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ORIGINAL ARTICLE

Efficacy of Remote Cognitive Behavioural Therapy for Insomnia in Improving Health Status of Patients with Insomnia Symptoms: A Meta-analysis

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Abstract

Background Insomnia is highly prevalent and cognitive behavioural therapy is the first-line treatment for it. This study aimed to assess the efficacy of remote cognitive behavioural therapy for insomnia, specifically, treatment fully delivered through the internet, mobile phones and telephones for sleep and other health outcomes in adults diagnosed with insomnia or reporting insomnia symptoms. This study also aimed to evaluate the effect of various intervention components as subgroup variables to explain the efficacy of remote cognitive behavioural therapy on health outcomes.

Methods Randomised controlled trial studies were obtained from five electronic databases. The PEDro scale was used to assess the quality of the studies. A random effect model was used to assess the mean difference, standardised mean difference and standard deviation of the outcome variables. Heterogeneity among the study articles was assessed using I^2 and Q tests. Egger regression analysis was used to assess publication bias.

Results Remote cognitive behavioural therapy for insomnia had significant and positive effects on improving sleep outcomes, depression, anxiety, fatigue and mental health compared with the control conditions. Its effect on physical health was not significant. The effect of the therapy was enhanced when the total length of intervention was shorter than 6 weeks, delivered via the internet and did not include therapist support.

Conclusion Remote cognitive behavioural therapy for insomnia is effective in improving sleep quality, depression, anxiety, fatigue and mental health in insomnia patients.

Keywords Insomnia · Cognitive behavioural therapy · CBT-I · Sleep quality · Sleep efficiency

Introduction

Insomnia is a common type of sleep disorder that is characterised by difficulty falling and remaining asleep, which leads to physical and mental distress during the daytime (Roth, 2007). There is a high prevalence of insomnia across the world. Studies have reported that the overall prevalence of insomnia symptoms among adults in America is over 20% (Dopheide, 2020; Ohayon, 2002) of the total population. A chronic condition of insomnia can lead to heavy burdens on quality of life and the economic condition of an individual, family and society (Daley et al., 2009; Kyle et al., 2010). In addition, insomnia can be a risk factor for other chronic and mental health problems, including cardiovascular diseases, diabetes, anxiety and depression (Guo et al., 2013; Medic et al., 2017).

Given the high prevalence and disease burdens, treatment of insomnia is imperative. Traditional pharmacological treatment for insomnia has risks of providing negative side effects. Further, the long-term effects are limited (Buscemi et al., 2007). In addition to pharmacological treatment, non-pharmacological treatment has been developed and recommended, aiming to provide fewer side effects as an adjunctive method of pharmacological treatment. Cognitive therapy, or cognitive restructuring, helps patients to identify

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negative understandings and beliefs about sleep and replace them with positive thoughts (Beck & Weishaar, 1989). Behavioural therapy, mainly sleep restriction and stimulus control, for treating insomnia focuses on developing a proper sleep schedule and using the bed only for sleep (Banks & Dinges, 2007; Bootzin et al., 1991). As a part of the non-pharmacological approach, sleep hygiene education involves teaching patients to create a proper bedroom environment and develop daily habits that promote better sleep (Hale & Marshall, 2019; Riemann, 2018). A well-developed cognitive behavioural therapy for insomnia (CBT-I) plan usually contains multiple components, such as a cognitive therapy component, behavioural therapy component, sleep hygiene and other components. The aim of CBT-I is to identify and change the sustaining factors of insomnia, including problematic thoughts, feelings and sleep behaviours.

The traditional way of delivering CBT-I is through face-to-face consultation sessions between therapists and patients; however, limitations still exist for face-to-face delivery. The concept of telemedicine, which refers to the delivery of treatment across a distance, has been developed since last century (Wootton, 2001). Adapting telemedicine concepts, remote CBT-I has been developed to be fully delivered through the internet, telephones and mobile phone applications (Salazar de Pablo et al., 2023). Studies have shown that remote CBT-I has a higher level of cost and clinical effectiveness compared with face-to-face treatments, especially for patients in rural areas because they can receive treatments at home without travelling to medical facilities (Hjelm, 2005; Wootton et al., 2017). In addition, remote CBT-I can be delivered using a minimum level of support from real therapists, which reduces the cost of treatment and is more scalable for patients (Fairburn & Patel, 2017; Karyotaki et al., 2017).

Although CBT-I was recommended as the first-line treatment for insomnia by the American College of Physicians (Qaseem et al., 2016), the actual dissemination of CBT-I remains challenging given the high cost of distribution and lack of professional therapists (Muench et al., 2022). Previously published meta-analysis studies have concluded that CBT-I has a significant effect in treating insomnia (Seyffert et al., 2016; Straten et al., 2018; Trauer et al., 2015; Zachariae et al., 2016; Zweerde et al., 2019a). Recent meta-analysis studies (Gao et al., 2022; Hasan et al., 2022; Simon et al., 2023) have mentioned that remote CBT-I has significant effects on improving sleep in insomnia patients. However, these studies mainly focused on the effect of CBT-I on sleep outcomes. Patients who had insomnia were frequently reported as experiencing depression, anxiety and daytime fatigue problems, including a decreased quality of life, which were also important factors when evaluating the overall health of these patients. Other studies (Alimoradi et al., 2022; Cunningham & Shapiro, 2018; Lee et al., 2023) have concluded that remote CBT-I has positive effects on depression, anxiety and quality of life; however, the effects of the detailed intervention design and various CBT-I components were not well explained.

To address the research gaps, this study aimed to provide a comprehensive overview of the efficacy of remote CBT-I on not only sleep outcomes but also co-existing depression and anxiety symptoms, daytime fatigue and quality of life-related physical and mental health in patients who have been diagnosed with insomnia disorder or are reporting insomnia symptoms. Subgroup analysis was conducted to assess the effect of remote CBT-I characteristics and components on the overall impact of remote CBT-I treatment. The results of this study will contribute to the theoretical understanding of remote CBT-I in treating insomnia and assist the development of proper treatment plans in clinical conditions, which may help to disseminate remote CBT-I.

Methods

The procedure of this study was developed using the preferred reporting items for systematic reviews and meta-analysis (PRISMA) guidelines (Liberati et al., 2009). This study was registered at the international prospective register of systematic reviews (PROSPERO) and the registration ID is CRD42020200091. The research protocol can be found at the following website: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42020200091.

Database Search

A whole database search and study selection process was completed by two researchers independently. A third researcher was consulted in cases of disagreement until consensus was reached. Relevant studies were searched for in five electronic databases: PubMed, Scopus, EMBASE, Cochrane Library and PsycINFO. Grey literature was acquired from ProQuest Central: Dissertations and Thesis. A Boolean approach was used to search for the following keywords in titles and abstracts: 'insomnia' OR 'sleep' AND 'remote CBT' OR 'telehealth' AND 'cognitive behavioural therapy' OR 'CBT' AND 'internet' OR 'telephone' OR 'mobile phone' AND 'randomised controlled trial' OR 'randomised controlled trial' OR 'RCT'. The search results from the five defined databases were exported into EndNote X9 software, in which duplicates across the databases were removed. The titles and abstracts of the articles were then examined, and articles focusing on remote CBT and insomnia were excluded from the study. The researchers then conducted a further review of the full text of the articles and screened the eligible articles for data analysis in accordance with the designed inclusion and exclusion criteria.

Study Selection

The following inclusion and exclusion criteria were developed according to the population, intervention, control and outcomes (PICO) approach (Leonardo, 2018).

Inclusion Criteria

P: The target population in the studies were over 18 years in age and had been diagnosed with insomnia (regardless of disease severity) according to valid definitions, guidelines or surveys (Association, 2013; Buysse et al., 1989; Insomnia, 1993; Sateia, 2014). Articles that reported the recruitment of subjects using self-reported insomnia symptoms without specific diagnostic criteria were also included.

I: The intervention described in the articles included at least one behavioural component (e.g. sleep restriction, stimulus control) and one cognitive component (e.g. cognitive restructure) and at least four intervention sessions. The number of other components in the intervention plan was not limited. The intervention was remotely delivered via telephone, internet or mobile phone applications.

C: Participants in the control groups received normal care for insomnia, including basic sleep education and pharmacological intervention (Riemann et al., 2017), or were put on a waitlist and received intervention later. Participants in the control groups could also receive face-to-face CBT-I.

O: The primary outcomes in this study were subjective sleep outcomes, including insomnia severity measured by the insomnia severity index (Insomnia, 1993), sleep quality measured by the Pittsburgh sleep quality index (Buysse et al., 1989), total sleep time, sleep efficiency, sleep onset latency, wake after sleep onset and number of awakenings. Secondary outcomes in this study included depression symptoms, anxiety symptoms, fatigue and quality of life-related physical and mental health. Depression symptoms were measured by scores of depression scales (Beck et al., 1996; Eaton et al., 2004; Hamilton, 1986; Yesavage, 1988; Zung, 1965), and anxiety symptoms were measured by anxiety scales (Beck et al., 1988; Bieling et al., 1998; Zigmond & Snaith, 1983). The fatigue outcome was measured by the scores of fatigue scales (Krupp et al., 1989; Smets et al., 1995). The quality of life-related health outcomes were measured by the scores of the physical health and mental health sections in quality of life surveys (SF-12, SF-36 or any other verified quality of life surveys comprising physical health and mental health sections) (Ware et al., 1994). Articles reporting at least one of the primary outcomes were included. For all outcome variables, articles should report the means and standard deviations before and after intervention for the intervention and control groups or mean differences with standard deviations.

In addition, the article should involve a randomised controlled trial design, in which participants were randomly assigned to intervention or control groups, having no restrictions in sample size and length of follow-up. There were no restrictions on language and publication date. The full text of the article was available online or through reasonable attempts, such as sending emails directly to the authors to request the full text of the articles.

Exclusion Criteria

The participants in the study were diagnosed with severe psychiatric diseases that exerted cognitive or behavioural impairment, such as schizophrenia, severe depression and severe bipolar disorders. The study design did not use remote CBT-I intervention or did not include any control groups. The study was also excluded if participants in the control group received any form of complementary or non-pharmacological intervention for insomnia other than CBT-I, including light therapy, mindfulness therapy, homeopathy and acupuncture (Riemann et al., 2017). The study did not provide complete data for at least one of the primary outcomes. The articles were literature reviews or study protocols. Duplicated articles, journal articles that were not peer-reviewed and low-quality studies scoring 3 or lower on the physiotherapy evidence database (PEDro) scale (Verhagen et al., 1998) were also excluded.

Quality Assessment

The quality assessment of studies was completed by two researchers independently using the PEDro scale (Verhagen et al., 1998). The PEDro scale evaluates the quality of randomised controlled trials by giving scores ranging from 0 to 10. The marking criteria include random allocation of subjects, concealed allocation of subjects, similar baseline characteristics, blinding to all subjects, blinding to all therapists, blinding to assessors who assessed the key outcomes, enough outcome measures obtained, subjects received intervention or control condition as study designed, presence of between-group comparison analysis and presence of point measures and measures of variability. One point is given if the study completely meets each of the criterion, otherwise no point is given. The quality of studies was categorised into four levels: low quality (≤ 3 points), moderate quality (4–5 points), good quality (6–8 points) and excellent quality (9–10 points) (Cashin & McAuley, 2020).

Data Extraction

The data extraction process was completed by two researchers independently. In cases of disagreement, the third researcher was invited to review and confirm the data. If the

article provided results for post-intervention and follow-up, the results for post-intervention and the longest follow-up time were extracted. When the published articles did not provide enough data, reasonable attempts, such as direct email requests to the corresponding authors, were made to acquire the full data sets of the studies.

Characteristics of Included Studies

The following characteristics of included studies were extracted: author, year of publication, location (name of country), sample size, average age of participants, gender (number and percentage of female), type of disease, including comorbidity, diagnosis criteria of insomnia, description of intervention, delivery format, use of manual, duration of treatment, length of longest follow-up, therapist support, percentage of participants that completed the treatment, description of control condition, outcome variable names and PEDro score.

Primary and Secondary Outcomes

The means and standard deviations for the primary and secondary outcomes were extracted from the included studies for the intervention and control groups before and after intervention. The extracted data were exported into an Excel document.

Subgroup Variables

The designs and groupings of the subgroup variables were in accordance with the recommended CBT-I design and characteristics from the published CBT-I guidelines for treating insomnia (Perlis et al., 2005). The characteristics of intervention were collected from each study and manually coded into subgroups. The subgroup variables included overall dropout rate (0 for $< 20\%$ and 1 for $\geq 20\%$), length of intervention (0 for ≤ 6 weeks and 1 for > 6 weeks), length of follow-up (0 for ≤ 3 months and 1 for > 3 months), delivery format (0 for telephone, 1 for internet and 2 for mobile phone applications), presence of therapist support (0 for self-help and 1 for guided), control condition (0 for no treatment, 1 for other treatment and 2 for education and information) and presence of important components, including sleep hygiene, relapse prevention, relaxation training, sleep education and homework (0 for not present and 1 for present).

Statistical Analysis

The software used for data analysis in this study was STATA 17.0. The significance level was set as 0.05 (two-sided) and a p value of less than 0.05 was considered to be statistically significant. A separate meta-analysis using a random effects model, which provided a statistical parameter of the variations among the studies (DerSimonian & Kacker, 2007), was performed for each of the primary and secondary outcomes. The meta-analysis was conducted separately for the post-intervention and follow-up results. Given that all of the outcome variables in this study were continuous variables, pooled mean differences (MD) that had 95% confidence intervals (CIs) were used in the results presentation. Forest plots were plotted to give a straightforward overview of the results. A standardised mean difference (SMD) that had a CI of 95% was used to measure the effect size of the variables. The SMD was calculated by dividing the mean difference by the pooled standard deviation (Hedges & Olkin, 2014). A SMD between 0.2 and 0.5 indicated a small effect size, between 0.5 and 0.8 a medium effect size and greater than 0.8 a large effect size (Ferguson, 2009).

