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CLINICAL REVIEW

Effects of cognitive behavioral therapy for insomnia (CBT-I) on quality of life: A systematic review and meta-analysis☆

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SUMMARY

The effects of cognitive behavioral therapy for insomnia (CBT-I) have consistently been shown to improve insomnia symptoms and other health-related outcomes, but the effects on QoL have been inconsistent. Many factors including the type CBT-I delivery and type of instrument used to assess QoL make the topic complex. The present systematic review and meta-analysis synthesized the evidence of CBT-I efficacy on QoL outcomes across different populations, delivery modes, and methodological aspects.

Following the guidelines on preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA), a literature search was conducted through *PubMed, Web of Science, Scopus,* and *PsycINFO* using keywords from relevant MeSH terms based on PICOS (Participants, Intervention, Comparison, Outcome and Study) criteria. Clinical trials investigating the effect of CBT-I as an intervention on QoL with any kind of control group were eligible if they reported mean scores and variation of QoL. Meta-analysis using a random-effect model was conducted to calculate the standardized mean differences (SMDs) in a set including all identified studies, as well as in three sub-sets: face-to-face CBT-I using randomized controlled trials (RCTs), online CBT-I using RCTs, and one-group pre- and post-treatment design.

A total of 24 studies comprising 1977 participants (808 in an intervention group) from 12 countries were eligible for meta-analysis. The overall pooled estimate of SMD of QoL when all 24 studies were included was 0.47 (95% CI: 0.22; 0.72; $I^2 = 84.5\%$; $tau^2 = 0.31$; $p < 0.001$). The overall pooled estimate of SMD of QoL was 0.46 (95% CI: 0.01−0.90; $I^2 = 87.5\%$; $tau^2 = 0.48$, $p < 0.001$) for intervention groups with face-to-face CBT-I compared to controls; 0.47 (95% CI: 0.02−0.92; $I^2 = 88.3\%$; $tau^2 = 0.36$; $p = 0.04$) for intervention groups with digital CBT-I compared to controls, and 0.46 (95% CI: 0.12−0.80; $I^2 = 52.9\%$; $tau^2 = 0.07$; $p = 0.08$) for one-group pre- and post-comparison using CBT-I intervention compared to baseline. Moreover, effects of CBT-I on QoL were different across populations (pooled SMD = 0.59 for

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patients with insomnia; 0.29 for patients with insomnia comorbid with another major disorder; and 0.48 for other conditions) and types of QoL instruments (pooled SMD = 0.36 for disease-specific QoL instrument not on insomnia, 0.43 for generic QoL instrument, and 0.67 for a single-QoL-item instrument). The probability of publication bias was ruled out in overall and design specific sub-group analysis based on funnel plot and Egger's test.

In conclusion, this meta-analysis confirmed a moderate, overall effect of CBT-I in improving QoL. However, due to small power and heterogeneity, future studies are needed to better explore the impact of moderating factors such as mode of delivery and type of QoL measure for assessment used.

Abbreviations

BZRAs	benzodiazepine receptor agonists
CBT	cognitive behavioral therapy
CBT-I	cognitive behavioral therapy for chronic insomnia
CI	confidence interval
ES	effect size
PICOS	Participants, Intervention, Comparison, Outcome and Study
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PROSPERO	International Prospective Register of Systematic Reviews
QoL	quality of life
RCTs	randomized controlled trials
ROB	risk of bias
SD	standard deviation
SF-36	Short-Form 36
SMD	standardized mean difference

Introduction

The issue of insomnia symptoms or sleep problems (including difficulties in sleep initiation and sleep maintenance, waking up too early, nonrestorative sleep, and poor sleep quality) is of serious concern [1]. More specifically, prior systematic reviews and meta-analyses have reported that the worldwide prevalence of insomnia among the general population is approximately 22% [2], while prevalence of insomnia among individuals with a specific condition may up to 40% (e.g., patients with obstructive sleep apnea) [3]. Moreover, insomnia disorder (hereafter insomnia) may develop when insomnia symptoms or sleep problems worsen. A range of negative conditions (e.g., somatic complaints, psychological distress, mental health, physical fatigue, and impaired quality of life [QoL]) are associated with insomnia, although the causal relationship between insomnia and negative conditions has diverse findings. For example, recent evidence has shown that previous insomnia is associated with individuals' later psychological distress [4], while other evidence has shown that individuals with higher levels of psychological distress are more likely to have sleep problems [5]. Moreover, insomnia has been identified as a robust risk factor for a range of mental health disorders and medical morbidities [6–8]. In other words, insomnia could be a cause of specific health outcomes, and insomnia could also be a consequence resulting from specific health problems.

Approximately 40% of individuals with insomnia have been reported to have a comorbid psychiatric condition (e.g., depression, psychotic disorder, attention deficit hyperactivity disorder, and psychoactive substance use) [9,10]. This implies that individuals suffering from insomnia are likely to have additional health concerns in addition to insomnia. Therefore, an individual's development and overall health are likely to be compromised by insomnia [11], which may result in further high societal costs. For example, prior research has demonstrated that an individual with insomnia who has received no treatment as compared with those who remitted from insomnia lost approximately 0.08 quality-adjusted life-year (on a 0–1 scale), cost more than US $242 per month on medical expenditure, and lost US $143 per month on productivity [12]. It has also been reported that the annual expenditure including direct and indirect costs for treating insomnia in the United States has exceeded $100 billion [13]. Consequently, finding effective ways to treat insomnia is important because this might prevent individuals with insomnia from future detrimental consequences and eventually lessen the healthcare burden for the society [14].

Apart from pharmacological treatment, cognitive behavioral therapy (CBT) specifically designed to treat insomnia (i.e., CBT-I), is recommended as the first line of treatment [15–18] and a standardized protocol has been developed [15]. The major benefit of providing CBT-I instead of prescribing medication for individuals with insomnia is that the current evidence for sleep medications only supports short-term use and effects and that CBT-I has superior long-term effects [19]. Additionally, although CBT-I may cause side-effects or adverse reactions, the severity level is less when compared to drug dependence, drug overuse, comorbid chronic pain, and accidents due to taking sleeping medication [19,20]. In addition to having a beneficial effect on insomnia symptoms, CBT-I has been found to be effective in reducing depression, anxiety, and chronic pain, and increasing sleep-related quality of life [21–26]. However, to the best of the present authors' knowledge, no prior studies have summarized the current evidence whether CBT-I is effective in relation to individuals' QoL.

QoL is a broad concept, and global definitions have been suggested. For example, 'the degree of satisfaction or dissatisfaction felt by individuals with various aspects of their lives', 'a person's sense of wellbeing, his satisfaction or dissatisfaction with life, or his happiness or unhappiness', or 'the individual's achievement of a satisfactory social situation within the limits of perceived physical capacity' [27]. QoL is very often seen as multidimensional construct, and although it is sometimes assessed with only a single global item, the most common way is to use psychometric scales that include items assessing dimensions such as physical/somatic, material, psychological/mental, social, functional, and emotional wellbeing, along with personal development and activity [27,28]. It has been noted that QoL should be conceptualized as an umbrella term that is defined and assessed in many ways, and that this heterogeneity calls for researchers to specifically define how they operationalize QoL in their studies, and for readers of published studies to pay attention to how the construct was assessed [28]. In

medical and health-related research, an important difference is that between a more broadly defined QoL, including many dimensions, and a health-related QoL focusing mostly on how somatic and psychological symptoms affects everyday function and well-being [27,28]. Most studies have used generic QoL instruments assessing how insomnia impacts on QoL, and results indicated that both primary (syndromic) and secondary (symptomatic) insomnia were associated with impaired QoL [29]. Furthermore, sleep-related QoL instruments have been developed [29,30] because sleep is essential for an individual to have typical development, energy resumption, and good psychosocial health [11]. Therefore, when individuals have insomnia problems, they are likely to have impaired QoL because they do not have typical development, energy resumption, and good psychosocial health, which are all important factors for good QoL.

