Efficacy of eHealth vs. in-person cognitive behavioral therapy for insomnia: A Systematic Review and Meta-Analysis of equivalence

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Abstract

Background: Insomnia is a prevalent condition with significant health, societal, and economic impacts. Cognitive Behavioral Therapy for Insomnia (CBTI) is recommended as the first-line treatment. With limited accessibility to in-person delivered CBTI (ipCBTI), electronically delivered (eHealth) CBTI (eCBTI), ranging from telephone- and videoconference delivered interventions to fully automated web-based programs and mobile applications, has emerged as an alternative. However, the relative efficacy of eCBTI compared to ipCBTI has not been conclusively determined.

Objective: To test the comparability of eCBTI and ipCBTI through a systematic review and meta-analysis of equivalence based on randomized trials directly comparing the two delivery formats.

Methods: A comprehensive search across multiple databases was conducted, leading to the identification and analysis of 15 unique randomized head-to-head comparisons of ipCBTI and eCBTI. Data on sleep and non-sleep outcomes were extracted and subjected to both conventional meta-analytical methods and equivalence testing based on predetermined equivalence margins derived from previously suggested minimal important differences (MIDs). Supplementary Bayesian analyses were conducted to determine the strength of the available evidence.

Results: The meta-analysis included 15 studies with a total of 1,100 participants. Conventional comparisons generally favored ipCBTI. However, the effect sizes were small, and the two delivery formats were statistically significantly equivalent for most sleep and non-sleep outcomes. Additional within-group analyses showed that both formats led to statistically significant improvements in insomnia severity, sleep quality, and secondary outcomes like fatigue, anxiety, and depression. Heterogeneity analyses highlighted the role of treatment duration and drop-out rates as potential moderators of the differences in treatment efficacy.

Conclusions: eCBTI and ipCBTI were found to be statistically significantly equivalent for treating insomnia for most examined outcomes, indicating eCBTI as a clinically relevant alternative to ipCBTI. This supports the expansion of eCBTI as a viable option to increase accessibility to effective insomnia treatment. Nonetheless, further research is needed to address the limitations noted, including the high risk of bias in some studies and the potential impact of treatment duration and drop-out rates on efficacy.

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Background: Insomnia is a prevalent condition with significant health, societal, and economic impacts. Cognitive Behavioral Therapy for Insomnia (CBTI) is recommended as the first-line treatment. With limited accessibility to in-person delivered CBTI (ipCBTI), electronically delivered (eHealth) CBTI (eCBTI), ranging from telephone- and videoconference delivered interventions to fully automated web-based programs and mobile applications, has emerged as an alternative. However, the relative efficacy of eCBTI compared to ipCBTI has not been conclusively determined.

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Keywords: sleep disturbance; digital; telehealth; face-to-face; head-to-head comparison; CBTI;

Introduction

Insomnia, characterized by difficulties initiating or maintaining sleep, which are perceived as distressing and result in significant impairment of daytime functioning, is a common concern in the general population [1]. It is estimated that around 20% of the population experience episodic symptoms of insomnia, resulting in negative consequences for daytime functioning, e.g., fatigue, with approximately 10% fulfilling the diagnostic criteria for an insomnia disorder [1]. The association between insomnia and adverse physical and mental health outcomes has been thoroughly documented, with numerous prospective studies showing increased risk of developing cardiovascular disease [2, 3], infectious diseases such as the common cold or pneumonia [4, 5], all-cause dementia [6] [7], mental disorders such as depression and anxiety [8], and social withdrawal and loneliness [9, 10]. In addition, not only short but also long sleep duration, both possible indicators of sleep disturbances, have been associated with increased mortality [11, 12]. Beyond the personal health implications, insomnia is associated with societal costs through increased healthcare utilization, higher levels of work absenteeism, diminished work-related productivity, reduced learning capacity, and poorer academic performance [13-15]. This underlines the extensive societal and economical burdens posed by untreated sleep disturbances.

