaellie 2016 98 105 93.33 [87.64; 97.44]
[65] Vuletic 2016 321 356 90.17 [86.84; 93.06]
[56] Hong 2015 71 96 73.96 [64.67; 82.30]
[52] Al-Ameri 2019 27 42 64.29 [49.09; 78.19]
[62] Kalmbach 2018 114 181 62.98 [55.81; 69.89]
[53] Albicini 2016 26 47 55.32 [40.86; 69.35]
[48] Meares 2011 32 62 51.61 [39.10; 64.02]
[49] Hou 2013 21 69 30.43 [20.07; 41.87]
[49] Hou 2013 18 69 26.09 [16.33; 37.16]
[57] Jain 2014 24 122 19.67 [13.05; 27.24]
Combined prevalence . 62.55 [44.50; 78.99]
Heterogeneity: I^2 = 98%, τ^2 = 0.0892, χ^2_{10} = 430.55 (p < 0.01)
studytype = records
[63] Towns 2015 145 158 91.77 [86.92; 95.61]
[59] Martindale 2017 63 72 87.50 [78.73; 94.28]
[58] Lu 2019 234 279 83.87 [79.31; 87.97]
[67] Julien 2017 123 157 78.34 [71.53; 84.47]
[55] Farrell-Carnahan 2013 88 114 77.19 [69.00; 84.47]
[60] Mollayeva 2015 65 94 69.15 [59.40; 78.12]
[61] Beetar 1996 83 127 65.35 [56.83; 73.41]
[54] Farrell-Carnahan 2015 17 40 42.50 [27.49; 58.22]
[50] Pugh 2019 9267 93003 9.96 [9.77; 10.16]
Combined prevalence . 68.29 [48.78; 84.98]
Heterogeneity: I^2 = 100%, τ^2 = 0.0892, χ^2_8 = 2561.15 (p = 0)
Combined prevalence . 65.18 [51.98; 77.31]
Heterogeneity: I^2 = 100%, τ^2 = 0.0892, χ^2_{19} = 5081.77 (p = 0)
Residual heterogeneity: I^2 = NA%, χ^2 = NA (p = NA)
0
20
40
60
80
100
Prevalence (%)