Given that insomnia and sleep problems have been related to a range of factors that are also relevant for (or overlap with) the concept of QoL, it is reasonable to assume that the level of sleep difficulties are related to QoL [31,32] and especially health-related QoL, and that successful treatment of insomnia should increase it. Studies have found that pharmacological therapies can improve sleep and subsequently elevate QoL, with the effects maintained for two to 6 mo [29]. More specifically, benzodiazepine receptor agonists (BZRAs) appear to be effective for patients with major insomnia given the QoL outcomes of previous randomized controlled trials (RCTs) [33,34]. Several RCTs have identified an improvement in QoL after CBT-I with longer effects (e.g., 1 y) than that of pharmacotherapy [29,35–39].

The efficacy findings regarding the effects of CBT-I on QoL among individuals with insomnia appear to be diverse. For example, Edinger et al. [39] found a large significant effect (effect size [ES] = 1.73) of CBT-I on QoL among fibromyalgia patients in an RCT, while Alessi et al. [40] found a non-significant effect (ES = −0.45) of CBT-I on QoL among older veterans in an RCT. Given that different studies may have different features in their designs (e.g., using a generic QoL instrument or a sleep-specific QoL instrument; RCTs vs. uncontrolled trials; large sample size vs. small sample size; blinding), conclusions regarding the effects of CBT-I on QoL can be difficult to draw. Therefore, there is a need to comprehensively synthesize the current evidence on this topic. A systematic review and meta-analysis can provide both qualitative and quantitative evidence concerning the efficacy of CBT-I on QoL among individuals with insomnia or at risk of insomnia. Moreover, CBT-I has expanded from being delivered face-to-face to also be delivered online, as guided or un-guided self-helps programs on the internet or via smartphone applications [38,41–46]. It is unclear whether different ways of delivering CBT-I affect QoL outcomes. Consequently, there is a need to examine how CBT-I impacts QoL and if this differs among populations (including insomniacs, patients with other primary disorders, other conditions) and other factors. Moreover, given the recent popularity and increased use of online delivery of the CBT-I, alongside the advancement of technology [25], there is also a need to examine the efficacy of CBT-I on QoL outcomes and its variation over a range of factors (e.g., in-person offline and online delivery).

Aims of the present study

The primary aim of the present study was to investigate the efficacy of CBT-I in improving QoL outcomes. The secondary aims were to identify the 1) long-term effect of CBT-I on QoL through follow-ups, 2) potential sources of heterogeneity in effect of CBT-I on QoL, and 3) extent to which these factors influence QoL, also when examining offline (in-person face-to-face) CBT-I and online CBT-I separately.

Methods

Study design and registration

The present systematic review and meta-analysis was carried out utilizing the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [47]. A systematic literature search was carried out utilizing four academic databases (please see Search strategy section for details), and relevant studies were extracted and their methodological quality was assessed using the Cochrane Risk of Bias (ROB) Assessment Tool [48]. Findings were synthesized using a meta-analysis approach. The protocol was registered in the PROSPERO International Prospective Register of Systematic Reviews under (ID code: CRD42021274245 [49]).

Outcomes and sub-groups

The primary outcome of the study was QoL, including all types of QoL. Sub-groups being explored were type of participants (insomniacs, patients with other primary disorders, or other conditions), type of QoL measure (general, specific [i.e., disease specific such as epilepsy], or single item) and type of support (individual, group, or combined). Possible factors of heterogeneity that were explored included blinding, type of control group, participants' mean age, session numbers, intervention hours, country, QoL measures, and participants. Factors for QoL that were also examined were different delivery modes of CBT-I (i.e., offline [in-person face-to-face] vs. online) and study designs were applied (i.e., one-group pre- and post-treatment trials analyzed separately).

Search strategy

A comprehensive search through four academic databases of *PubMed, Web of Science, Scopus, and PsycINFO* was conducted during the first week of September, 2021. For comprehensiveness, gray literature was reviewed by hand by searching through the references of included papers. The search was performed using keywords from relevant MeSH terms. Keywords were selected based on the PICOS (Participants, Intervention, Comparison, Outcome and Study) criteria to answer the research question (where P = participants receiving CBT-I; I = CBT-I in some form; C = none or some control group; O = QoL; S = RCT or non-controlled). In the study, CBT-I was selected as the intervention and QoL was selected as the outcome as two main search components. Database search strategies use a combination of the following keyword sets within the titles, abstracts and keywords: ('cognitive behavioral therapies' OR 'cognitive therapy' OR 'cognitive psychotherapy' OR 'cognition therapy') AND ('quality of life' OR 'health related quality of life' OR 'HRQOL') AND ('disorders of initiating and maintaining sleep' OR 'DIMS' OR 'early awakening' OR 'nonorganic insomnia' OR 'primary insomnia' OR 'transient insomnia' OR 'rebound insomnia' OR 'secondary insomnia' OR 'sleep initiation dysfunction' OR 'sleeplessness' OR 'insomnia disorder' OR 'insomnia' OR 'chronic insomnia' OR 'psychophysiological insomnia'). More specifically, DIMS is the acronym of disorders (D) of initiating (I) and maintaining (M) sleep (S). To have a comprehensive search and respecting the issue that QoL might be assessed but not reported in the title or abstract, search for 'quality of life' was set within all fields of paper. The search syntax was customized based on the specific attributes of each database. Each database was reviewed from inception until the end of August 2021.

Study selection and eligibility criteria

Based on title and abstract, retrieved potential studies were scrutinized. Duplicates and irrelevant studies were removed. The full texts of potentially relevant papers were reviewed for eligibility criteria. The eligibility criteria included 1) clinical trials investigating the efficacy of CBT-I as an intervention on QoL with any kind of control group (or no control group) and 2) the study participants reported a problem with insomnia. Studies with the following conditions were excluded. Those that: 1) did not report mean (SD) score for QoL; 2) carried out an observational study; and 3) carried out a review study. No limitation was set regarding language, participant age, ethnicity, gender, or sample size. The reason for setting no limitation on sample size was to increase the generalizability of the study results and study the role of different variables in the impact of CBT-I intervention on QoL. However, small sample sizes are likely to cause bias in the meta-analysis findings. Also, different designs of clinical trials possess different features in terms of study bias. Therefore, some statistical strategies were carried out to take care of these issues. Please see Data synthesis section for details.

Quality assessment

Two members of the research team independently assessed the risk of bias using the Cochrane ROB Assessment Tool [48]. Selection bias (random sequence generation, allocation concealment), performance bias (blinding of participants and personnel), detection bias (blinding of outcome assessment), attrition bias (incomplete outcome data), reporting bias (selective reporting), and other bias (sample size estimation, complete definition of intervention sessions and outcomes for intervention and control group) were assessed using this checklist. No study was excluded based on the quality, but the impact of study quality on the pooled ES was assessed via subgroup analysis.

Data extraction and management

After screening, selecting, and evaluating the quality of selected studies, data were extracted using pre-designed *Excel* spreadsheet. Information included the first author's name, year of publication, country of the study, sample size, and mean age, measure time points, intervention description, and numerical data regarding QoL measures. The three phases of the study selection, quality assessment, and data extraction were carried out independently by two of the research team. Disagreements were resolved through discussion.