While hypnotic medications are commonly used to treat insomnia, they are not recommended for long-term use due to the risk of developing tolerance and dependence [16] as well as a wide range of adverse consequences, including daytime drowsiness, impaired cognitive function, increased risk of accidents or falls, and rebound insomnia upon discontinuation [17, 18]. Instead, the major sleep medicine and research organizations recommend cognitive behavioral therapy for insomnia (CBTI) as the first-line treatment for insomnia [19-21]. CBTI usually involves a combination of two or more of the following five components [17]: (a) *sleep restriction therapy*, aiming at promoting more efficient and consolidated sleep patterns by first reducing the time spent awake in bed and then gradually allowing the person to increase time in bed [22], (b) *stimulus-control therapy*, which aims

to strengthen the connection between the bed and sleep by associating the bed and bedroom with sleep rather than wakefulness [23], c) *relaxation techniques*, which aims to reduce stress, anxiety, and tension that may interfere with falling asleep or staying asleep [24], (d) *cognitive therapy*, which targets negative thought patterns and maladaptive beliefs about sleep [25], and (e) *sleep hygiene education*, focusing on establishing healthy habits and optimizing the sleep environment to promote better sleep [26]. Several meta-analyses have supported the efficacy of CBTI in treating insomnia, both short-term [16, 27] and long-term [28], and not only insomnia as the primary problem, but also comorbid insomnia, e.g., in chronic pain patients [29] and cancer survivors [30]. Compared with pharmacotherapy, CBTI has been found to be at least as effective in reducing insomnia symptoms and generally demonstrates more durable effects than pharmacotherapy [31].

Nonetheless, substantial challenges remain in extending assistance to those affected. Individuals with insomnia rarely receive guideline-compliant treatment, hindered by various obstacles. These include insufficient numbers of trained CBTI providers, low rates of referral by primary care physicians, and geographical and physical barriers that deter patients from receiving help [32-34]. To address these challenges, several alternative eHealth delivery formats of CBTI have been developed and evaluated [32]. These alternatives include telephone- and videoconference-delivered CBTI and fully automated web-based programs and mobile applications.

Recently published meta-analyses have revealed statistically significant and clinically meaningful effects of eHealth CBTI (eCBTI) on various measures, including insomnia severity, self-reported sleep quality, and sleep diary-based outcomes such as sleep onset latency (SOL), wake after sleep onset (WASO), total sleep time (TST), and sleep efficiency (SE) [35, 36]. This efficacy extends not only to individuals with insomnia as their primary concern [37, 38] but also to those with comorbid insomnia, e.g., cancer survivors [39]. Still, the results of recent systematic reviews and network meta-analyses comparing various delivery formats of CBTI suggest that in-person delivered CBTI (ipCBTI) is generally superior to eCBTI and more so for insomnia severity than for sleep diary

outcomes [40, 41]. In contrast, a network meta-analysis investigating a Food and Drug Administration (FDA) authorized prescription eCBTI compared to traditional ipCBTI found that eCBTI was the most efficacious regarding insomnia severity [42].

The inconclusive results of the existing meta-analyses could be due to their reliance on both direct and indirect comparisons, and variations in treatment length, dosage, content, and control group types across studies of both formats which may compromise comparability [41]. To date, no meta-analysis has focused exclusively on randomized trials, conducting direct head-to-head comparisons of eCBTI and ipCBTI, and it thus remains unclear how well the two delivery formats compare in terms of efficacy.

Additionally, when examining the equivalence or non-equivalence of two interventions with meta-analysis, the conventional non-superiority null hypothesis test procedure is insufficient. Here, a non-significant result merely indicates a failure to reject the null hypothesis of no difference, which cannot conclusively determine non-equivalence or equivalence [43]. To truly test whether treatments are equivalent, we must reject the null hypothesis of non-equivalence, i.e., that differences in effect sizes are as large or larger than a predetermined equivalence margin [44]. When choosing equivalence margins, one will usually base these on previously determined minimal important differences (MIDs), referring to the minimal difference in an outcome of interest that can be viewed as clinically meaningful [45].

Given the prevalence of insomnia and the need for diverse treatment approaches, establishing the equivalence or non-equivalence of digital and traditional CBTI delivery formats is crucial. The possible equivalence or non-equivalence of eCBTI and ipCBTI has not yet been subjected to meta-analysis. The aim of the present study was, therefore, to test the comparability of eCBTI and ipCBTI with a systematic review and meta-analysis of equivalence based on randomized trials directly

comparing the two delivery formats.

Methods

The study was registered with the International Prospective Register of Systematic Reviews (PROSPERO) (registration number: CRD42023390811) and conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement [46].

Search strategy

The electronic databases of CINAHL, Cochrane, EMBASE, PsycInfo, and PubMed were searched for publications from the earliest time available until Jan 5, 2024. Keywords related to insomnia (e.g., sleep disturbance OR sleep disorder) were combined with keywords related to CBTI (e.g., cognitive behavioral OR CBT) and keywords pertaining to eHealth (e.g., telehealth OR digital). The search strings were constructed in collaboration with a skilled librarian. See Appendix, Table A1, for detailed search strings for each database. The electronic database searches were supplemented with backward searches of reference lists of included studies. No separate protocol in addition to the one registered with PROSPERO was prepared. The main methodological changes to the original registered protocol were: a) the search date was changed from 1991 to earliest time available due to the inclusion of additional electronic delivery formats, e.g., telephone-based interventions, and b) we also extracted data on secondary non-sleep outcomes of fatigue, anxiety, and depression.