Heterogeneity of the studies was assessed using I^2 values (Higgins et al., 2003) and Q tests (Huedo-Medina et al., 2006). The I^2 value ranged from 0 to 100%. An I^2 value larger than 50% for a certain variable indicated that there was a high heterogeneity and a subgroup analysis was required to examine the possible causes. A greater Q test value also indicated a higher level of heterogeneity. Sensitivity analysis was conducted by removing one study at a time from the meta-analysis to examine the stability of the pooled results and the potential source of the heterogeneity.

Egger's regression analysis (Lin & Chu, 2018) was used to investigate the potential publication bias among the studies for each of the primary and secondary outcomes. The results are presented as Egger's t values that have 95% CIs and p values. A p value greater than 0.05 indicated that the publication bias was not statistically significant. Funnel plots were presented to assist in the evaluation of publication bias.

Results

Literature Search and Study Selection

During the database search, 1849 relevant studies were identified from the five defined databases and 152 items of grey literature from other sources. The earliest record available for title and abstract examination was published in 1993 (Morin et al., 1993). A total of 546 duplicates were removed and the remaining 1455 studies underwent title and abstract examination. After the screening of titles and abstracts, 1204 articles that did not focus on remote CBT-I or insomnia were excluded from this study. The total number of articles eligible for full-text assessment was 251. Another 209 studies were excluded during full-text assessment and the final number of studies eligible for data analysis was 42. The PRISMA flow chart of the literature search and screening is presented in Fig. 1.

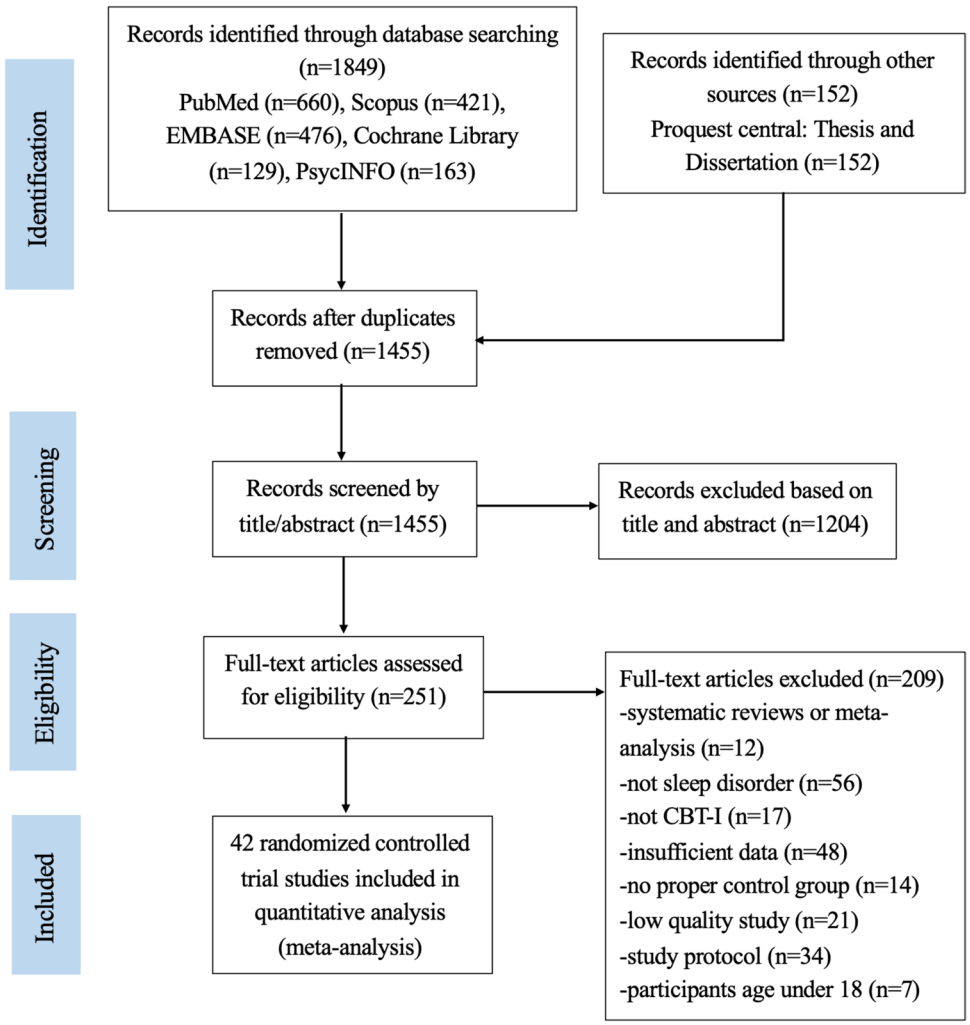

Fig. 1 PRISMA flow chart for study selection

Characteristics of Included Studies

A total of 10,496 participants were included in the 42 studies (Abdelaziz et al., 2022; Ahorsu et al., 2020; Arnedt et al., 2013, 2021; Blom et al., 2015; Brenes et al., 2012; Chan et al., 2023; Chapoutot et al., 2021; Cheng et al., 2019; Espie et al., 2012; Freeman et al., 2015, 2017; Gieselmann & Pietrowsky, 2019; Glozier et al., 2019; Godzik et al., 2021; Hagatun et al., 2019; Ho et al., 2014; Horsch et al., 2017; Hürlimann et al., 2023; Jernelöv et al., 2012; Kaldo et al., 2015; Kalmbach et al., 2020; Lancee et al., 2016; Lokman et al., 2017; Lorenz et al., 2019; McCurry et al., 2016, 2021; Morris et al., 2016; Oswald et al., 2022; Rajabi Majd et al., 2020; Ritterband et al., 2009, 2017; Siebmanns et al., 2021; Straten et al., 2014; Thorndike et al., 2013; Vedaa et al., 2020; Vincent & Lewycky, 2009; Yeung et al., 2022; Zachariae et al., 2018; Zhang et al., 2023; Zweerde et al., 2019b, 2020). The average age ranged from 25 to 72 years old. Among the participants, 8558 were female (81.5%). All of the participants in the included studies had insomnia and some of them had been diagnosed with other diseases, including epilepsy, depression, anxiety, cancer, kidney disease and cardiovascular disease. Participants in intervention groups all received remote CBT-I interventions delivered via telephone, internet or mobile phone applications. A total of 16 studies used study manuals. The total length of intervention ranged from 12 days to three months. The content of the interventions was delivered by trained therapists in 21 studies, and self-help content were provided in the other 21 studies. There was an overall high rate of completion for the interventions: the lowest compliance rate was 48% in one of the studies (Cheng et al., 2019). The control group design was divided into three categories: participants did not receive any CBT-I treatment, participants received information or education about sleep and insomnia, or participants received intervention content through face-to-face delivery. All of the 42 studies reported at least one of the primary outcomes. Among the 42 included studies, five were moderate quality, 21 were high quality and 16 were excellent quality. Details of study characteristics are displayed in Table 1.

Table 1 Characteristics of included studies

References	Location	Sample size	Age (mean)	Gender: female, n (%)	Disorder	Diagnosis of insomnia	Intervention	Format
Abdelaziz et al., (2022)	Saudi Arabia	80	53	80 (100%)	Insomnia	ISI > 7, PSQI > 5	Six online weekly CBT modules via WhatsApp or email containing cognitive intervention, psychoeducation and behavioural intervention	Internet
Ahorsu et al., (2020)	Iran	320	38	187 (58%)	Insomnia, epilepsy	ISI > 15	Weekly contents focusing on relaxation training, sleep education, cognitive restructuring, action planning and coping planning	Mobile app
Arnedt et al., (2021)	USA	65	47	46 (71%)	Chronic insomnia	ICSD-3	Six sessions on sleep restriction, stimulus control, cognitive restructuring, relaxation training, constructive worry and relapse prevention	Internet
Arnedt et al., (2013)	USA	30	39	27 (90%)	Chronic insomnia	Research Diagnostic Criteria for insomnia	Four telephone sessions on behavioral strategies, cognitive restructuring, sleep hygiene and relapse prevention	Telephone
Blom et al., (2015)	Sweden	48	54	23 (48%)	Insomnia	ISI	Eight online sessions on sleep restriction, stimulus control, sleep education, cognitive restructuring, sleep hygiene, worry handling and relapse prevention	Internet

Table 1 (continued)

References	Location	Sample size	Age (mean)	Gender: female, n (%)	Disorder	Diagnosis of insomnia	Intervention	Format
Brenes et al., (2012)	USA	60	69	50 (83%)	Insomnia, anxiety, depression	DSM-4	Workbook chapters about treatment rationale, relaxation training, cognitive restructuring, problem-solving, thought stopping, behavioral activation, in vivo exposure and relapse prevention with 5 telephone sessions	Telephone
Chan et al., (2023)	China	320	27	167 (65%)	Insomnia, depression	DSM-5, ISI > 7, PHQ-9 > 9	Six online weekly CBT modules on sleep restriction, stimulus control, cognitive therapy, relaxation training and sleep hygiene with homework	Mobile app
Chapoutot et al., (2021)	France	32	48	24 (75%)	Insomnia	ICSD-3	Individual video conference sessions on sleep restriction, stimulus control and cognitive therapy	Internet
Cheng et al., (2019)	USA	658	45	520 (79%)	Insomnia	DSM-5	Six core sessions of CBT-I containing behavioral components, cognitive components, relaxation strategies and sleep hygiene	Internet
Espie et al., (2012)	UK	164	49	120 (73%)	Insomnia	GBSS	Behavioral strategies, cognitive restructuring, relaxation training and sleep hygiene delivered by an automated virtual therapist	Internet
Freeman et al., (2017)	UK	3755	25	2676 (72%)	Insomnia, anxiety, depression, paranoia	Sleep Condition Indicator < 16	Six weekly sessions on behavioral strategies, cognitive restructuring and sleep education	Internet

Table 1 (continued)

References	Location	Sample size	Age (mean)	Gender: female, n (%)	Disorder	Diagnosis of insomnia	Intervention	Format
Freeman et al., (2015)	USA	118	55	118 (100%)	Insomnia, breast cancer	Self-report	Videoconferencing sessions on behavioral strategies (behavioural therapy) and cognitive restructuring	Internet
Gieselmann and Pietrowsky (2019)	Germany	73	40	38 (52%)	Insomnia	Research Diagnostic Criteria for insomnia	Imagination exercise, sleep hygiene, sleep restriction, cognitive therapy and review sessions delivered through synchronous text-based chats	Internet
Glozier et al., (2019)	Australia	87	58	0 (0%)	Insomnia, anxiety, depression	ISI > 14	Six online modules incorporating sleep restriction, stimulus control, sleep hygiene, cognitive restructuring and relapse prevention	Internet
Godzik et al., (2021)	USA	30	65	23 (77%)	Insomnia	Self-report	Six online CBT-I learning modules on sleep education, behavioural therapy and cognitive therapy	Internet
Hagatun et al., (2019)	Norway	181	45	122 (67%)	Insomnia	DSM-4	Six online weekly sessions on sleep restriction, stimulus control, cognitive restructure, sleep hygiene and relapse prevention	Internet
Ho et al., (2014)	China	312	39	222 (71%)	Insomnia	Self-report	Five mobile phone-delivered sessions on sleep restriction, stimulus control, sleep hygiene, cognitive restructuring, relaxation training and relapse prevention	Internet

Table 1 (continued)

References	Location	Sample size	Age (mean)	Gender: female, n (%)	Disorder	Diagnosis of insomnia	Intervention	Format
Horsch et al., (2017)	Netherlands	151	40	94 (62%)	Insomnia	DSM-5	Mobile application covering sleep diary, relaxation exercise, sleep restriction, sleep education and cognitive therapy over six weeks	Mobile app
Hürlimann et al., (2023)	Switzerland	386	48	301 (78%)	Insomnia	Self-report	Online CBT-I sessions on sleep restriction, stimulus control, sleep hygiene, cognitive restructuring and relaxation training	Internet
Jernelöv et al., (2012)	Sweden	133	48	109 (82%)	Insomnia	ISI, Research Diagnostic Criteria for insomnia	Self-help book on sleep restriction, stimulus control, sleep hygiene, cognitive restructuring and relaxation training with telephone consulting sessions	Telephone
Kaldo et al., (2015)	Sweden	148	48	116 (78%)	Insomnia	ISI, Research Diagnostic Criteria for insomnia	Online modules about sleep information, sleep hygiene, sleep medication, sleep restriction, stimulus control, stress management, managing fatigue, handling negative thoughts and planning ahead	Internet
Kalmbach et al., (2020)	USA	91	29	91 (100%)	Insomnia	ISI ≥ 10	Six digital sessions on behavioral strategies, cognitive restructuring, relaxation training and sleep hygiene	Internet
Lancee et al., (2016)	Netherlands	90	41	73 (81%)	Insomnia	DSM-5, ISI > 10	Online weekly face-to-face sessions on psychoeducation, relaxation exercise, sleep hygiene, sleep restriction and cognitive exercises	Internet

Table 1 (continued)

References	Location	Sample size	Age (mean)	Gender: female, n (%)	Disorder	Diagnosis of insomnia	Intervention	Format
Lokman et al., (2017)	Netherlands	329	43	249 (75%)	Insomnia, Depression	IDS-SR	Self-help interventions on relaxation training, cognitive restructuring, worry control and behavioral changing	Internet
Lorenz et al., (2019)	Germany	56	43	39 (70%)	Insomnia	ISI ≥ 8	Six fully automated sessions on psychoeducation, sleep restriction, relaxation training, sleep hygiene, cognitive restructuring and changing sleep-related behaviors	Internet
McCurry et al., (2021)	USA	282	70	211 (75%)	Insomnia, chronic pain	ISI ≥ 11	Six telephone CBT-I sessions on sleep restriction, stimulus control, cognitive therapy, sleep hygiene and relapse prevention	Telephone
McCurry et al., (2016)	USA	106	55	106 (100%)	Insomnia	ISI	Six telephone sessions on sleep hygiene, sleep restriction, stimulus control and cognitive therapy	Telephone
Morris et al., (2016)	UK	138	20	93 (67%)	Insomnia, anxiety	Self-report	Six online modules covering psychoeducation, sleep restriction, stimulus control, sleep hygiene, cognitive restructuring and relaxation training	Internet
Oswald et al., (2022)	USA	30	58	N/A	Insomnia, breast cancer	Clinically significant insomnia symptoms	Weekly 90-min sessions for six weeks over videoconference. Contents include sleep restriction, stimulus control, cognitive therapy, sleep hygiene and relapse prevention	Internet