Data synthesis

Data were analyzed using STATA Software Version 14. The meta-analysis was performed using a random effect model with the DerSimonian and Laird weighted method [50]. Standardized mean difference was the selected key measure. The pooled standardized mean difference (SMD) with 95% confidence interval (CI) was reported. SMD effect size of 0.2−0.5 is considered as small effect size; 0.5−0.8 is considered as medium effect size; and greater than 0.8 is interpreted as large effect size [51]. Heterogeneity between studies was estimated using I^2 index and an $I^2 < 25\%$ is considered mild heterogeneity, between 25% and 50% is considered moderate heterogeneity, and above 50% is considered severe heterogeneity [52,53]. Subgroup and meta-regression analyses were performed to investigate potential sources of heterogeneity (e.g., intervention time of CBT-I). More specifically, different study designs (i.e., face-to-face RCT design, online RCT design, and one-group pre- and post-treatment trial) were analyzed separately in the subgroup analyses. Glass's *d* method was used to calculate the effect size for studies having a small sample size (i.e., <20 participants) with the consideration of weighting on the sample size. In addition, the effect sizes of studies with small sample sizes were investigated based on sensitivity analysis. Publication bias was assessed using the funnel plot and Begg's tests [54]. Probable publication bias was corrected using Fill and Trim method [55]. Sensitivity analysis was performed using the Jackknife method [56] to determine the small study effect of individual studies on the outcome. The Jackknife method is also known as the 'one-out method', and was used to evaluate the quality and consistency of the results. These were evaluated by removing each study individually.

Results

Study screening and selection process

The initial search in the four academic databases resulted in the retrieval of 1221 papers: *Scopus* (n = 266), *PubMed* (n = 375), *ISI Web of Knowledge* (n = 506), and *PsycINFO* (n = 74). After removing duplicate papers, a further 883 papers were screened based on title, abstract, and results sections. Finally, 206 papers appeared to be potentially eligible and their full-texts were reviewed. From this process, 24 studies met the eligibility criteria and were pooled in the meta-analysis. Fig. 1 shows the search process based on the PRISMA flowchart.

Study description

A total of 24 studies comprising 1977 participants (808 in an intervention group) from 12 countries (Canada, China, Finland, Hong Kong, Iran, Korea, Netherland, Norway, Sweden, Switzerland, UK, and USA) were included in final synthesis. The USA had the most studies (n = 8). The smallest sample size was 10, and the largest sample size was 320. The mean age of participants ranged from 14.9 to 72.1 y. Most studies were RCTs (n = 19) and others were one group pre- and post-treatment trials. Most studies were not blinded (n = 14), six studies were single-blinded, two were double-blinded, and two were assessor-blinded. CBT-I was provided in offline (face-to-face) mode in 16 studies, and eight studies used an online method using internet-based platforms to provide the interventional content. Individual intervention was provided in 12 studies, small-group intervention in four studies, large-group intervention in two studies, and a combination of individual and group intervention in the remaining six studies. In the RCTs, eight studies had active control with sleep-related education, six studies had waiting list control, and four studies had treatment as usual control group. Only one study compared CBT-I with a hypnotic drug as control group. Session numbers varied from two to 10 sessions with average of six sessions. Total interventional hours varied from 3.5 to 36 h with average of 10 h. QoL was assessed with a variety of measures, and the Short-Form 36 (SF-36) was the most frequent measure (n = 8). Time to follow-up varied from 1 mo (one study), 3 mo (three studies), 4 mo (two studies), 6 mo (six studies), and 12 mo (two studies). Table 1 provides the summary characteristics of all included studies. Also Table S1 in supplementary provide characteristics of CBT-I intervention in included studies.

Methodological quality assessment

Assessment of methodological quality of studies based on the Cochrane ROB Assessment Tool showed that most of the studies were at low risk of bias regarding random sequence generation, completely defining outcome measures and essential details of

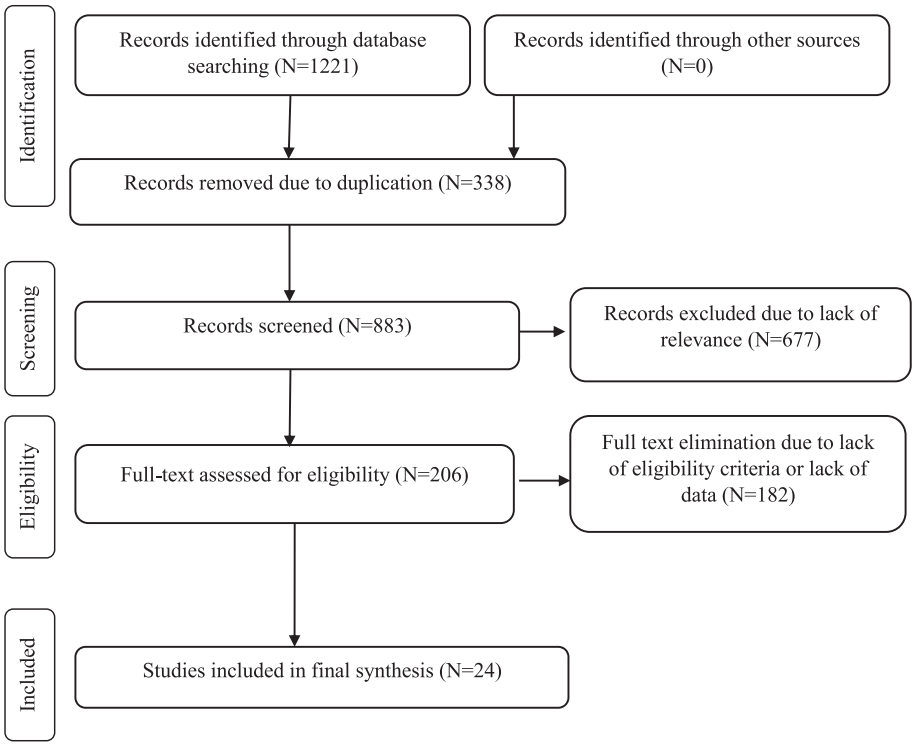

Fig. 1. PRISMA flowchart.

intervention. Almost all studies had no selective reporting or incomplete data outcome. Blinding of participants, personnel, and outcome assessor was not performed in most studies. Fig. 2 shows the representation of the quality of selected studies.

Overall outcome measure of CBT-I on QoL

The pooled estimate of SMD of QoL when all 24 studies were included was 0.47 (95% CI: 0.22–0.72; $I^2 = 84.5\%$; $tau^2 = 0.31$; $p < 0.001$) for intervention group with CBT-I compared to control (Fig. 3), which indicates a significant small to moderate effect of CBT-I on QoL. Sensitivity analysis with the Jackknife method did not show a small study effect (Fig. S1). Funnel plot (Fig. S2) and Egger's test ($p = 0.89$) ruled out the probability of publication bias. The results of subgroup analysis (Table 2) showed that the point estimate of the ES of CBT-I on QoL was the same in before/after trials (i.e., within-group effects) compared to randomized controlled trials (i.e., between-group effects). The overall point estimate of the ES of CBT-I on QoL was different based on participants groups (participants with other conditions: 0.48; patients with other primary disorders: 0.29; insomniacs: 0.59). Single item QoL measures showed highest the point estimate (ES = 0.67) vs. specific QoL measures (ES = 0.37) and general measures (ES = 0.43). However, these differences were not significant considering the overlapping 95% CI of estimated effect sizes in subgroups. Based on multivariable meta-regression (Tables 3 and 4) type of blinding, number of sessions, and participants' mean age were the most significant variables and explained 37.14% variance in effect of CBT-I on QoL.

