COGNITIVE BEHAVIOURAL THERAPY FOR INSOMNIA IN CANCER SURVIVORS: AN UPDATED SYSTEMATIC REVIEW AND META-ANALYSIS

by © Lauren Squires

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Abstract

Background: Cancer survivors are at greater risk of insomnia relative to the general population. The evidence for the efficacy of cognitive behavioural therapy for insomnia (CBT-I) amongst cancer survivors continues to grow. The objective of this systematic review and meta-analysis was to provide an up-to-date assessment of the efficacy of CBT-I in cancer survivors and explore its effect on comorbid symptoms.

Method: Searches were conducted of *PubMed*, *EMBase*, *PsycINFO*, clinicaltrials.gov and the World Health Organization's international clinical trials registry for studies published up to August 2020. Studies were included if they assessed the efficacy of CBT-I for improving insomnia severity in adults diagnosed with cancer. Our primary measure of interest was insomnia severity. Secondary outcomes included: actigraphy and diary measured sleep continuity, subjective sleep quality, fatigue, mood, quality of life, and pain severity. The protocol for this systematic review and meta-analysis was pre-registered on PROSPERO (CRD42020169986).

Results: Twenty-two studies including 1461 participants met the eligibility criteria. CBT-I significantly improved insomnia severity (Hedges' $g = 0.78$ and a 7.81-point decrease in mean ISI score), with durable benefits at 3- and 6-month follow-up. CBT-I produced significant small to large effects for the following secondary outcomes: sleep efficiency (sleep diary: $g = 0.71$ and a 12.32% increase), wake after sleep onset (actigraphy: $g = 0.21$ and a 10.61-minute decrease; sleep diary: $g = 0.60$ and a 26.24-minute decrease), total sleep time (actigraphy: $g = 0.30$ and a 23.29-minute decrease; sleep diary: $g = 0.21$ and a 30.12-minute increase), sleep onset latency (actigraphy: $g = 0.29$ and a 3.40-minute decrease; sleep diary: $g = 0.65$ and a 20.58-minute decrease), sleep quality ($g = 0.70$ and a 4.62-point decrease in mean PSQI score), anxiety ($g = 0.28$), depression ($g = 0.31$), fatigue ($g = 0.35$), and overall quality of life ($g = 0.31$). There were

insufficient data to analyse the effect of CBT-I on pain outcomes. Subgroup analyses revealed no significant difference between in-person and self-help CBT-I, and effects were stronger for trials that used non-active comparison groups.

Conclusion: Our results demonstrate the robust efficacy and durability of CBT-I for the treatment of insomnia in cancer survivors and supports that CBT-I can produce concomitant benefits on other symptoms. Implementation efforts are needed to ensure that people with cancer have access to CBT-I as the recommended first-line treatment for insomnia.

Keywords: cancer, insomnia, cognitive behavioural therapy for insomnia, meta-analysis

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Insomnia in the General Population

Insomnia is a sleep-wake disorder characterized by dissatisfaction with sleep quality or quantity that involves difficulties falling and/or staying asleep three or more times per week for at least 3 months, despite adequate opportunity for sleep (American Psychiatric Association, 2013). As of 2015, insomnia affected approximately 24% of Canadians age 18 and older (Chaput et al., 2018). In addition to sleep difficulties, those diagnosed with insomnia disorder are also 2.4 times more likely to report various chronic health problems, such as arthritis, chronic pain, ulcers, and hypertension (Daley, Morin, LeBlanc, Grégoire, Savard, et al., 2009). Insomnia is also associated with higher work absenteeism and reduced productivity, which can amount to a high economic burden and impact overall health and wellbeing, with annual costs (direct and indirect) amounting to $5,010 for those with insomnia disorder compared to $421 for good sleepers age 18-83 as of 2009 (Daley, Morin, LeBlanc, Grégoire, & Savard, 2009). Approximately 76% of these annual costs are attributed to accumulated work absenteeism or reduced productivity (Daley, Morin, LeBlanc, Grégoire, & Savard, 2009). It is also important to note that a three-year longitudinal study of insomnia prevalence by Morin and colleagues found that, of the participants with insomnia disorder at baseline, approximately 41% still presented with insomnia disorder after three years (Morin et al., 2009), emphasizing the fact that insomnia disorder can become a chronic condition for if not treated.

Insomnia in Cancer Survivors

According to the Canadian Cancer Statistics Advisory Committee, approximately 1 in 2 Canadians will be diagnosed with cancer in their lifetime (Canadian Cancer Statistics Advisory

Committee, 2019), with 225,800 new cases of cancer estimated for 2020 (Brenner et al., 2020). From 2012 to 2014, the population-based five- and ten-year survival rates for all cancers combined increased to 63% and 54%, respectively (Canadian Cancer Statistics Advisory Committee, 2019). Because overall cancer survivorship has increased in recent years, it is becoming more apparent that the challenges of those diagnosed with cancer do not end when treatment ends. Instead, dealing with cancer and its effects extends into the survivorship period, which also comes with unique challenges. One such challenge that may arise at the point of diagnosis, during treatment, and beyond is insomnia (Savard & Morin, 2001).

Insomnia has the potential to occur before cancer treatment begins and persist despite improvements in other parameters such as tumour presence, anxiety, and distress (Schieber et al., 2019). Of notable interest are findings from Savard and colleagues (Savard, Ivers, et al., 2011), in which approximately 60% of participants diagnosed with cancer experienced clinically relevant symptoms of insomnia or met criteria for insomnia disorder prior to receiving surgery. This number decreased to approximately 36% at the end of the 18-month study period, which is still greater than that of the general population. There are several potential reasons for this, including the emotional consequences of the initial cancer diagnosis, the physical impact of invasive medical treatments and their side effects, and the functional disruption that the diagnosis and treatment can have on daily routines and habits (Clark et al., 2004; Palesh et al., 2010). Evidence also supports that cancer survivors continue to experience insomnia symptoms after their cancer treatment has finished (Schieber et al., 2019).

Impact of Insomnia on Those Diagnosed with Cancer

The impact and consequences of insomnia in cancer survivors can be extensive. Greater insomnia severity in cancer survivors is associated with an increased risk of developing

infections (Ruel et al., 2020; Ruel et al., 2015) and a worsening of cancer-related symptoms such as cognitive impairments and mood disturbances (Caplette-Gingras et al., 2013; Fleming et al., 2010; Liou et al., 2019). These factors can then reduce the quality of life of those diagnosed with cancer shortly after diagnosis. For example, a longitudinal study of ovarian cancer survivors by Ross and colleagues demonstrated that those with insomnia reported significantly lower quality of life at three and six months after diagnosis compared to those without insomnia (Ross et al., 2020). They found this association to be strongest for physical and functional well-being, meaning that insomnia had a large impact on participants' perception of the severity of physical treatment side effects (e.g., nausea, lack of energy, pain, etc.) and aspects of daily functioning (e.g., being able to work and do things they enjoy) (Cella et al., 1993; Ross et al., 2020). Some cancer survivors have also reported that they were more overwhelmed by their insomnia and resulting issues than they were from cancer treatment itself (Fleming et al., 2010). Even after the completion of treatment, survivors report that they continue to experience cognitive disturbances, inability to share a bed with their partner, and worry as a consequence of their insomnia (Reynolds-Cowie & Fleming, 2020; Savard, Ivers, et al., 2011; Schieber et al., 2019).

Insomnia can exist independently, but its severity is often influenced and worsened by other comorbid conditions, (e.g., anxiety, depression, fatigue, pain, etc.) (Bean et al., 2021; Garland et al., 2018; Schieber et al., 2019). Cancer survivors reporting insomnia symptoms are six times more likely to report symptoms of depression and five times more likely to report fatigue symptoms than those without insomnia symptoms (Haque et al., 2020). In a study of 413 women diagnosed with breast cancer, approximately half of the variance in Insomnia Severity Index score was explained by anxiety, depression, fatigue, and pain, while the other half of the variance was explained by insomnia alone (Gehrman et al., 2017). Yet another longitudinal study

assessing the one-year prevalence rates of cancer-related insomnia found an association between the presence of insomnia, depression, anxiety, and fatigue at baseline and the presence of insomnia one year later in women (Schieber et al., 2019). The same study also found that insomnia and depression was correlated with insomnia after one year in men (Schieber et al., 2019). The symptom burden of insomnia in addition to its comorbidities have the potential to persist into survivorship, which can further negatively impact the quality of life of cancer survivors (Wu & Harden, 2015).

Behavioural and Cognitive Theories of Insomnia Development and Maintenance

The Behavioural 3P Model of Insomnia

There are many factors that contribute to the development and maintenance of insomnia that generally fall under predisposing, precipitating, and perpetuating factors (or '3P') as defined by Spielman and colleagues (Spielman et al., 1987).

Predisposing Factors. Predisposing factors for insomnia generally increase vulnerability to the development of insomnia. A common predisposing factor is a family history of insomnia (LeBlanc et al., 2009) or other mental health conditions (e.g., anxiety and depression) (Garland et al., 2018; Savard & Morin, 2001).

Female sex is another critical factor that has the potential to impact sleep, in part due to hormone fluctuations (i.e., during menstruation, menopause, etc.) (Baker et al., 2015; Pusalavidyasagar et al., 2018) and societal expectations and demands (Sidani et al., 2019). In multiple studies, women diagnosed with breast and gynecologic cancers have been observed to experience higher rates of insomnia compared to those diagnosed with other types of cancers (Palesh et al., 2010; Savard et al., 2009). Similarly, those who were pre-menopausal prior to diagnosis and treatment may experience medical menopause as a result of treatments for breast

or gynecologic cancers (Hall et al., 2014). Experiencing symptoms of menopause (e.g., hot flashes) in addition to treatment side effects may worsen insomnia symptoms in women with cancer, with increased hot flash severity being related to increased insomnia symptom severity (Savard, Savard, et al., 2011).

Although older age (i.e., 60 years of age and older) is associated with problems staying asleep in the general population given that total sleep time (TST) and sleep efficiency (SE) have been found to decrease with age (Ohayon et al., 2004), several cancer-specific studies have found that younger age (i.e., less than 50 years of age) is associated with a greater risk of developing insomnia and other sleep disturbances among cancer patients (Hall et al., 2014; Palesh et al., 2010; Price et al., 2009; Savard, Simard, Hervouet, et al., 2005). This may be due to the fact that young adults have to negotiate cancer's impacts on education and careers (Panjwani et al., 2019; Raque-Bogdan et al., 2015), and may not be as financially stable (Mahon et al., 2021), which can contribute to cancer-related uncertainty (Panjwani et al., 2019). Even after treatment ends, this uncertainty is related to higher levels of reported sleep disturbances, fatigue, and mood disturbances among younger cancer survivors (Hall et al., 2014).

Precipitating Factors. Factors that precipitate insomnia development are acute events that trigger initial onset. Events related to health, work, or school are common precipitating factors of insomnia. These events can be positive or negative, but people often perceive the events precipitating their insomnia as negative (Bastien et al., 2004). The impact of precipitating factors on insomnia severity is generally highest at the onset of insomnia symptoms and decrease with time (Spielman et al., 1987).

A diagnosis of cancer and the onset of treatment may be the primary precipitator of insomnia in cancer survivors, with many cancer survivors attributing their insomnia to their

thoughts and emotions, both general and sleep-related (Shaffer et al., 2020). A qualitative study of insomnia development and maintenance in cancer survivors by Garland and colleagues (Garland et al., 2018) found that some participants saw their cancer diagnosis and treatment and its emotional impacts as the main predisposing factor for their insomnia. Indeed, the above-mentioned longitudinal study by Savard and colleagues (Savard, Ivers, et al., 2011) found that approximately 60% of their 962 participants presented with clinically-relevant insomnia symptoms or insomnia disorder at the perioperative phase (i.e., around the time when they received surgical treatment). It is possible that the stress of initial diagnosis and treatment onset contributed to this prevalence rate.

Insomnia onset could also be triggered by various aspects of cancer treatment and prevention (e.g., chemotherapy, surgeries, etc.) (Garland et al., 2018; Savard et al., 2015). Cancer surgeries can be a notable precipitating factor (Savard et al., 2009), possibly due to the experience of pain after or anxiety before cancer surgery (Sun et al., 2020). Chemotherapy, radiation, and hormonal treatments can also contribute to the development of insomnia due to their physical side effects (e.g., nausea, hot flashes, pain, etc.) (Ross et al., 2020; Savard et al., 2015). Aside from the medical components of treatment, some may find it difficult to adjust to an empty schedule and boredom resulting from the discontinuation of work or school due to cancer treatment (Fleming et al., 2010). Finally, cognitions surrounding sleep and its role in cancer treatment and remission may contribute to the development of insomnia. These thoughts include worries about delayed recovery in the presence of insomnia, or believing that sleep has to be of high quality in order for cancer to move into remission (Savard & Morin, 2001).

Perpetuating Factors. As insomnia persists, the role of perpetuating factors become more prominent and the impact of the precipitating event lessens (Perlis, 2017; Spielman et al.,

1987). Perpetuating factors are generally behaviors that an individual uses to compensate for their lack of good sleep that actually promote the maintenance of insomnia (Perlis, 2017). This includes such things as: napping or spending extra time in bed, increasing caffeine consumption to induce wakefulness during the daytime, or increasing alcohol and hypnotic use during the nighttime to induce sleepiness (Spielman et al., 1987).

A person's cognitions can also maintain insomnia by increasing arousal, and making it more difficult to fall asleep (Norell-Clarke et al., 2014). Worrying, dysfunctional beliefs about sleep, monitoring (e.g., watching the clock), and safety behaviours (e.g., going to bed earlier than usual out of fear of being tired the next day) are associated with insomnia symptoms (Norell-Clarke et al., 2014). The presence of worrying and dysfunctional beliefs about sleep are also related to persistent insomnia over an extended amount of time (Spielman et al., 1987).

The factors that perpetuate insomnia among those diagnosed with cancer are similar to those observed among the general population; however, they may be tied (either directly or indirectly) to their cancer diagnosis and treatment. Chemotherapy among those diagnosed with cancer can contribute to experiences of fatigue, which lends itself to survivors using compensatory measures, such as spending more time in bed to manage the fatigue they are experiencing (Garland et al., 2018). In addition, many take prescription or over-the-counter sleep aids during and after treatment (Moore et al., 2011; Ross et al., 2020; Slade et al., 2020), which then makes it more challenging to return to a normal sleeping pattern once they are discontinued or tolerance occurs (Garland et al., 2018).

The Cognitive Model of Insomnia

The cognitive model developed by Harvey, explains insomnia development and maintenance through a process involving negative sleep-related cognitions and subsequent

compensatory measures, which results in arousal (Harvey, 2002). This arousal then contributes to selectively paying attention to sleep and sleep-related cues, and distorted beliefs and attitudes about sleep. Taken together, these mechanisms end up contributing to actual deficits in sleep during the nighttime and decreased functionality during the daytime (Harvey, 2002). Simplified, insomnia is maintained through a self-perpetuating cycle in which arousal is experienced because of worries and negative thoughts about sleep, which then results in hyperfocusing on the inability to sleep (e.g., by constantly checking the clock). This then contributes to negative perceptions about sleep quality, which can perpetuate negative thoughts and worries about sleep that result in arousal. These cognitive processes can also contribute to safety behaviours, such as going to bed earlier than normal to compensate for a lack of sleep (Harvey, 2002; Norell-Clarke et al., 2014). In cancer survivors specifically these may look like napping during the day to or spending time in bed awake to compensate for fatigue due to cancer treatments.

Cognitive Behavioural Therapy for Insomnia (CBT-I)

Considering theories of insomnia development and maintenance by both Spielman (1987) and Harvey (2002), it is important to address cancer survivors' thoughts and feelings (i.e., cognitive factors) in addition to the behaviours they exhibit that contribute to insomnia development and maintenance. The leading non-pharmacological insomnia treatment is cognitive behavioural therapy for insomnia (CBT-I), the use of which is strongly recommended by the American Academy of Sleep Medicine (Edinger et al., 2021a). CBT-I is a multicomponent intervention that addresses patients' dysfunctional beliefs and attitudes surrounding their sleep along with behaviours that are not conducive to quality sleep (Garland, Johnson, et al., 2014), and gives patients the tools to prevent insomnia reoccurrence (Perlis, 2017). A recent systematic review and meta-analysis that was not specific to cancer found that CBT-I produces clinically

significant improvements in insomnia severity, insomnia remission rate, patients' beliefs and attitudes about sleep, daytime fatigue, and total wake time (Edinger et al., 2021b) when compared to control treatments. It may also provide benefits that are more durable and reduce the need for sleeping medications (Edinger et al., 2021a). In order to address and improve patients' behaviours and cognitions surrounding sleep, the following main components are used: stimulus control (i.e., limiting behaviours in the bedroom that are not conducive with sleep), sleep restriction (i.e., restricting time spent in bed to match current sleep ability), cognitive restructuring (i.e., targeting erroneous beliefs about sleep), relaxation training when indicated, and psychoeducation on sleep hygiene (Edinger et al., 2021a; Johnson et al., 2016).

Stimulus Control

Spending time awake in bed or engaging in arousing activities (e.g., using backlit devices, doing work/homework, worrying, or watching television (Bootzin & Perlis, 2011; Perlis, 2017)) in the bedroom can allow for the formation of associations that promote wakefulness. Stimulus control is a process of reassociating the bed with successful sleep experiences. For stimulus control to be effective, the patient is asked to only engage in sleep and sex in the bedroom and to engage in all other activities elsewhere in the home. The patient is also instructed to not get into bed until they begin to feel sleepy and, if they are not asleep after approximately 15 minutes of trying, to get out of bed and go to another room to engage in a relaxing activity and to return to the bed only when they feel sleepy again. This way, the brain will be prevented from associating the bedroom with wakefulness, and will further associate the bedroom with sleep (Perlis, 2005; Perlis, 2017).

Sleep Restriction

The sleep restriction component of CBT-I involves matching the patient's current sleep diary measured total sleep time (TST) with their time in bed (TIB) in order to increase their sleep drive and sleep efficiency (i.e., the ratio of total sleep time to time spent in bed) (Perlis, 2005; Perlis, 2017). The individual's TST at the start of treatment may be less than their individual sleep need or desired TST. To increase the patient's sleep efficiency, the CBT-I therapist initially compresses their TIB by giving them a later bedtime, which encourages them to fall asleep faster upon getting into bed. Over time, the patient's sleep efficiency will improve as the discrepancy between their TST and TIB closes and they become less accustomed to spending long periods of time in bed awake. Once an ideal sleep efficiency is achieved (i.e., 85% or greater), the CBT-I therapist begins a process called sleep titration (Kyle et al., 2015), during which TIB is increased by 15-30 minutes until they reach their sleep requirement (Kyle et al., 2015). Sleep restriction ultimately solidifies the association between the patient's bedroom and sleep while helping to deepen their sleep and increase its quality (Perlis, 2005).

While sleep restriction is an essential component of CBT-I, it also presents potential drawbacks such as increases in daytime sleepiness, fatigue, and psychomotor difficulties, particularly when treatment is first introduced and the patient's TST is shortened (Edinger et al., 2021a, 2021b). While issues such as these may cause impairments at the beginning of treatment, their impact is small for the majority of patients and they generally subside as treatment progresses (Edinger et al., 2021a, 2021b).