Table 1 (continued)

References	Location	Sample size	Age (mean)	Gender: female, n (%)	Disorder	Diagnosis of insomnia	Intervention	Format
Rajabi Majd et al., (2020)	Iran	312	36	174 (56%)	Insomnia	DSM-5, ISI > 10	Self-help weekly contents covering sleep education, sleep restriction, stimulus control, sleep hygiene, cognitive restructuring and problem solving	Mobile app
Ritterband et al., (2017)	USA	303	43	218 (72%)	Insomnia	Self-report SOL > 30 min, TST < 6.5 h	Six online modules incorporating sleep restriction and stimulus control, sleep hygiene, cognitive restructuring and relapse prevention	Internet
Ritterband et al., (2009)	USA	44	45	34 (76%)	Insomnia	DSM-4	Six online modules incorporating sleep restriction and stimulus control, sleep hygiene, cognitive restructuring and relapse prevention	Internet
Siebmanns et al., (2021)	Sweden	48	72	17 (35%)	Insomnia, cardiovascular disease	Verified diagnosis of insomnia	Nine online modules covering sleep education, sleep restriction, stimulus control, sleep hygiene, cognitive restructuring and relaxation training guided by a nurse	Internet
Thorndike et al., (2013)	USA	45	45	34 (77%)	Insomnia	DSM-4	Six online modules incorporating sleep restriction and stimulus control, sleep hygiene, cognitive restructuring and relapse prevention	Internet
van der Zweerde et al., (2020)	Netherlands	134	50	87 (65%)	Insomnia	WASO ≥ 30 min ≥ 3 days per week	Five lessons covering psychoeducation, stimulus control, relaxation training and cognitive restructuring	Internet

Table 1 (continued)

References	Location	Sample size	Age (mean)	Gender: female, n (%)	Disorder	Diagnosis of insomnia	Intervention	Format
van der Zweerde et al., (2019b)	Netherlands	104	45	85 (82%)	Insomnia	ISI	Five online sessions covering sleep restriction, stimulus control, sleep hygiene, cognitive restructuring, relaxation training and relapse prevention	Internet
van Straten et al., (2014)	Netherlands	118	49	83 (76%)	Insomnia	DSM-4, self-report	Six weekly online sessions covering sleep restriction, stimulus control, sleep hygiene, cognitive restructuring, relaxation training and relapse prevention with homework	Internet
Vedaa et al., (2020)	Norway	1721	44	1167 (68%)	Insomnia	ISI > 12	Six online modules incorporating sleep restriction and stimulus control, sleep hygiene, cognitive restructuring and relapse prevention	Internet
Vincent and Lewycky (2009)	Canada	118	N/A	79 (67%)	Insomnia	Research diagnostic criteria for insomnia	Five online sessions containing cognitive therapy, sleep restriction, relaxation training and sleep hygiene with homeworks	Internet
Yeung et al., (2022)	USA	325	70	243 (75%)	Insomnia, osteoarthritis	Not provided	Six telephone sessions on sleep restriction, stimulus control, sleep hygiene, and cognitive restructuring, with homework	Telephone
Zachariae et al., (2018)	Denmark	255	50	255 (100%)	Insomnia	Self-report, PSQI	Six online modules incorporating sleep restriction and stimulus control, sleep hygiene, cognitive restructuring and relapse prevention	Internet

Table 1 (continued)

References	Location	Sample size	Age (mean)	Gender: female, n (%)	Disorder	Diagnosis of insomnia	Intervention	Format
Zhang et al., (2023)	China	82	50	56 (68%)	Insomnia	ICSD-3, ISI > 14	Six-week self-guided CBT-I containing sleep hygiene education, stimulation control, relaxation therapy, sleep restriction, and cognitive therapy	Mobile app

References	Manual	Length of intervention	Follow up	Therapist support	Compliance	Control	Key outcomes	PEDro score
Abdelaziz et al., (2022)	No	6 weeks	Post intervention	Professors in psychiatric mental health nursing and obstetric and gynecological nursing	92%	No intervention	ISI, PSQI, sleep diary	8
Ahorsu et al., (2020)	No	6 weeks	6 months	Self-help	100%	Sleep education	ISI, PSQI, sleep diary, HADS	6
Arnedt et al., (2021)	No	3 months	3 months	Experienced diplomate	95%	Face-to-face CBT	ISI, Sleep diary, MFI, PHQ-9, GAD-7, WSAS, SF-12	9
Arnedt et al., (2013)	Yes	8 weeks	3 months	3 clinical psychologists, expertise in CBT-I	88%	Sleep education	ISI, PSQI, sleep diary, QIDS, STAI-T, MFI, SF-12	5
Blom et al., (2015)	Yes	8 weeks	6 months	Trained psychiatrist	98%	Group CBT	ISI, Sleep diary, MADRS-S	9
Brenes et al., (2012)	Yes	12 weeks	6 months	1 Doctoral level psychology student, 1 master's level social worker	92%	Education only	STAI-T, ISI, SF-36, BDI	9
Chan et al., (2023)	Yes	6 weeks	3 months	Self-help	68%	Waitlist control	ISI, PSQI, CES-D, HADS, SF-12	8
Chapoutot et al., (2021)	No	8 weeks	Post intervention	2 trained psychologists	94%	Waitlist control	ISI, PSQI, Sleep diary, QD2A, WHOQOL	7
Cheng et al., (2019)	No	6 weeks	Post intervention	Self-help	48%	Sleep education	ISI, QIDS	9
Espie et al., (2012)	Yes	6 weeks	8 weeks	Online programs	82%	Treatment as usual	Sleep diary	9
Freeman et al., (2017)	No	10 weeks	3 months	Self-help	70%	Treatment as usual	ISI, PHQ-9, GAD-7	5
Freeman et al., (2015)	Yes	5 weeks	3 months	1 licensed professional counselor, 1 family medicine physician	88%	Waitlist control	PSQI, SF-36, FACIT-F	6
Gieselmann and Pietrowsky (2019)	No	4 weeks	2 months	3 psychology students, 5 psychologists	90%	Waitlist control	PSQI, Sleep diary, STAI-T, FSS	6

Table 1 (continued)

References	Manual	Length of intervention	Follow up	Therapist support	Compliance	Control	Key outcomes	PEDro score
Glozier et al., (2019)	No	12 weeks	6 months	Self-help	86%	Insomnia education	ISI, CES-D	5
Godzik et al., (2021)	No	6 weeks	2 weeks	Self-help	87%	Psychoeducation	ISI, DASS-21, WHO-QOL	7
Hagatun et al., (2019)	No	9 weeks	6 months	Self-help	78%	Sleep education	ISI, sleep diary	9
Ho et al., (2014)	No	6 weeks	3 months	2 experienced clinical psychologists	61%	Waitlist control	Sleep diary, ISI, PSQI, HADS, SF-36, MFI	9
Horsch et al., (2017)	Yes	7 weeks	3 months	Self-help	51%	Waitlist control	Sleep diary, ISI, PSQI, HADS, CES-D	5
Hürlimann et al., (2023)	No	4 weeks	3 months	Self-help	59%	Waitlist control	ISI	6
Jernelöv et al., (2012)	Yes	6 weeks	3 months	Clinical psychologists in final year training	95%	Waitlist control	Sleep diary, ISI, Day time fatigue	7
Kaldo et al., (2015)	No	8 weeks	12 months	Trained clinical psychologists	98%	Inactive treatment (CBT-control)	ISI, sleep diary	6
Kalmbach et al., (2020)	No	6 weeks	Post intervention	Self-help	99%	Sleep education	ISI, PSQI, EPDS	6
Lancee et al., (2016)	No	6 weeks	6 months	Self-help	90%	Waitlist control	ISI, sleep diary, CES-D, HADS-A	6
Lokman et al., (2017)	No	3 months	6 months	Self-help	72%	Waitlist control	IDS-SR, GAD-7, sleep diary	5
Lorenz et al., (2019)	No	12 days	12 months	Self-help	93%	Waitlist control	ISI, BDI-II	9
McCurry et al., (2021)	Yes	8 weeks	12 months	1 MS-level psychologist, 1 PhD nurse, 1 PhD social worker	86%	Education only	ISI, PHQ, FSS	8
McCurry et al., (2016)	No	8 weeks	3 months	1 social worker, 1 psychologist without prior experience in CBT	83%	Waitlist control	ISI, PSQI, Sleep diary	9
Morris et al., (2016)	No	6 weeks	Post intervention	Self-help	81%	Waitlist control	PSQI, BDI-II, STAI-S	7
Oswald et al., (2022)	Yes	6 weeks	Post intervention	1 licensed psychologist, 1 psychology graduate student	97%	Waitlist control	ISI, sleep efficiency	8
Rajabi Majd et al., (2020)	No	6 weeks	6 months	Self-help	100%	Sleep education	ISI, PSQI, HADS	9
Ritterband et al., (2017)	No	9 weeks	12 months	Self-help	91%	Sleep education	ISI, sleep diary	9
Ritterband et al., (2009)	No	9 weeks	Post intervention	Self-help	96%	Waitlist control	ISI, sleep diary	9
Siebmanns et al., (2021)	No	9 weeks	6 months	1 registered nurse	88%	Education only	ISI, SF-12	7
Thorndike et al., (2013)	Yes	9 weeks	Post intervention	Self-help	96%	Waitlist control	BDI-II, STPI, SF-12	8
van der Zweerde et al., (2020)	No	5 weeks	Post intervention	Mental health nurses, recently graduated psychologists	100%	Treatment as usual	ISI, sleep diary, HADS, FSS	6

Table 1 (continued)

References	Manual	Length of intervention	Follow up	Therapist support	Compliance	Control	Key outcomes	PEDro score
van der Zweerde et al., (2019b)	No	9 weeks	Post intervention	Clinical psychology graduate students	87%	Sleep diary monitoring	Sleep diary, PHQ-9, ISI, FSS, HADS	9
van Straten et al., (2014)	Yes	6 weeks	3 months	CBT coaches	86%	Waitlist control	PSQI, sleep diary, HADS, CES-D	6
Vedaa et al., (2020)	No	9 weeks	Post intervention	Self-help	65%	Sleep education	ISI, sleep diary, HADS, SF-12	9
Vincent and Lewycky (2009)	Yes	5 weeks	4 weeks	Study coordinator	67%	Waitlist control	ISI, sleep diary, MFI	7
Yeung et al., (2022)	Yes	8 weeks	12 months	Qualified CBT therapist	N/A	Education only	ISI	6
Zachariae et al., (2018)	Yes	9 weeks	6 weeks	Self-help	80%	Waitlist control	ISI, PSQI, FACIT-F, Sleep diary	9
Zhang et al., (2023)	Yes	6 weeks	6 months	Self-help	94%	Education only	ISI, sleep diary, FSS, GAD-7, PHQ-9, SF-12	9

BDI Beck Depression Inventory, *CBT* cognitive behavioral therapy, *CDMI* complaint-directed mini-interventions, *CES-D* Centre of Epidemiological Studies Depression Scale, *DASS-21* Depression, Anxiety and Stress Scale, *DSM-4* diagnostic and statistical manual of mental disorders, fourth edition, *DSM-5* diagnostic and statistical manual of mental disorders, fifth edition, *EPDS* Edinburgh Postnatal Depression Scale, *FACIT-F* Functional Assessment of Chronic Illness Therapy Fatigue Scale, *FSS* Fatigue Severity Scale, *GAD-7* Generalized Anxiety Disorder 7-item scale, *GBSS* Great British Sleep Survey, *HADS* Hospital Anxiety and Depression Scale, *ICSD-3* International Classification of Sleep Disorders-Third Edition, *IDS-SR* Inventory of Depressive Symptomatology Self-Report, *ISI* Insomnia Severity Index, *MADRS-S* Montgomery Åsberg Depression Rating Scale-Self Rated, *MFI* Multidimensional Fatigue Inventory, *PHQ-9* Patient Health Questionnaire 9-item scale, *PROMIS-Fatigue 7* Patient Reported Outcomes Management Information System Fatigue 7—item Short Form, *PSQI* Pittsburgh Sleep Quality Index, *QD2A* 12 item self-report inventory on depressive symptomatology, *QIDS* Quick Inventory of Depressive Symptomatology, *SF-12* 12-item Short-Form Health Survey, *SF-36* 36-item Medical Outcomes Study Short-Form General Health Survey, *STAI-T* State-Trait Anxiety Inventory-Trait subscale, *STPI* State Trait Personality Inventory, *UK* United Kingdom, *USA* United States of America, *WHOQOL* World Health Organization Quality of Life Questionnaire, *WSAS* Work and Social Adjustment Scale

Effect of Remote CBT-I on Sleep Outcomes

The results of the meta-analysis of the primary and secondary outcomes are presented in Tables 2 and 3. The forest plots for the meta-analysis are presented in Figs. 2 and 3.