Outcome measure based on mode of delivery and study design

Outcome measure face-to-face CBT-I on QoL in RCT studies: The pooled estimate of SMD of QoL was 0.46 (95% CI: 0.01–0.90; $I^2 = 87.5\%$; $tau^2 = 0.48$; $p < 0.001$) in favor of the face-to-face CBT-I intervention group when compared to controls in the eleven included RCT trials (Fig. 4), which indicates significant moderate effect. Sensitivity analysis with the Jackknife method did not show a small study effect (Fig. S3). Funnel plot (Fig. S4) and Egger's test ($p = 0.96$) ruled out the probability of publication bias. The results of subgroup analysis (Table 2) showed that the point estimate of the ES of offline (face-to-face) CBT-I for insomniac, patients with other primary disorders, and participants with other conditions were 0.59, 0.25, and 0.39, respectively. However, these differences were not significant. Based on multivariable meta-regression (Tables 3 and 4), type of blinding and number of sessions were the most significant variables which explained 79.92% variance in effect of CBT-I on QoL. Within this group, four studies reported results of 6-mo follow-up with pooled estimate effect of 0.35 (95% CI: −0.20 to 0.90; $I^2 = 68.9\%$; $tau^2 = 0.52$; $p = 0.02$). Also, two studies reported results of 12-mo follow-up with pooled estimate effect of 0.04 (95% CI: −0.35 to 0.43; $I^2 = 0\%$; $tau^2 = 0.46$; $p = 0.60$).

Outcome measure online CBT-I on QoL in RCT studies: The pooled estimate of SMD of QoL was 0.47 (95% CI: 0.02–0.92; $I^2 = 88.3\%$; $tau^2 = 0.36$; $p = 0.04$) in favor of the intervention group in the eight RCT trials comparing online CBT-I to controls (Fig. 5). Sensitivity analysis with the Jackknife method did not show a small study effect (Fig. S5). Funnel plot (Fig. S6) and Egger's test ($p = 0.87$) ruled out the probability of publication bias. The results of subgroup analysis (Table 2) showed that the point estimate of the ES of online CBT-I was 0.73, 0.58 and 0.16 respectively for insomniac participants, participants with other conditions, and patients with other primary disorders regarding the improved QoL. Also, the greatest effect of the intervention was observed when the QoL was measured using a single-item compared to generic or specific QoL instrument (0.67 vs. 0.37, and 0.31). However, these differences were not statistically significant. Based on multivariable meta-regression (Tables 3 and 4) type of blinding and participants' mean age were the most significant variables which explained 34.69% variance in effect of online CBT-I on QoL.

Table 1
Summary characteristics of included studies.

First author	Year	Country	Design	Blinding	Participants	Participants groups	Insomnia definition	Sample size	Mean age	QoL measure	Type of QoL measure	Quality score
Palermo [69]	2017	USA	One group trial	Not blinded	Adolescents with physical and psychiatric comorbidities	Patients with other primary disorders	Difficulty initiating or maintaining sleep three or more nights during the past month and significant daytime impairment in at least one domain	40	14.93	HRQOL	General measure	4
Birling [70]	2018	China	One group trial	Not blinded	Insomniacs	Insomniacs	Insomnia disorder based on DSM-5	72	50	SF36	General measure	5
Jansson-Fröjmark [71]	2020	Sweden	One group trial	Not blinded	Patients with co-morbid generalized anxiety disorder	Patients with other primary disorders	Insomnia disorder based on DSM-5	59	46.7	Brunnsviken Brief Quality of Life	General measure	7
Järnefelt [72]	2012	Finland	One group trial	Not blinded	Chronic insomniacs	Insomniacs	Individuals who had consulted Occupational Health Services personnel because of insomnia, or to whom OHS physicians had prescribed sleep promoting medication	33	44.4	SF36	General measure	5
Quesnel [73]	2003	Canada	One group trial	Not blinded	Women treated for nonmetastatic breast cancer	Patients with other primary disorders	Diagnostic criteria for a chronic insomnia disorder, as defined by the combined criteria of the International Classification of Sleep Disorders (American Sleep Disorders Association, 1997) and the 4th edition of the Diagnostic and Statistical Manual of Mental Disorders	10	54.3	QLQ-C30	Specific measure	5
Sandlund [74]	2018	Sweden	RCT	Single blind	Primary care patients who meet the criteria for insomnia disorder	Insomniacs	Patients with insomnia were recruited to the study when they consulted their primary health care physician, who made a preliminary assessment of the patient's insomnia symptoms and health status	165	55	SF36	General measure	7
Omvik [75]	2008	Norway	RCT	Double blind	Older patients suffering from chronic insomnia	Insomniacs	DSM-IV diagnosis of primary insomnia for a minimum of 6 mo	46	59.74	SF36	General measure	8
Wong_Sample11 [38]	2020	Hong Kong	RCT	Assessor blind	Insomniacs	Insomniacs	DSM-5 criteria for insomnia disorder	210	38.2	SF6D	General measure	8
Edinger [39]	2005	UK	RCT	Single blind	Fibromyalgia patients	Patients with other primary disorders	Structured interview criteria for insomnia (Sleep Disorders according to DSM-III-R)	47	48.6	SF36	General measure	9
Ham [76]	2020	Korea	RCT	Single blind	Middle-aged women with insomnia	Insomniacs	Insomnia Severity Index [ISI] $\geq$ 10	58	53.83	Menopausal quality of life	Specific measure	8
Taylor [36]	2014	USA	RCT	Not blinded	College Students	Other conditions	Insomnia disorder based on DSM-5	34	19.71	Q-LES-QSF	Specific measure	6
Kalmbach [77]	2019	USA	RCT	Single blind	Postmenopausal women with insomnia	Other conditions	Insomnia disorder based on DSM-5	50	56.44	SF36	General measure	5
Dirksen [78]	2007	USA	RCT	Not blinded	Breast cancer survivors	Patients with other primary disorders	Women were included if they were concerned about their sleep, reported impaired daytime functioning and disturbed sleep including: (a) sleep onset latency and/or wake	81	57.2	FACT-B	General measure	6

							after sleep onset of 30 min or more on three nights per week for 2 wk (corroborated through the daily sleep diaries) and (b) a disturbed sleep complaint of at least 3 mo					
Savard [37]	2005	Canada	RCT	Single blind	Breast cancer patients	Patients with other primary disorders	Combined criteria of the International Classification of Sleep Disorders and of the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition	57	54.81	QLQ-C33	Specific measure	6
Harvey [79]	2015	USA	RCT	Single blind	Bipolar disorder I participants	Patients with other primary disorders	General insomnia disorder, as defined by the International Classification of Sleep Disorders (2nd ed.; American Academy of Sleep Medicine, 2005), and DSM—IV—TR criteria for primary insomnia	58	37.7	Q-LES-QSF	Specific measure	6
Taylor [80]	2015	USA	RCT	Not blinded	Persistent insomnia and hypnotic dependency	Insomniacs	Interview	23	50.1	SF36	General measure	5
Wong_Sample2 [38]	2020	Hong Kong	RCT	Assessor blind	Insomniacs	Insomniacs	DSM-5 criteria for insomnia disorder	210	36.9	SF6D	General measure	6
Thorndike [45]	2013	USA	RCT	Not blinded	Adults with comorbid psychological and fatigue symptoms	Patients with other primary disorders	DSM-4R criteria for insomnia disorder	45	44.68	SF12	General measure	7
Krieger [43]	2019	Switzerland	RCT	Not blinded	Insomniacs	Insomniacs	Acute or chronic insomnia according to the International Classification of Sleep Disorders (ICSD-3)	104	42.17	QoL VAS	Single item measure	7
Ahorsu [41]	2020	Iran	RCT	Double blind	Patients with epilepsy	Patients with other primary disorders	Moderate or severe insomnia as indicated by a score of 15 or higher on the Insomnia Severity Index (ISI)	320	38.37	Quality of Life in Epilepsy-31 Inventory	Specific measure	4
van Straten [46]	2013	Netherland	RCT	Not blinded	General population with insomnia	Insomniacs	Insomnia disorder based on DSM-IV	118	49.4	QoL VAS	Single item measure	4
Kim [42]	2017	Korea	RCT	Not blinded	Nurses	Other conditions	Subjectively complaining of insomnia, waking up after sleep for more than 30 min due to irregular sleep, and optimal sleep time. Those whose sleep efficiency is less than 80%	55	27.2	WHOQOL-BREF	General measure	5
Ritterband [44]	2012	USA	RCT	Not blinded	Cancer survivors	Patients with other primary disorders	DSM-IV-TR definition of insomnia	29	53.7	SF12	General measure	8
Belleville [81]	2007	Canada	RCT	Not blinded	Chronic users of hypnotics	Insomniacs	Difficulty with initiating or maintaining sleep (i.e., sleep-onset latency or wake after sleep onset _ 30 min or involuntary final awakening after less than 6 h of sleep) more than three nights a week for at least 6 mo	53	55.3	SF36	General measure	7