Inclusion and exclusion criteria

Based on the PICO (Population, Intervention, Comparison, Outcome) approach [47], the following inclusion criteria were used: **Population:** Adults and adolescents (≥12 years) with a) self-reported poor sleep quality and/or symptoms of insomnia assessed with relevant instruments, e.g., the Insomnia Severity Index (ISI) [48] or the Pittsburgh Sleep Quality Index (PSQI) [49] or b) with an insomnia diagnosis established by a structured clinical interview. Studies of children <12 years,

together with studies focusing on other medical sleep disorders (e.g., sleep apnea, narcolepsy), were excluded. No exclusions were made based on comorbid disorders. **Intervention:** electronically-delivered (eHealth) cognitive behavioral therapy for insomnia (eCBTI), defined as CBTI delivered remotely or using digital means without in-person contact, e.g., by telephone or video, web-based CBTI, or smartphone-based CBTI. CBTI was defined as any combination of two or more of the standard CBTI components, i.e., sleep restriction therapy, stimulus-control therapy, relaxation, cognitive therapy, and sleep hygiene education. Other eHealth interventions aimed at treating insomnia, e.g., mindfulness-based interventions, were excluded, as were stand-alone CBTI components. **Comparison:** eCBTI had to be directly compared with in-person delivered CBTI (ipCBTI), defined as any combination of two or more standard CBTI components delivered in person, either individually or in group format. Other in-person-delivered interventions aimed at treating insomnia, including stand-alone CBTI components, were excluded. **Outcomes:** Studies should report means with standard deviations (SDs) or standard errors (SEs), change scores, effect sizes (e.g., Cohen's *d*), or data that could be converted into an effect size for at least one relevant sleep outcome, i.e., insomnia severity or clinically significant sleep disturbance assessed with relevant scales, e.g., the Insomnia Severity Index (ISI) [48] and the Pittsburgh Sleep Quality Index (PSQI) [49], or structured clinical interviews, or a relevant sleep parameter assessed with sleep diary, actigraphy, or polysomnography (PSG). Only randomized controlled trials (RCTs) published in English in peer-reviewed journals were included. Case studies, open trials, and other non-RCTs were excluded, together with studies with sample sizes <10.

Study selection and data extraction

Identified references were imported into the online software program Covidence [50]. After duplicate removal, title and abstract screening was performed, followed by full-text screening. One author (SK) conducted the final search, with three authors (SK, DC, PC) conducting the screening process independently. Discrepancies were resolved through discussions and, in case of disagreement, by

including a fourth author (RZ). The primary outcome was total sleep disturbance calculated as the combined, i.e., averaged, results for insomnia severity and/or sleep quality assessed with validated scales, e.g., ISI, PSQI, or similar. Secondary sleep outcomes were insomnia severity measured with the ISI, sleep quality measured with the PSQI, and the sleep diary and/or actigraphy-based outcomes of SOL, WASO, TST, and SE calculated as TST relative to time in bed (TiB). In addition, we extracted data on the secondary non-sleep outcomes of fatigue, anxiety, and depression, and for potential between-study characteristics as moderators of the difference between ipCBTI and eCBTI, including mean sample age, the proportion of women in the sample, study drop-out rates, type and degree of therapist contact, number of treatment sessions, treatment length, and the type and number of CBTI components in each condition. Three authors extracted data from the included studies independently and discrepancies were resolved through discussion and by including a fourth author (RZ).

Risk of bias assessment

The revised Cochrane Risk of Bias tool (ROB 2) [51] was used to evaluate the risk of bias in the included studies. Five sources of bias were assessed: (1) bias arising from the randomization process, (2) bias due to deviations from intended interventions, (3) bias due to missing outcome data, (4) bias in the measurement of the outcome, and (5) bias in the selection of the reported result. All studies were evaluated for each of the five potential sources of bias and rated as either "low risk", "high risk", or "some concerns" on the primary outcome of sleep disturbance. In addition, an overall assessment of the risk of bias was conducted for each study. As the number of drop-outs in studies investigating eCBTI is generally high with mean attrition rates ranging from 22% to 25% [36, 52], it was decided to use a less conservative criterion in domain 3. We thus considered the availability of data from ≥90% of participants at post-intervention sufficient. The assessments were conducted independently by three authors (SK, DC, and PC). Disagreements were solved by negotiation.