A total of 34 studies reported the insomnia severity index as an outcome measurement. We found that there was an overall significant reduction in insomnia severity for participants in the remote CBT-I intervention groups compared with the control groups, given that there was a larger reduction in the average insomnia severity index scores than in the control groups (MD = − 3.92, 95% CI − 4.57 to − 3.26, $p < 0.001$, $I^2 = 96.65$) and a large effect size (SMD = − 1.45, 95% CI − 2.13 to − 0.78, $p < 0.001$, $I^2 = 99.54$). Given the high level of heterogeneity, subgroup analysis was conducted for the insomnia severity index. The results are presented in Table 3. According to the subgroup analysis, the subgroup variables that provided the greatest effect in reducing insomnia severity was form of delivery. CBT-I delivered through the internet (MD = − 4.19, 95% CI − 5.04 to − 3.34, $p < 0.001$, $I^2 = 97.40$) more effectively reduced insomnia severity index scores than telephone-delivered CBT-I (MD = − 3.58, 95% CI − 4.38 to − 2.79, $p < 0.001$, $I^2 = 80.86$) and CBT-I delivered through mobile phone applications (MD = − 2.92, 95% CI − 4.62 to − 1.22, $p < 0.001$, $I^2 = 82.17$). In addition, remote CBT-I significantly reduced insomnia severity index scores compared with no treatment (MD = − 4.62, 95% CI − 5.53 to − 3.71, $p < 0.001$, $I^2 = 95.89$) and education only conditions (MD = − 3.87, 95% CI − 4.66 to − 3.08, $p < 0.001$, $I^2 = 91.20$) but showed similar effects in reducing insomnia severity compared with other deliveries of CBT-I intervention (MD = − 0.53, 95% CI − 1.63 to − 0.58, $p > 0.05$, $I^2 = 0.00$).

The Pittsburgh sleep quality index was reported by 14 studies. There was an overall significant improvement in sleep quality, measured by the reduction of Pittsburgh sleep quality index scores in the remote CBT-I intervention groups compared with the control groups (MD = − 2.68,

Table 2 Overall effect of remote CBT-I on primary and secondary outcomes (pre-intervention vs. post-intervention)

Variables	Studies (n)	Participants (N)	Mean difference			Effect size			Publication bias
			Mean difference (95% CI)	*Q* test	I^2 (%)	Standardized mean difference (95% CI)	*Q* test	I^2 (%)	Egger's t (95% CI)
Insomnia Severity Index	34	9420	− 3.92*** (− 4.57, − 3.26)	985.06***	96.65***	− 1.45*** (− 2.13, − 0.78)	867.34***	99.54***	0.45 (− 1.12, 1.75)
Pittsburgh Sleep Quality Index	14	1798	− 2.68*** (− 3.10, − 2.25)	80.33***	86.18***	− 1.46*** (− 2.24, − 0.68)	317.52***	98.11***	− 1.24 (− 2.20, 0.61)
Total sleep time	25	4461	13.35*** (7.65, 19.05)	280.54***	95.42***	0.69* (0.10, 1.28)	392.57***	98.73***	1.44 (− 0.28, 1.57)
Sleep efficiency	25	4403	6.40*** (4.67, 8.13)	653.13***	97.24***	1.26*** (0.57, 1.96)	669.35***	98.98***	0.56 (− 1.23, 2.14)
Sleep onset latency	23	4314	− 11.78*** (− 15.74, − 7.82)	261.52***	96.37***	− 0.95*** (− 1.38, − 0.51)	465.24***	97.39***	− 0.20 (− 2.43, 2.00)
Wake after sleep onset	18	3871	− 16.25*** (− 22.39, − 10.11)	2411.16***	98.71***	− 1.96* (− 3.52, − 0.40)	732.60***	99.75***	1.38 (− 0.74, 3.49)
Number of awakenings	10	1084	− 0.41** (− 0.64, − 0.17)	24.65**	61.33**	− 0.37** (− 0.64, − 0.10)	31.09**	76.98**	0.49 (− 2.39, 3.69)
Depression	22	5914	− 2.13*** (− 2.95, − 1.32)	96.04***	88.06***	− 0.48*** (− 0.68, − 0.28)	168.14***	90.63***	− 0.98 (− 2.22, 0.80)
Anxiety	17	5008	− 1.51*** (− 2.01, − 1.02)	206.77***	93.11***	− 0.74*** (− 1.16, − 0.33)	219.32***	97.35***	− 0.64 (− 1.83, 0.99)
Fatigue	10	2775	− 1.77*** (− 2.68, − 0.87)	86.55***	86.89***	− 0.62* (− 1.15, − 0.09)	179.29***	96.55***	1.60 (− 0.55, 3.00)
Physical Health	9	2602	− 0.51 (− 2.88, 1.86)	343.16***	96.20***	− 0.26 (− 1.19, 0.66)	157.46***	98.72***	0.76 (− 2.24, 4.36)
Mental Health	9	2326	4.27** (1.71, 6.84)	95.32***	92.24***	0.81* (0.10, 1.51)	112.45***	96.80***	− 0.64 (− 4.15, 2.38)

*$p < 0.05$, **$p < 0.01$, ***$p < 0.001$

Table 3 Overall effect of remote CBT-I on primary and secondary outcomes (pre-intervention vs. longest follow-up)

Variables	Studies (n)	Participants (N)	Mean difference			Effect size			Publication bias
			Mean difference (95% CI)	*Q* test	I^2 (%)	Standardized mean difference (95% CI)	*Q* test	I^2 (%)	Egger's t (95% CI)
Insomnia Severity Index	23	6937	− 3.97 (− 4.81, − 3.14)***	172.37***	96.16***	− 1.34 (− 1.96, − 0.72)***	497.42***	99.16***	0.27 (− 1.74, 2.24)
Pittsburgh Sleep Quality Index	15	1858	− 2.42 (− 2.89, − 1.96)***	79.88***	88.35***	− 1.26 (− 2.02, − 0.49)**	331.87***	98.11***	0.15 (− 1.43, 1.64)
Total sleep time	21	4005	13.50 (6.23, 20.76)***	155.37***	91.27***	0.36 (0.14, 0.59)**	127.26***	89.28***	1.10 (− 5.90, 1.91)
Sleep efficiency	20	3918	5.69 (3.82, 7.56)***	314.76***	96.02***	1.03 (0.49, 1.57)***	395.27***	98.09***	− 0.87 (− 3.47, 1.44)
Sleep onset latency	19	3858	− 11.27 (− 15.80, − 6.73)***	225.07***	95.61***	− 0.85 (− 1.28, − 0.41)***	294.41***	97.03***	− 0.17 (− 2.85, 2.42)
Wake after sleep onset	15	3495	− 16.89 (− 24.02, − 9.75)***	2260.07***	98.45***	− 1.93 (− 3.70, − 0.15)*	483.68***	99.79***	1.17 (− 1.19, 4.01)
Number of awakenings	7	809	− 0.47 (− 0.74, − 0.19)***	20.59**	69.17**	− 0.53 (− 0.98, − 0.07)*	27.32***	87.97***	0.34 (− 4.18, 5.45)
Depression	20	4717	− 2.49 (− 3.37, − 1.60)***	59.04***	85.04***	− 0.52 (− 0.74, − 0.30)***	131.60***	88.11***	− 0.53 (− 1.78, 1.07)
Anxiety	17	4754	− 1.73 (− 2.27, − 1.19)***	209.30***	93.47***	− 0.78 (− 1.19, − 0.36)***	207.84***	96.99***	− 1.33 (− 1.88, 0.43)
Fatigue	8	2336	− 1.63 (− 2.77, − 0.49)**	85.46***	91.35***	− 0.69 (− 1.36, − 0.01)*	177.85***	96.43***	1.98 (− 0.41, 3.82)
Physical Health	8	2241	− 0.27 (− 3.16, 2.61)	343.55***	97.06***	− 0.26 (− 1.33, 0.81)	157.35***	98.41***	1.05 (− 1.79, 4.45)
Mental Health	9	2285	4.53 (1.96, 7.09)***	93.85***	91.78***	0.83 (0.13, 1.53)*	111.59***	96.48***	− 0.58 (− 3.69, 2.25)

*$p < 0.05$, **$p < 0.01$, ***$p < 0.001$

95% CI − 3.10 to − 2.25, $p < 0.001$, $I^2 = 86.18$), which had a large effect size (SMD = − 1.46, 95% CI − 2.24 to − 0.68, $p < 0.01$, $I^2 = 98.11$). Subgroup analysis was conducted for the Pittsburgh sleep quality index. The results are presented in Table 3. The subgroup analysis showed that the Pittsburgh sleep quality index scores were greatly affected by the forms of CBT-I delivery. CBT-I delivered via telephone (MD = − 1.60, 95% CI − 1.77 to − 1.43, $p > 0.05$, $I^2 = 0.00$) had a smaller effect on reducing Pittsburgh sleep quality index scores than therapy delivered through the internet (MD = − 2.79, 95% CI − 3.26 to − 2.32, $p < 0.001$, $I^2 = 52.29$) and mobile applications (MD = − 3.09, 95% CI − 3.66 to − 2.52, $p < 0.001$, $I^2 = 0.00$). The level of sleep quality index scores was not significantly affected by other subgroup variables.

For sleep outcomes from sleep diaries, there was a significant increase in total sleep time in the remote CBT-I intervention groups compared with the control groups (MD = 13.35, 95% CI 7.65–19.05, $p < 0.001$, $I^2 = 95.42$), which had a medium effect size (SMD = 0.69, 95% CI 0.10–1.28, $p < 0.01$, $I^2 = 98.73$). The results of the subgroup analysis on total sleep time are presented in Table 4. A more significant improvement in total sleep time could be found in studies that had a lower dropout rate (MD = 15.91, 95% CI 7.95–23.86, $p < 0.001$, $I^2 = 84.78$) than studies that had a dropout rate greater than 20% (MD = 8.74, 95% CI − 2.10 to 15.37, $p < 0.05$, $I^2 = 97.19$). Moreover, greater improvement in total sleep time was observed when intervention was shorter than six weeks (MD = 20.19, 95% CI 11.23–29.14, $p < 0.001$, $I^2 = 95.50$) compared with interventions longer

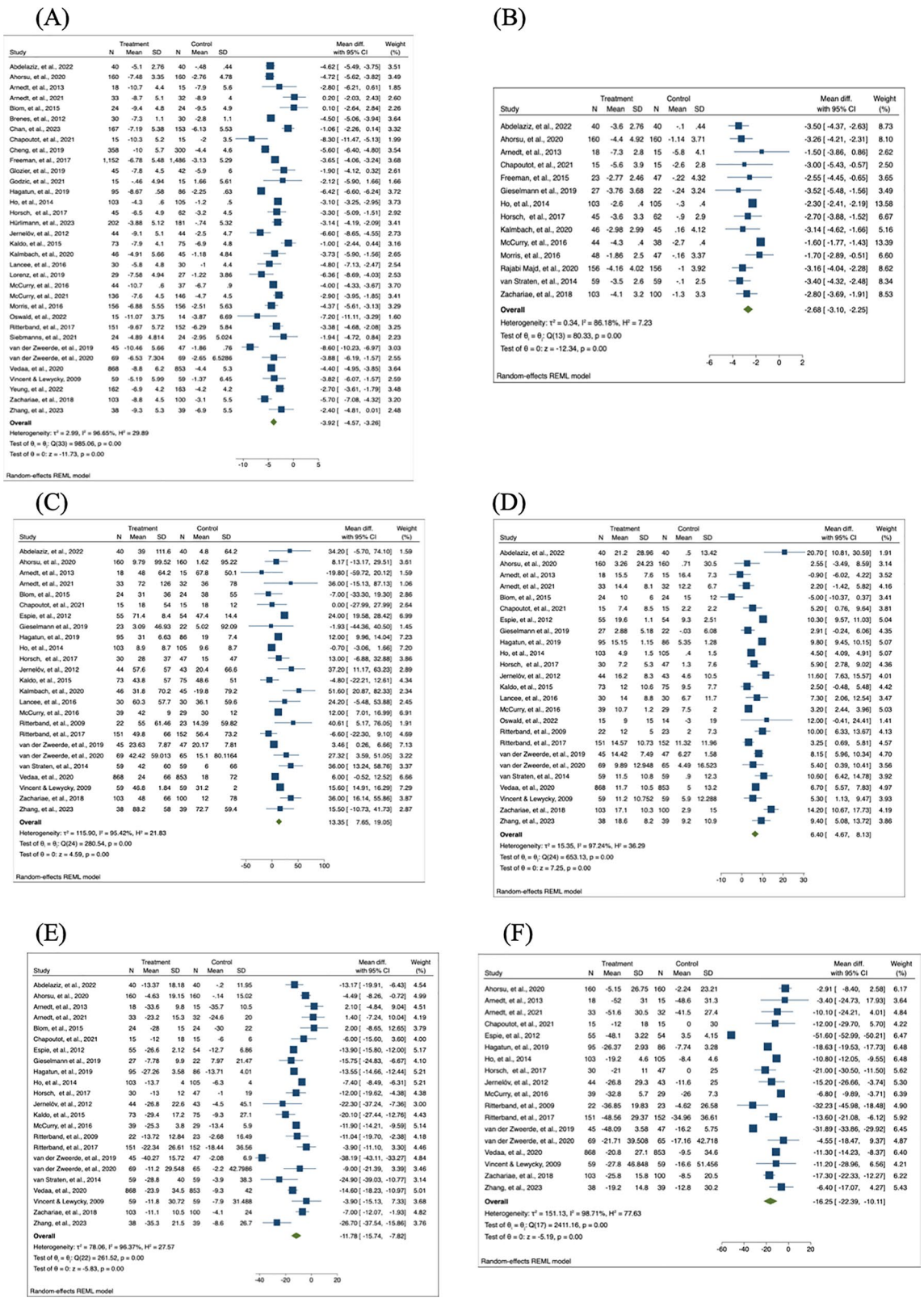

Fig. 2 Forest plots of the effect of remote CBT-I on sleep outcomes. **A** Insomnia Severity Index; **B** Pittsburgh Sleep Quality Index; **C** total sleep time; **D** sleep efficiency; **E** sleep onset latency; **F** wake after sleep onset