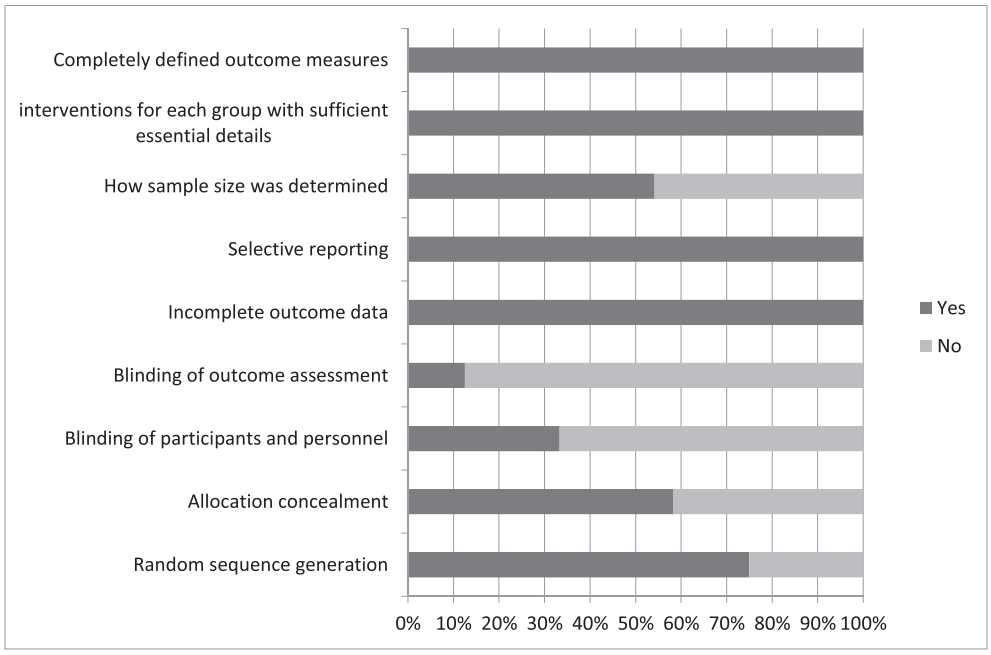

Fig. 2. Quality assessment of included studies.

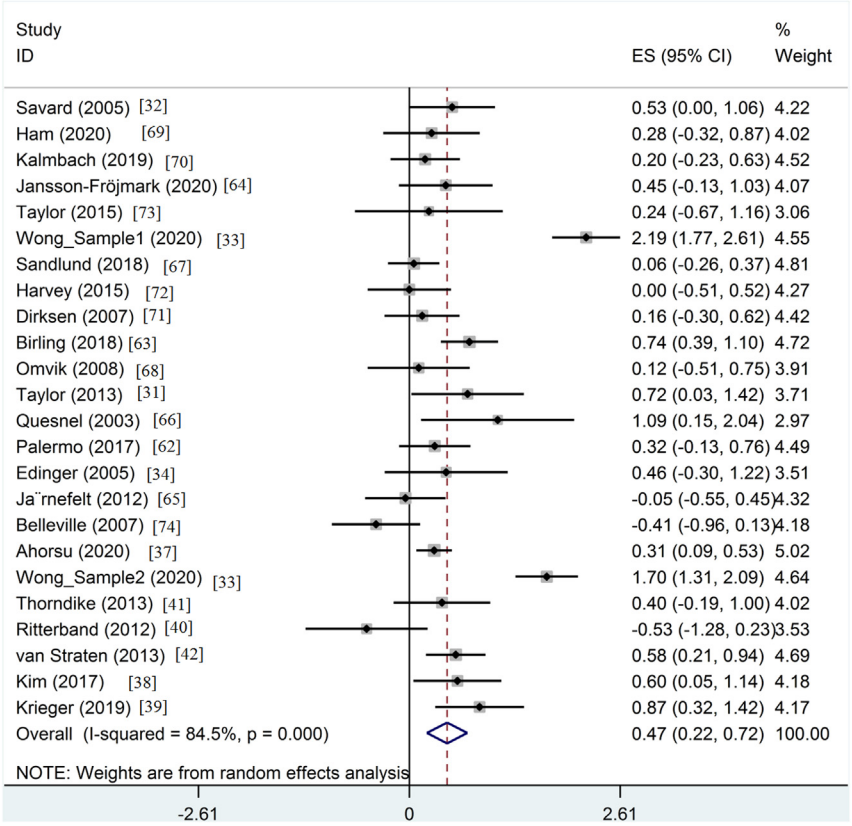

Fig. 3. Forest Plot displaying the overall estimated pooled effect size of CBT-I on QoL.

Within this group, two studies reported results of 3-mo follow-up with pooled estimate effect of 0.11 (95% CI: −0.37 to 0.59; $I^2 = 52.3\%$; $tau^2 = 0.45$; $p = 0.07$). Also, two studies reported results of 6-mo follow-up with pooled estimate effect of 0.21 (95% CI: −0.30; 0.72 $I^2 = 35.3$; $tau^2 = 0.54$; $p = 0.07$).

Outcome measure online CBT-I on QoL in one-group pre- and post-treatment trial: All of the five non-RCT trials were delivered as offline (face-to-face) CBT-I. The pooled estimate of SMD of QoL was 0.46 (95% CI: 0.12–0.80; $I^2 = 52.9\%$; $tau^2 = 0.07$; $p = 0.08$) after intervention with CBT-I compared to baseline (Fig. 6), which

Table 2
Results of subgroup analysis.

Variable		Overall effect of CBT on QoL					Design specific effect of CBT on QoL								
							RCTs with face to face CBT-I					RCTs with online CBT-I			
		No. studies	Pooled SMD	95% CI	I^2 (%)	tau^2	No. studies	Pooled SMD	95% CI	I^2 (%)	tau^2	No. studies	Pooled SMD	95% CI	I^2 (%)	tau^2
Design	RCTs	19	0.46	0.16; 0.77	87.1	0.38										
	One group before/after trials	5	0.46	0.12; 0.79	53.5	0.08										
Participants	Other conditions	4	0.48	0.22; 0.72	0	0	2	0.39	−0.11; 0.88	37.1	0.05	2	0.58	0.28; 0.89	0	0
	Patients with other primary disorders	10	0.29	0.13; 0.46	12.1	0.009	4	0.25	−0.02; 0.52	0	0	3	0.16	−0.28; 0.59	56.3	0.09
	Insomniac patients	10	0.59	0.04; 1.14	92.6	0.71	5	0.59	−0.37; 1.55	94.3	1.11	3	0.73	−0.51; 1.97	94.8	1.14
Blinding	Not blinded	14	0.37	0.15; 0.59	55.9	0.09	3	0.32	−0.04; 0.67	0	0	6	0.29	−0.14; 0.71	72.8	0.20
	Blinded	10	0.59	0.11; 1.07	92.2	0.54	8	0.48	−0.09; 1.06	90.9	0.62	2	0.99	−0.37; 2.36	97.3	0.94
QoL measure	Specific measure	6	0.36	0.15; 0.57	15	0.01	4	0.35	0.04; 0.65	10.8	0.01	1	0.31	0.09; 0.53	–	–
	General measure	16	0.43	0.06; 0.81	89.1	0.50	7	0.50	−0.17; 1.17	92	0.72	5	0.37	−0.51; 1.26	92.4	0.93
	Single item	2	0.67	0.36; 0.97	0	0						2	0.67	0.02; 0.92	0	0
Mode of CBT-I provision	Face to face CBT-i	Individual					6	0.24	−0.01; 0.48	0	0					
		Group					3	0.92	−0.43; 2.28	96.9	1.38					
		Combined					2	0.20	−0.16; 0.57	0	0					
	Online CBT-I	Guided										3	0.35	−0.34; 1.04	83.6	0.31
		Unguided										5	0.53	−0.15; 1.20	91.4	0.52
Overall estimated SMD		24	0.47	0.22; 0.72	84.5	0.31	11	0.46	0.01 ; 0.90	87.5	0.48	8	0.472	0.02; 0.92	88.3	0.36