Cognitive Restructuring

In addition to engaging in problem behaviours around sleep, some patients may hold erroneous beliefs about sleep or experience worrying thoughts surrounding their sleep that can contribute to the maintenance of their insomnia. For example, a patient may believe that they

must get eight hours of sleep every night to be a good sleeper and feel well-rested the next morning. Or, while trying unsuccessfully to sleep, they may worry that their functioning the next day will be diminished due to their lack of sleep (Harvey et al., 2007; Norell-Clarke et al., 2014). The purpose of the cognitive restructuring component is to challenge these erroneous thoughts and beliefs that the patient may hold about their sleep (Harvey et al., 2007). In doing so, the patient will not only be more inclined to relax when they go to bed, but they may also stop putting pressure on themselves to sleep for a certain amount of time. In essence, this component aims to reduce the patient's cognitive arousal in the bedroom by explicitly targeting the dysfunctional beliefs and attitudes that help to create and maintain their worries. This component may also include some relaxation training (e.g., deep breathing exercises, progressive muscle relaxation, etc.), to make it so that the patient can relax while in bed and trying to fall asleep. However, the inclusion of relaxation training is dependent upon individual CBT-I therapists and the type of techniques that would benefit individual patients (Perlis, 2005).

Sleep Hygiene

Sleep hygiene involves educating the patient on ways to maintain healthy sleep habits, which can prevent a worsening of insomnia symptoms and increase total sleep time (Perlis, 2005). This component is implemented by outlining common ways to improve sleep hygiene (e.g., reducing alcohol, caffeine, and nicotine consumption, exercising regularly, only sleeping as much as you need, etc.) and providing further guidance on how to employ the listed strategies. Psychoeducation on sleep hygiene gives patients the tools to modify their sleep habits and maintain the changes they have made during therapy.

Efficacy of CBT-I for Cancer Survivors

Cognitive behavioural therapy for insomnia (CBT-I) has been consistently efficacious in improving insomnia symptom severity in those diagnosed with cancer (Garland, Johnson, et al., 2014; Johnson et al., 2016). A previous systematic review and meta-analysis by Johnson and colleagues found that, compared to other treatments and wait-list controls, cancer survivors who received CBT-I reported improved insomnia symptom severity, sleep efficiency (SE), sleep onset latency (SOL), and wake after sleep onset (WASO) (Johnson et al., 2016). The mode of delivery of CBT-I for cancer survivors has also varied, with evidence that it can be delivered effectively via the internet (Zachariae et al., 2018; Zhou & Recklitis, 2020), videos (Savard et al., 2021), telemedicine (McCarthy et al., 2018), to groups of individuals (Garland, Carlson, et al., 2014), and via self-help manuals (Savard, Villa, et al., 2011). However, further research is needed to assess whether self-help treatments are as effective or durable when compared to CBT-I conducted with a trained therapist.

While CBT-I is primarily used to treat insomnia and improve sleep quality in cancer survivors, it has also been shown to reduce the burden of other conditions in a symptom cluster with insomnia. In addition to improving insomnia, CBT-I reduces depression (Peoples et al., 2019) and cancer-related fatigue (Espie et al., 2008; Fleming et al., 2014; Heckler et al., 2016; Savard et al., 2014), and increases overall quality of life in cancer survivors (Peoples et al., 2017). Preliminary research suggests that CBT-I may also improve perceived cognitive impairment (Quesnel et al., 2003), making it a potent intervention for many co-occurring symptoms.

Importance of the Present Review

It is necessary to conduct an updated systematic review and meta-analysis for several reasons. First, there have been a number of additional randomized-controlled trials (RCTs)

published after the previous meta-analysis by Johnson and colleagues (Johnson et al., 2016) whose findings must be assessed collectively. Second, the primary outcome of the previous review was sleep efficiency (SE) and not insomnia severity, which we consider to be the more relevant outcome of CBT-I due to its subjective nature compared to SE. Assessing self-reported insomnia severity using a measure such as the Insomnia Severity Index (Morin, 1993) captures issues that are directly related to the diagnostic criteria for insomnia disorder present in the DSM-5, such as difficulty falling or staying asleep, dissatisfaction with sleep quality, and impairment in different areas of functioning (American Psychiatric Association, 2013). While an SE of 85% or greater is considered ideal, it is possible for someone to present with an ideal SE value while experiencing clinically relevant insomnia. For example, if someone got out of bed when having difficulty falling asleep as opposed to lying in bed awake, their time in bed (TIB) value would not reflect their trouble sleeping and the time they spent awake out of bed and would therefore not have as great of an impact on their SE. Third, there has been an increased focus within the literature on self-help and virtual CBT-I interventions which could not be examined by Johnson and colleagues (Johnson et al., 2016). Finally, to our knowledge, no meta-analyses have assessed the efficacy of CBT-I for the treatment of factors that are often comorbid with insomnia in cancer survivors, such as poor sleep quality, fatigue, anxiety, depression, overall quality of life, and pain severity.

Objective

The primary objective of our systematic review and meta-analysis is to quantify the efficacy and durability of CBT-I compared to other pharmacological and non-pharmacological treatments for improving insomnia severity and symptoms of comorbid conditions in cancer survivors. Our secondary aims were to quantify the efficacy and durability of CBT-I on insomnia

and secondary outcomes by mode of treatment (face-to-face vs. not) and comparison group (active vs. not).

Methods

Protocol and Registration

The protocol for this systematic review and meta-analysis was pre-registered on PROSPERO (CRD42020169986) and adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Moher et al., 2009) outlined in Appendix 1.

Eligibility Criteria

Study Design

Studies using a randomized controlled trial (RCT) were eligible to be included in the present systematic review and meta-analysis due to their high internal validity and ability to determine causality (Johnson et al., 2016).

Participants

Studies were included if their samples consisted of adults (18 years of age or older) who had been diagnosed with any type of cancer at any stage who also presented with clinically-relevant levels of insomnia as determined by a valid assessment measure (e.g., the Insomnia Severity Index (Morin, 1993); the Diagnostic and Statistical Manual of Mental Disorders (American Psychiatric Association, 2013)).

Interventions

Studies were included if they assessed the efficacy of CBT-I as a non-pharmacological treatment for insomnia. In order to be considered CBT-I, the intervention had to have included sleep restriction, stimulus control, and cognitive restructuring components (Johnson et al., 2016).

Comparisons

For the purpose of the present review, we compared CBT-I to any other active (e.g., pharmacotherapy, other psychotherapies, mindfulness-based therapies, exercise, usual care) or non-active treatments (e.g., wait-list, placebo). Given that the goal of the present review is to compare CBT-I to non-CBT treatments, studies were excluded if they included other CBT or CBT-I treatments as their only comparison/control intervention.

Outcomes

Studies were eligible if they included at least one empirically validated measure of insomnia severity (e.g., the ISI). Insomnia severity was selected as our primary outcome because insomnia by definition is a subjective appraisal of sleep. Secondary outcomes included sleep parameters (i.e., SOL, WASO, SE, and TST) measured by both wrist actigraphy and sleep diary, subjective sleep quality, fatigue, depression and anxiety symptoms, overall quality of life, and pain severity. We also examined the long-term treatment durability of these outcomes at follow-up time points.

Search Methods

The following electronic databases were searched, with the search limited to articles published in English up to and including August 2020: *PubMed*, *EMBase*, *PsycINFO*, and clinicaltrials.gov and the World Health Organization's (WHO) international clinical trials registry platform via the Cochrane central register of randomized controlled trials (CENTRAL) database. *ProQuest* was also searched for grey literature. To enhance our search strategy, we also scanned the references of each study that met our inclusion criteria. The search strategy used for *PubMed* is as follows:

((“Cognitive Therapy” [Mesh]) OR (cognitive or behavio* or therapy)) AND ((“Sleep Initiation and Maintenance Disorders”

[Mesh]) OR (insomnia or sleep or sleep disturbance [Title/Abstract])) AND (("Neoplasms" [Mesh]) OR (cancer or carcinoma or neoplasm*[Title/Abstract])). The *PubMed* RCT filter was then applied to the search results.

Data Collection and Analysis

Study Selection

Two reviewers independently screened the titles and abstracts of the studies exported to Rayyan (Ouzzani et al., 2016) against inclusion criteria. Those that met inclusion criteria proceeded to full text review by the same reviewers. Disagreements during each stage of the selection process were resolved via consensus or arbitration by the primary supervisor.

Data Extraction

A standardized data extraction form was used to extract the following from included studies: participant sample characteristics (i.e., sample size, mean age, standard deviation, cancer type and stage); intervention characteristics (i.e., intervention format, intervention intensity); comparison treatment characteristics (i.e., type of comparison/control group used); and outcomes (i.e., primary and secondary outcome measures used in each trial). A separate form was used to extract statistical data as they pertained to pre- and post-treatment and follow-up means and standard deviations of insomnia severity and secondary outcomes. Study authors were contacted via email when data were missing.

Data from studies included in the systematic review and meta-analysis by Johnson and colleagues (Johnson et al., 2016) were obtained from the review authors. Secondary outcome data relevant to the current meta-analysis that were not included in their review were extracted from the articles or obtained via e-mails sent to the authors of the original studies.

Risk of Bias Assessment and Quality Assessment

Risk of bias and quality assessments were performed using a scale initially created for assessing the quality of psychological trials for pain by Yates and colleagues (Yates et al., 2005). The overall score ranges from 0-35 and consists of two subscales. The treatment quality subscale ranges from 0-9 and assesses treatment content, duration of treatment, manualisation, therapist training and patient engagement. The quality of study design and methods subscale ranges from 0-26 and assesses inclusion and exclusion criteria, attrition, sample characteristics, randomization, justification of outcomes, follow-up length, appropriateness of statistical analyses, and choice of control group (Yates et al., 2005). Our assessments were carried out independently by two raters using a standardized form. Disagreements were resolved via consensus or third-party arbitration by the primary supervisor.

Summary Measures

The efficacy of CBT-I as compared to other pharmacological, non-pharmacological, wait list control, or treatment as usual interventions was assessed using Comprehensive Meta-Analysis (CMA) software. CBT-I was compared to control interventions using Hedges' *g* (Hedges, 1981), which was calculated using mean pre- and post-treatment scores and standard deviations within CMA. To calculate the standardized mean difference needed to calculate Hedges' *g*, the following equation was used within CMA: Standard difference in means = Raw mean difference/Pooled SD for post-treatment scores. Raw means and standard deviations were used. In cases where standard error values or 95% confidence intervals were reported in place of standard deviations, the following calculations were used to calculate standard deviation: $SD = SE*\sqrt{N}$ when given standard error, and $SD = \sqrt{N}*[(\text{upper limit} - \text{lower limit})/(2*t_{critical})]$ when given 95% confidence intervals. When standard deviations were not provided and could not be calculated, study authors were contacted via e-mail.

Assessment of Heterogeneity

Heterogeneity was assessed using both I^2 and prediction intervals. With respect to the former, I^2 represents the proportion of overall variability attributable to variation in the magnitude of the "true" effect between studies as opposed to sampling error, for example. This measure is common but has been criticized in recent years because it is difficult to interpret and not intrinsically meaningful (Borenstein et al., 2017). I^2 was still calculated, however, to provide a marker to indicate when to conduct meta-regression analyses to assess potential sources of statistical heterogeneity. Confidence intervals for I^2 were calculated using the test-based method outlined by Higgins and Thompson (Higgins & Thompson, 2002). Prediction intervals (PI's) are also reported characterize the degree that the underlying effect differs across studies and provide a measure of the range of effects expected in the event that one decided to conduct a new, well-powered study with methods similar to those included in the model (Borenstein et al., 2017).

Additional Analyses

To assess the potential effects of type of control group (active vs. non-active) and type of CBT-I intervention (in-person vs. self-help CBT-I), subgroup analyses were planned a priori. In addition to these analyses, meta-regression analyses were performed for outcomes with significant statistical heterogeneity as determined by an I^2 value greater than 50%. When meta-regressions were performed, the planned moderators were mean participant age, participant sex, and overall treatment quality score.

Estimation of Practical Significance

Estimating practical significance is important due to the arbitrary nature of null hypothesis statistical testing and the p level of .05. When providing pooled effect sizes, it is important to indicate whether or not the effect would be meaningful in a clinical context.

Practical significance was estimated by two means. First, pooled effect sizes were compared to the approximate benchmark of $g = 0.42$ provided by Ferguson (Ferguson, 2009). In addition to this benchmark, practical significance was estimated by calculating mean difference values from pre- to post-treatment and post-treatment to follow-up time points to assess the size of the outcomes of interest. These values were then compared to values reported in the literature that are indicative of clinically significant change.

Publication Bias

Small sample effects (often thought to be indicative of publication bias (Egger et al., 1997)) were assessed using funnel plots and the Begg's test (Begg & Mazumdar, 1994). Orwin's fail-safe N (Orwin, 1983) was also used, which was calculated using the following formula: $k_0 = k[(ESk/ESc) - 1]$, whereby k corresponds to the total number of, comparisons, ESk is the pooled effect size, and ESc is the criterion effect size, which was set at 0.20.

Results

Systematic Review

Study Identification

Searches returned 606 unique citations. As shown in Figure 1, 37 articles underwent full-text review, with 22 RCTs fulfilling inclusion criteria, including the nine articles analyzed by Johnson and colleagues (Dirksen & Epstein, 2008; Epstein & Dirksen, 2007; Espie et al., 2008; Fiorentino et al., 2010; Garland, Carlson, et al., 2014; Matthews et al., 2014; Ritterband et al., 2012; Savard et al., 2014; Savard, Simard, Ivers, et al., 2005), and unpublished dissertation corresponding to one of the articles analyzed by Johnson and colleagues was also identified (Fiorentino, 2008), and an additional article identified through a grey literature search (Agyemang, 2016). Fifteen articles were original reports with the remining articles reporting on

secondary analyses (Dirksen & Epstein, 2008; Fiorentino et al., 2010; Garland et al., 2016; Heckler et al., 2016; Peoples et al., 2017; Peoples et al., 2019; Savard et al., 2016). Articles that utilized the same dataset were represented by their parent article in the event that they did not provide new information for a particular outcome. If these articles contributed data that the parent study did not for certain outcomes, data on those outcomes were extracted. In addition, each secondary study received the same quality rating score as its respective parent study. In total, 22 studies were included in the current meta-analysis.

It must be noted that one article and its corresponding secondary analysis utilized a three-arm design (in-person CBT-I vs. video-based CBT-I vs. control) (Savard et al., 2016; Savard et al., 2014). To include this analysis in the current meta-analysis, the CBT-I interventions were compared to the same control group, meaning that these effects violated the assumption of independence between effects. To determine the degree of this violation, a sensitivity analysis was conducted for the primary outcome in which the video-based CBT-I vs. control comparison was removed, as the in-person CBT-I arm used a treatment modality that was more consistent with the majority of the included studies. Because the sensitivity analysis did not have a large impact on the overall effect size for this outcome (Hedges' $g = 0.77$ before the sensitivity analysis vs. $g = 0.78$ with one treatment arm removed) and dependency is only present for one of the included studies, we are not concerned about the small influence of data dependency on the current meta-analysis.

Study Characteristics

Table 1 outlines the characteristics of the included articles as they pertain to sample characteristics, study design, and details of the included CBT-I interventions. In total, 1,461 participants were included, with sample sizes ranging from 21 to 255 participants. Seven studies

exclusively assessed women with breast cancer (Epstein & Dirksen, 2007; Fiorentino, 2008; Irwin et al., 2017; Matthews et al., 2014; Savard et al., 2014; Savard, Simard, Ivers, et al., 2005; Zachariae et al., 2018), while the remaining studies assessed men and women diagnosed with a variety of cancers (Agyemang, 2016; Casault et al., 2015; Espie et al., 2008; Garland, Carlson, et al., 2014; Garland et al., 2019; Mercier et al., 2018; Ritterband et al., 2012; Roscoe et al., 2015).

Of the 15 original reports, seven used individual in-person CBT-I as their treatment intervention (Epstein & Dirksen, 2007; Espie et al., 2008; Fiorentino, 2008; Garland et al., 2019; Matthews et al., 2014; Roscoe et al., 2015; Savard, Simard, Ivers, et al., 2005); three used internet-delivered CBT-I (iCBT-I) (Agyemang, 2016; Ritterband et al., 2012; Zachariae et al., 2018); two used self-help CBT-I (Casault et al., 2015; Mercier et al., 2018); two used group CBT-I (Garland, Carlson, et al., 2014; Irwin et al., 2017); and one used both individual in-person and video-based CBT-I (Savard et al., 2014). The duration of CBT-I treatments ranged from six to 12 weeks, generally with one session per week ranging from 30 to 120 minutes. CBT-I interventions were compared to active and non-active treatments: three were compared to treatment-as-usual (Agyemang, 2016; Casault et al., 2015; Espie et al., 2008), four to a wait list control (Fiorentino et al., 2010; Ritterband et al., 2012; Savard, Simard, Ivers, et al., 2005; Zachariae et al., 2018), two to no treatment (Roscoe et al., 2015; Savard et al., 2014) one to sleep education (Epstein & Dirksen, 2007), one to acupuncture (Garland et al., 2019), one to mindfulness-based stress reduction (MBSR) (Garland, Carlson, et al., 2014), one to Tai Chi Chih (TCC) (Irwin et al., 2017), one to a behavioural placebo treatment (BPT) (Matthews et al., 2014), and one to an at-home aerobic exercise program (Mercier et al., 2018). One of the included studies and three out of four of its secondary analyses originally presented with four groups: CBT-I paired with armodafinil, CBT-I paired with a placebo, armodafinil alone, and a placebo

alone (Garland et al., 2016; Heckler et al., 2016; Peoples et al., 2017; Roscoe et al., 2015). The groups assessed in each of the aforementioned articles were aggregated into CBT-I or no CBT-I because armodafinil (alone and paired with CBT-I) did not significantly impact any of the outcomes assessed. Eleven of the included primary studies performed a follow-up assessment (Casault et al., 2015; Espie et al., 2008; Garland, Carlson, et al., 2014; Garland et al., 2019; Irwin et al., 2017; Matthews et al., 2014; Mercier et al., 2018; Roscoe et al., 2015; Savard et al., 2016; Savard, Simard, Ivers, et al., 2005; Zachariae et al., 2018).

Risk of Bias Assessment and Quality Assessment

Quality assessment of the included 15 primary analyses are presented in Table 2. Overall quality assessment scores ranged from 22-34 (out of a possible 35). The mean total quality rating score for the included studies is 27.93 (*SD* = 3.60). While there are no formal cut-off scores for different quality rating categories for this scale, the means and standard deviations obtained in the validity testing of the Yates scale are as follows: 'excellent' = 22.7 (*SD* = 1.95); 'average' = 18.71 (*SD* = 2.25); 'poor' = 12.10 (*SD* = 3.17) (Yates et al., 2005). Therefore, the average overall quality score of the included studies would be considered excellent. Based on the scores obtained through validity testing, none of the included studies are of poor quality.

Meta-Analysis

Primary Outcome

Insomnia Severity. There was little variability in measures used to assess insomnia severity. Only one of the included trials used a measure other than the Insomnia Severity Index (ISI), which used the Athens Insomnia Severity Index (Irwin et al., 2017). CBT-I resulted in significant improvements in insomnia severity compared to control treatments from pre- to post-treatment, corresponding to a 7.81 point reduction in mean ISI score, with a large effect size

when pooled across studies (Table 3 and Figure 2), $g = 0.78$ [95% CI: 0.57, 0.98] [95% PI: 0.066, 1.48], $Z = 7.43$, $p < .001$. There was significant evidence of statistical heterogeneity, $Q = 39.64$, $p < .001$, $I^2 = 64.69\%$ [95% CI: 38.70%, 79.66%].