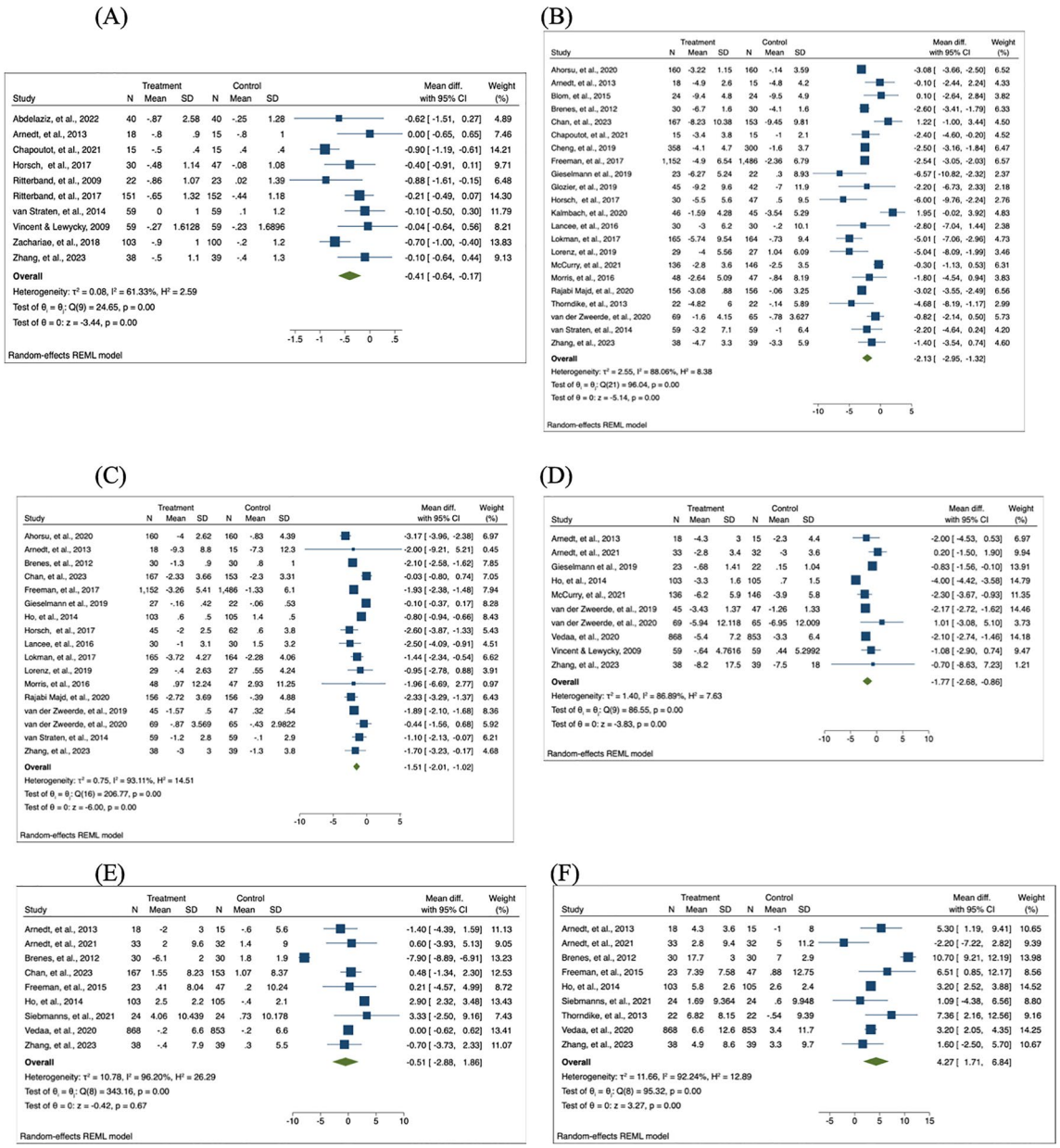

Fig. 3 Forest plots of the effect of remote CBT-I on sleep and health outcomes. **A** Number of awakenings; **B** depression; **C** anxiety; **D** fatigue; **E** physical health; **F** mental health

than six weeks (MD = 7.90, 95% CI 2.54–13.27, $p < 0.01$, $I^2 = 76.81$). Greater improvement in total sleep time was also observed in studies that had a shorter follow-up period (MD = 18.62, 95% CI 10.26–26.98, $p < 0.001$, $I^2 = 96.71$) compared with studies that had a longer follow-up (MD = 7.71, 95% CI 1.74–13.67, $p < 0.05$, $I^2 = 55.99$). Other effective subgroup characteristics for total sleep time included internet delivery and presence of relaxation training.

Sleep efficiency was improved in remote CBT-I intervention groups compared with control groups (MD = 6.40, 95% CI 4.67–8.13, $p < 0.001$, $I^2 = 97.24$), which had a large effect size (SMD = 1.26, 95% CI 0.57–1.96, $p < 0.01$, $I^2 = 98.98$). Subgroup analysis was conducted on sleep efficiency. The results are displayed in Table 4. There was a more significant increase in sleep efficiency in studies that had a shorter follow-up (MD = 7.52, 95% CI 5.41–9.63, $p < 0.001$, $I^2 = 95.18$) than studies that had a longer follow-up (MD = 4.47, 95% CI 1.69–7.25, $p < 0.001$, $I^2 = 96.15$). Telephone-delivered CBT-I showed a limited effect in improving sleep efficiency (MD = 1.96, 95% CI − 1.73 to 5.65, $p > 0.05$, $I^2 = 58.57$) compared

Table 4 Subgroup analysis on Insomnia Severity Index and Pittsburgh Sleep Quality Index

Subgroups	Insomnia Severity Index						Pittsburgh Sleep Quality Index					
	Study (n)	MD (95% CI)	SMD (95% CI)	MD I^2 (%)	MD Q test	p Between	Study (n)	MD (95% CI)	SMD (95% CI)	MD I^2 (%)	MD Q test	p Between
Dropout rate						< 0.001						< 0.001
< 20%	26	− 3.80*** (− 4.65, − 2.96)	− 1.10*** (− 1.55, − 0.66)	91.42***	147.80***		12	− 2.75*** (− 3.25, − 2.24)	− 1.14*** (− 1.64, − 0.63)	68.03***	61.06***	
≥ 20%	8	− 4.25*** (− 5.18, − 3.32)	− 2.56* (− 5.07, − 0.05)	97.86***	821.14***		2	− 2.30*** (− 2.41, − 2.20)	− 3.31 (− 8.08, 1.47)	0	0.44	
Length of intervention						< 0.001						< 0.001
≤ 6 weeks	16	− 3.90*** (− 4.64, − 2.96)	− 1.17*** (− 1.79, − 0.55)	86.17***	91.44***		9	− 2.89*** (− 3.35, − 2.43)	− 1.49** (− 2.55, − 0.44)	57.72**	22.94**	
> 6 weeks	18	− 3.88*** (− 4.98, − 2.78)	− 1.72** (− 2.90, − 0.54)	97.63***	437.12***		5	− 2.21*** (− 2.93, − 1.49)	− 1.40* (− 2.65, − 0.14)	58.28*	10.86*	
Length of follow-up												
≤ 3 months	20	− 4.02*** (− 4.87, − 3.18)	− 1.10*** (− 1.61, − 0.58)	94.57***	157.77***	< 0.001	10	− 2.73*** (− 3.16, − 2.30)	− 1.41** (− 2.37, − 0.45)	47.86*	18.03*	< 0.001
> 3 months	14	− 3.76*** (− 4.85, − 2.68)	− 1.98** (− 3.48, − 0.48)	96.38***	325.80***		4	− 2.26*** (− 3.60, − 1.64)	− 1.58* (− 3.12, − 0.05)	81.42***	23.15***	
Form of delivery						< 0.001						< 0.001
Telephone	5	− 3.58*** (− 4.38, − 2.79)	− 2.22* (− 4.21, − 0.24)	80.86**	15.28**		2	− 1.6 (− 1.77, − 1.43)	− 2.21 (− 5.71, 1.28)	0	0.01	
Internet	25	− 4.19*** (− 5.04, − 3.34)	− 1.44** (− 2.27, − 0.60)	97.40***	924.19***		9	− 2.79*** (− 3.26, − 2.32)	− 1.52** (− 2.57, − 0.47)	52.29*	17.47*	
Mobile app	4	− 2.92** (− 4.62, − 1.22)	− 0.63** (− 1.05, − 0.20)	82.17***	23.48***		3	− 3.09*** (− 3.66, − 2.52)	− 0.79*** (− 0.94, − 0.64)	0	0.57	
Therapist support						< 0.001						< 0.001
Self-help	21	− 4.21*** (− 5.09, − 3.32)	− 1.27** (− 2.16, − 0.38)	94.89***	357.18***		7	− 2.86*** (− 3.27, − 2.44)	− 0.79*** (− 0.91, − 0.67)	0	5	
Guided	13	− 3.44*** (− 4.33, − 2.56)	− 1.75** (− 2.81, − 0.69)	94.41***	83.83***		7	− 2.59*** (− 3.28, − 1.90)	− 2.13** (− 3.60, − 0.67)	94.89***	64.49	
Control						< 0.001						< 0.001
No treatment	17	− 4.62*** (− 5.53, − 3.71)	− 1.61*** (− 2.33, − 0.88)	95.89***	134.14***		10	− 2.58*** (− 3.09, − 2.07)	− 1.76** (− 2.82, − 0.70)	90.37***	68.18***	
Other treatment	3	− 0.53 (− 1.63, 0.58)	− 0.11 (− 0.36, 0.13)	0	1.02		0	N/A	N/A	N/A	N/A	
Education only	14	− 3.87***	− 1.57*	91.20***	223.16***		4	− 3.10***	− 0.77***	0	1.89	

Table 4 (continued)

Subgroups	Insomnia Severity Index						Pittsburgh Sleep Quality Index					
	Study (n)	MD (95% CI)	SMD (95% CI)	MD I^2 (%)	MD Q test	p Between	Study (n)	MD (95% CI)	SMD (95% CI)	MD I^2 (%)	MD Q test	p Between
		(− 4.66, − 3.08)	(− 2.98, − 0.17)					(− 3.67, − 2.52)	(− 0.92, − 0.62)			
Sleep hygiene						< 0.001						< 0.001
No	4	− 4.53***	− 1.70*	77.82***	9.03*		2	− 2.72***	− 0.74**	0	0.08	
		(− 6.71, − 2.37)	(− 3.36, − 0.04)					(− 4.22, − 1.22)	(− 1.16, − 0.31)			
Yes	30	− 3.85***	− 1.42***	96.95***	975.72***		12	− 2.68***	− 1.57**	88.75***	79.72***	
		(− 4.55, − 3.15)	(− 2.16, − 0.68)					(− 3.13, − 2.23)	(− 2.47, − 0.67)			
Relapse prevention						< 0.001						< 0.001
No	11	− 4.01***	− 0.89***	75.85***	39.85***		6	− 2.89***	− 0.99***	31.45	6.33	
		(− 4.71, − 3.30)	(− 1.19, − 0.60)					(− 3.56, − 2.22)	(− 1.32, − 0.65)			
Yes	23	− 3.84***	− 1.71**	98.01***	935.84***		8	− 2.58***	− 1.81**	92.24***	65.66***	
		(− 4.76, − 2.91)	(− 2.70, − 0.72)					(− 3.12, − 2.04)	(− 3.16, − 0.47)			
Relaxation training						< 0.001						< 0.001
No	15	− 3.74***	− 1.64*	95.94***	345.05***		7	− 2.49***	− 1.22**	63.70**	22.75**	
		(− 4.79, − 2.70)	(− 3.02, − 0.27)					(− 3.19, − 1.80)	(− 2.10, − 0.34)			
Yes	19	− 4.04***	− 1.31***	94.93***	161.63***		7	− 2.82***	− 1.69*	62.72**	18.65**	
		(− 4.90, − 3.18)	(− 1.92, − 0.70)					(− 3.33, − 2.31)	(− 3.03, − 0.35)			
Sleep education						< 0.001						< 0.001
No	14	− 4.28***	− 1.75*	95.47***	195.86***		6	− 2.82***	− 0.85***	0	1.93	
		(− 5.51, − 3.04)	(− 3.15, − 0.35)					(− 3.40, − 2.25)	(− 1.03, − 0.67)			
Yes	20	− 3.64***	− 1.25***	93.40***	115.64***		8	− 2.82***	− 1.94**	93.87***	73.24***	
		(− 4.33, − 2.96)	(− 1.90, − 0.60)					(− 3.33, − 2.31)	(− 3.25, − 0.63)			
Homework						< 0.001						< 0.001
No	23	− 4.22***	− 1.26***	95.12***	166.14***		10	− 2.82***	− 1.59**	82.32***	53.36***	
		(− 5.00, − 3.44)	(− 1.82, − 0.70)					(− 3.40, − 2.25)	(− 2.68, − 0.49)			
Yes	11	− 3.31***	− 1.86*	95.22***	258.95***		4	− 2.64***	− 1.12***	0	0.33	
		(− 4.49, − 2.12)	(− 3.68, − 0.05)					(− 3.22, − 2.06)	(− 1.57, − 0.67)			

*$p < 0.05$, **$p < 0.01$, ***$p < 0.001$

with internet-delivered (MD = 6.97, 95% CI 4.97–8.96, $p < 0.001$, $I^2 = 97.56$) and mobile application-delivered CBT-I (MD = 6.35, 95% CI 3.17–9.54, $p < 0.001$, $I^2 = 39.55$). Remote CBT-I had a greater effect on sleep efficiency when the intervention was shorter than 6 weeks, delivered by internet, had no treatment in the control group and provided a relaxation training component.