indicates the significant reductions of QoL after CBT-I. Sensitivity analysis with the Jackknife method did not show a small study effect (Fig. S7). Funnel plot (Fig. S8) and Egger's test ($p = 0.06$) ruled out probability of publication bias. None of the examined variables in subgroup analysis or meta-regression (Table 3) were found to be a potential source of heterogeneity.

Discussion

The present systematic review and meta-analysis showed that CBT-I can improve QoL outcomes significantly (overall SMD = 0.47, offline [face-to-face] CBT-I SMD = 0.46, online CBT-I SMD = 0.47) when compared to different control groups in the RCTs. The probability of a small study effect and publication bias was ruled out in overall and design-specific sub-group analysis. Moreover, a high level of heterogeneity was observed in both face-to-face online CBT-I as compared with one-group pre- and post-treatment trials. This higher level of heterogeneity might be due to applying single-item QoL-measures, which appears to inflate results and cause heterogeneity. Moreover, most studies synthesized in the present systematic review and meta-analysis did not utilize blinding to control placebo effects. Therefore, it is possible that the findings of CBT-I are likely to be overestimated. However, when the present meta-analysis used meta-regression to explore the blinding effect, the findings showed that studies with blinding had significantly stronger effects of CBT-I on QoL than did those without blinding (coefficient = 0.31; SE = 0.13; $p = 0.01$). This finding somewhat indicates that placebo effects might not be a significant confounder that compromise the internal validity of these analyzed studies.

Long-term efficacy of CBT-I was shown in both offline (face-to-face) CBT-I and online CBT-I, although not significantly. Long-terms efficacy of CBT has been demonstrated for different psychological problems (e.g., anxiety and depression) [57]. Some evidence has also shown that CBT-I has long-term efficacy on QoL of up to 12 mo [19]. The results of the present study indicated non-significant long-term effects on QoL (although the effects were positive). One possible reason for the non-significant findings is the lack of statistical power. There were only four studies assessing 6-mo effects of face-to-face CBT-I on QoL, two studies assessing 12-mo effects of offline (face-to-face) CBT-I on QoL, and two studies assessing 6-mo effects of online CBT-I on QoL. Moreover, different types of QoL (e.g., general QoL and sleep-related QoL) were used across these studies. Consequently, more evidence testing the long-term efficacy of CBT-I on QoL is needed testing the different types of QoL.

An important finding from the present systematic review and meta-analysis is that having a major comorbid disorder (e.g., cancer, psychiatric symptoms) may reduce the effects of CBT-I on QoL among individuals with insomnia. Indeed, individuals with chronic insomnia gained a moderate effect size of OoL improvement after receiving CBT-I (SMD = 0.59; 95% CI = 0.04, 1.14), while individuals with a major disorder in addition to insomnia only had small effect (SMD = 0.29; 95% CI = 0.13, 0.46). CBT-I posits some important components (e.g., relaxation training) [58] that could be directly beneficial for individuals' QoL [59]. The CBT-I also has other components (e.g., education, behavioral strategies, and cognitive therapy) that might be indirectly beneficial for individuals' QoL through the improvement of insomnia and sleep hygiene [25]. However, when individuals have other diseases in addition to insomnia, the benefits of CBT-I on their QoL may be reduced because these individuals may have their QoL impaired not only by insomnia but also by the other condition. For example, cancer patients may have treatment side effects and insomnia to impair their QoL [60] and the side effects cannot be relieved using

Table 3
Results of uni-variable meta-regression.

Variable	Overall effect of CBT on QoL						Design specific effect of CBT on QoL																	
							RCTs with face to face CBT-I[a]						RCTs with online CBT-I						One group trials[b]					
	No. of studies	Coeff.	S.E.	*p*	I^2 res. (%)	Adj. R^2 (%)	*Tau*^{2}	No. of studies	Coeff.	S.E.	*p*	I^2 res. (%)	Adj. R^2 (%)	*Tau*^{2}	No. of studies	Coeff.	S.E.	*p*	I^2 res. (%)	Adj. R^2 (%)	*Tau*^{2}	No. of studies	Coeff.	S.E.	*p*	I^2 res. (%)	Adj. R^2 (%)	*Tau*^{2}
Blinding	24	0.33	0.11	0.01	79.91	33.38	0.20	11	0.48	0.18	0.03	72.8	46.51	0.19	8	0.34	0.19	0.12	87.24	27.85	0.30							
Type of control group	24	0.02	0.092	0.83	85.01	−4.67	0.31	11	0.08	0.21	0.70	88.34	−9.32	0.40	8	0.004	0.23	0.98	89.90	−19.46	0.50							
participants mean age	24	−0.02	0.01	0.14	83.73	7.09	0.28	11	0.13	0.28	0.66	88.15	−8.01	0.39	8	−0.05	0.02	0.10	87.30	29.93	0.29	5	0.01	0.01	0.52	57.93	−42.9	0.12
Sessions no	24	−0.13	0.07	0.07	80.21	16.22	0.25	11	−0.31	0.08	0.003	56.46	72.19	0.10	8	−0.11	0.25	0.69	87.98	−14.60	0.48	5	0.03	0.10	0.80	63.24	−69.22	0.12
Total intervention hours	16	−0.01	0.02	0.65	87.69	−5.29	0.41	7	−4.50	0.08	1	92.59	−21.10	0.64	5	−0.01	0.03	0.74	89.65	−30.80	0.72	4	−0.02	0.06	0.77	52.94	−300	0.12
Country	24	0.01	0.04	0.85	85.12	−5.42	0.31	11	0.04	0.07	0.55	87.82	−6.25	0.38	8	−0.02	0.08	0.77	87.77	−15.91	0.49	5	−0.003	0.06	0.96	63.33	−59.77	0.11
QoL measure	24	0.02	0.04	0.58	85.15	−4.41	0.31	11	−0.006	0.05	0.90	88.69	−11.66	0.40	8	0.08	0.11	0.48	89.92	−9.22	0.46	5	0.06	0.06	0.38	59.34	−21.11	0.08
Participants	24	0.10	0.17	0.59	84.51	−3	0.31	11	0.13	0.28	0.66	88.15	−8.01	0.39	8	0.12	0.34	0.73	89.16	−16.68	0.49	5	−0.15	0.40	0.73	64.69	−80.91	0.13
ROB scores	24	0.01	0.09	0.90	84.78	−5	0.31	11	0.16	0.16	0.34	86.25	3.13	0.35	8	−0.14	0.18	0.47	89.93	−10.29	0.46	5	0.03	0.21	0.91	64.38	−65.57	0.12

[a] I^2 and Tau^2 were 0 in this group for all variables.
[b] All studies were not blinded, provided individual intervention with self-control group.