Seven of the included studies assessed insomnia severity at 3-month follow-up (Casault et al., 2015; Matthews et al., 2014; Mercier et al., 2018; Roscoe et al., 2015; Savard et al., 2016; Savard, Simard, Ivers, et al., 2005; Zachariae et al., 2018), and eight at 6-month follow-up (Casault et al., 2015; Garland, Carlson, et al., 2014; Garland et al., 2019; Irwin et al., 2017; Matthews et al., 2014; Mercier et al., 2018; Savard et al., 2016; Savard, Simard, Ivers, et al., 2005). Insomnia severity data at 3-months could not be obtained for one trial (Matthews et al., 2014). As displayed in Table 4, the improvement in insomnia severity following CBT-I treatment compared to control treatments at post-treatment remained significant at 3-month follow-up ($Z = 3.22$, $p = .001$) with a small to medium effect size, $g = 0.42$ [95% CI: 0.16, 0.68] [95% PI: -0.33, 1.17]. There was significant evidence of statistical heterogeneity for insomnia severity at this time point, $Q = 15.31$, $p = .022$, $I^2 = 60.80\%$ [95% CI: 10.07%, 82.91%]. Improvements were also statistically significant from post-treatment to 6-month follow-up ($Z = 3.01$, $p = .002$) with a small effect size, $g = 0.33$ [95% CI: 0.12, 0.54] [95% PI: -0.27, 0.94]. There was also significant evidence of statistical heterogeneity at this time point, $Q = 17.41$, $p = .026$, $I^2 = 54.04\%$ [95% CI: 2.36%, 78.37%]. Reductions in the mean ISI score were maintained at 3- and 6-months follow-up.

Secondary Outcomes

Sleep Quality. Eight trials assessed sleep quality as an outcome variable. There was little variation in the measures used, with one study using sleep diary to assess sleep quality (Epstein & Dirksen, 2007), and seven using the Pittsburgh Sleep Quality Index (Fiorentino et al., 2010;

Garland, Carlson, et al., 2014; Garland et al., 2019; Irwin et al., 2017; Mercier et al., 2018; Roscoe et al., 2015; Zachariae et al., 2018). As seen in Table 3 and Figure 2b, CBT-I resulted in significant improvements in sleep quality from pre- to post-treatment compared to control treatments, $Z = 4.12$, $p < .001$, with a large pooled effect size, $g = 0.70$ [95% CI: 0.37, 1.03] [95% PI: -0.39, 1.79] corresponding to a 4.62 point reduction in mean PSQI score. There was significant evidence of statistical heterogeneity ($Q = 31.09$, $p < .001$, $I^2 = 77.49\%$ [95% CI: 55.30%, 88.60%]).

Three studies assessed subjective sleep quality at 3-month follow-up (Irwin et al., 2017; Mercier et al., 2018; Zachariae et al., 2018), and four studies assessed sleep quality at 6-month follow-up (Garland, Carlson, et al., 2014; Garland et al., 2019; Irwin et al., 2017; Mercier et al., 2018). Improvements to sleep quality from post-treatment to 3-months did not remain statistically significant, $Z = 0.79$, $p = .43$, and the effect size was small, $g = 0.090$ [95% CI: = -0.14, 0.32] [95% PI: -1.38, 1.56]. In contrast, improvements to sleep quality from post-treatment to 6-months were statistically significant, $Z = 1.97$, $p = .049$, however the effect size remained small, $g = 0.28$ [95% CI: 0.001, 0.57] [95% PI: -0.75, 1.32]. Reductions in the mean PSQI score were maintained at 3- and 6-months follow-up. There was no statistically significant evidence of statistical heterogeneity at 3- or 6-months follow-up.

Sleep Diary. Data for SOL, WASO, TST, and SE measured by sleep diary at 3-months and 6-months could not be obtained for two separate studies (Fiorentino et al., 2010; Matthews et al., 2014).

Sleep Onset Latency (SOL). As shown in Table 3 and Figure 3a, CBT-I resulted in significant reductions in sleep onset latency (SOL) compared to control treatments from pre- to post-treatment with a medium to large effect size, $g = 0.65$ [95% CI: 0.44, 0.86] [95% PI: -0.11,

1.41], $Z = 6.11$, $p < .001$, corresponding to a 20.58 minute reduction. However, there was significant evidence of statistical heterogeneity, $Q = 39.60$, $p < .001$, $I^2 = 69.90\%$ [95% CI: 47.74%, 82.66%].

As shown in Table 4, changes persisted at 3-month follow-up with a small pooled effect size, $g = 0.31$ [95% CI: 0.090, 0.53] [95% PI: -0.21, 0.83], $Z = 2.76$, $p = .006$, and at 6-months again with a small effect size, $g = 0.29$ [95% CI: 0.14, 0.44] [95% PI: 0.026, 0.56], $Z = 3.85$, $p < .001$. Reductions in SOL measured by sleep diary were maintained at 3- and 6-months follow-up. As shown in Tables 4 and 5, there was no significant evidence of statistical heterogeneity for SOL measured by sleep diary at 3- or 6-months follow-up.

Wake After Sleep Onset (WASO). As shown in Table 3 and Figure 3b, CBT-I resulted in significant improvements from pre- to post-treatment with a medium pooled effect size, $g = 0.60$, [95% CI: 0.42, 0.77] [95% PI: -0.0077, 1.20], $Z = 6.55$, $p < .001$, which corresponded to a 26.24 minute reduction. However, there was evidence of statistical heterogeneity, $Q = 34.42$, $p = .002$, $I^2 = 59.32\%$ [95% CI: 28.06%, 77.00%].

Improvements to WASO persisted with a small pooled effect size at 3-month follow-up, $g = 0.38$ [95% CI: 0.12, 0.64] [95% PI: -0.35, 1.11], $Z = 2.83$, $p = .005$, and 6-month follow-up, $g = 0.38$ [95% CI: 0.20, 0.55] [95% PI: -0.039, 0.79], $Z = 4.24$, $p < .001$ (Tables 4 and 5). The mean reduction in WASO measured by sleep diary was maintained at 3- and 6-months follow-up. There was no significant evidence of statistical heterogeneity for this outcome at 3- or 6-months follow-up.

Total Sleep Time (TST). As shown in Table 3 and Figure 3c, CBT-I resulted in significant improvements from pre- to post-treatment compared to control treatments with a small pooled effect size, $g = 0.21$ [95% CI: 0.10, 0.32] [95% PI: 0.093, 0.33], $Z = 3.86$, $p < .001$,

corresponding to a 30.12 minute increase. There was no significant evidence of statistical heterogeneity for this outcome from pre- to post-treatment.

As shown in Tables 4 and 5, these improvements persisted at 3-month follow-up with a small effect size, $g = 0.26$ [95% CI: 0.089, 0.43] [95% PI: 0.035, 0.48], $Z = 2.99$, $p = .003$, at 6-month follow-up again with a small pooled effect size, $g = 0.18$ [95% CI: 0.040, 0.32] [95% PI: 0.012, 0.34], $Z = 2.53$, $p = .011$. The mean increase in TST measured by sleep diary was maintained at follow-up time points. There was no significant evidence of statistical heterogeneity at 3- or 6-months follow-up.

Sleep Efficiency (SE). As shown in Table 3 and Figure 3d, CBT-I resulted in significant improvements in sleep efficiency (SE) from pre- to post-treatment with a large pooled effect size, $g = 0.71$ [95% CI: 0.553, 0.856] [95% PI: 0.29, 1.12], $Z = 9.11$, $p < .001$, which corresponded to a 12.32% increase. There was no significant evidence of statistical heterogeneity at this time point.

These improvements after CBT-I compared to control treatments remained statistically significant from post-treatment to 3-months with a small to moderate effect size, $g = 0.43$ [95% CI: 0.14, 0.72] [95% PI: -0.43, 1.29], $Z = 2.93$, $p = .003$. Improvements from post-treatment to 6-months were also statistically significant with a small effect size, $g = 0.38$ [95% CI: 0.21, 0.55] [95% PI: -0.020, 0.78], $Z = 4.36$, $p < .001$ (Tables 4 and 5). The mean increase in SE measured by sleep diary was maintained at 3- and 6-months follow-up. There was no evidence of significant statistical heterogeneity at 3- or 6-months follow-up.

Actigraphy. A meta-analysis could not be conducted for SOL, WASO, TST, and SE at 3-months follow-up given only one study reported the results of actigraphy at this time point

(Mercier et al., 2018). There was no significant evidence of statistical heterogeneity for any actigraphy-measured sleep outcomes at any time point.

Sleep Onset Latency (SOL). As shown in Table 3 and Figure 4a, CBT-I resulted in significant reductions in SOL measured by actigraphy from pre- to post-treatment with a small pooled effect size, $g = 0.29$ [95% CI: 0.095, 0.49] [95% PI: 0.014, 0.57], $Z = 2.91$, $p = .004$, which corresponded to a 3.40 minute reduction. As shown in Table 5, these improvements persisted at 6-months follow-up with a small effect size, $g = 0.25$ [95% CI: 0.032, 0.47] [95% PI: -0.10, 0.60], $Z = 2.24$, $p = .025$. Reductions in mean SOL measured by actigraphy were also maintained at 6-months follow-up.

Wake After Sleep Onset (WASO). CBT-I resulted in significant improvements in WASO from pre- to post-treatment with a small pooled effect size, $g = 0.21$, [95% CI: 0.022, 0.41] [95% PI: -0.039, 0.47], $Z = 2.19$, $p = .029$ (Table 3 and Figure 4b), corresponding to a 10.61 minute reduction. As shown in Table 5, these improvements did not persist at 6-months follow-up and the pooled effect size remained small, $g = 0.11$ [95% CI: -0.10, 0.33] [95% PI: -0.24, 0.47], $Z = 1.03$, $p = .30$. Mean reductions in WASO measured by actigraphy were also not maintained at follow-up.

Total Sleep Time (TST). CBT-I resulted in significant improvements to actigraphic TST from pre- to post-treatment with a small to medium pooled effect size, $g = 0.30$ [95% CI: 0.11, 0.50] [95% PI: 0.051, 0.56], $Z = 3.08$, $p = .002$ (Table 3 and Figure 4c), corresponding to a 23.29 minute reduction. As reported in Table 5, improvements after CBT-I from post-treatment to 6-months did not remain statistically significant, and the pooled effect size remained small, $g = 0.15$ [95% CI: -0.20, 0.51] [95% PI: -0.20, 0.51], $Z = 1.38$, $p = .17$. Mean reductions in TST measured by actigraphy were maintained at follow-up.

Sleep Efficiency (SE). As shown in Table 3 and Figure 4d, CBT-I did not result in statistically significant improvements in actigraphic SE from pre- to post-treatment, and the pooled effect size was small, $g = 0.18$ [95% CI: -0.008, 0.38] [95% PI: -0.068, 0.44], $Z = 1.88$, $p = .061$, corresponding to a 1.70% increase. CBT-I also did not significantly improve SE measured by actigraphy at 6-months follow-up, and the pooled effect size remained small, $g = 0.12$ [95% CI: -0.099, 0.34] [95% PI: -0.23, 0.47], $Z = 1.07$, $p = .28$. However, increases in mean SE measured by actigraphy were maintained at follow-up.

Fatigue. Eleven trials assessed fatigue as an outcome variable. As seen in Table 3 and Figure 5a, CBT-I resulted in significant improvements in fatigue symptoms from pre- to post-treatment compared to control treatments, $Z = 4.72$, $p < .001$ with a small pooled effect size, $g = 0.35$ [95% CI: 0.21, 0.50] [95% PI: -0.018, 0.73]. There was no significant evidence of statistical heterogeneity at this time point.

Six studies assessed fatigue at 3-month follow-up (Casault et al., 2015; Heckler et al., 2016; Matthews et al., 2014; Savard et al., 2016; Savard, Simard, Ivers, et al., 2005; Zachariae et al., 2018), and seven at 6-month follow-up (Casault et al., 2015; Espie et al., 2008; Garland et al., 2019; Irwin et al., 2017; Matthews et al., 2014; Savard et al., 2016; Savard, Simard, Ivers, et al., 2005). As seen in Table 4, improvements in fatigue after CBT-I compared to control treatments from post-treatment to 3-months were statistically significant ($Z = 2.10$, $p = .035$) with a small effect size, $g = 0.16$ [95% CI: 0.011, 0.31] [95% PI: -0.018, 0.73]. From post-treatment to 6-months, improvements were not statistically significant ($Z = 1.46$, $p = .15$) with a small effect size, $g = 0.11$ [95% CI: -0.036, 0.25] [95% PI: -0.071, 0.28]. There was no significant evidence of statistical heterogeneity at 3- or 6-months follow-up.

Depression. Twelve trials assessed depression as an outcome variable. As seen in Table 3 and Figure 5b, CBT-I resulted in significant improvement in depression symptoms from pre- to post-treatment compared to control treatments, $Z = 5.20$, $p < .001$ and a small pooled effect size, $g = 0.31$ [95% CI: 0.20, 0.43] [95% PI: 0.18, 0.44]. There was no significant evidence of statistical heterogeneity for depression from pre- to post-treatment.

Five studies assessed depression symptoms at 3-month follow-up (Casault et al., 2015; Matthews et al., 2014; Peoples et al., 2019; Savard et al., 2016; Savard, Simard, Ivers, et al., 2005), while eight assessed it at 6-month follow-up (Casault et al., 2015; Espie et al., 2008; Garland, Carlson, et al., 2014; Garland et al., 2019; Irwin et al., 2017; Matthews et al., 2014; Savard et al., 2016; Savard, Simard, Ivers, et al., 2005). Improvements in depression following CBT-I treatment compared to control treatments from post-treatment to 3-months were not statistically significant ($Z = 1.56$, $p = .12$) with a small effect size, $g = 0.14$ [95% CI: -0.037, 0.32] [95% PI: -0.18, 0.44]. However, as seen in Table 5 these improvements were statistically significant from post-treatment to 6-months ($Z = 2.45$, $p = .014$) while the effect size remained small, $g = 0.17$ [95% CI: 0.033, 0.30] [95% PI: 0.0067, 0.33]. There was no significant evidence of statistical heterogeneity at 3- or 6-months follow-up.

Anxiety. Ten trials assessed anxiety as an outcome variable. As shown in Table 3 and Figure 4c, CBT-I resulted in significant improvements in anxiety symptoms from pre- to post-treatment compared to control treatments, $Z = 4.23$, $p < .001$ and a small pooled effect size, $g = 0.28$ [95% CI: 0.15, 0.41] [95% PI: 0.13, 0.42]. There was no significant evidence of statistical heterogeneity from pre- to post-treatment.

Four studies assessed anxiety symptoms at 3-month follow-up (Casault et al., 2015; Matthews et al., 2014; Savard et al., 2016; Savard, Simard, Ivers, et al., 2005), and seven at 6-

month follow-up (Casault et al., 2015; Espie et al., 2008; Garland, Carlson, et al., 2014; Garland et al., 2019; Matthews et al., 2014; Savard et al., 2016; Savard, Simard, Ivers, et al., 2005). As seen in Table 4, improvements after CBT-I compared to control treatments from post-treatment to 3-months did not remain statistically significant ($Z = 1.12$, $p = .26$) with a small effect size, $g = 0.11$ [95% CI: -0.082, 0.30] [95% PI: -0.23, 0.42]. These improvements also did not remain statistically significant from post-treatment to 6-months ($Z = 1.42$, $p = .16$) with a small effect size, $g = 0.10$ [95% CI: -0.039, 0.24] [95% PI: -0.073, 0.28]. There was no significant evidence of statistical heterogeneity at 3- or 6-months follow-up.

Quality of Life. Ten trials assessed quality of life as an outcome variable. Quality of life data of two trials were not included in the meta-analysis because they used measures that could not be used to calculate an overall score from subscale scores (Garland et al., 2019; Ritterband et al., 2012). As seen in Table 3 and Figure 5d, CBT-I resulted in significant improvements in overall quality of life (QOL) from pre- to post-treatment compared to control treatments, $Z = 4.21$, $p < .001$ and a small pooled effect size $g = 0.31$ [95% CI: 0.17, 0.45] [95% PI: 0.14, 0.48]. There was no significant evidence of statistical heterogeneity from pre- to post-treatment for overall quality of life.

Five studies assessed overall quality of life at 3-month follow-up (Casault et al., 2015; Matthews et al., 2014; Peoples et al., 2017; Savard et al., 2016; Savard, Simard, Ivers, et al., 2005), and five at 6-month follow-up (Casault et al., 2015; Espie et al., 2008; Matthews et al., 2014; Savard et al., 2016; Savard, Simard, Ivers, et al., 2005). From post-treatment to 3-months, improvements in quality of life after CBT-I compared to control treatments persisted ($Z = 2.27$, $p = .023$) with a small effect size, $g = 0.20$ [95% CI: 0.027, 0.38] [95% PI: -0.14, 0.48]. As seen in Table 5, improvements from post-treatment to 6-months were not statistically significant ($Z =$

1.80, p = .071) with a small effect size, g = 0.16 [95% CI: -0.014, 0.33] [95% PI: -0.084, 0.40]. There was no significant evidence of statistical heterogeneity at 3- or 6-months follow-up.

Pain Severity. Only one trial assessed pain severity as an outcome variable using the Brief Pain Inventory (Garland et al., 2019) which precluded the use of meta-analysis. This RCT found acupuncture to be more effective for improving pain severity at post-treatment, but this difference was not significant at the 5-month follow-up time point.

Subgroup Analyses

Type of Control Treatment. For this particular subgroup analysis, studies that utilized wait-list controls or no treatment were coded as 'non-active', and those that utilized treatments other than CBT-I (e.g., acupuncture (Garland et al., 2019), Tai Chi Chih (Irwin et al., 2017), behavioural placebo treatment (Matthews et al., 2014), treatment as usual (TAU)) were coded as active. Subgroup analyses comparing studies that used active and non-active control treatments could not be completed for the secondary outcomes of SOL measured by actigraphy and subjective sleep quality due to only having two comparisons for the non-active controls subgroup.

Results of subgroup analyses conducted to assess the effect of CBT-I on studies using active and non-active control treatments are displayed in Table 6. Of notable importance are the results of the subgroup analysis pertaining to insomnia severity, which indicated that the effect of CBT-I on insomnia severity was significantly greater for studies that utilized non-active control treatments, Q = 7.96, p = .005. While all but WASO and SE measured by actigraphy remained statistically significant with a wide range of small to large effect sizes (0.21 to 1.02), the difference between studies that utilized active control treatments and those that utilized non-active controls was not statistically significant for any of the secondary outcomes.

Mode of CBT-I Intervention. Trials that utilized CBT-I interventions that involved in-person contact with a therapist were categorized as ‘in-person’, and those that utilized CBT-I interventions that were conducted primarily independently by participants (e.g., via web-based programs, booklets, etc.) were categorized as ‘self-help’. One trial included in-person and video-based CBT-I as part of a three-arm RCT with representative arms being included in their respective categories(Savard et al., 2014). Subgroup analyses for SOL, WASO, TST, and SE measured by actigraphy could not be conducted due to having two comparisons for the self-help CBT-I group.

Results of subgroup analyses conducted to assess the effect of in-person CBT-I compared to self-help CBT-I are displayed in Table 7. Analyses of all of the included outcomes with the exception of anxiety and overall quality of life for the self-help CBT-I subgroup were statistically significant for both subgroups. Regarding comparisons between subgroups, sleep onset latency measured by subjective sleep diary was the only outcome that presented a statistically significant difference between studies that utilized in-person CBT-I and those that utilized self-help CBT-I, $Q = 4.66$, $p = .031$. In this case, CBT-I was more efficacious for studies using in-person CBT-I, $g = 0.80$ [95% CI: 0.57, 1.03], than those using self-help CBT-I, $g = 0.37$ [95% CI: 0.062, 0.69]. More importantly, there was no statistically significant difference between in-person and self-help CBT-I for any other outcomes.

Meta-Regression

Due to statistically significant heterogeneity for insomnia severity, SOL measured by sleep diary, and WASO measured by sleep diary, meta-regressions were conducted for each of these outcomes. There was significant evidence of statistical heterogeneity for sleep quality, however a meta-regression was not conducted because there was less than 10 comparisons

(Higgins et al., 2020). The following were assessed as potential moderators: mean age of participants; percentage of male participants; and total quality assessment score (assessed using the total Yates quality assessment score for each study). A summary of moderator analyses is displayed in Table 8.