The meta-analysis found that remote CBT-I effectively shortened the sleep onset latency time compared with the control conditions (MD = − 11.78, 95% CI − 15.74 to − 7.82, $p < 0.001$, $I^2 = 96.37$), which had a large effect size (SMD = − 0.95, 95% CI − 1.38 to − 0.51, $p < 0.001$, $I^2 = 97.39$). The subgroup analysis results for sleep onset latency are presented in Table 5. The subgroup variable that provided the greatest effect on sleep onset latency was relaxation training. Studies that included relaxation training (MD = − 15.15, 95% CI − 22.13 to − 8.16, $p < 0.01$, $I^2 = 97.01$) showed a greater improvement in sleep onset latency than studies that did not include relaxation training (MD = − 9.26, 95% CI − 13.03 to − 5.49, $p < 0.001$, $I^2 = 87.88$). Other effective subgroups included intervention length shorter than six weeks, internet delivery, no treatment in control group and sleep hygiene.

Likewise, remote CBT-I had a significant effect on improving wake after sleep onset. The average wake time after sleep onset was significantly shortened in intervention groups compared with control groups (MD = − 16.25, 95% CI − 22.39 to − 10.11, $p < 0.001$, $I^2 = 98.71$), which had a large effect size (SMD = − 1.96, 95% CI − 3.52 to − 0.40, $p < 0.001$, $I^2 = 99.75$). Given the high level of heterogeneity, subgroup analysis was performed on wake after sleep onset. The results can be found in Table 5. Therapist support and sleep hygiene were the two subgroup variables that had the greatest effect on shortening wake time after sleep onset. Wake time after sleep onset was more effectively shortened in studies that used self-help interventions (MD = − 18.97, 95% CI − 26.66 to − 11.28, $p < 0.001$, $I^2 = 98.77$) than in studies providing therapist-guided interventions (MD = − 9.20, 95% CI − 20.68 to − 6.00, $p < 0.001$, $I^2 = 49.23$). Studies that included a sleep hygiene component (MD = − 17.05, 95% CI − 23.65 to − 10.45, $p < 0.001$, $I^2 = 94.36$) had a greater effect on wake after sleep onset than studies that did not (MD = − 7.40, 95% CI − 18.34 to 3.55, $p > 0.05$, $I^2 = 0.00$). Other effective subgroup characteristics included a follow-up shorter than three months, internet delivered, no treatment in control group and relaxation training.

The number of awakenings was also significantly improved in remote CBT-I intervention groups compared with control groups (MD = − 0.41, 95% CI − 0.64 to − 0.17, $p < 0.01$, $I^2 = 61.33$), which had a medium effect size (SMD = − 0.37, 95% CI − 0.64 to − 0.10, $p < 0.01$, $I^2 = 76.98$).

Similar meta-analysis results for all sleep outcomes were found when comparing pre-intervention with post-intervention and follow-up. All of the Q test results were consistent with the I^2 results in all analyses, indicating the same levels of heterogeneity in all sleep outcomes and subgroup variables. In all subgroup analysis, the p values between groups were smaller than 0.001, which suggested that there was a significant difference between groups for each of the subgroup variables.

Effect of Remote CBT-I on Depression and Anxiety Symptoms

The scores of depression scales were measured in 22 studies, and a total of 5914 participants were included in these studies. The meta-analysis showed that remote CBT-I intervention significantly improved the depressive symptoms, given that the average score of depression scales in the intervention groups was significantly lower than in the control groups (MD = − 2.13, 95% CI − 2.95 to − 1.32, $p < 0.001$, $I^2 = 88.06$), which had a medium effect size (SMD = − 0.48, 95% CI − 0.68 to − 0.28, $p < 0.001$, $I^2 = 90.63$) immediately after intervention. Given the high level of heterogeneity, subgroup analysis was performed on depression. The results are presented in Table 6. The subgroup variable that provided the greatest effect on depression was the form of delivery. Depression scale scores were more significantly reduced when the intervention was delivered through internet (MD = − 2.37, 95% CI − 3.49 to − 1.26, $p < 0.001$, $I^2 = 83.00$) and mobile phone applications (MD = − 2.31, 95% CI − 4.23 to − 0.38, $p < 0.05$, $I^2 = 93.55$). However, telephone-delivered interventions (MD = − 1.14, 95% CI − 2.82 to 0.54, $p > 0.05$, $I^2 = 85.34$) did not provide a significant effect on depression scale scores. Depression was also improved when the studies had a longer intervention period, longer follow-up, provided self-help materials, had no treatment in the control group and included sleep hygiene and relaxation training components.

Anxiety scales were measured in 17 studies, which used 5,008 participants. Similarly to depression, remote CBT-I showed a greater effect on anxiety than control conditions because the average scores for anxiety scales in intervention groups were more effectively reduced than the scores in the control groups (MD = − 1.51, 95% CI − 2.01 to − 1.02, $p < 0.001$, $I^2 = 93.11$), which had a medium effect size (SMD = − 0.74, 95% CI − 1.16 to − 0.33, $p < 0.001$, $I^2 = 97.35$) at post-intervention. Subgroup analysis was conducted on anxiety and the results can be found in Table 6. Studies that provided a relaxation training component (MD = − 1.59, 95% CI − 2.08 to − 1.09, $p < 0.001$, $I^2 = 91.19$) had the greatest effect on anxiety scale scores compared with studies that did not (MD = − 1.21, 95% CI − 3.16 to − 0.74, $p > 0.05$, $I^2 = 88.65$). Anxiety was also

Table 5 Subgroup analysis on total sleep time and sleep efficiency

Subgroups	Total sleep time						Sleep efficiency					
	Study (n)	MD (95% CI)	SMD (95% CI)	MD I^2 (%)	MD Q test	p Between	Study (n)	MD (95% CI)	SMD (95% CI)	MD I^2 (%)	MD Q test	p Between
Dropout rate						< 0.001						< 0.001
< 20%	20	15.91*** (7.95, 23.86)	0.40** (0.17, 0.62)	84.78***	96.64***		20	6.40*** (4.16, 8.65)	0.93*** (0.43, 1.43)	93.63***	271.88***	
≥ 20%	5	8.74* (2.10, 15.37)	2 (− 1.01, 5.01)	97.19***	178.36***		5	6.62*** (4.52, 8.72)	2.58 (− 0.24, 5.39)	97.37***	374.07***	
Length of intervention						< 0.001						< 0.001
≤ 6 weeks	12	20.19*** (11.23, 29.14)	1.09 (− 0.14, 2.32)	95.50***	201.43***		12	7.71*** (5.48, 9.94)	1.25** (0.44, 2.06)	92.67***	216.39***	
> 6 weeks	13	7.90** (2.54, 13.27)	0.36* (0.04, 0.68)	76.81***	43.07***		13	5.26*** (2.73, 7.79)	1.28* (0.13, 2.42)	97.10***	340.03***	
Length of follow-up												
≤ 3 months	16	18.62*** (10.26, 26.98)	0.89* (− 0.03, 1.81)	96.71***	261.35***	< 0.001	16	7.52*** (5.41, 9.63)	1.19*** (0.57, 1.81)	95.18***	253.86***	< 0.001
> 3 months	9	7.71* (1.74, 13.67)	0.37 (− 0.06, 0.80)	55.99	12.17		9	4.47** (1.69, 7.25)	1.4 (− 0.27, 3.07)	96.15***	298.66***	
Form of delivery						< 0.001						< 0.001
Telephone	2	2.52 (− 26.00, 31.03)	0.43 (− 1.04, 1.89)	58.34	2.4		2	1.96 (− 1.73, 5.65)	0.95 (− 1.14, 3.05)	58.57	2.41	
Internet	20	14.95*** (7.70, 22.20)	0.80* (0.06, 1.53)	97.29***	277.01***		20	6.97*** (4.97, 8.96)	1.39** (0.54, 2.24)	97.56***	517.44***	
Mobile app	3	11.87* (− 0.85, 24.59)	0.15 (− 0.04, 0.33)	0	0.2		3	6.35*** (3.17, 9.54)	0.61* (0.04, 1.18)	39.55	3.52	
Therapist support						< 0.001						< 0.001
Self-help	15	14.57*** (8.05, 21.08)	1.01* (0.02, 1.99)	95.02***	105.64***		14	7.39*** (5.66, 9.13)	1.60** (0.44, 2.76)	93.24***	96.27***	
Guided	10	11.08* (0.35, 22.50)	0.25 (− 0.01, 0.52)	87.83***	45.09***		11	5.34** (1.80, 8.87)	0.85** (0.27, 1.44)	97.45***	60.38***	
Control						< 0.001						< 0.001
No treatment	15	17.25*** (9.97, 24.53)	1.00* (0.03, 1.97)	95.75***	248.33***		16	7.82*** (5.91, 9.73)	1.37*** (0.78, 1.95)	94.80***	288.20***	
Other treatment	3	− 2.38 (− 16.34, 11.59)	0.01 (− 0.26, 0.29)	0	2.36		3	0.37 (− 3.91, 4.66)	0.05 (− 0.44, 0.54)	72.77*	6.15*	
Education only	7	8.72	0.35	73.21**	17.10**		6	5.58**	1.63*	95.08***	69.61***	

Table 5 (continued)

Subgroups	Total sleep time						Sleep efficiency					
	Study (n)	MD (95% CI)	SMD (95% CI)	MD I^2 (%)	MD Q test	p Between	Study (n)	MD (95% CI)	SMD (95% CI)	MD I^2 (%)	MD Q test	p Between
		(− 0.25, 17.69)	(− 0.15, 0.85)					(2.36, 8.81)	(− 0.88, 4.14)			
Sleep hygiene						< 0.001						< 0.001
No	2	14.71	0.32*	53.03	2.13		2	5.29**	0.48*	0	0	
		(− 11.98, 41.40)	(0.01, 0.63)					(1.96, 8.61)	(0.08, 0.88)			
Yes	23	13.30***	0.73*	95.94***	278.36		23	6.50***	1.32**	97.71***	651.74***	
		(7.33, 19.27)	(0.09, 1.37)					(4.61, 8.38)	(0.57, 2.07)			
Relapse prevention						< 0.001						< 0.001
No	8	18.97***	1.44	62.96**	21.57**		7	7.47***	1.40*	82.09***	38.99***	
		(12.53, 25.40)	(− 0.43, 3.32)					(4.61, 10.34)	(0.14, 2.66)			
Yes	17	11.24**	0.36**	93.00***	107.96***		18	5.95***	1.21**	97.86***	562.95***	
		(4.23, 18.24)	(0.12, 0.61)					(3.81, 8.09)	(0.36, 2.07)			
Relaxation training						< 0.001						< 0.001
No	12	8.95**	0.94	92.77***	45.72***		13	5.20***	1.20*	97.05***	340.41***	
		(2.52, 15.38)	(− 0.34, 2.21)					(2.55, 7.86)	(0.05, 2.35)			
Yes	13	19.46***	0.48***	91.68***	125.85***		12	7.63***	1.33**	92.33***	219.65***	
		(10.32, 28.59)	(0.21, 0.75)					(5.60, 9.65)	(0.53, 2.13)			
Sleep education						< 0.001						< 0.001
No	11	11.61*	0.37*	90.81***	41.60***		10	6.17***	1.42*	91.49***	90.75***	
		(1.45, 21.78)	(0.04, 0.71)					(3.51, 8.83)	(− 0.03, 2.87)			
Yes	14	14.59***	0.98*	94.96***	212.10***		15	6.60***	1.16**	97.08***	281.09	
		(7.37, 21.82)	(0.08, 2.04)					(4.19, 9.00)	(0.46, 1.86)			
Homework						< 0.001						< 0.001
No	16	12.73**	0.40**	91.62***	133.37***		16	6.39***	1.23***	95.81***	287.72***	
		(5.04, 20.41)	(0.12, 0.67)					(4.49, 8.29)	(0.60, 1.85)			
Yes	9	14.25***	1.27*	90.77**	25.97**		9	6.48***	1.33***	92.20***	68.60***	
		(7.21, 21.28)	(− 0.39, 2.93)					(2.52, 10.44)	(0.33, 3.00)			