CBT-I. In other words, cancer patients' QoL may get improved only for the insomnia problems but not for the side effect problems.

Most QoL measures used in the analyzed studies in the present systematic review and meta-analysis were general (16 studies), often health-related QoL, with only six being disease-specific QoL instruments. Moreover, none of the six disease-specific QoL instruments were sleep-related. No significant effects caused by type of QoL-measure were found. The largest effects of CBT-I on QoL were found in general health-related assessment using single-item QoL instruments. However, only two trials used this type of measure. Therefore, great caution in the interpretation of the findings is called for. Future studies should further investigate if single-item measures systematically provide larger effects and if this might be due to their more general and brief nature making them more subjective and possibly more strongly influenced by changes in the primary symptom measures.

A somewhat more robust finding, although still not significant, was that disease-specific QoL instruments showed larger effects than general health-related measures (besides the single-item measures). Their focus on the improvement of disease symptoms (e.g., seizure for individuals with epilepsy) might make them more sensitive to change, although the effects of CBT-I on disease-specific QoL instruments might not be direct but rather mediated by better sleep, which in turn improves the primary health concern and the QoL related to it. Additionally, very few of the included studies coded as using a general QoL measure assessed a concept of QoL that went beyond general health. Therefore, the multidimensional aspect in the QoL [27,28] was not and could not be fully investigated in the present systematic review and meta-analysis. Finally, most studies included in the present meta-analysis for synthesis used a generic QoL instrument or a disease-specific QoL instrument not relevant to sleep. Therefore, whether CBT-I has specific effects on sleep-related QoL does not have sufficient evidence to be concluded using the present meta-analysis results, although the effects are very likely to exist. Future studies using a specific measure assessing sleep-related QoL (e.g., Glasgow Sleep Impact Index [30]) are needed to answer this research question.

Given that insomnia is found to be an important factor contributing poor QoL [20], the improvement in insomnia or insomnia symptoms is likely to elevate the QoL [61–64], although this association was not evaluated in the present study. Moreover, prior evidence shows that CBT-I can effectively decrease other stressors (e.g., depression) that jeopardize individuals' QoL [21–25]. Therefore, the effects of CBT-I on QoL could possibly be explained by the improvement of CBT-I on psychological and physical health. More specifically, individuals with insomnia are likely to have better physical fitness, cognitive functions, and energy after they improve their sleep [11]. Such improvements of physical and psychological health may subsequently elevate the QoL for individuals with insomnia [25]. Consequently, the effects of CBT-I on QoL as synthesized in the present systematic review and meta-analysis could in part be explained by the effects on mental and physical health.

Some studies found that online self-help CBT-I (e.g., using the internet or smartphone app) [42,43,46] can increase QoL, and the SMD was very similar to offline CBT-I, but the heterogeneity was larger and the effects non-significant. Although the development of online and other forms of self-help CBT-I is mature with solid evidence on insomnia symptoms [26,65–68], its effects on QoL are currently difficult to determine given that only few studies have used QoL as an outcome (only eight studies were identified in the literature) and that the effect seems to be rather small also for offline CBT-I. In addition to the low statistical power, the diversity of delivery methods used in the online CBT-I, where there is a

Table 4
Results of multivariable[a] meta-regression.

Overall effect of CBT on QoL				RCTs with face-to-face CBT-I				RCTs with online CBT-I			
Variables	Coefficient	S.E.	*p*	Variables	Coefficient	S.E.	*p*	Variables	Coefficient	S.E.	*p*
Blinding	0.31	0.13	0.02	Blinding	0.25	0.17	0.18	Blinding	0.24	0.20	0.28
Sessions no	−0.02	0.08	0.84	Sessions no	−0.24	0.09	0.02	Participants mean age	−0.03	0.03	0.24
Participants mean age	−0.02	0.01	0.13								
Between-study variance (tau^2)	0.19			Between-study variance (tau^2)	0.72			Between-study variance (tau^2)	0.27		
% residual variation due to heterogeneity (I^2 residual)	79.16			% residual variation due to heterogeneity (I^2 residual)	48.22			% residual variation due to heterogeneity (I^2 residual)	88.44		
Proportion of between-study variance explained (Adjusted R^2)	37.14			Proportion of between-study variance explained (Adjusted R^2)	79.92			Proportion of between-study variance explained (Adjusted R^2)	34.69		

[a] Variable with $p < 0.20$ were selected to enter in multi-variable model.

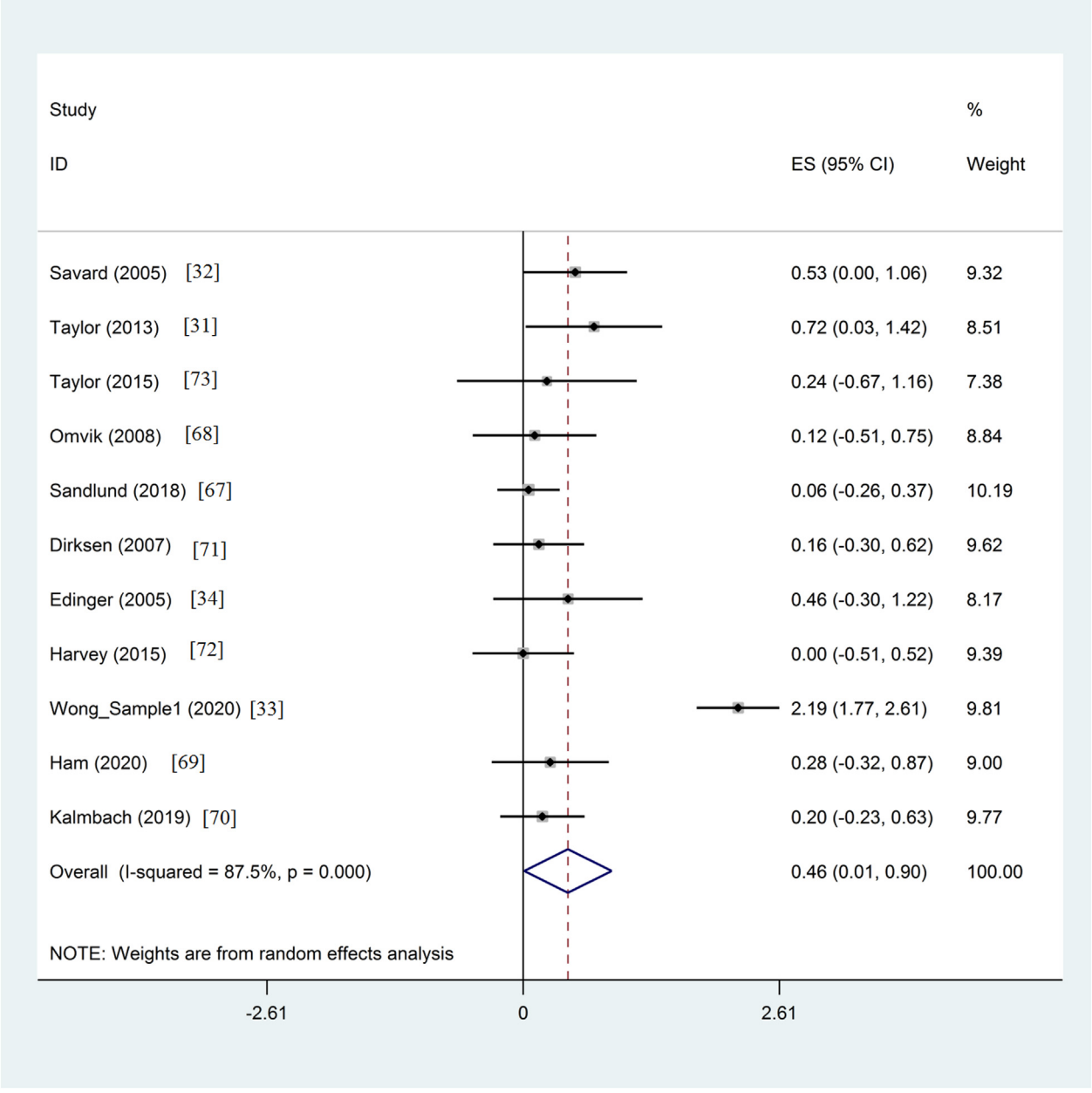

Fig. 4. Forest Plot displaying the estimated pooled effect size of CBT-I on QoL among RCT studies with face-to-face CBT-I.