Data analysis

Hedges's g, a variation of Cohen's *d* correcting for possible bias due to small sample size [53], was used as the standardized effect size (ES). All ES calculations were based on differences between ipCBTI and eCBTI intervention groups in changes (means and SDs) from pre- to post-intervention, and pre-intervention to follow-up, standardized by change score SDs. If the relevant data were not reported, we contacted the authors, requesting them to provide this information. We also analyzed the mean differences across the different sleep-related outcomes, i.e., mean differences in ISI and PSQI scores, percentages for SE, and minutes for SOL, WASO, and TST. ESs were pooled using the inverse variance method, taking the precision of each study into account. A random-effects model was used in all analyses, with positive ESs indicating ipCBTI being more efficacious than eCBTI. If studies reported results for more than one measure per outcome, e.g., insomnia severity or sleep quality, we chose the most commonly used outcome measure, i.e., ISI for insomnia severity and the PSQI for sleep quality, so that only one result per study was used in each data synthesis, ensuring the independence of results.

Differences between ipCBTI and eCBTI were first analyzed using a conventional random effects test of superiority for results at both post-intervention (post) and follow-up (FU). The pooled ESs were then subjected to analyses of equivalence [44], testing whether the confidence interval fell within an equivalence interval based on the clinical significance thresholds (or minimal important differences, MIDs) previously suggested for the various sleep outcome measures. The MIDs were thus 0.5 SD for the standardized mean differences of sleep disturbance, insomnia severity, sleep quality, SE, SOL, WASO, and TST, as suggested in a previous study [54]. The MIDs for the mean differences were 4.4 points on the PSQI [55], and 5% for SE, 10 min for SOL, and 15 min for WASO and TST [54]. The 6 point MID previously suggested for the ISI [56] was based on an analysis of within-subject improvement, i.e., minimal important change (MIC). We used 0.5 × the average SD of 4.2 (= 2.6 points) for ISI at baseline in patients with insomnia reported in the original validation paper [48].

This SD corresponds well with the average SD of 4.1 found for ISI scores across studies at baseline in the present review. The equivalence interval of ± 0.25 SD for depression was chosen based on the MID previously suggested [57]. As no specific MIDs were available for the measures of fatigue and anxiety, ± 0.5 SD was chosen as the equivalence interval for these measures [58]. The equivalence test is based on two one-sided tests, with the two interventions considered to be statistically significantly equivalent if the largest of the two *p*-values is < .05 [44].

Heterogeneity was explored by calculating the I^2 statistic [59, 60]. In addition, we calculated the 95% prediction interval, i.e., the interval in which 95% of future observations from the same family of studies are expected to fall [61]. Possible reasons for heterogeneity of the differences between ipCBTI and eCBTI were explored with moderator analyses comparing the ESs of studies according to the following study characteristics: Mean sample age, the proportion of women in the sample (%), overall study drop-out (%), the difference in drop-out between eCBTI and ipCBTI (%), therapist contact in the eCBTI condition (reference: fully automated, i.e., no direct or indirect therapist contact), number of treatment sessions, and treatment duration (weeks). In addition, we explored the possible role of the number of CBTI components used in ipCBTI and eCBTI respectively. Both categorical and continuous moderators were analyzed with meta-regression when K (the number of studies in the analysis) was ≥10.

When K ≥ 10, the possibility of publication bias was evaluated with funnel plots and Egger's method [62]. If the results were suggestive of publication bias, we planned to calculate an adjusted ES using the Duval and Tweedie trim and fill method [63]. The calculations were conducted with Comprehensive Meta-Analysis, Version 4 [64] and various formulas in Microsoft Excel.

Finally, to assess the potential efficacy of each condition, we calculated the pooled within-participant differences for each condition at post-intervention and FU for all outcomes.