*$p < 0.05$, **$p < 0.01$, ***$p < 0.001$

Table 6 Subgroup analysis on sleep onset latency and wake after sleep onset

Subgroups	Sleep onset latency						Wake after sleep onset					
	Study (n)	MD (95% CI)	SMD (95% CI)	MD I^2 (%)	MD Q test	p Between	Study (n)	MD (95% CI)	SMD (95% CI)	MD I^2 (%)	MD Q test	p Between
Dropout rate						< 0.001						< 0.001
< 20%	18	− 12.17*** (− 17.25, − 7.09)	− 0.84*** (− 1.28, − 0.40)	93.50***	186.28***		13	− 16.69*** (− 25.07, − 8.31)	− 1.97 (− 4.04, 0.11)	97.77***	1157.81***	
≥ 20%	5	− 11.10*** (− 14.68, − 7.52)	− 1.32* (− 2.56, − 0.09)	91.41***	66.79***		5	− 14.45*** (− 18.87, − 10.03)	− 1.98 (− 4.06, 0.11)	94.55***	109.38***	
Length of intervention						< 0.001						< 0.001
≤ 6 weeks	10	− 12.78*** (− 17.35, 8.22)	− 0.93*** (− 1.43, − 0.43)	90.49***	61.88***		7	− 15.16* (− 28.52, − 1.79)	− 2.45 (− 6.13, 1.23)	99.21***	1944.70***	
> 6 weeks	13	− 10.57** (− 16.54, − 4.60)	− 0.96** (− 1.64, − 0.27)	96.19***	156.57***		11	− 16.91*** (− 22.36, − 11.45)	− 1.68* (− 3.03, − 0.34)	95.67***	261.67***	
Length of follow− up						< 0.001						< 0.001
≤ 3 months	15	− 12.47*** (− 17.79, − 7.16)	− 0.87*** (− 1.36, − 0.39)	95.47***	200.63***		12	− 19.35*** (− 27.67, − 11.03)	− 2.27* (− 4.48, − 0.05)	98.67***	2018.29***	
> 3 months	8	− 10.54*** (− 16.27, − 4.81)	− 1.09* (− 1.98, − 0.20)	94.07***	46.09***		6	− 10.22*** (− 15.88, − 4.57)	− 1.38 (− 3.19, 0.43)	89.44***	84.35***	
Form of delivery						< 0.001						< 0.001
Telephone	2	− 5.3 (− 19.00, 8.40)	− 1.14 (− 3.77, 1.49)	92.90***	14.09***		2	− 6.73*** (− 9.79, − 3.67)	− 0.61 (− 1.54, 0.32)	0	0.1	
Internet	18	− 12.31*** (− 16.87, − 7.75)	− 0.97*** (− 1.48, − 0.46)	96.64***	226.58***		13	− 19.17*** (− 26.62, − 11.73)	− 2.54* (− 4.66, − 0.42)	99.07	2237.03***	
Mobile app	3	− 13.58* (− 26.00, − 1.16)	− 0.66* (− 1.15, − 0.16)	89.13***	15.79***		3	− 9.74 (− 20.68, 1.21)	− 0.44 (− 0.97, 0.09)	80.25**	10.48*	
Therapist support						< 0.001						< 0.001
Self-help	13	− 11.98*** (− 17.73, − 6.23)	− 1.04** (− 1.72, − 0.37)	96.52***	154.83***		13	− 18.97*** (− 26.66, − 11.28)	− 2.42* (− 4.56, − 0.27)	98.77***	1789.02***	
Guided	10	− 11.27*** (− 16.53, − 6.00)	− 0.83** (− 1.32, − 0.33)	91.25***	47.32***		5	− 9.20*** (− 20.68, − 6.00)	− 0.85* (− 1.68, − 0.02)	49.23***	7.29***	
Control						< 0.001						< 0.001
No treatment	14	− 13.87*** (− 18.82, − 8.92)	− 1.13*** (− 1.65, − 0.62)	95.19***	178.74***		11	− 20.10*** (− 28.92, − 11.28)	− 2.55* (− 4.93, − 0.17)	98.83***	2065.88***	
Other treatment	3	− 5.88 (− 20.42, 8.65)	− 0.26 (− 0.92, 0.40)	87.82***	18.37***		1	− 10.1 (− 24.21, 4.01)	− 0.35 (− 0.84, 0.14)	N/A	N/A	
Education only	6	− 9.82*	− 0.87	95.19***	51.12***		6	− 10.76***	− 1.2	89.28***	57.19***	

Table 6 (continued)

Subgroups	Sleep onset latency						Wake after sleep onset					
	Study (n)	MD (95% CI)	SMD (95% CI)	MD I^2 (%)	MD Q test	p Between	Study (n)	MD (95% CI)	SMD (95% CI)	MD I^2 (%)	MD Q test	p Between
		(− 17.20, − 2.43)	(− 1.98, 0.24)					(− 16.31, − 5.22)	(− 3.06, 0.66)			
Sleep hygiene						< 0.001						< 0.001
No	2	− 7.13	− 0.28	0	0.14		2	− 7.4	− 0.18	0	0.42	
		(− 14.72, 0.46)	(− 0.59, 0.03)					(− 18.34, 3.55)	(− 0.49, 0.13)			
Yes	21	− 12.14***	− 1.00***	96.90***	260.26		16	− 17.05***	− 2.18*	98.92***	2403.14***	
		(− 16.40, − 7.88)	(− 1.47, − 0.54)					(− 23.65, − 10.45)	(− 3.92, − 0.44)			
Relapse prevention						< 0.001						< 0.001
No	7	− 13.67***	− 1.00**	0	11.37		5	− 21.43*	− 3.13	94.36***	140.97***	
		(− 15.34, − 11.99)	(− 1.62, − 0.37)					(− 38.61, − 4.26)	(− 8.32, 2.06)			
Yes	16	− 11.25***	− 0.93**	96.90***	260.26***		13	− 14.20***	− 1.54**	97.39***	419.54***	
		(− 16.56, − 5.94)	(− 1.50, − 0.36)					(− 19.32, − 9.07)	(− 2.71, − 0.37)			
Relaxation training						< 0.001						< 0.001
No	12	− 9.26***	− 0.81*	87.88***	47.84***		9	− 14.23***	− 1.21*	87.05***	76.52***	
		(− 13.03, − 5.49)	(− 1.44, − 0.18)					(− 18.67, − 9.79)	(− 2.40, − 0.02)			
Yes	11	− 15.15***	− 1.09***	97.01***	196.00***		9	− 17.72**	− 2.76	99.17***	1963.13***	
		(− 22.13, − 8.16)	(− 1.70, − 0.48)					(− 28.54, − 6.90)	(− 5.72, 0.21)			
Sleep education						< 0.001						< 0.001
No	10	− 11.99**	− 1.02***	95.35***	148.90***		9	− 16.92***	− 1.78*	94.07***	162.08***	
		(− 19.87, − 4.11)	(− 1.60, − 0.48)					(− 22.85, − 11.00)	(− 3.45, − 0.12)			
Yes	13	− 11.33***	− 0.80*	87.30***	75.47***		9	− 16.44**	− 2.17	99.13***	2190.00***	
		(− 14.53, − 6.05)	(− 1.51, − 0.09)					(− 27.25, − 5.62)	(− 4.97, 0.63)			
Homework						< 0.001						< 0.001
No	14	− 12.39***	− 1.04***	97.00***	209.14***		13	− 17.08***	− 2.13*	98.59***	2195.45***	
		(− 18.10, − 6.69)	(− 1.60, − 0.48)					(− 24.63, − 9.53)	(− 4.18, − 0.08)			
Yes	9	− 10.79***	− 0.80*	81.99***	37.40***		5	− 13.68**	− 1.55	90.35***	38.98***	
		(− 15.53, − 6.05)	(− 1.51, − 0.09)					(− 24.01, − 3.36)	(− 3.77, 0.66)			

*$p < 0.05$, **$p < 0.01$, ***$p < 0.001$

improved when the remote CBT-I intervention had the following characteristics: an intervention period longer than six weeks, a follow-up longer than three months, self-help and a relaxation training component.

Similar meta-analysis results were found at the post-intervention and follow-up timepoints. The Q test results were consistent with the I^2 results, showing the same levels of heterogeneity. The p between groups were all smaller than 0.001, suggesting that the difference between groups for each of the subgroup variables was significant (Table 7).

Effect of Remote CBT-I on Fatigue

A total of 10 studies reported fatigue as an outcome measurement. The total number of participants in these studies was 2775. We found that the level of fatigue measured by fatigue scales was significantly reduced in remote CBT-I intervention groups compared with the control groups (MD = − 1.77, 95% CI − 2.68 to − 0.87, $p < 0.01$, $I^2 = 86.89$), and there was a medium effect size (SMD = − 0.62, 95% CI − 1.15 to − 0.09, $p < 0.05$, $I^2 = 96.55$). The Q test result were consistent with the I^2 result, indicating a significantly high level of heterogeneity.

Effect of Remote CBT-I on Quality of Life-Related Physical and Mental Health

The scores of quality of life-related physical health were reported in nine studies, and the total number of participants was 2602. The meta-analysis showed that the score difference between remote CBT-I intervention groups and control groups was not significant (MD = − 0.51, 95% CI − 2.88 to 1.86, $p > 0.05$, $I^2 = 96.20$), and the effect size was small (SMD = − 0.26, 95% CI − 1.19 to 0.66, $p > 0.05$, $I^2 = 98.72$).

The scores of quality of life-related mental health were reported in nine studies, and the total number of participants was 2285. Unlike the physical health scores, a greater improvement in mental health scores was observed in remote CBT-I intervention groups than the control groups (MD = 4.27, 95% CI 1.71–6.84, $p < 0.01$, $I^2 = 92.24$), which had a large effect size (SMD = 0.81, 95% CI 0.10–1.51, $p < 0.05$, $I^2 = 96.80$). In addition, the Q test results for physical health and mental health were consistent with the I^2 results, representing the same level of heterogeneity.

Publication Bias

Egger's regression test was conducted to assess the publication bias of all outcomes. The results are summarised in Table 2. No significant publication bias was found for all of the research outcomes, including the insomnia severity index ($t = 0.45$, 95% CI − 1.12 to 1.75, $p > 0.05$), the Pittsburgh sleep quality index ($t = -1.24$, 95% CI − 2.20 to 0.61, $p > 0.05$), total sleep time ($t = 1.44$, 95% CI − 0.28 to 1.57, $p > 0.05$), sleep efficiency ($t = -0.56$, 95% CI − 1.23 to 2.14, $p > 0.05$), sleep onset latency ($t = -0.20$, 95% CI − 2.43 to 2.00, $p > 0.05$), wakening after sleep onset ($t = 1.38$, 95% CI − 0.74 to 3.49, $p > 0.05$), number of awakenings ($t = 0.49$, 95% CI − 2.39 to 3.69, $p > 0.05$), depression ($t = -0.98$, 95% CI − 2.22 to 0.80, $p > 0.05$), anxiety ($t = -0.64$, 95% CI − 1.83 to 0.99, $p > 0.05$), fatigue ($t = 1.60$, 95% CI − 0.55 to 3.00, $p > 0.05$), physical health ($t = 0.76$, 95% CI − 2.24 to 4.36, $p > 0.05$) and mental health ($t = -0.64$, 95% CI − 4.15 to 2.38, $p > 0.05$). The funnel plots are provided in Supplementary Figs. 1 and 2. Visual inspection of the funnel plots found a symmetric distribution of mean difference for all outcome variables except the Pittsburgh sleep quality index. In addition, results from the sensitivity analysis suggested that removing any single study did not change the overall publication bias results. Therefore, no significant publication bias was found for all outcome variables.

Discussion

This meta-analysis included 42 randomised controlled trial studies that included a total of 10,496 participants. The results from this meta-analysis showed that remote CBT-I intervention was effective in improving sleep outcomes (insomnia severity index, Pittsburgh sleep quality index, total sleep time, sleep efficiency, sleep onset latency, wakening after sleep onset and number of awakenings), depression symptoms, anxiety symptoms, fatigue and quality of life-related mental health. Remote CBT-I intervention did not have significant effects on quality of life-related physical health.

Effect of Remote CBT-I Approach on Sleep Outcomes

Remote CBT-I was significantly effective in improving overall sleep quality and reducing insomnia severity, which is consistent with prior studies (Seyffert et al., 2016; Zachariae et al., 2016). One of the major goals of CBT-I interventions is to limit sleep opportunities during the day to increase the pressure for sleep at normal sleep times, leading to an improved homeostatic regulation of sleep (Koffel et al., 2015; Smith et al., 2002). The establishment of a regulated sleep cycle through a CBT-I approach has produced positive effects on not only overall sleep quality and the reduction of insomnia severity but also the improvement in total sleep time, sleep efficiency, sleep onset latency, wake after sleep onset and number of awakenings.

The subgroup analysis identified sleep hygiene and relaxation training as effective components, and the results were consistent with prior studies (Chung et al., 2018; Garcia et al., 2018; Hayes-Skelton & Lee, 2020; Pardo Cebrián &

Table 7 Subgroup analysis on depression and anxiety

Subgroups	Depression						Anxiety					
	Study (n)	MD (95% CI)	SMD (95% CI)	MD I^2 (%)	MD Q test	p Between	Study (n)	MD (95% CI)	SMD (95% CI)	MD I^2 (%)	MD Q test	p Between
Dropout rate						< 0.001						< 0.001
< 20%	18	− 1.76*** (− 2.66, − 0.86)	− 0.47*** (− 0.72, − 0.21)	84.14***	85.01***		13	− 1.48*** (− 2.12, − 0.84)	− 0.74** (− 1.28, − 0.21)	90.82***	159.72***	
≥ 20%	4	− 3.39*** (− 4.79, − 1.98)	− 0.50*** (− 0.64, − 0.36)	85.55**	8.53*		4	− 1.57*** (− 2.30, − 0.83)	− 0.75* (− 1.34, − 0.17)	87.23***	30.58***	
Length of intervention						< 0.001						< 0.001
≤ 6 weeks	11	− 1.75** (− 2.90, − 0.59)	− 0.44** (− 0.75, − 0.13)	89.13***	48.75***		10	− 1.30** (− 2.04, − 0.55)	− 0.53** (− 0.83, − 0.22)	94.00***	80.17***	
> 6 weeks	11	− 2.56*** (− 3.74, − 1.37)	− 0.52*** (− 0.78, − 0.25)	84.58***	45.02***		7	− 1.91*** (− 2.08, − 1.74)	− 1.09* (− 2.05, − 0.13)	0	3.87	
Length of follow-up												
≤ 3 months	12	− 1.65** (− 2.91, − 0.40)	− 0.29** (− 0.49, − 0.09)	89.72***	62.14***	< 0.001	10	− 1.10*** (− 1.72, − 0.49)	− 0.73* (− 1.39, − 0.06)	94.77***	149.54***	< 0.001
> 3 months	10	− 2.94*** (− 3.27, − 2.61)	− 0.71*** (− 1.04, − 0.39)	0	13.77		7	− 2.15*** (− 2.68, − 1.62)	− 0.76** (− 1.19, − 0.32)	49.13	11.05	
Form of delivery						< 0.001						< 0.001
Telephone	3	− 1.14 (− 2.82, 0.54)	− 0.57 (− 1.58, 0.44)	85.34***	16.39***		2	− 2.10*** (− 2.58, − 1.62)	− 1.2 (− 3.18, 0.77)	0	0	
Internet	14	− 2.37*** (− 3.49, − 1.26)	− 0.38*** (− 0.55, − 0.22)	83.00***	42.30***		10	− 1.21*** (− 1.73, − 0.68)	− 0.77* (− 1.42, − 0.12)	92.53***	141.49***	
Mobile app	5	− 2.31* (− 4.23, − 0.38)	− 0.67* (− 1.20, − 0.14)	93.55***	18.31**		5	− 1.95** (− 3.09, − 0.81)	− 0.53** (− 0.85, − 0.21)	84.57***	34.62***	
Therapist support						< 0.001						< 0.001
Self-help	15	− 2.48*** (− 3.52, − 1.43)	− 0.51*** (− 0.74, − 0.27)	90.03***	50.34***		11	− 1.86*** (− 2.44, − 1.28)	− 0.73* (− 1.27, − 0.18)	82.00***	37.19***	
Guided	7	− 1.38* (− 2.49, − 0.28)	− 0.43* (− 0.85, − 0.01)	70.48***	24.35***		6	− 0.92* (− 1.64, − 0.21)	− 0.85* (− 1.49, − 0.21)	93.26***	54.53***	
Control						< 0.001						< 0.001
No treatment	12	− 2.89*** (− 4.14, − 1.63)	− 0.43*** (− 0.61, − 0.25)	76.82***	34.09***		12	− 1.20*** (− 1.72, − 0.67)	− 0.70* (− 1.25, − 0.16)	93.06***	153.75***	
Other treatment	1	0.1 (− 2.64, 2.84)	0.02 (− 0.55, 0.59)	N/A	N/A		0	N/A	N/A	N/A	N/A	
Education only	9	− 1.61**	− 0.54*	91.53***	58.66***		5	− 2.39***	− 0.85*	41.39	5.85	