Mean Age of Participants. Mean age of participants explained 51% of the variance in insomnia severity, $Q = 6.44$, $p = .011$, whereby studies with a higher participant mean age reported lower Hedges' *g* values. It also explained 41% of the variance in SOL (Diary), $Q = 5.82$, $p = .016$, whereby studies with a higher mean age reported greater Hedges' *g* values. Mean participant age explained 7% of the variance of WASO (Diary), and this value was not statistically significant, $Q = 1.94$, $p = .16$.

Participant Sex. The proportion of male participants explained 40% of the variance in SOL (Diary), $Q = 4.56$, $p = .033$. Studies with a greater proportion of male participants reported greater Hedges' *g* values. However, this moderator explained 0% of the variance in insomnia severity and WASO (Diary).

Total Quality Assessment Score. Total quality assessment score (measured by the Yates quality rating scale (Yates et al., 2005)) explained 63% of the variance in insomnia severity, $Q = 9.48$, $p = .0021$, whereby studies with higher overall study quality reported lower Hedges' *g* values. It also explained 20% of the variance of WASO (Diary), however this was not statistically significant, $Q = 2.22$, $p = .14$. Total quality assessment score explained 0% of the variance of SOL (Diary).

Publication Bias

For the primary outcome of insomnia severity, visual inspection of the funnel plot did not show asymmetry (Figure 6a) and Begg's test for asymmetry was not statistically significant,

Kendall's tau = 0.0286, p = .441. Funnel plots of secondary outcomes are displayed in Figures 6 to 9. While visual inspections of funnel plots for certain secondary outcomes (i.e., objective sleep outcome variables, subjective sleep quality, depression symptoms, overall quality of life) visually presented varying degrees of asymmetry, Begg's test was statistically significant for sleep onset latency measured by actigraphy only, Kendall's tau = -0.733, p = .019. All other secondary outcome p-values for Begg's test ranged from .070 to .48.

Orwin's fail-safe N values from pre- to post-treatment ranged from 0 (sleep efficiency measured by actigraphy) to 43.50 (insomnia severity). Using insomnia severity as an example, this means that approximately 44 studies would need to be identified that report null effects in order to diminish the observed effect of CBT-I on insomnia severity (g = 0.78) below the criterion effect size (g = 0.20). The range of fail-safe N values were considerably lower for 3-month follow-up (0 to 7.70) and 6-month follow-up times (0 to 8.10).

Discussion

Main Findings

The present study was a systematic review and meta-analysis assessing the efficacy of CBT-I for cancer survivors. Our objective was to provide an up-to-date assessment of the effect of CBT-I on insomnia severity and common comorbid conditions, such as depression, anxiety, and fatigue. Conducting this review was necessary given the fact that the meta-analysis by Johnson and colleagues (Johnson et al., 2016) was conducted more than five years ago. Even though the median time required for an update is approximately 5.5 years, some systematic reviews and meta-analyses are out of date within two years (Higgins et al., 2020; Shojania et al., 2007). As well, the present study includes 22 RCT's as opposed to the 8 RCT's included by Johnson and colleagues (2016). Given the number of RCT's published since the cutoff date of

November 2014 employed by Johnson and colleagues (2016), it was important to ensure the conclusions made continued to reflect the literature to date while also providing new evidence pertaining to comorbidities and different types of CBT-I interventions.

In total there are five main findings to address: first, that CBT-I is efficacious for the treatment of insomnia and the improvement of subjective and objective sleep outcomes; second, that CBT-I produced significant effects for some conditions comorbid with insomnia in people diagnosed with cancer; third, that CBT-I is more efficacious that no treatment as well as other active treatments in general; fourth, that self-help CBT-I may be as efficacious as in-person CBT-I, which has larger implications for the accessibility of CBT-I treatment; and finally, that mean participant age and sex explained significant amounts of variation in statistical heterogeneity of insomnia severity and SOL measured by sleep diary.

Effect of CBT-I on Insomnia and Sleep Outcomes

Our results demonstrate the robust and consistent efficacy of CBT-I in cancer survivors. The effect size observed herein for insomnia severity was $g = 0.78$, which is very similar to the effect size of $d = 0.78$ reported by Johnson and colleagues (2016). This corresponded to a reduction of approximately 8 points in the mean Insomnia Severity Index (ISI) score from pre- to post-treatment, which is a clinically significant reduction (Savard, Savard, et al., 2005). CBT-I was also efficacious for improving insomnia severity from pre- to post-treatment and at three- and six-months follow-up with mean ISI scores remaining below 8, which is the threshold at which cancer survivors are likely to present with sleep difficulties (Savard, Savard, et al., 2005). While this is a promising finding, it is important to note that our Hedges' g value of 0.33 observed at six-months follow-up is smaller than the pooled effect size of $d = 0.55$ observed by Johnson and colleagues at six-months follow-up (Johnson et al., 2016). In addition to this, our

pooled effect size does not meet the benchmark for practical significance of approximately g = 0.42 outlined by Ferguson (2009). This discrepancy may be due to the fact that the present meta-analysis includes a greater number of studies and therefore more data. However, not all of the included studies conducted follow-up assessments, which may have had additional impacts on our pooled effect size at six-months follow-up.

This is the first study to comprehensively assess both sleep diary and actigraphy measured sleep in cancer survivors after receiving CBT-I. Statistically significant effects in all subjective sleep continuity outcomes, subjective sleep quality, and all actigraphy measured sleep variables with the exception of sleep efficiency were observed. CBT-I was associated with clinically meaningful reductions of approximately 20 minutes in SOL (g = 0.65) and 25 minutes in WASO (g = 0.60) measured by sleep diary from pre- to post-treatment, respectively. Post-treatment mean differences for the CBT-I group were below the 30-minute benchmark for SOL and WASO that is indicative of possible insomnia and an SE less than the optimal value of 85% (Buysse et al., 2006). Both SOL and WASO values measured by sleep diary remained below this benchmark at three- and six-months follow-up for the CBT-I group, while WASO measured by sleep diary remained above 30 minutes for the control group. CBT-I also contributed to a 12% improvement in SE measured by sleep diary from pre- to post-treatment (g = 0.71), which resulted in a post-treatment SE of 86%, compared to a 6% increase to an SE of approximately 79% for control conditions. These values remained at about 86% for the CBT-I group at three- and six-months follow-up, while SE measured by sleep diary remained below 85% for the control condition at follow-up. Our sleep diary findings are consistent with the findings of Johnson and colleagues (2016) at post-treatment as well as 6-months follow-up. Our pooled effects pertaining to TST at pre- to post-treatment (g = 0.21) were consistent with those of a

meta-analysis by Ma and colleagues that assessed the efficacy of CBT-I in breast cancer survivors, in which pooled effects were small (g = 0.22) but statistically significant at post-treatment (Ma et al., 2021). Finally, CBT-I contributed to a reduction of approximately 5 points in the Pittsburgh Sleep Quality Index (PSQI) total score to a value of 6.89 at post-treatment (g = 0.70), which is consistent with Ma and colleagues' (2021) finding that CBT-I contributes to large improvement in PSQI score (g = -0.66). While the cutoff for poor sleepers is generally set at scores greater than 5 (Buysse et al., 1989), recommendations have been made to increase the cutoff score to 8 for cancer survivors (Carpenter & Andrykowski, 1998; Mystakidou et al., 2007). Therefore, mean PSQI scores at post-treatment and follow-up time points for the CBT-I group may be indicative of clinically-meaningful changes in subjective sleep quality.

Despite these encouraging findings, there were notable discrepancies between subjective and objective sleep outcomes regarding pooled effect sizes as well as durability of effects. For example, the effect size for sleep onset latency (SOL) measured by sleep diary was larger (g = 0.65) than SOL measured by actigraphy (g = 0.29). In addition, CBT-I contributed to a 4-minute reduction in SOL measured by actigraphy, while the reduction for SOL measured by sleep diary was approximately 20 minutes. Total sleep time (TST) is the only sleep outcome in which pre- to post-treatment effect sizes are similar between sleep diary and actigraphy (g = 0.21 and g = 0.30, respectively). There were also differences in durability between sleep outcomes measured by sleep diary and actigraphy: while diary-measured outcomes (with the exception of TST) remained durable at 3- and 6-months follow-up, actigraphy-measured outcomes largely did not. For example, WASO measured by sleep diary remained below 30 minutes at 6-months follow-up, while WASO measured by actigraphy was approximately 60 minutes. The discrepancy between subjective and objective outcomes is consistent with a meta-analysis by Mitchell and

colleagues, in which CBT-I contributed to moderate to large effects in SOL, WASO, and SE measured by sleep diary in adults with insomnia, but only small effects in SOL measured by actigraphy (Mitchell et al., 2019). In addition to this, CBT-I was found to have a moderate negative effect on TST measured by actigraphy, indicating a reduction in TST (Mitchell et al., 2019).

It is worth noting that CBT-I may influence cancer survivors' subjective perceptions about the quantity and quality of their sleep on their diary reports more than it does their actigraphy-measured sleep outcomes. Previous research has demonstrated that sleep-diary and actigraphy-measured sleep are frequently discordant in insomnia disorder (Mitchell et al., 2019). People with insomnia have been found to misperceive how long it takes them to fall asleep and their total sleep time (Harvey & Tang, 2012), while good sleepers are usually able to perceive their sleep accurately without the same discrepancies between objective and subjective sleep outcomes (Harvey & Tang, 2012; Tulk et al., 2020). Further, while all of the sleep outcomes measured by sleep diary with the exception of TST were practically significant, the sleep outcomes measured by actigraphy were not. This may be a result of the lower number of included studies that assessed actigraphy-measured sleep (6-7 as opposed to 14-15 for subjective sleep outcomes). Correlations between actigraphy and diary-measured sleep have been found to be low (Aili et al., 2017), and actigraphy has been shown to underestimate certain sleep parameters such as TST and SE (Dietch & Taylor, 2021; Palesh et al., 2017), which also could have influenced our findings. As such, firm conclusions cannot be made about the practical significance of CBT-I for objective sleep outcomes based on the present review alone.

Effect of CBT-I on Comorbid Symptoms

This is the only study to comprehensive describe the effect of CBT-I on comorbid symptoms in cancer survivors, including fatigue, depression and anxiety symptoms, and overall quality of life. We observed that CBT-I contributed to small but statistically significant improvements in fatigue, depression and anxiety symptoms, and overall quality of life at post-treatment. There were not enough studies to allow us to assess the effect of CBT-I on pain outcomes. While none of these findings met the benchmark for practical significance outlined above and did not remain durable at 3- and 6-months follow-up, they are of particular importance as many cancer survivors experience mood disturbances, decreased quality of life, and increased fatigue in addition to insomnia (Gehrman et al., 2017; Lis et al., 2008; Ross et al., 2020). There are a number of potential reasons for the lack of practical significance and depreciation in durability, one of which may be the small number of studies for each outcome at follow-up time points. In addition, active controls were pooled with non-active controls; it is possible that pooled effects may have been practically significant and remained durable if they had only been compared to non-active controls. Because of factors such as these, further research is needed to provide strong evidence of the practicality and durability of CBT-I for improving symptoms comorbid with insomnia in cancer survivors.

Our findings are somewhat consistent with findings from a network meta-analysis by Ballesio and colleagues, who found that individual in-person CBT-I contributed to a small statistically significant effect for depression symptoms when compared with placebos ($d = 0.34$), but no modality of CBT-I delivery (group in-person, individual in-person, or self-help) contributed to improvement in fatigue symptoms (Ballesio et al., 2018). While our depression findings are consistent with these findings, we found that CBT-I contributed to small but statistically significant improvements in fatigue ($g = 0.35$). A number of factors could have

contributed to this discrepancy, the most prominent of which is the difference in participant comorbidities. While our meta-analysis focused on cancer survivors only, Ballesio and colleagues used a heterogenous sample that included participants diagnosed with cancer in addition to those with other mental and physical comorbidities, such as depression, post-traumatic stress disorder, fibromyalgia, and chronic pain (Ballesio et al., 2018). Those diagnosed with cancer are different from the general population in that they have been found to have prevalence rates of depression greater than that of the general population, sometimes as high as 2-3 times greater (Caruso et al., 2017), and experience greater levels of fatigue (Hinz et al., 2020) and anxiety (Hinz et al., 2019). These and other factors such as responses to chemotherapy and reactions to diagnosis in general may have influenced some of the discrepancies between our findings and the findings of Ballesio and colleagues (2018).

Type of Control Treatment

Because it is to be expected that the effect of CBT-I would be greater for studies that used non-active control treatments (i.e., studies that compared CBT-I to no treatment at all), it was necessary to assess the effect of CBT-I compared to other active treatments pooled together. We found that the effect of CBT-I was significantly greater among those studies that used non-active control treatments compared to those that used active treatments. Comparing an active treatment such as CBT-I to non-active controls sets a low threshold for detecting significant effects, and CBT-I unsurprisingly cleared this threshold (e.g., Hedges' $g = 1.02$ for insomnia severity). CBT-I also passed the threshold for detecting effects when compared to other active treatments, although pooled effect sizes were lower (e.g., $g = 0.56$ for insomnia severity). This finding is consistent with the above-mentioned meta-analysis by Ma and colleagues (2021), in which Hedges' *g* values were greater for studies that used non-active control treatments

compared to those that used active treatments (g = -0.85 compared to -0.66, respectively). However, we tested for superiority as opposed to non-equivalence, and active control treatments were pooled into one active control group for the purposes of the analysis. This means that we cannot make a strong conclusion that CBT-I is efficacious compared to specific active control treatments; rather, it produces larger effect sizes than other active options in general. While CBT-I is the gold-standard non-pharmacological treatment for insomnia and produces larger effect sizes than other active treatments in general, individual patients may have personal preferences that lead them to choose another treatment over CBT-I. Indeed, this would be more reflective of real world practice where an individual would choose a treatment that is in line with their preferences and values and may impact the outcomes of the trial (Delevry & Le, 2019). The current meta-analysis provides critical information to assist patients and providers make informed treatment decisions; however, more research is needed to determine the effect of preference on CBT-I treatment outcome.

Efficacy of Self-Help CBT-I

Given the need to improve access to CBT-I there has been an increased effort on evaluating alternative delivery models to the traditional face-to-face. While this is laudable, it requires an assessment of whether the effects of the alternative delivery models meet the bar set by face-to-face CBT-I provision. We found that CBT-I treatment modality (in-person vs. self-help) did not significantly impact its efficacy, emphasizing the fact that CBT-I is efficacious for a variety of outcomes regardless of treatment modality. Other meta-analyses with heterogenous participant samples that have also shown that self-help interventions are effective for alleviating insomnia symptoms and symptoms related to sleep outcomes (Ho et al., 2020; Ye et al., 2016; Zachariae et al., 2016). One meta-analysis assessing the efficacy of eCBT-I (i.e., CBT-I

delivered electronically) among a heterogenous group of adults with insomnia found a large effect of eCBT-I on insomnia severity from pre- to post-treatment (Hedges' $g = 1.09$), and medium effect sizes for sleep outcome variables (Zachariae et al., 2016). This finding in particular has important implications to accessibility of CBT-I treatment and treatment adherence more broadly, as people with insomnia view efforts to increase access to CBT-I via digital means favourably (Cheung et al., 2019).

Possible Effects of Participant Age and Sex

When assessing the efficacy of CBT-I, it is important to gain a better understanding of possible reasons for heterogeneity as they pertain to specific groups that may gain particular benefit from CBT-I. To our knowledge, the present meta-analysis is the first to present preliminary findings on the efficacy of CBT-I based on participant age and sex in cancer survivors. We found that mean participant age explained statistically significant amounts of variance in the statistical heterogeneity of both insomnia severity and SOL measured by sleep diary, with increased participant age being related to lower Hedges' *g* values for the effect of CBT-I on insomnia severity and higher values for the effect of CBT-I on SOL measured by sleep diary. Because older adults experience age-related changes to sleep continuity (Ohayon et al., 2004), they may see greater benefits as a result of CBT-I in areas of sleep continuity such as SOL as opposed to insomnia severity. Older adults diagnosed with cancer in particular are also more likely to present with an increased number of comorbidities, such as congestive heart failure, diabetes, hypertension, and dementia (Piccirillo et al., 2008), that may impact their sleep. However, future research is required to expand upon the nature of these relationships.

We also found that participant sex explained a significant amount of the statistical heterogeneity in SOL measured by sleep diary, with the percentage of male participants being

related to greater Hedges' *g* values. There are different avenues from which to approach this finding: first, it is possible that male participants may have accrued more benefits from CBT-I in relation to diary-reported SOL compared to female participants. While differences in CBT-I response specific to cancer survivors have yet to be examined, preliminary findings of a CBT-I intervention in adults diagnosed with fibromyalgia found differences in treatment responses in which male participants experienced improvements in areas such as sleep disturbances and pain-related anxiety, while female participants experienced improvements in areas such as depression and sleep onset latency (Lami et al., 2016). It is also possible that female participants may have been experiencing premature menopause as a result of treatment for sex-specific cancers (Hall et al., 2014), which can contribute to increased rates of insomnia and other sleep disturbances (Savard et al., 2009). It follows that treatment effects such as these may have impacted the benefit that female participants gained from CBT-I treatment with regard to SOL.

Limitations

The present systematic review and meta-analysis was not without limitations. First, there was variability in the duration of follow-up time points. For example, not all of the included studies assessed the efficacy of CBT-I at three- and six-months follow-up, which limits our ability to fully capture its durability over time. Second, there was a very large proportion of female participants in the included studies, ranging from 56.9% to 100%. This may limit the generalizability of our findings given the lower proportion of male participants and the potential for sex and gender differences in cancer experiences, adherence to treatment, etc. Third, all of the included studies were conducted in upper-income countries, and all but one was conducted in a predominantly English speaking country. This may bias our findings to favour upper-income countries, which does not take into account the potential differences in efficacy of CBT-I in

lower-middle-income countries. Finally, the included studies did not report whether participants' onset of insomnia symptoms predated or came after their cancer diagnosis. Because cancer treatment can impact insomnia symptom severity (Savard et al., 2015), this could have impacted our findings.

In addition to the above limitations pertaining to the literature at large, there are limitations pertaining to the present review specifically that must be acknowledged. First, effects were pooled across a diverse range of control conditions (e.g., no treatment, active control interventions such as acupuncture, etc.). This may have impacted our overall findings, as the effects of CBT-I were greater for studies that used a non-active control condition as opposed to pooled active control conditions. Second, more than one statistical test was performed for multiple outcomes without adjusting for inflation in error. While the statistical tests performed in the current review were outline a priori as recommended by the Cochrane collaboration (Higgins et al., 2020), the large number of planned statistical tests and the lack of adjustment may have inflated the error present in our analyses. Third, two analyses were conducted for the same trial in the case of one study (Savard et al., 2014) and its secondary analysis (Savard et al., 2016) with three treatment arms, which violated the assumption of data dependency. While the influence of this violation was thought to be small based on the subsequent sensitivity analysis, data dependence was not formally accounted for in this review. Fourth, one of the listed inclusion criteria was the inclusion of participants presenting with clinically-relevant insomnia as measured by an appropriate assessment tool as opposed to a clinical diagnosis of insomnia disorder determined by clinical interview. While using the presence of clinically-relevant insomnia may have more real-world utility, it still means that the presence of insomnia disorder cannot be confirmed for all participants in the included studies. Finally, analyses for certain

outcomes (e.g., sleep quality at 3-months follow-up) include a small number of studies that may not be sufficient to make strong conclusions.