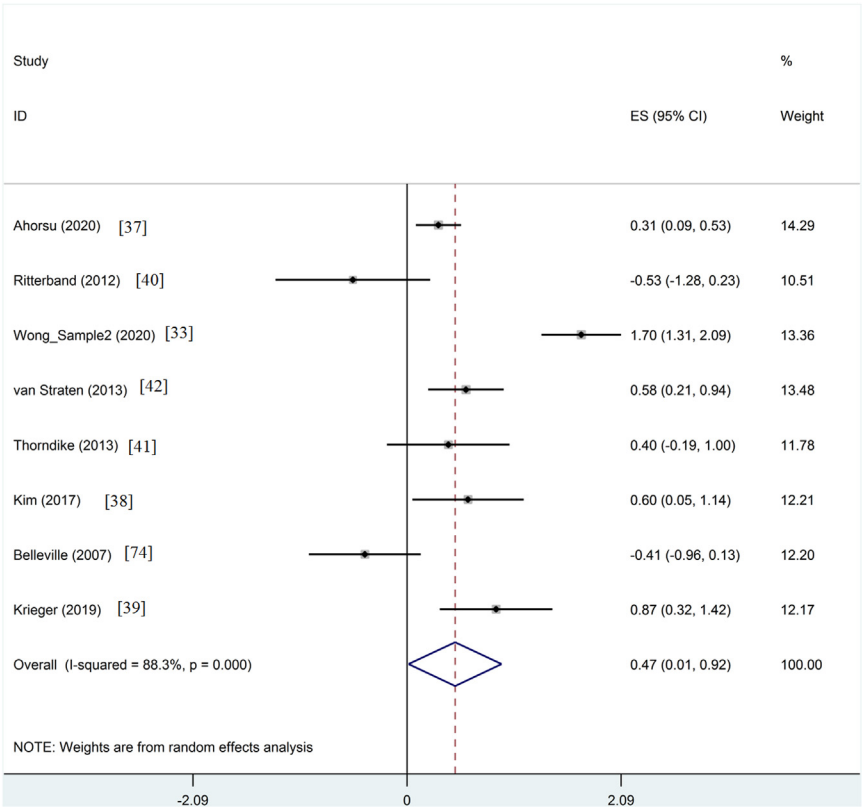

Fig. 5. Forest Plot displaying the estimated pooled effect size of CBT-I on QoL among RCT studies with online CBT-I.

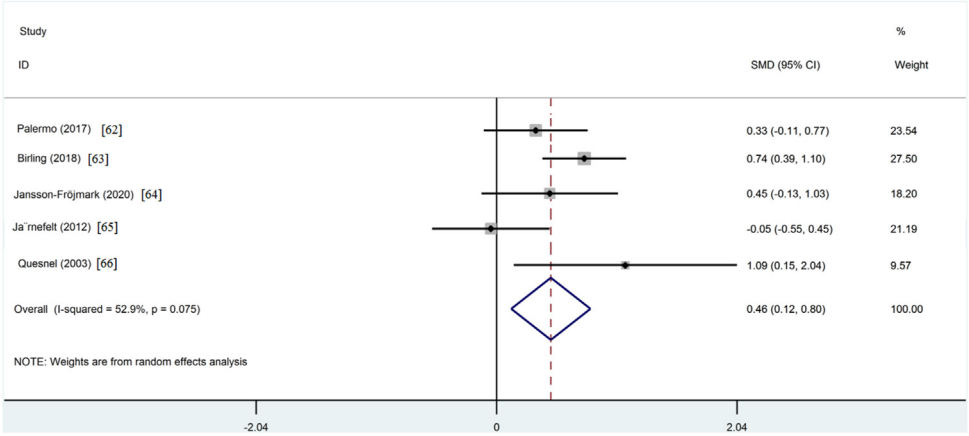

Fig. 6. Forest Plot displaying the estimated pooled effect size of CBT-I on QoL among one group trial studies.

tendency for guided online CBT-I to be superior to unguided, may also contribute to the heterogeneity of effects on QoL. Consequently, the effects of online CBT-I might be diluted across these few studies examining its effects on QoL.

Limitations

The present systematic review and meta-analysis has a number of limitations. First, the format (e.g., type of delivery, support, length, and duration) of the CBT-I was diverse among the studies evaluated. Therefore, it is unclear whether the diversity of the CBT-I contributes to different findings regarding the effectiveness of QoL. Although the present systematic review and meta-analysis separated out a major diverse feature in the CBT-I (i.e., offline [face-to-face] mode vs. online mode), other variations of the CBT-I (e.g., telephone-based CBT-I and shortened CBT-I) were not taken into account. Also, both offline and online CBT-I can take many forms of varying quality. However, given that stratifying all the variations in CBT-I would have resulted in small numbers of studies for meta-analysis, the present study chose not to control this confounder. Second, the QoL instruments were assessed using self-reports. Therefore, the biases

caused by self-reports such as social desirability bias cannot be controlled for. However, given that the QoL instruments used in the analyzed studies were all psychometrically sound, this limitation is unlikely to be serious. Third, the effect of CBT-I synthesized in the present systematic review and meta-analysis was low (between group SMD = 0.20–0.22; one-group design SMD = 0.46). This indicates that the risk of being underpowered was quite high in the present study. Therefore, further studies assessing QoL are needed.

Conclusion

CBT-I has previously been shown to be an effective intervention for insomnia, and the current systematic review indicates a potential but small effect on QoL. The results are primarily generalizable to general (instead of disease-specific) health-related QoL, because this was the most common type of QoL assessed in the studies. Effects of online CBT-I on QoL were found to be non-significant, although this could be related to low-power and heterogeneity. Similarly, more statistical power is needed to examine CBT-I effects on different types of QoL. Therefore, additional studies are needed to investigate the effects of offline (in-person face-to-face) and online CBT-I on QoL, and researchers are encouraged to include QoL as an outcome measure in future trials.

Practice points

1) Insomnia disorder (or insomnia) is associated with low level of quality of life (QoL).
2) The effects of face-to-face cognitive behavioral therapy for insomnia (CBT-I) on QoL improvement are supported but not strong.
3) The effects of online CBT-I on QoL improvement are not fully supported. More evidence is needed to establish its long-term efficacy."

Research agenda

1) Using randomized controlled trial (RCT) designs and/or one-group pre- and post-treatment trials to assess the causality between cognitive behavioral therapy for insomnia (CBT-I) and quality of life (QoL) can provide healthcare providers direction in treating individuals with sleep problems to improve their QoL.
2) Evidence of CBT-I on sleep-related QoL is insufficient given that most studies included in the present meta-analysis assessed QoL using generic measures of QoL. Therefore, additional evidence is needed to examine whether CBT-I improves sleep-related QoL using specific instruments (e.g., Glasgow Sleep Impact Index).
3) Studies may want to explore potential mechanisms that explain the effects of CBT-I on QoL improvement found in the present systematic review and meta-analysis. For example, whether the QoL improvement is mediated by the reduction of insomnia symptoms or by the improvement of psychological health.

Conflicts of interest

The authors do not have any conflicts of interest to disclose.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.smrv.2022.101646.

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