Table 7 (continued)

Subgroups	Depression						Anxiety					
	Study (n)	MD (95% CI)	SMD (95% CI)	MD I^2 (%)	MD Q test	p Between	Study (n)	MD (95% CI)	SMD (95% CI)	MD I^2 (%)	MD Q test	p Between
		(− 2.72, − 0.50)	(− 0.97, − 0.11)					(− 2.98, − 1.81)	(− 1.49, − 0.21)			
Sleep hygiene						< 0.001						< 0.001
No	3	− 1.95**	− 0.85*	59.64	5.12		2	− 1.35	− 1.15	86.02**	7.15**	
		(− 3.17, − 0.73)	(− 1.69, − 0.01)					(− 2.97, 0.27)	(− 3.18, 0.88)			
Yes	19	− 2.20***	− 0.44***	90.26***	90.25***		15	− 1.54***	− 0.69**	93.83***	188.31***	
		(− 3.17, − 1.22)	(− 0.64, − 0.23)					(− 2.08, − 0.99)	(− 1.12, − 0.27)			
Relapse prevention						< 0.001						< 0.001
No	10	− 2.77***	− 0.45***	88.81***	34.89***		6	− 1.47**	− 0.34***	86.76***	61.70***	
		(− 4.22, − 1.32)	(− 0.66, − 0.24)					(− 2.33, − 0.60)	(− 0.41, − 0.28)			
Yes	12	− 1.71***	− 0.50**	84.82***	60.79***		11	− 1.54***	− 0.95**	93.83***	129.55***	
		(− 2.67, − 0.75)	(− 0.82, − 0.17)					(− 2.17, − 0.91)	(− 1.58, − 0.31)			
Relaxation training						< 0.001						< 0.001
No	7	− 1.75*	− 0.47*	80.78***	39.27***		3	− 1.21	− 0.44**	88.65***	19.47***	
		(− 3.15, − 0.34)	(− 0.88, − 0.07)					(− 3.16, 0.74)	(− 0.69, − 0.19)			
Yes	15	− 2.30***	− 0.48***	89.07***	54.96***		14	− 1.59***	− 0.84**	91.19***	139.39***	
		(− 3.32, − 1.28)	(− 0.72, − 0.25)					(− 2.08, − 1.09)	(− 1.33, − 0.34)			
Sleep education						< 0.001						< 0.001
No	11	− 2.58***	− 0.53**	85.49***	38.58***		7	− 1.57***	− 1.11*	92.18***	122.71***	
		(− 4.02, − 1.15)	(− 0.83, − 0.23)					(− 2.32, − 0.83)	(− 2.06, − 0.16)			
Yes	11	− 1.82***	− 0.44**	87.45***	57.46***		10	− 1.47***	− 0.51**	89.10***	71.45***	
		(− 2.79, − 0.86)	(− 0.72, − 0.15)					(− 2.17, − 0.77)	(− 0.81, − 0.21)			
Homework						< 0.001						< 0.001
No	15	− 2.45***	− 0.40***	86.81***	63.70***		11	− 1.46***	− 0.79**	92.88***	147.12***	
		(− 3.60, − 1.29)	(− 0.56, − 0.23)					(− 2.02, − 0.89)	(− 1.37, − 0.21)			
Yes	7	− 1.78**	− 0.63*	88.30***	26.99***		6	− 1.55**	− 0.66*	88.55***	41.90***	
		(− 2.93, − 0.62)	(− 1.14, − 0.12)					(− 2.52, − 0.58)	(− 1.25, − 0.07)			

*$p < 0.05$, **$p < 0.01$, ***$p < 0.001$

Calero, 2019). Sleep hygiene education teaches insomnia patients the right behaviours that promote sleep, such as keeping a quiet sleep environment and maintaining regular sleep schedules, while discouraging unhelpful behaviours, such as alcohol and tobacco intake (Morin & Insomnia, 2007). This is effective in improving sleep quality because it helps to develop habits that are advantageous for sleep (Morin & Insomnia, 2007). Relaxation training is also effective in improving sleep because it provides relaxation strategies for physical and mental conditions (Sateia & Insomnia, 2016; Zung, 1965). A more relaxed condition can decrease arousal at night and make it easier to fall asleep and therefore prolong the sleep duration (Buysse, 2013). Relapse prevention appeared to have limited effect, which was possibly because of other effects, given that the level of heterogeneity was still very high. Despite the limited effect, relapse prevention consolidates the acquired skills (Larimer et al., 1999); thus, researchers should be cautious when considering the exclusion of relapse prevention. In addition, sleep education had limited effects because it did not provide any practical skills. Finally, the effect of homework was not significant because in many of the studies, homework was given as recording sleep and filling in sleep diaries, which do not provide a direct effect on sleep improvement. However, we need to mention that completely discouraging homework is not recommended because the completion of homework is important in measuring participant adherence and data collection (Laloyaux et al., 2013).

In addition, sleep outcomes were more significantly improved in studies that had a shorter length of intervention, which differed from the findings of prior studies (Zachariae et al., 2016), in which greater effects were observed in longer interventions. A possible explanation for the difference is that patients might be less focused in longer interventions because they might forget to access the intervention sessions or just have a quick glance at the self-help materials after weeks of treatment. In addition, the dropout rate was closely related to the length of intervention. A longer intervention period usually leads to a higher dropout rate, which also affects the final effect of treatment.

We also found that the improvement in sleep outcomes was more significant in studies that had a shorter follow-up period. As described in prior studies (Jernelöv et al., 2022; Zweerde et al., 2019c), although the effect of CBT-I could last for over 12 months, the overall effect generally decreases over time, which means that the long-term effect of CBT-I is smaller than the short-term effect. The reason for this could be that the patients in intervention groups no longer adhere to the advantageous sleep behaviours developed during the intervention, leading to the increase of insomnia symptoms (Zweerde et al., 2019c).

For the delivery methods, patients can access the intervention content in the forms of voice, texts, videos, graphs and figures or facial expressions and gestures of the therapists, which can be viewed at any time through internet and mobile application delivery. All of the elements enhance the understanding of the intervention content. However, patients can only make voice contact with the therapists during the telephone sessions, and the opportunity for obtaining extra contact with the therapists after the telephone sessions is limited. Our findings on therapist support differed from prior studies (Zachariae et al., 2016) because self-help designs were more effective than guided ones. Although therapist support may enhance the adherence of participants, self-help materials are more flexible and enable participants to develop their own understanding and practice without being constrained by therapists.

In general, remote CBT-I had similar effects on sleep outcomes to face-to-face treatments. However, the number of studies that have directly compared the difference between remote CBT-I and face-to-face intervention is limited and further studies are required.

Effect of Remote CBT-I Approach on Depression and Anxiety Symptoms

Similar to the findings from prior studies (Carpenter et al., 2018; Hall et al., 2016; Koffel et al., 2015; Lattie et al., 2019), remote CBT-I was effective in reducing depression and anxiety symptoms in patients who had insomnia. Although most of the treatment content in this study targeted sleep behaviours, cognitive components in the interventions still retained the functions of rectifying negative thoughts and beliefs, which could also benefit depression and anxiety conditions (Larzelere & Wiseman, 2002). In addition, prior studies have mentioned that there is a close relationship between insomnia and depression and anxiety symptoms and the relationship is bidirectional (Dopheide, 2020). Treating insomnia is recognised as an important part of treating depression and anxiety. Remote CBT-I provides a significant effect on improving sleep quality and the improvement of sleep quality has a positive influence on daytime symptoms such as depression and pain (Koffel et al., 2015).

There are still differences between the subgroup analysis results for sleep outcomes, depression symptoms and anxiety symptoms. Remote CBT-I showed a greater effect on depression and anxiety symptoms when the length of intervention was longer than 6 weeks. This is reasonable because insomnia is only one of the secondary manifestations of depression (Fang et al., 2019). A longer intervention period allows therapists to develop a closer relationship with patients and the therapists will have a greater chance to provide more specific psychological counselling to target the conditions of every single patients, for insomnia and other factors contributing to their depression and anxiety symptoms (Koffel et al., 2015). Sleep education did not seem

to have a great effect on depression and anxiety symptoms because the education content did not include information on depression and anxiety.

Effect of Remote CBT-I Approach on Fatigue

The relationship between sleep and fatigue has been well understood and described in many studies. Studies have claimed that the greatest cause of fatigue is the insufficiency of sleep (Caldwell et al., 2019), which explains the significant effect of remote CBT-I in reducing levels of fatigue. As discussed earlier, remote CBT-I significantly increased sleep quality and reduced insomnia severity, which prolonged the total sleep time at night and reduced the chance of sleep disruption. A regulated sleep cycle enabled the patients to be fully rested in bed and this directly reduced the level of fatigue during the day (Caldwell et al., 2019).

Effect of Remote CBT-I Approach on Quality of Life-Related Physical and Mental Health

Prior studies have mentioned that a chronic condition of insomnia exerts negative effects on mood and cognitive functions (Khan & Aouad, 2017). People in a constant bad mood tend to develop more negative thoughts, which impair overall mental health and quality of life. CBT-I interventions promote better rest and rectify negative thoughts of patients, leading to a positive attitude towards the surroundings and therefore improve mental health (González-Valero et al., 2019). The reason that remote CBT-I did not show a significant effect on physical health is that the CBT-I intervention that participants received focused on insomnia only and the content about other diseases and lifestyles were limited. Moreover, an improvement in physical health usually takes longer to be observed. Therefore, it is reasonable that physical health is not greatly affected by remote CBT-I treatment.

Strength, Limitations and Implications

This study performed a meta-analysis of 42 high-quality randomised controlled trial studies focusing on treating insomnia using remote CBT-I. Subgroup analysis was conducted to identify factors that may explain the effect of remote CBT-I intervention on the improvement of sleep patterns, depression symptoms and anxiety symptoms. This study used a high-quality study design and minimised publication bias.

There are a number of limitations of this study. First, patients who had been clinically diagnosed with insomnia disorder and patients who reported insomnia symptoms or poor sleep quality were included in this study; however, we were not able to perform subgroup analysis on the clinical diagnosis of insomnia and a cut-off for subjective measures. Second, most of the included randomised controlled trials did not provide clear comorbidity information for the participants; thus, we were not able to group comorbidities as subgroup variables and could not identify the effect of remote CBT-I on different comorbidities. During the subgroup analysis process, some groupings of the subgroup variables were presented in a limited number of studies; thus, the evaluation of these subgroup variables might not be possible. Finally, we observed high levels of heterogeneity for some outcomes in the meta-analysis and subgroup analysis, which means that heterogeneity was similar in the analyses for primary outcomes and the subgroup analysis provided a limited explanation of the high levels of heterogeneity. Another limitation was that we did not include an analysis of comorbidities in this study because most of the included randomised controlled trials did not provide clear comorbidity information for the participants; thus, we were not able to group comorbidities as subgroup variables. Therefore, further studies that include more studies are needed to support the findings from this study.

Overall, remote CBT-I intervention is a possible option for treating insomnia. When designing an intervention plan, it is necessary to retain participants in groups and minimise the dropout rate. The recommended intervention plan includes the following characteristics: total intervention period around six weeks, delivered through internet or mobile phone applications, more self-help content and include components such as sleep hygiene and relaxation training while avoiding complex homework that takes a long time to complete. Although the results indicate that relapse prevention and sleep education components provided a smaller influence on the overall intervention effect, this does not mean that these components can be excluded from the intervention design.

Conclusion

In conclusion, remote CBT-I intervention is effective in improving sleep-related outcomes, including insomnia severity as measured by the insomnia severity index, sleep quality as measured by the Pittsburgh sleep quality index, total sleep time, sleep efficiency, sleep onset latency, wake after sleep onset and number of awakenings, in insomnia patients. Remote CBT-I intervention can also improve other health outcomes, including depression, anxiety, fatigue and mental health. Remote CBT-I is more effective when delivered in a shorter period on the internet without therapist support. In addition to the most widely used components, such as sleep restriction, stimulus control and cognitive restructure, other components, such as sleep hygiene, relaxation training and homework, showed positive effects and can be considered to be included in treatment design. More studies that include randomised controlled trials that have

different designs are required in further studies to confirm the findings.

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Declarations

Conflict of Interest Dawei Xu, Zhanjiang Li, Unnah Leitner and Jing Sun have completed the Unified Competing Interest form and declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Informed Consent All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (national and institutional). Informed consent was obtained from all individual subjects participating in the study. Additional informed consent was obtained from any subjects for whom identifying information appears in this paper.

Animal Rights No animal studies were carried out by the authors for this article.

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