Future Directions

Recommendations for CBT-I Dissemination

Despite the clear benefits of CBT-I as emphasized by the findings of the present review, many of those diagnosed with cancer do not properly adhere to CBT-I treatment, are not referred, or cannot access it due to a lack of trained therapists in their area (Matthews et al., 2013; Perlis & Smith, 2008; Zhou et al., 2017). In a review of adult survivorship programs, only 13% of programs referred their patients to CBT-I treatment more than half of the time (Zhou et al., 2017). Even if patients do avail of CBT-I treatments, many do not adhere to them for a number of reasons including but not limited to accessibility, attitudes surrounding CBT-I, anxiety or depression symptoms, and beliefs about how effective it is (Matthews et al., 2013). Numbers of trained CBT-I practitioners and clinical psychologists with clinical sleep training are low given the prevalence of insomnia among those diagnosed with cancer (Thomas et al., 2016; Zhou et al., 2020). For example, a 2016 geographic patterning study by Thomas and colleagues identified 752 practitioners worldwide, with 659 identified in the United States and 37 in Canada (Thomas et al., 2016). Because of this lack of providers and other barriers such as high costs and lack of insurance coverage, CBT-I is inaccessible to a large portion of people diagnosed with cancer (Garland et al., 2021). A study conducted by Garland and colleagues found that approximately 71% of attendees at a workshop on improving sleep during cancer (composed of clinicians and patients/advocates) identified financial constraints and lack of insurance coverage as a barrier to accessing non-pharmacological insomnia treatments such as CBT-I and acupuncture (Garland et al., 2021). In addition to system-level barriers such as these, practical

barriers such as travel time can impact access to CBT-I (Koffel et al., 2018). This point is of particular concern in a Canadian context given that some of the highest new incidence rates of cancer are in the Atlantic region (Canadian Cancer Statistics Advisory Committee, 2019), which also has a high rural population (Statistics Canada, 2016). Self-help CBT-I may be an answer to issues of CBT-I accessibility by providing patients with lower-cost treatment that can be accessed from the comfort of their own home that is comparable in effectiveness to in-person treatment. Indeed, multiple meta-analyses have shown that self-help interventions are effective for alleviating symptoms of insomnia related to sleep outcomes (e.g., high sleep onset latency, high wake after sleep onset, etc.) (Ho et al., 2020; Ye et al., 2016; Zachariae et al., 2016). The effectiveness of these interventions may be due in part to their increased accessibility, which may improve treatment adherence (Zachariae et al., 2016). However, if self-help interventions are to be carried out they may need to be provided for a longer duration and include an element of personal clinical support for patients (Zachariae et al., 2016).

Recommendations for Future Research

There are a number of important future directions regarding the literature itself. First, the literature would benefit from more longitudinal RCT's to better assess the impact of CBT-I following treatment. While many of the included studies assessed insomnia severity at three- and six-months follow-up, it is important for longitudinal studies to be conducted wherever possible and for longer periods of time to understand how durable the efficacy of CBT-I is. In line with this, it is also important for future researchers to assess if periodic refreshers of the content of CBT-I treatments can help to maintain the effect of CBT-I over time. This would allow researchers and clinicians to better understand if the decreased effect sizes observed in the present meta-analysis are due to a low number of studies conducting analyses at follow-up or a

depreciation of effect over time. Third, we recommend future researchers assess the distinct contributions of different CBT-I components separately in cancer survivors specifically. While previous research using a dismantling study among adults with persistent insomnia disorder found full CBT-I to be more effective than behavioural therapy (BT) or cognitive therapy (CT) alone (Harvey et al., 2014), it is essential that this research is extended to those that have been diagnosed with cancer. This will allow researchers and clinicians alike to better understand which CBT-I components and individual therapies produce the greatest improvements among this population. Fourth, more studies focusing on the effects of CBT-I in males with cancer specifically and sex and gender differences in responses to CBT-I would be beneficial. The studies included in the present meta-analysis involved large proportions of female participants, which may have impacted the results. Fifth, we recommend further research to identify characteristics of cancer survivors who are more likely to respond to and benefit from CBT-I treatment, characteristics of non-responders, and viable alternatives to CBT-I for non-responders. For example, factors such as psychiatric comorbidities, pain, and medication changes have been found to impact the ability to fully engage in treatment for members of the general population (Baron & Hooker, 2017). Finally, upon further identifying reasons for non-response, it is necessary to investigate ways to improve the implementation of CBT-I to increase adherence and response in cancer survivors specifically. Some cancer survivors may not respond well to certain types of CBT-I for a variety of reasons, or they may not have the time or resources needed to access it. Previous research has found that combining CBT-I with other treatments such as mindfulness-based therapy (MBT) (Wong et al., 2016) and acceptance and commitment therapy (ACT) (Chapoutot et al., 2021) contributes to improvements in insomnia severity for adults diagnosed with insomnia. We recommend future researchers assess the potential benefits of

combination therapies such as these for improving insomnia severity in cancer survivors specifically to give clinicians the tools to meet patients where they are as opposed to applying one type of CBT-I to all patients.

Recommendations for Future Meta-Analyses

There are also important future directions to address with regard to the methods employed in the current meta-analysis. First, the literature would benefit from more meta-analyses that assess the different effects of CBT-I when compared to specific control treatments as more research is conducted on different treatments for insomnia. This would provide more specific findings pertaining to how specific treatments or types of treatments compare to CBT-I on their own as opposed to a pooled group of multiple unique treatments. Second, it would be beneficial for the authors of future meta-analyses to adjust for any potential inflations in error when performing multiple statistical tests for multiple outcomes. Finally, we recommend that future researchers conduct a meta-analysis in this area that only includes studies where participants have received a clinical diagnosis of insomnia disorder determined by clinical interview, as opposed to studies with participants identified as having insomnia disorder measured by an appropriate assessment tool. This will allow for a comparison of outcomes between those who have been formally diagnosed in a clinical setting and those who present with clinically-relevant insomnia without a formal diagnosis of insomnia disorder.

Conclusion

CBT-I remains an efficacious treatment for insomnia in cancer survivors while also contributing to improvements in other symptoms that can present throughout cancer diagnosis, treatment, and beyond. Therefore, CBT-I should continue to be recommended as a first-line treatment for insomnia in cancer survivors. Self-help CBT-I is also recommended for those who

cannot access in-person treatment. Further research is needed to assess sex and gender differences in its efficacy to determine what works best and for whom, and more longitudinal studies must be conducted to determine the long-term efficacy of CBT-I. In addition to this, more research is needed to assess the efficacy of self-help CBT-I compared to CBT-I delivered by a therapist so as to combat issues of accessibility and treatment adherence.

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Table 1

Characteristics of included studies.

First author (Date)	Country	Sample characteristics	Allocation	Screening tool	Treatment components	Length/number of sessions	Follow-up	Outcome measures
Agyemang (2016)	U.S.A.	Men & women, any diagnosis, stage 0-III	iCBT-I = 16 TAU = 15	DSM-IV	SR, SC, SH, CR	One Core per week for 6 weeks; 45-60 mins to complete	N/A	ISI, sleep diary, PHQ-9, GAD-7, FACT-G
Casault et al. (2015)	Canada	Men & women, any diagnosis, stage 0-III	mCBT-I = 20 No treatment = 18	IIS and ISI	SC, SR, CR, SH	One 10-15 page booklet per week for 6 weeks; 1 phone consult every 2 weeks for max 30 mins	3- & 6-mo	ISI, sleep diary, HADS, MFI, EROTC-QOL, DBAS-Brief, SBQ
*Epstein & Dirksen (2007)	U.S.A.	Women stage I-III BCa	CBT-I = 40 Sleep education = 41	Sleep diaries	SC, SR, SH	6 sessions, 1/wk: session 1 = 2 hrs; session 2-4 = ~ 1 hr; sessions 5-6 15-30 min phone consults	N/A	Sleep diary, actigraphy
*[a]Dirksen & Epstein (2007)								ISI, POMS/F, STAI-S, STAI-T, CESD, FACT-B
*Espie et al. (2008)	U.K.	Men & women, any diagnosis, stage 0-III	CBT-I = 100 TAU = 50	PSQI	SC, SR, CR	5 sessions: 50 mins/wk for 5 wks	6-mo	PSQI, ESS, HADS, FSI, FACT-G, sleep diary, actigraphy

*Fiorentino et al. (2008)	U.S.A	Women who were BCa survivors	CBT-I = 11 WLC = 10	DSM-IV	SC, SR, SH, CR	6 sessions: 1hr/wk for 6 wks	N/A	Actigraphy, ISI, PSQI, sleep diary, MOS-SF 36, FOSQ, CESD, BSI, MFSI-SF, GCS
*[b]Fiorentino et al. (2010)								Actigraphy, ISI, PSQI, sleep diary
*Garland et al. (2014)	Canada	Men & women, any diagnosis, stage 0-III	Group CBT-I = 47 MBCR = 64	DSM-IV	SC, SR, CR, RT	8 sessions: 90 mins/wk for 8 wks	5-mo	ISI, PSQI, CSSI, POMS-SF, DBAS, sleep diary, actigraphy
Garland et al. (2019)	U.S.A.	Men & women, any stage or diagnosis	CBT-I = 80 Acupuncture = 80	ISI and DSM-V	SR, SC, CR, RT, SH	7 sessions for 8 weeks: session 1 = 1 hr; sessions 2-5 = 30 mins/wk; sessions 6 and 7 = 30 mins/biweekly	5-mo	ISI, PSQI, sleep diary, BPI, MFSI-SF, HADS, PROMIS-Global
Irwin et al. (2017)	U.S.A.	Women, BCa	Group CBT-I = 45 Tai Chi Chih = 45	DSM-IV-TR, ICD	CR, SC, SR, SH, RT	8 sessions: 2 hrs/wk for 8 weeks; followed by 4 weeks of skill consolidation	6- & 15-mo	PSQI, AISI, sleep diary, MFI, ESS, IDSC
*Matthews et al. (2014)	U.S.A.	Women finished treatment for stage I-III BCa	CBT-I = 32 BPT = 28	IIS	SR, SC, CR	6 weekly sessions: sessions 1-3 and 6 in person, 30-45 mins; sessions 4 and 5	3- & 6-mo	ISI, EORTC-QLQ-C30, AFI, PFS, HADS, DBAS-16, PKT, sleep diary

						over phone 15-20 mins		
Mercier et al. (2018)	Canada	Men & women, any diagnosis, stage 0-III	Self-help CBT-I = 21 Aerobic exercise = 20	ISI	SC, SR, CR, SH	1 video segment (5-20 mins each) and 1 booklet/wk for 6 wks	3- & 6-mo	ISI, PSQI, sleep diary, EX diary, GLTEQ
*Ritterband et al. (2012)	U.S.A.	Men & women, any stage or diagnosis	SHUTi = 14 WLC = 14	DSM-IV-TR	SR, SC, SH, CR	6 Cores: 45-60 mins each, available for 9 wks	N/A	ISI, sleep diary, MFSI-SF, HADS, SF-12
Roscoe et al. (2015)	U.S.A.	Men & women, finished treatment for any cancer at any stage or diagnosis	CBT-I = 47 no CBT-I = 49	DSM-IV	SC, SR, CR, SH	7 sessions: 1, 2, & 4 in person (30-60 mins); 3, 5, & 6 by phone (15-30 mins)	3-mo	ISI, PSQI
[c]Garland et al. (2016)								Sleep diary
[c]Heckler et al. (2016)								BFI, FACIT-F
[c]Peoples et al. (2017)								FACT-G
[c]Peoples et al. (2019)								PHQ-9
*Savard et al. (2005)	Canada	Women finished	CBT-I = 28 WLC = 30	ICSD, DSM-IV	SC, SR, CR, SH	8 sessions: 90 mins/wk for 8 wks	3-, 6-, & 12-mo	IIS, sleep diary, PSG, ISI, HADS, MFI, EORTC QLQ-C30

		treatment for stage I-III BCa						
*Savard et al. (2014)	Canada	Women, stage 0-III BCa	PCBT-I = 81 VCBT-I = 80 no CBT-I = 80	ISI	SC, SR, CR, SH	PCBT-I: 6 sessions, 50 mins/wk for 6 wks VCBT-I: 1 video (5-20 mins) & 1 booklet/wk for 6 wks	N/A	ISI, sleep diary, IIS, MFI, HADS, EORTC QLQ-C30, DBAS, actigraphy
[d]Savard et al. (2016)							3-, 6-, & 12-mo	
Zacharie et al. (2018)	Denmark	Women, stage 0-III BCa	iCBT-I = 133 WLC = 122	PSQI	SR, SC, CR, SH	6 Cores: 45-60 mins each, available for 9 wks	15 wk	ISI, PSQI, sleep diary, FACIT-F

Abbreviations. AFI = Attentional Function Index; AISI = Athens Insomnia Scale; BFI = Brief Fatigue Inventory; BPI = Brief Pain Inventory; BPT = Behavioral Placebo Treatment; BSI = Brief Symptom Inventory; CBT-I = cognitive behavioural therapy for insomnia; iCBT-I = internet cognitive behavioural therapy for insomnia; CES-D = Center for Epidemiologic Studies – Depression Scale; CR = cognitive restructuring; CSSI = Calgary Symptoms of Stress Inventory; DBAS-Brief = Dysfunctional Beliefs and Attitudes about Sleep Scale – Brief; DSM-IV; Diagnostic and Statistical Manual of Mental Disorders 4th edition; DSM-V = Diagnostic and Statistical Manual of Mental Disorders 5th edition; EORTC-QOL = European Organization for Research and Treatment of Cancer quality of life; ESS = Epsworth Sleepiness Scale; EX diary = exercise diary; FSI = Fatigue Symptom Inventory; FACT-B = Functional Assessment of Cancer Therapy-Breast; FACT-G = Functional Assessment of Cancer Therapy-General; FACIT-F = Functional Assessment of Chronic Illness Therapy-Fatigue; FOSQ = Functional Outcomes of Sleep Questionnaire; FSI = Fatigue Symptom Inventory; GCS = Greene Climacteric Scale; GLTEQ = Godin Leisure-Time Exercise; ICSD = International Classification of Sleep Disorders; IDSC = Inventory for Depressive Symptomology – Clinician; IIS = Insomnia Interview Schedule; ISI = Insomnia Severity Index; MBSR = Mindfulness-based cancer recovery; MFI = Multidimensional Fatigue Inventory; MFSI-SF = Multidimensional Fatigue Symptom Inventory – Short Form; PFS = Piper Fatigue Scale; PHQ-9 = Patient Health Questionnaire; PKT = Patient Knowledge Test; POMS-SF = Profile of Mood States – Short Form; PROMIS-Global = Patient – Reported Outcomes Measurement Information System; PSG = polysomnography; RT = relaxation training; SC = stimulus control; SF-12 = Medical Outcomes Study Short Form 12 Health Survey; SF-36 = Medical Outcomes Study Short Form 36 Health Survey; SH = sleep hygiene; SR = sleep restriction; STAI = State – Trait Anxiety Inventory

* Denotes articles that were included in the previous systematic review and meta-analysis by Johnson and colleagues (2016).
[a] Denotes articles that are secondary studies of Epstein and Dirksen (2007).
[b] Denotes articles that are secondary studies of Fiorentino (2008).
[c] Denotes articles that are secondary studies of Roscoe and colleagues (2015).
[d] Denotes articles that are secondary studies of Savard and colleagues (2014).

Table 2

Quality assessment of included studies.

Quality rating possible score	Ayemang (2016)	Casault (2015)	*Epstein (2007)	*Espie (2008)	*Fiorentino (2008)	*Garland (2014)	Garland (2019)	Irwin (2017)
Treatment quality								
Treatment contact/setting 0,2	2	2	2	2	2	2	2	2
Treatment duration 0,1	0	1	1	1	1	1	1	1
Manualization 0,2	2	2	2	2	2	2	2	2
Adherence to manual 0,1	1	1	1	1	1	0	1	1
Therapist training 0,2	2	1	2	2	2	2	2	2
Patient engagement 0,1	1	1	1	1	1	1	1	0
Total treatment quality	8	8	9	9	9	8	9	8
Quality of design/methods								
Sample criteria 0,1	1	1	1	1	1	1	1	1
Evidence criteria met 0,1	1	1	1	1	1	1	1	1
Attrition 0,2	1	1	1	2	1	2	2	2
Rate of attrition 0,1	1	0	1	1	1	1	0	1
Sample characteristics 0,1	1	1	1	1	1	1	1	1
Group equivalence 0,1	1	1	1	1	1	1	1	1
Randomization 0,2	1	2	1	1	1	2	2	2
Allocation bias 0,1	0	1	0	0	0	1	1	1
Measurement bias 0,1	0	1	0	0	0	0	1	1
Treatment expectations 0,1	0	0	0	0	0	0	0	0
Justification of outcomes 0,2	2	1	2	2	2	2	2	2
Validity of outcomes 0,2	2	2	2	2	2	2	2	2
Reliability and sensitivity 0,2	2	2	2	2	2	2	2	2
Follow-up 0,1	0	1	0	1	0	0	0	1
Power calculation 0,1	0	1	1	1	0	1	1	1

Sufficient sample size 0,1	0	1	1	0	0	1	1	1
Planned data analysis 0,1	1	1	1	1	1	1	1	1
Statistics reporting 0,1	1	1	1	0	0	1	1	1
Intention to treat analysis 0,1	1	1	0	1	0	1	1	1
Control group 0,2	0	0	2	0	0	2	2	2
Total quality of design/methods	16	20	19	18	14	23	24	26
Overall quality	24	28	28	27	23	31	33	34

Note. Maximum treatment quality score = 9; maximum quality of design/methods score = 35

* Denotes studies included in the previous meta-analysis

Table 2.

Quality assessment of included studies (continued).

Quality rating possible score	*Matthews (2014)	Mercier (2018)	*Ritterband (2012)	Roscoe (2015)	*Savard (2005)	*Savard (2014)	Zacharie (2018)
Treatment quality							
Treatment contact/setting 0,2	2	2	2	2	2	2	2
Treatment duration 0,1	1	1	1	1	1	1	1
Manualization 0,2	2	1	2	2	2	2	2
Adherence to manual 0,1	1	1	0	0	0	1	0
Therapist training 0,2	2	1	0	1	2	2	0
Patient engagement 0,1	1	1	1	1	1	1	1
Total treatment quality	9	7	6	7	8	9	6
Quality of design/methods							
Sample criteria 0,1	1	1	1	1	1	1	1
Evidence criteria met 0,1	1	1	1	1	1	1	1
Attrition 0,2	1	1	1	1	1	1	1
Rate of attrition 0,1	1	1	1	1	1	0	1
Sample characteristics 0,1	1	1	1	1	1	1	1
Group equivalence 0,1	1	1	1	1	1	1	1
Randomization 0,2	1	2	1	1	0	2	1
Allocation bias 0,1	1	1	0	1	0	1	0
Measurement bias 0,1	0	0	0	1	0	0	1
Treatment expectations 0,1	0	0	0	0	0	0	0
Justification of outcomes 0,2	2	2	2	2	2	2	2
Validity of outcomes 0,2	2	2	2	2	2	2	2
Reliability and sensitivity 0,2	2	2	2	2	2	2	2
Follow-up 0,1	1	1	0	0	1	1	0
Power calculation 0,1	1	1	0	1	1	1	1
Sufficient sample size 0,1	1	1	0	0	1	1	0
Planned data analysis 0,1	1	1	1	1	1	1	1

Statistics reporting 0,1	0	1	1	0	1	1	1
Intention to treat analysis 0,1	1	1	1	1	1	1	1
Control group 0,2	2	2	0	0	2	2	0
Total quality of design/methods	21	24	16	18	20	22	18
Overall quality	30	31	22	25	28	31	24

Note. Maximum treatment quality score = 9; maximum quality of design/methods score = 35
* Denotes studies included in the previous meta-analysis

Table 3

Between-group meta-analysis statistics and fail-safe N's from pre- to post-treatment.

Outcomes	Pre	Post	M Diff	*k*	ES	95%	95% PI	*Z*	Statistical heterogeneity			Fail-
	M(SD)	M(SD)			(*g*)	CI			I^2	*Q*	95% CI	safe N
[a]Insomnia				15	0.78	0.57,	0.066,	7.43***	64.69%	39.64***	38.70%,	43.50
CBT-I	16.15(4.34)	8.34(4.92)	-7.81			0.98	1.48				79.66%	
Control	16.32(4.57)	12.86(5.16)	-3.46									
SOL (Act)				6	0.29	0.095,	0.014,	2.91**	0%	3.47	0%,	2.70
CBT-I	15.23(11.91)	11.83(13.74)	-3.40			0.49	0.57				74.35%	
Control	17.98(19.49)	15.33(15.56)	-2.65									
SOL (Diary)				15	0.65	0.44, 0.86	-0.11, 1.41	6.11***	69.90%	46.51***	47.74%, 82.66%	33.75
CBT-I	39.73(29.90)	19.15(17.80)	-20.58									
Control	39.70(30.97)	31.75(25.40)	-7.95									
WASO (Act)				7	0.21	0.022, 0.41	-0.039, 0.47	2.19*	0%	1.78	0%, 70.90%	0.35
CBT-I	68.66(36.22)	58.05(27.37)	-10.61									
Control	76.52(34.90)	69.74(32.58)	-6.78									
WASO (Diary)				15	0.60	0.42, 0.78	-0.0077, 1.20	6.54***	59.32%	34.42**	28.06%, 77.00%	30.0
CBT-I	52.23(34.66)	25.99(23.09)	-26.24									
Control	54.45(34.69)	41.45(30.19)	-13.00									
TST (Act)				7	0.30	0.11,	0.051,	3.08**	0%	3.27	0%,	3.50
CBT-I	423.63(68.68)	400.34(67.86)	-23.63			0.50	0.56				70.90%	
Control	427.25(61.04)	426.59(51.24)	-0.66									
TST (Diary)				15	0.21	0.10, 0.32	0.093, 0.33	3.86***	0%	10.45	0%, 53.66%	0.75
CBT-I	382.33(73.37)	412.45(61.74)	30.12									

Control	375.27(72.71)	398.84(69.93)	23.57									
SE (Act)				7	0.18	-0.008, 0.38	-0.068, 0.44	1.88	0%	2.03	0%, 70.90%	0
CBT-I	82.35(8.36)	84.05(7.56)	1.70									
Control	81.17(8.03)	82.53(7.55)	1.36									
SE (Diary)				14	0.71	0.55, 0.86	0.29, 1.12	9.11***	39.02%	21.32	0%, 67.69%	35.70
CBT-I	74.18(11.79)	86.50(8.49)	12.32									
Control	73.96(12.25)	79.10(11.58)	5.14									
[b]Sleep quality				8	0.70	0.38, 1.03	-0.39, 1.79	4.12***	77.49%	31.09***	0%, 88.60%	20.0
CBT-I	11.51(2.97)	6.89(3.05)	-4.62									
Control	11.96(3.00)	9.72(3.41)	-2.24									
Fatigue	-	-	-	13	0.35	0.21, 0.50	-0.018, 0.73	4.72***	33.42%	18.02	0%, 65.64%	9.75
Depression	-	-	-	14	0.31	0.20, 0.43	0.18, 0.44	5.20***	0%	9.82	0%, 55.12%	7.70
Anxiety	-	-	-	11	0.28	0.15, 0.41	0.13, 0.42	4.23***	0%	4.61	0%, 37.53%	4.40
Quality of life	-	-	-	10	0.31	0.17, 0.45	0.14, 0.48	4.21***	0%	3.99	0%, 62.47%	5.50

Abbreviations. M = mean; M Diff = mean difference; SD = standard deviation; SE (Act) = sleep efficiency measured by actigraphy; SE (Diary) = sleep efficiency measured by self-report sleep diary; SOL (Act) = sleep onset latency measured by actigraphy; SOL (Diary) = sleep onset latency measured by self-report sleep diary; TST (Act) = total sleep time measured by actigraphy; TST (Diary) = total sleep time measured by self-report sleep diary; WASO (Act) = wake after sleep onset measured by actigraphy; WASO (Diary) = wake after sleep onset measured by self-report sleep diary; 95% CI = 95% confidence interval; 95% PI = 95% prediction interval.

Note. A default of 0% was applied to outcomes with a negative value for the lower 95% confidence limit for I^2.

Mean values could not be calculated for Fatigue, Depression, Anxiety, and QOL outcomes because several different measures were used to assess these outcomes.

[a]Insomnia values from Irwin and colleagues (2017) were excluded from mean calculations of insomnia severity because the Insomnia Severity Index was not used.
[b]Sleep quality values from Epstein and Dirksen (2007) were excluded from mean calculations of sleep quality because the Pittsburgh Sleep Quality Index was not used.

k = number of comparisons
* $p < .05$
** $p < .01$
*** $p < .001$

Table 4

Between-group meta-analysis statistics and fail-safe N's from post-treatment to 3-months follow-up.

	Post	3-months	M Diff						Statistical heterogeneity			Fail-
Outcomes	M(SD)	M(SD)		*k*	ES (*g*)	95% CI	95% PI	*Z*	I^2	*Q*	95% CI	safe N
Insomnia				7	0.42	0.16, 0.68	-0.33, 1.17	3.22**	60.80%	15.31*	10.07%, 82.91%	7.70
CBT-I	7.03(4.44)	7.33(4.77)	0.30									
Control	11.91(5.55)	9.91(5.74)	-2.00									
SOL (Diary)				6	0.31	0.090, 0.53	-0.21, 0.83	2.76**	29.14%	7.06	0%, 71.04%	3.30
CBT-I	17.59(15.05)	17.89(13.99)	0.30									
Control	31.52(21.96)	28.44(24.06)	-3.08									
WASO (Diary)				6	0.38	0.12, 0.64	-0.0034, 1.20	2.83**	48.84%	9.77	0%, 79.75%	5.40
CBT-I	25.16(19.97)	26.28(21.89)	1.12									
Control	47.26(33.74)	36.71(32.02)	-10.55									
TST (Diary)				7	0.26	0.089, 0.43	0.093, 0.33	2.99**	0%	3.25	0%, 70.90%	2.10
CBT-I	421.09(55.21)	430.75(56.54)	9.66									
Control	417.97(65.74)	421.78(71.66)	3.81									
SE (Diary)				5	0.43	0.14, 0.72	-0.29, 1.12	2.93**	49.80%	7.97	0%, 81.64%	5.75
CBT-I	86.71(7.41)	86.27(8.11)	-0.44									
Control	79.16(10.82)	82.55(11.10)	3.39									
Sleep quality				3	0.090	-0.14, 0.32	-1.38, 1.56	0.79	0%	1.39	0%, 89.66%	0
CBT-I	6.36(2.85)	6.36(2.87)	0									
Control	9.38(3.63)	9.13(3.92)	-0.25									
Fatigue	-	-	-	7	0.16	0.011, 0.31	-0.018, 0.73	2.10*	0%	0.66	0%, 70.90%	0

Depression	-	-	-	6	0.14	-0.037, 0.32	-0.18, 0.44	1.56	0%	2.54	0%, 74.71%	0
Anxiety	-	-	-	5	0.11	-0.082, 0.30	-0.13, 0.42	1.12	0%	0.59	0%, 79.29%	0
Quality of life	-	-	-	6	0.20	0.027, 0.38	-0.14, 0.48	2.27*	0%	2.79	0%, 74.71%	0

Abbreviations. M = mean; M Diff = mean difference; SD = standard deviation; SE (Diary) = sleep efficiency measured by self-report sleep diary; SOL (Diary) = sleep onset latency measured by self-report sleep diary; TST (Diary) = total sleep time measured by self-report sleep diary; WASO (Diary) = wake after sleep onset measured by self-report sleep diary; 95% CI = 95% confidence interval; 95% PI = 95% prediction interval.

Note. A default of 0% was applied to outcomes with a negative value for the lower 95% confidence limit for I^2.

Mean values could not be calculated for Fatigue Depression, Anxiety, and Quality of life outcomes because several different measures were used to assess these outcomes.

k = number of comparisons
* $p < .05$
** $p < .01$
*** $p < .001$

Table 5

Between-group meta-analysis statistics and fail-safe N's from post-treatment to 6-months follow-up.

Outcomes	Post	6-months	M Diff	*k*	ES	95%	95%	*Z*	Statistical heterogeneity			Fail-
	M(SD)	M(SD)			(*g*)	CI	PI		I^2	*Q*	95% CI	safe N
[a]Insomnia				9	0.33	0.12,	-0.27,	3.09**	54.04%	17.41*	2.36%,	5.85
CBT-I	7.80(4.69)	7.75(4.72)	-0.05			0.54	0.94				78.37%	
Control	11.53(5.41)	9.46(5.59)	-2.07									
SOL (Act)				5	0.25	0.032,	-0.10,	2.24	0%	3.60	0%,	1.25
CBT-I	11.52(12.41)	14.19(20.76)	2.67			0.47	0.60				79.29%	
Control	14.42(14.69)	14.04(20.45)	-0.38									
SOL (Diary)				9	0.29	0.14, 0.44	0.026, 0.56	3.85***	12.91%	9.19	0%, 54.89%	4.05
CBT-I	18.80(17.64)	18.57(18.05)	-0.23									
Control	30.21(22.18)	24.22(22.94)	-5.99									
WASO (Act)				5	0.11	-0.10, 0.33	-0.24, 0.47	1.03	0%	1.18	0%, 79.29%	0
CBT-I	63.13(32.71)	62.01(36.13)	-1.12									
Control	69.57(35.30)	68.22(34.41)	-1.35									
WASO (Diary)				9	0.38	0.20, 0.55	-0.039, 0.79	4.24***	33.24%	11.98	0%, 69.29%	8.10
CBT-I	28.19(23.89)	29.03(25.41)	0.84									
Control	48.44(36.01)	37.02(34.85)	-11.42									
TST (Act)				5	0.15	-0.065,	-0.20,	1.38	0%	1.41	0%,	0
CBT-I	399.02(63.95)	404.41(67.39)	5.39			0.37	0.51				79.29%	
Control	429.36(54.05)	426.10(67.46)	-3.26									
TST (Diary)				9	0.18	0.040, 0.32	0.012, 0.34	2.53*	0%	2.48	0%, 64.89%	0
CBT-I	412.42(57.04)	427.15(57.63)	14.73									

Control	411.72(68.17)	426.62(65.99)	14.90									
SE (Act)				5	0.12	-0.099, 0.34	-0.23, 0.47	1.07	0%	1.34	0%, 79.29%	0
CBT-I	82.68(8.88)	82.51(9.72)	-0.17									
Control	82.30(7.94)	81.30(10.85)	-1.00									
SE (Diary)				9	0.38	0.21, 0.55	-0.020, 0.78	4.36***	30.86%	11.57	0%, 68.10%	8.10
CBT-I	86.89(8.07)	86.99(8.23)	0.10									
Control	80.19(10.59)	83.44(10.47)	3.25									
Sleep quality				4	0.28	0.001, 0.57	-0.75, 1.32	1.97	46.09%	5.57	0%, 82.12%	1.60
CBT-I	7.17(2.86)	7.41(3.13)	0.24									
Control	9.05(3.28)	8.02(3.62)	-1.03									
Fatigue	-	-	-	8	0.11	-0.036, 0.25	-0.071, 0.28	1.46	0%	1.11	0%, 67.67%	0
Depression	-	-	-	9	0.17	0.033, 0.30	0.0067 0.33	2.45*	0%	5.99	0%, 64.89%	0
Anxiety	-	-	-	8	0.10	-0.039, 0.24	-0.073, 0.28	1.42	0%	1.00	0%, 67.67%	0
Quality of life	-	-	-	6	0.16	-0.014, 0.33	-0.084, 0.40	1.80	0%	2.68	0%, 74.71%	0

Abbreviations. M = mean; M Diff = mean difference; SD = standard deviation; SE (Act) = sleep efficiency measured by actigraphy; SE (Diary) = sleep efficiency measured by self-report sleep diary; SOL (Act) = sleep onset latency measured by actigraphy; SOL (Diary) = sleep onset latency measured by self-report sleep diary; TST (Act) = total sleep time measured by actigraphy; TST (Diary) = total sleep time measured by self-report sleep diary; WASO (Act) = wake after sleep onset measured by actigraphy; WASO (Diary) = wake after sleep onset measured by self-report sleep diary; 95% CI = 95% confidence interval; 95% PI = 95% prediction interval.

Note. A default of 0% was applied to outcomes with a negative value for the lower 95% confidence limit for I^2.

Mean values could not be calculated for Fatigue, Depression, and Quality of life outcomes because several different measures were used to assess these outcomes.

[a]Insomnia values from Irwin and colleagues (2017) were excluded from mean calculations of insomnia severity because the Insomnia Severity Index was not used.

k = number of comparisons
* $p < .05$
** $p < .01$
*** $p < .001$

Table 6

Between-group subgroup analysis statistics of studies using active vs. non-active control treatments from pre- to post-treatment.

Outcomes	Type of Control Group	Pre M(SD)	Post M(SD)	M Diff	*k*	ES (*g*)	95% CI	*Z*	Q
[a]Insomnia severity	Active				8	0.56	0.34, 0.78	5.00***	7.96**
	CBT-I	17.39(4.38)	8.86(5.30)	-8.53					
	Control	17.06(4.91)	12.14(5.52)	-4.92					
	Non-active				7	1.02	0.79, 1.26	8.43***	
	CBT-I	14.91(4.31)	7.82(4.54)	-7.09					
	Control	15.55(4.23)	13.59(5.05)	-1.96					
SOL (Diary)	Active				9	0.75	0.50, 1.00	5.88***	1.53
	CBT-I	44.61(34.45)	21.14(19.49)	-23.47					
	Control	42.66(31.56)	32.77(27.31)	-9.89					
	Non-active				6	0.50	0.20, 0.81	3.27**	
	CBT-I	32.41(23.08)	16.17(14.77)	-16.24					
	Control	35.27(30.09)	30.22(22.53)	-5.05					
WASO (Act)	Active				4	0.21	-0.012, 0.43	1.86	0.011
	CBT-I	69.19(39.75)	57.69(33.82)	-11.50					
	Control	68.56(33.56)	63.85(35.97)	-4.71					
	Non-active				3	0.23	-0.16, 0.63	1.16	
	CBT-I	67.97(31.51)	58.53(18.77)	-9.44					
	Control	87.14(36.69)	77.59(28.07)	-9.55					
WASO (Diary)	Active				9	0.52	0.29, 0.75	4.47***	1.00
	CBT-I	50.76(34.78)	25.96(24.64)	-24.80					
	Control	54.39(34.82)	38.90(29.83)	-15.49					
	Non-active				6	0.71	0.43, 0.98	5.02***	
	CBT-I	54.44(34.49)	26.03(20.76)	-28.41					
	Control	54.54(34.50)	45.29(30.72)	-9.25					
TST (Act)	Active				4	0.23	0.005, 0.45	2.01*	2.07
	CBT-I	419.00(77.79)	395.86(69.05)	-23.14					

	Control	419.99(69.12)	411.71(59.15)	-8.28					
	Non-active				3	0.56	0.16, 0.96	2.75**	
	CBT-I	429.81(56.54)	406.33(66.28)	-23.48					
	Control	436.92(50.26)	446.43(40.69)	9.51					
TST (Diary)	Active				9	0.18	0.034, 0.33	2.42*	0.39
	CBT-I	378.05(78.73)	410.03(66.72)	31.98					
	Control	366.74(74.68)	396.19(70.81)	29.45					
	Non-active				6	0.25	0.090, 0.41	3.08**	
	CBT-I	388.73(65.34)	416.07(54.28)	27.33					
	Control	388.07(69.79)	402.82(68.61)	14.75					
SE (Act)	Active				4	0.19	-0.028, 0.41	1.71	0.025
	CBT-I	82.38(9.69)	84.25(9.18)	1.87					
	Control	82.29(8.72)	83.35(8.58)	1.06					
	Non-active				3	0.16	-0.24, 0.55	0.78	
	CBT-I	82.32(6.58)	83.78(5.39)	1.46					
	Control	79.69(7.12)	81.44(6.17)	1.75					
SE (Diary)	Active				8	0.63	0.42, 0.83	6.02***	1.29
	CBT-I	73.19(12.59)	85.74(9.33)	12.55					
	Control	72.93(12.33)	79.32(11.53)	6.39					
	Non-active				6	0.80	0.58, 1.03	6.96***	
	CBT-I	75.50(10.73)	87.52(7.37)	12.02					
	Control	75.33(12.15)	78.79(11.64)	3.46					
Fatigue	Active	-	-	-	6	0.40	0.17, 0.62	3.49***	0.24
	Non-active	-	-	-	7	0.32	0.10, 0.53	2.91**	
Depression	Active	-	-	-	8	0.28	0.13, 0.43	3.66***	0.40
	Non-active	-	-	-	6	0.36	0.17, 0.55	3.75***	
Anxiety	Active	-	-	-	6	0.21	0.039, 0.38	2.40*	1.27
	Non-active	-	-	-	5	0.36	0.17, 0.55	3.66***	
Quality of life	Active	-	-	-	5	0.42	0.20, 0.63	3.78***	1.70

Non-active	-	-	-	5	0.22	0.030, 0.42	2.27*

Abbreviations. M = mean; M Diff = mean difference; SD = standard deviation; SE (Act) = sleep efficiency measured by actigraphy; SE (Diary) = sleep efficiency measured by self-report sleep diary; SOL (Diary) = sleep onset latency measured by self-report sleep diary; TST (Act) = total sleep time measured by actigraphy; TST (Diary) = total sleep time measured by self-report sleep diary; WASO (Act) = wake after sleep onset measured by actigraphy; WASO (Diary) = wake after sleep onset measured by self-report sleep diary; 95% CI = 95% confidence interval; 95% PI = 95% prediction interval.

Note. Mean values could not be calculated for Fatigue, Depression, Anxiety, and Quality of life outcomes because several different measures were used to assess these outcomes.

[a]Insomnia values from Irwin and colleagues (2017) were excluded from mean calculations of insomnia severity because the Insomnia Severity Index was not used.

k = number of comparisons
* $p < .05$
** $p < .01$
*** $p < .001$

Table 7

Between-group subgroup analysis statistics of studies using in-person vs. self-help CBT-I interventions from pre- to post-treatment.

Outcomes	CBT-I Intervention	Pre M(SD)	Post M(SD)	M Diff	*k*	ES (*g*)	95% CI	*Z*	*Q*
[a]Insomnia severity	In-person				9	0.67	0.42, 0.91	5.28***	2.09
	CBT-I	17.34(4.23)	8.93(5.19)	-8.41					
	Control	17.78(4.06)	13.20(5.03)	-4.58					
	Self-help				6	0.97	0.64, 1.30	5.76***	
	CBT-I	14.57(4.49)	7.56(4.49)	-7.01					
	Control	14.39(5.24)	12.42(5.63)	-1.97					
SOL (Diary)	In-person				9	0.80	0.57, 1.03	6.85***	4.66*
	CBT-I	42.72(33.62)	18.33(17.78)	-24.39					
	Control	38.77(25.37)	30.46(22.16)	-8.31					
	Self-help				6	0.37	0.062, 0.69	2.35*	
	CBT-I	35.23(24.32)	20.39(17.32)	-14.84					
	Control	41.10(39.37)	33.69(30.26)	-7.41					
WASO (Diary)	In-person				9	0.57	0.34, 0.79	4.89***	0.21
	CBT-I	55.22(33.02)	27.85(24.96)	-27.37					
	Control	60.77(35.39)	46.44(33.95)	-14.33					
	Self-help				6	0.66	0.34, 0.97	4.10***	
	CBT-I	47.75(37.13)	23.19(20.29)	-24.56					
	Control	44.97(33.65)	33.97(24.55)	-11.00					
TST (Diary)	In-person				9	0.16	0.023, 0.29	2.29*	2.02
	CBT-I	377.33(69.02)	401.12(59.22)	23.79					
	Control	374.80(70.10)	401.19(67.39)	26.39					
	Self-help				6	0.32	0.14, 0.50	3.42**	
	CBT-I	389.81(79.90)	429.44(65.52)	39.63					
	Control	375.97(76.64)	395.31(73.74)	19.34					
SE (Diary)	In-person				8	0.70	0.50, 0.90	6.89***	0.014
	CBT-I	73.83(11.60)	86.59(8.57)	12.76					

	Control	74.06(11.05)	80.10(10.18)	6.04					
	Self-help				6	0.72	0.45, 0.98	5.33***	
	CBT-I	74.63(12.06)	86.38(8.38)	11.75					
	Control	73.82(13.86)	77.75(13.44)	3.93					
Fatigue	In-person	-	-	-	9	0.38	0.20, 0.56	4.05***	0.24
	Self-help	-	-	-	4	0.30	0.021, 0.57	2.11*	
Depression	In-person	-	-	-	10	0.31	0.18, 0.45	4.68***	0.005
	Self-help	-	-	-	4	0.30	0.042, 0.57	2.27*	
Anxiety	In-person	-	-	-	7	0.29	0.14, 0.43	3.82***	0.072
	Self-help	-	-	-	4	0.25	-0.016, 0.51	1.84	
Quality of life	In-person	-	-	-	7	0.35	0.18, 0.52	4.06***	0.78
	Self-help	-	-	-	3	0.20	-0.079, 0.48	1.41	

Abbreviations. M = mean; M Diff = mean difference; SD = standard deviation; SE (Diary) = sleep efficiency measured by self-report sleep diary; SOL (Diary) = sleep onset latency measured by self-report sleep diary; TST (Diary) = total sleep time measured by self-report sleep diary; WASO (Diary) = wake after sleep onset measured by self-report sleep diary.

Note. Mean values could not be calculated for Fatigue, Depression, and Quality of life outcomes because several different measures were used to assess these outcomes.

[a]Insomnia values from Irwin and colleagues (2017) were excluded from mean calculations of insomnia severity because the Insomnia Severity Index was not used.

k = number of comparisons
* $p < .05$
** $p < .01$
*** $p < .001$

Table 8

Summary of moderator analyses for outcomes with statistically significant heterogeneity.

Outcomes	Moderator	*k*	Regression Coefficient	95% Confidence Interval	*Z*	*Q* (Test of the Model)
Insomnia severity						
	Mean Age	15	-0.066	-0.12, -0.015	-2.55*	6.48*
	Participant Sex (% Male)	15	-0.0037	-0.019, 0.011	-0.48	0.23
	Total Quality Score	15	-0.068	-0.11, -0.025	-3.08**	9.49**
SOL (Diary)						
	Mean Age	15	0.063	0.012, 0.11	2.41*	5.79*
	Participant Sex (% Male)	15	0.013	0.0011, 0.026	2.13*	4.53*
	Total Quality Score	15	-0.021	-0.087, 0.045	-0.62	0.38
WASO (Diary)						
	Mean Age	15	-0.037	-0.089, 0.015	-1.40	1.96
	Participant Sex (% Male)	15	-0.0026	-0.015, 0.0099	-0.41	0.17
	Total Quality Score	15	-0.039	-0.090, 0.012	-1.49	2.21

Abbreviations. SOL (Diary) = sleep onset latency measured by sleep diary; WASO (Diary) = wake after sleep onset measured by sleep diary

Note. k = number of comparisons

* $p < .05$
** $p < .01$
*** $p < .001$

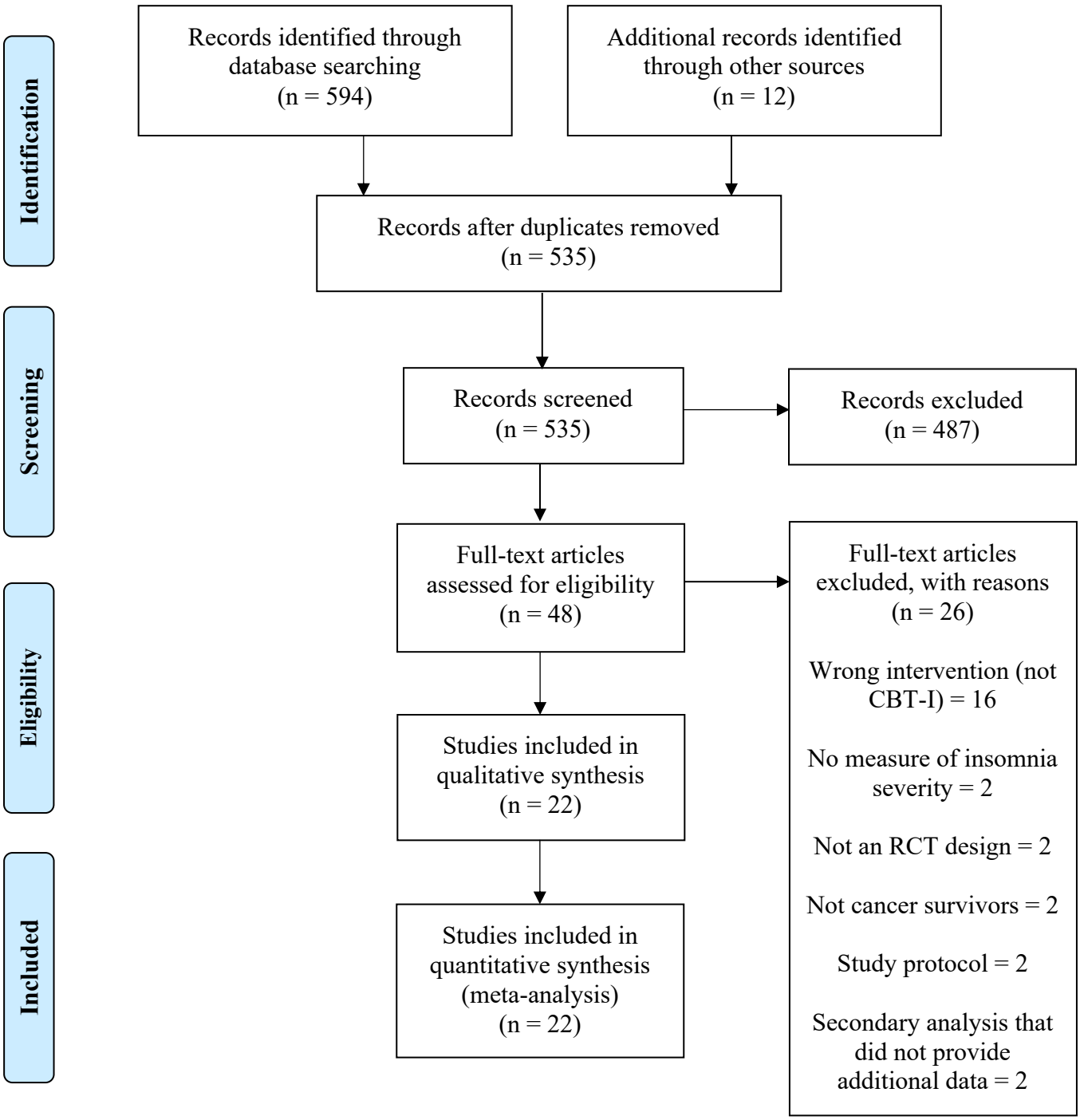
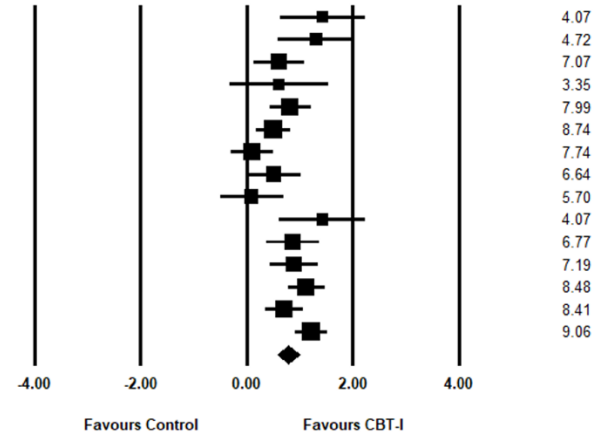


Figure 1. PRISMA flow diagram of studies included and excluded at each stage of the systematic review.

a)

Study name	Outcome	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value	Relative weight
Ayemang (2016)	Insomnia severity	1.421	0.413	0.171	0.611	2.230	3.438	0.001	4.07
Casault (2015)	Insomnia severity	1.302	0.365	0.133	0.586	2.018	3.565	0.000	4.72
Epstein (2007)	Insomnia severity	0.600	0.239	0.057	0.132	1.068	2.511	0.012	7.07
Fiorentino (2010)	Insomnia severity	0.600	0.477	0.227	-0.334	1.535	1.259	0.208	3.35
Garland (2014)	Insomnia severity	0.811	0.198	0.039	0.422	1.200	4.087	0.000	7.99
Garland (2019)	Insomnia severity	0.490	0.166	0.028	0.164	0.815	2.950	0.003	8.74
Irwin (2017)	Insomnia severity	0.089	0.209	0.044	-0.321	0.499	0.424	0.672	7.74
Matthews (2014)	Insomnia severity	0.505	0.259	0.067	-0.002	1.013	1.950	0.051	6.64
Mercier (2018)	Insomnia severity	0.086	0.307	0.094	-0.514	0.687	0.282	0.778	5.70
Ritterband (2012)	Insomnia severity	1.416	0.413	0.170	0.607	2.225	3.430	0.001	4.07
Roscoe (2015)	Insomnia severity	0.857	0.253	0.064	0.362	1.353	3.390	0.001	6.77
Savard (2005)	Insomnia severity	0.875	0.233	0.054	0.418	1.332	3.751	0.000	7.19
Savard (2014a)	Insomnia severity	1.109	0.177	0.031	0.762	1.456	6.263	0.000	8.48
Savard (2014b)	Insomnia severity	0.697	0.180	0.032	0.343	1.050	3.864	0.000	8.41
Zacharie (2018)	Insomnia severity	1.208	0.152	0.023	0.910	1.507	7.941	0.000	9.06
		0.775	0.104	0.011	0.571	0.980	7.434	0.000	



b)

Study name	Outcome	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value	Relative weight
Epstein (2007)	Sleep quality	0.180	0.234	0.055	-0.279	0.639	0.769	0.442	12.94
Fiorentino (2010)	Sleep quality	0.332	0.470	0.221	-0.590	1.254	0.706	0.480	7.40
Garland (2014)	Sleep quality	1.460	0.214	0.046	1.039	1.880	6.807	0.000	13.47
Garland (2019)	Sleep quality	0.428	0.167	0.028	0.101	0.756	2.562	0.010	14.71
Irwin (2017)	Sleep quality	0.296	0.210	0.044	-0.116	0.708	1.408	0.159	13.58
Mercier (2018)	Sleep quality	0.572	0.313	0.098	-0.041	1.185	1.828	0.068	10.84
Roscoe (2015)	Sleep quality	1.296	0.274	0.075	0.758	1.834	4.723	0.000	11.85
Zacharie (2018)	Sleep quality	0.897	0.147	0.022	0.609	1.185	6.111	0.000	15.21
		0.700	0.170	0.029	0.367	1.032	4.123	0.000	

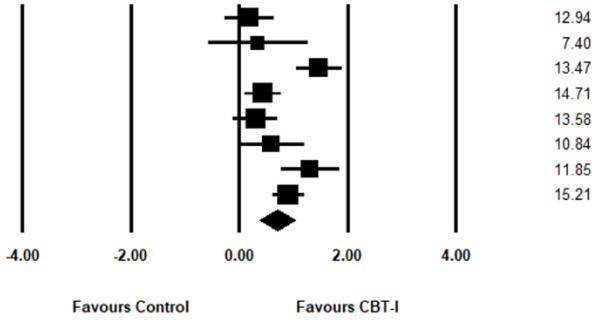


Figure 2. a) Improvement of insomnia severity from pre- to post-treatment by study and overall. b) Improvement of subjective sleep quality from pre-to post-treatment by study and overall.

Abbreviations. CBT-I = cognitive behavioural therapy for insomnia.

Note. Savard (2014a) denotes in-person CBT-I vs. control and Savard (2014b) denotes video-based CBT-I vs. control.

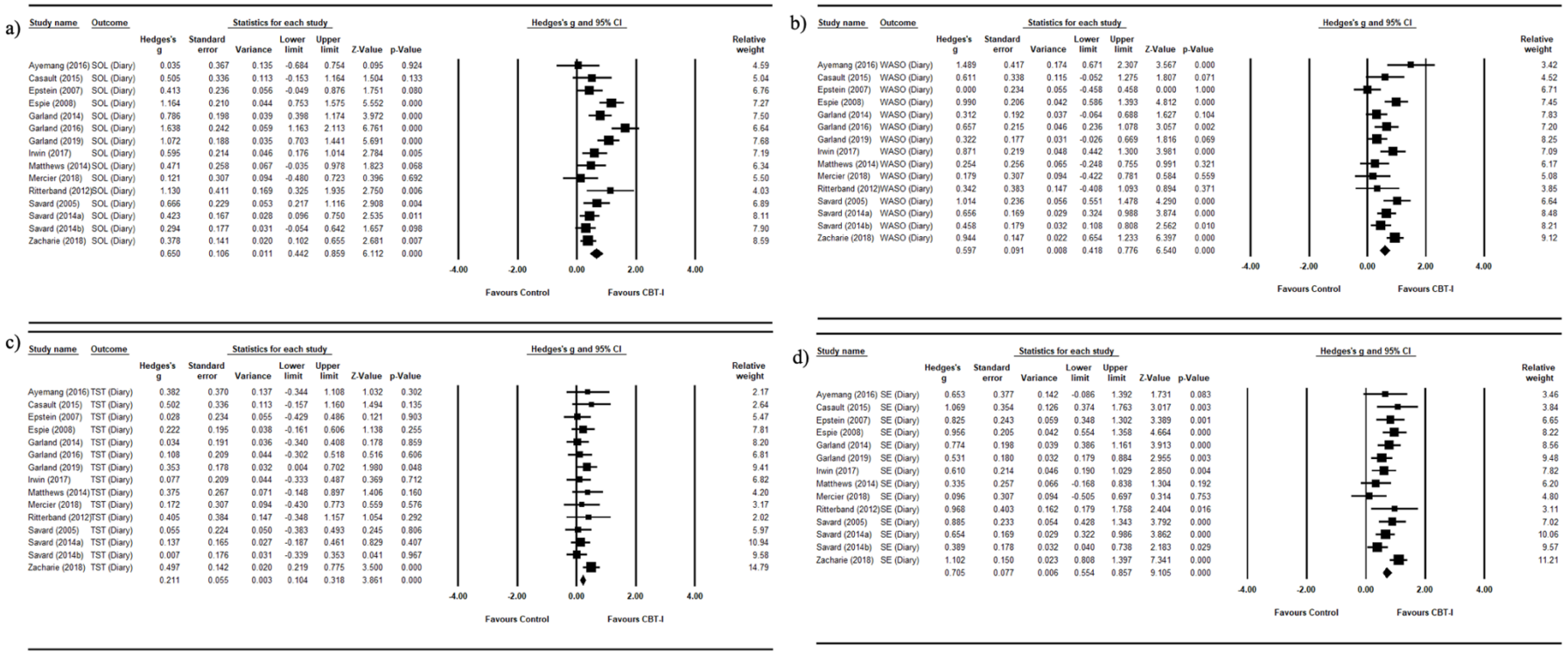


Figure 3. a) Improvement of sleep onset latency (SOL) measured by sleep diary from pre- to post-treatment by study and overall. b) Improvement of wake after sleep onset (WASO) measured by sleep diary from pre-to post-treatment by study and overall. c) Improvement of total sleep time (TST) measured by sleep diary from pre-to post-treatment by study and overall. d) Improvement of sleep efficiency (SE) measured by sleep diary from pre-to post-treatment by study and overall.

Abbreviations. CBT-I = cognitive behavioural therapy for insomnia; SE (Diary) = sleep efficiency measured by sleep diary; SOL (Diary) = sleep onset latency measured by sleep diary; TST (Diary) = total sleep diary measured by sleep diary; WASO (Diary) = wake after sleep onset measured by sleep diary.

Note. Savard (2014a) denotes in-person CBT-I vs. control and Savard (2014b) denotes video-based CBT-I vs. control.

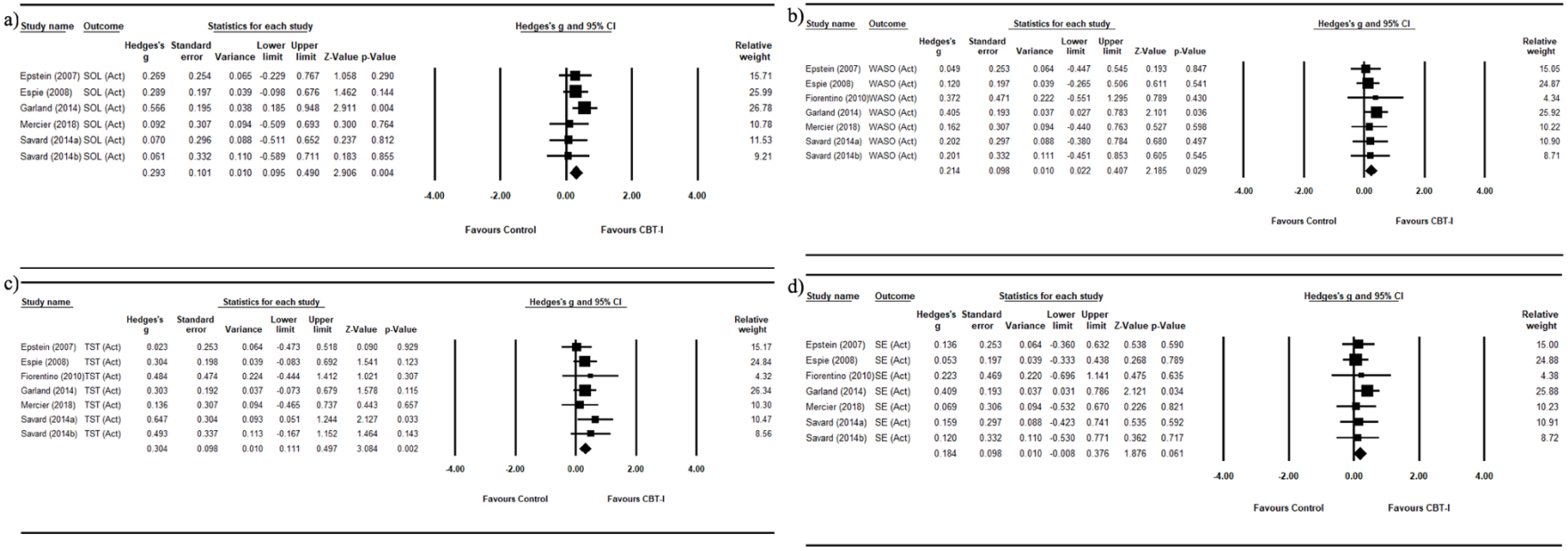


Figure 4. a) Improvement of sleep onset latency (SOL) measured by actigraphy from pre- to post-treatment by study and overall. b) Improvement of wake after sleep onset (WASO) measured by actigraphy from pre-to post-treatment by study and overall. c) Improvement of total sleep time (TST) measured by actigraphy from pre-to post-treatment by study and overall. d) Improvement of sleep efficiency (SE) measured by actigraphy from pre-to post-treatment by study and overall.

Abbreviations. CBT-I = cognitive behavioural therapy for insomnia; SE (Act) = sleep efficiency measured by actigraphy; SOL (Act) = sleep onset latency measured by actigraphy; TST (Act) = total sleep diary measured by actigraphy; WASO (Act) = wake after sleep onset measured by actigraphy.

Note. Savard (2014a) denotes in-person CBT-I vs. control and Savard (2014b) denotes video-based CBT-I vs. control.

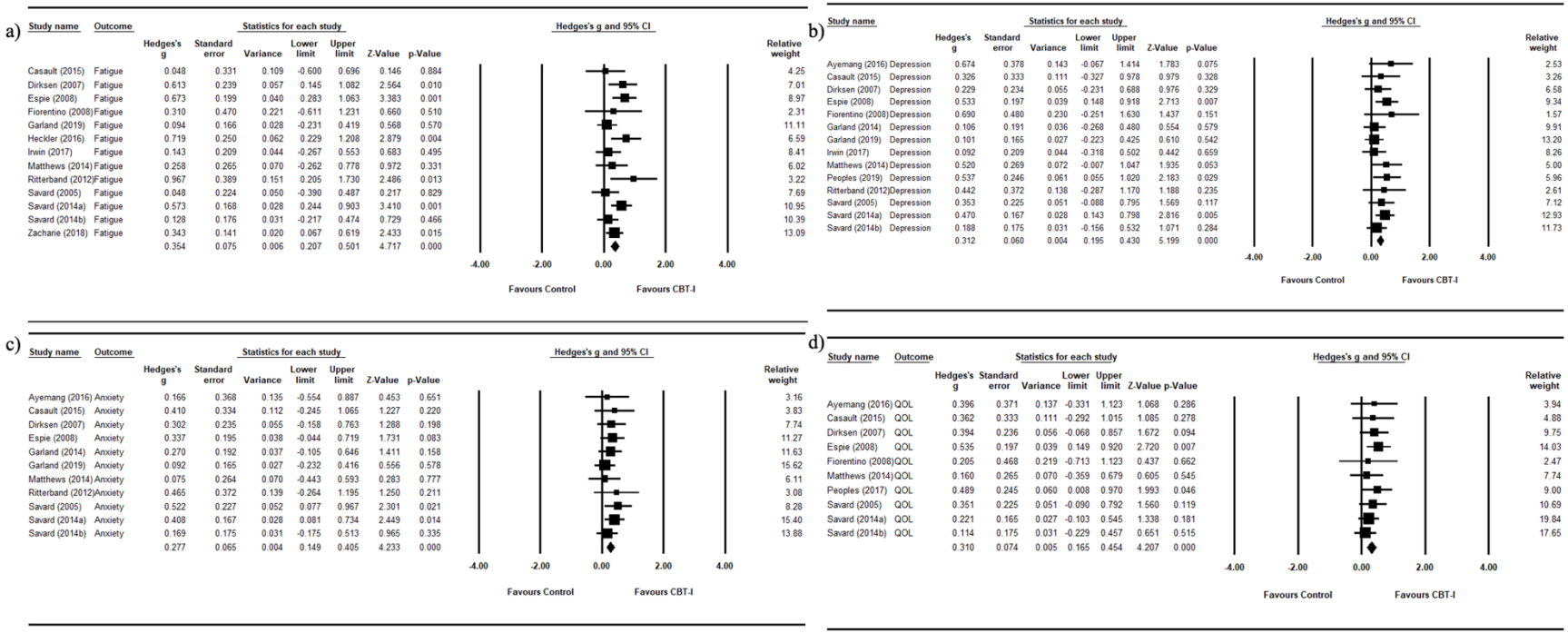


Figure 5. a) Improvement of fatigue from pre- to post-treatment by study and overall. b) Improvement of depression symptoms from pre-to post-treatment by study and overall. c) Improvement of anxiety symptoms from pre-to post-treatment by study and overall. d) Improvement of overall quality of life from pre-to post-treatment by study and overall.

Abbreviations. CBT-I = cognitive behavioural therapy for insomnia; QOL = overall quality of life.

Note. Savard (2014a) denotes in-person CBT-I vs. control and Savard (2014b) denotes video-based CBT-I vs. control.

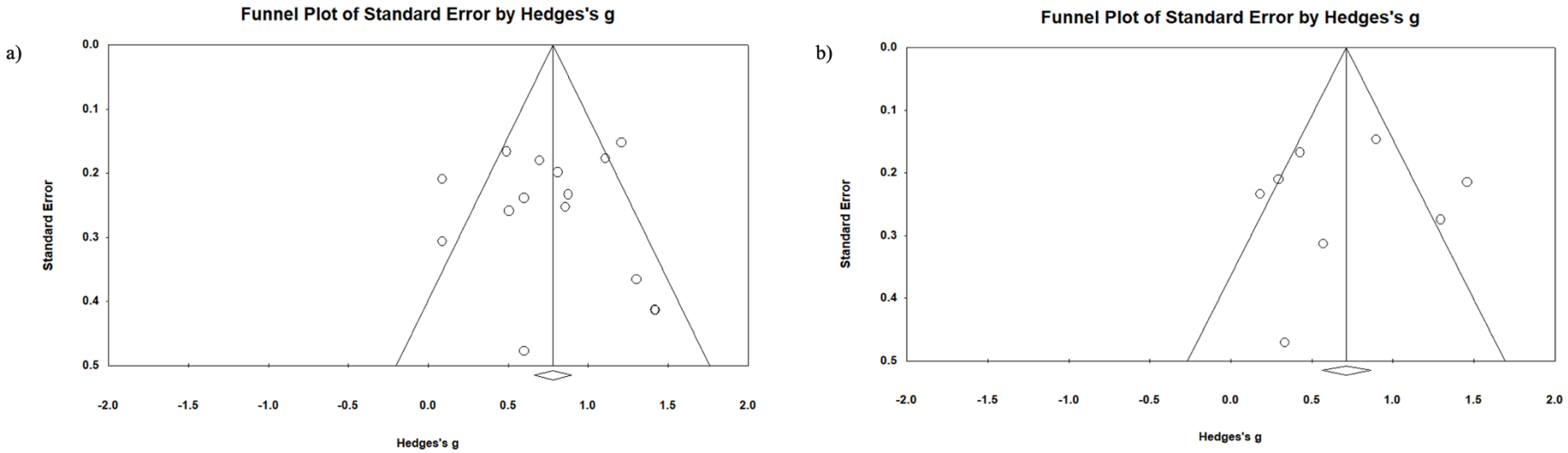


Figure 6. a) Funnel plot of standard error by Hedges' *g* for insomnia severity from pre- to post-treatment. b) Funnel plot of standard error by Hedges' *g* for subjective sleep quality from pre- to post-treatment.

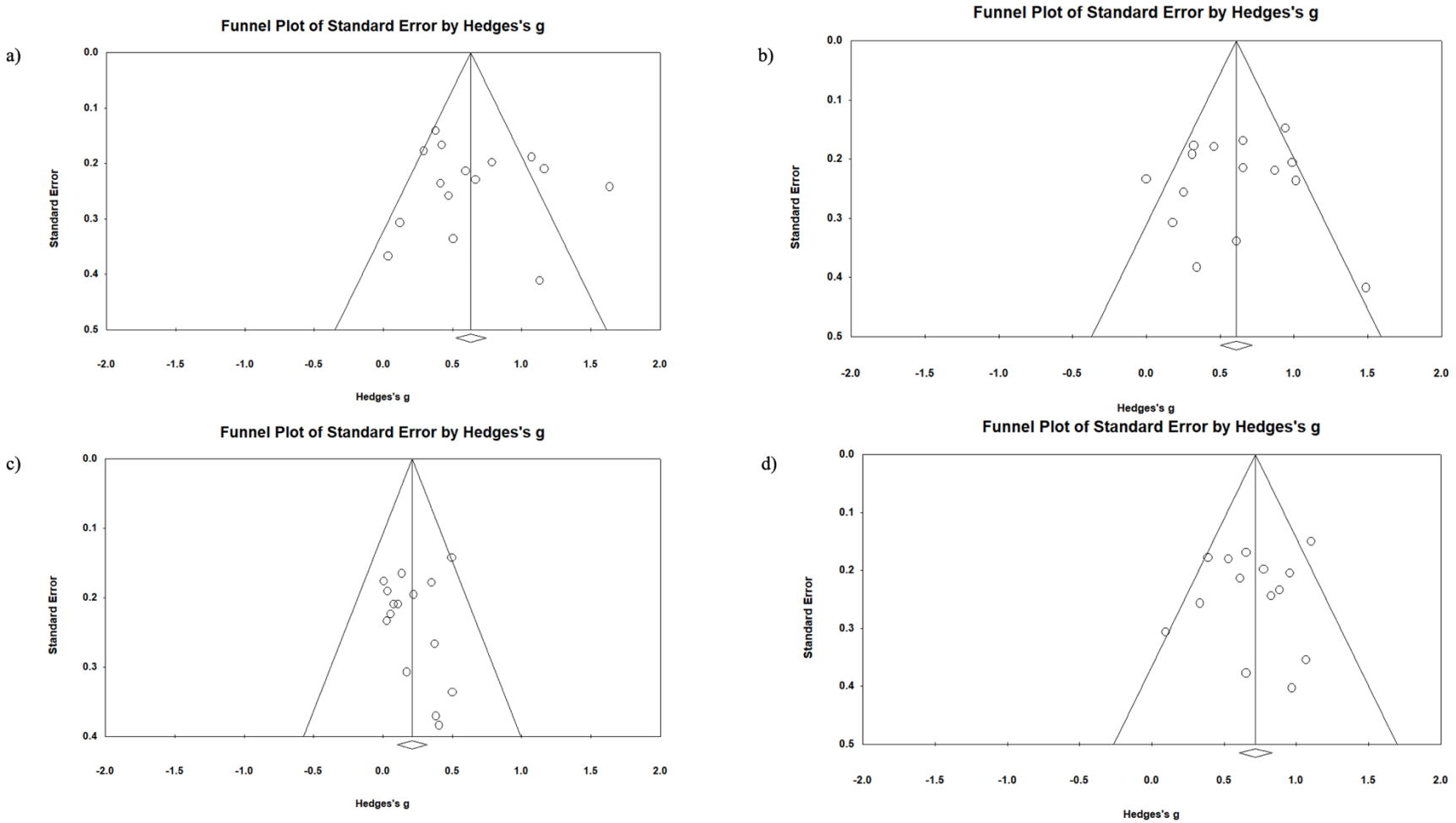


Figure 7. a) Funnel plot of standard error by Hedges' *g* for sleep onset latency (SOL) measured by sleep diary from pre- to post-treatment. b) Funnel plot of standard error by Hedges' *g* for wake after sleep onset (WASO) measured by diary from pre- to post-treatment. c) Funnel plot of standard error by Hedges' *g* for total sleep time (TST) measured by sleep diary from pre- to post-treatment. d) Funnel plot of standard error by Hedges' *g* for sleep efficiency (SE) measured by sleep diary from pre- to post-treatment.

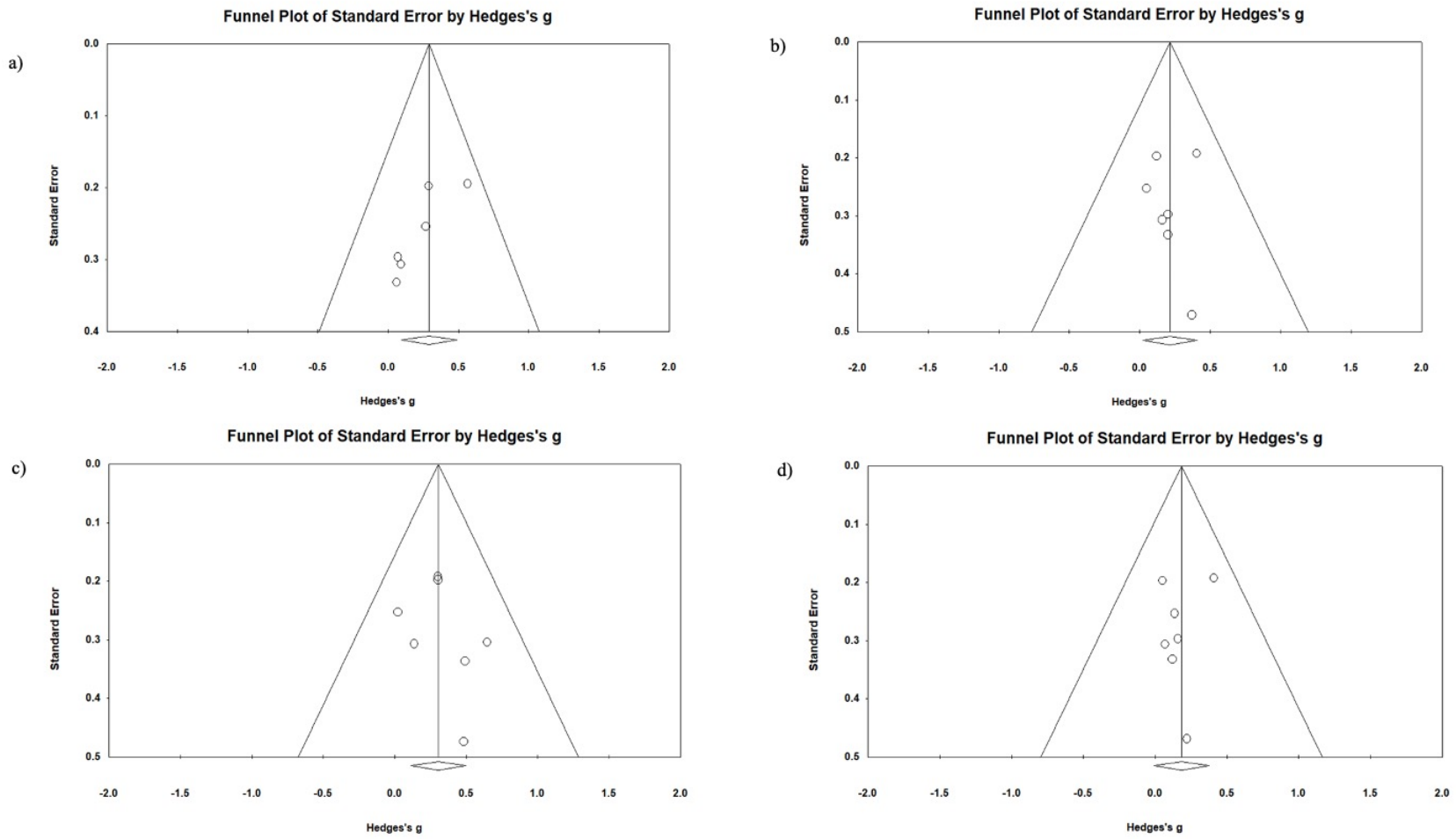


Figure 8. a) Funnel plot of standard error by Hedges' *g* for sleep onset latency (SOL) measured by actigraphy from pre- to post-treatment. b) Funnel plot of standard error by Hedges' *g* for wake after sleep onset (WASO) measured by actigraphy from pre- to post-treatment. c) Funnel plot of standard error by Hedges' *g* for total sleep time (TST) measured by actigraphy from pre- to post-treatment. d) Funnel plot of standard error by Hedges' *g* for sleep efficiency (SE) measured by actigraphy from pre- to post-treatment.

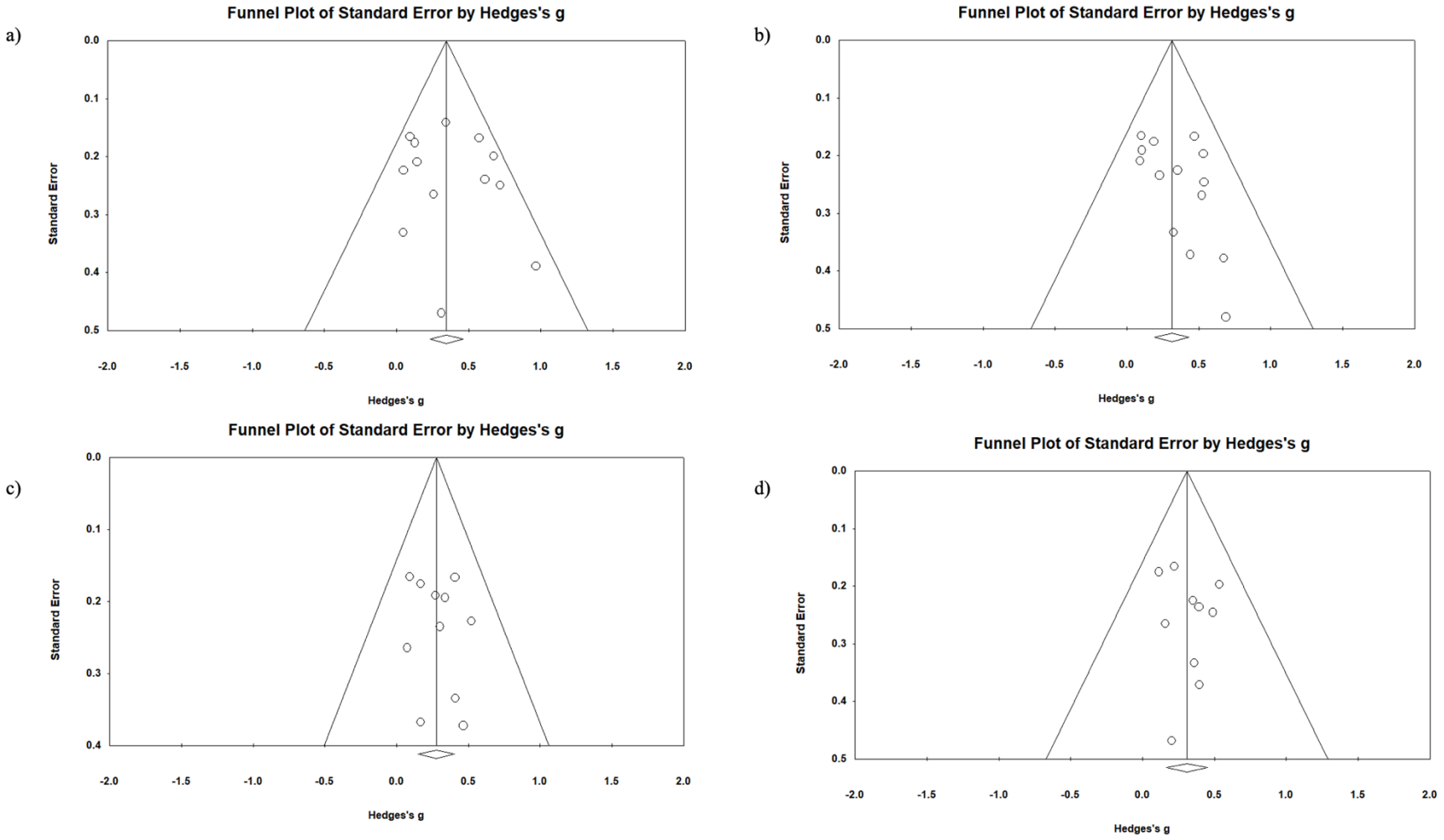


Figure 9. a) Funnel plot of standard error by Hedges' *g* for fatigue from pre- to post-treatment. b) Funnel plot of standard error by Hedges' *g* for depression symptoms from pre- to post-treatment. c) Funnel plot of standard error by Hedges' *g* for anxiety symptoms from pre- to post-treatment. d) Funnel plot of standard error by Hedges' *g* for overall quality of life from pre- to post-treatment.

Appendix 1. *PRISMA checklist.*

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	i
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	ii
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	1
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	13
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	14
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	14
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	15
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	15
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	16

Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	16
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	14
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	16
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	17
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	17
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	19
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	18
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	19
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	20
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	22
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	22
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	22
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	33

Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	31
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	34
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	43
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	48
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	iv