Supplementary Bayesian analyses

To aid the interpretation of the results, we conducted a supplementary Bayesian Model-Averaged

meta-analysis [65] of the overall comparisons of ipCBTI and eCBTI at post-intervention and follow-up. The procedure examined the results of four models: a) The fixed-effect null hypothesis, i.e., that the difference between ipCBTI and eCBTI is non-zero (fH_0), b) the fixed-effect alternative hypothesis, i.e., that the difference is zero (fH_1), c) the random-effects null hypothesis (rH_0), and d) the random effects alternative hypothesis (rH_1). Bayesian Model-Averaged analysis thus avoids selecting either a fixed- or random-effects model and addresses two questions in light of the observed data: What is the plausibility that the overall effect is zero, i.e., equivalent, and is there between-study variability in the effect sizes? Bayesian methods enable direct probability statements about the hypotheses themselves and avoid other issues associated with null-hypothesis significance testing, such as the over-reliance on relatively arbitrary *p*-value thresholds and the dichotomization of results into “significant” and “non-significant” [66]. We chose an uninformed prior probability, i.e., 25%, of the four models and 2000 iterations. Concerning parameter distributions, we chose previously recommended defaults [65], using a zero-centered Cauchy prior with a scale of 0.707 for the effect size and an empirically informed prior distribution of non-zero between-study deviation estimates from 705 meta-analyses [67]. This distribution has been approximated by an Inverse-Gamma (1, 0.15) prior on the standard deviation (Tau) [65]. The Bayesian analyses were conducted with the computer software JASP, Version 16 [68]. All data included in this review are available in tables and figures in the manuscript or the Appendix.

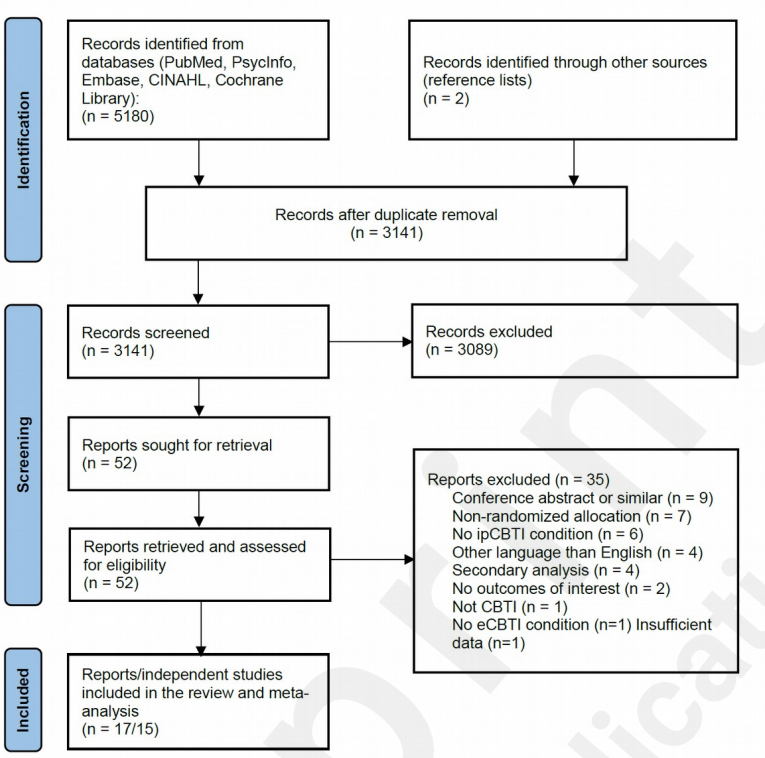
Results

Study selection

A total of 5180 records were identified via databases, and two additional records via reference lists. After 2039 duplicates were removed, 3141 references were screened by title and abstract. Full-text screening was carried out for 52 records, and after assessing eligibility, we identified 17 full-text reports of 15 unique randomized head-to-head comparisons of ipCBTI and eCBTI. The results of the

study selection process are shown in Figure 1.

Figure 1. Study selection flowchart



Study characteristics

The characteristics of the included studies are summarized in Table 1. Most of the studies were conducted in the U.S. (K=5), followed by Canada (K=3) and the Netherlands (K=2). The rest of the studies (K=5) were all conducted in different countries. A total of 1100 participants were included in the 15 studies, of which 61.3% were women. The mean age of the total sample was 40.6 years, with mean sample ages ranging from 15.5 to 55.1 years. Most studies focused on insomnia as the primary problem (K=11), and four studies focused on patients with comorbid insomnia, i.e., abstinent alcoholics (K=1), breast cancer survivors (K=1), and patients with PTSD (K=2). All studies had insomnia as an inclusion criterion, either based on diagnostic criteria, validated questionnaires, or quantitative criteria such as SOL, WASO or early morning awakening (EMA) of ≥30 minutes at least three nights a week or SE <85%.

Reported sleep outcomes were insomnia severity (K=13), with the ISI being the most frequently used

instrument (K=11), and sleep quality (K=5), with the PSQI being used by all studies reporting this outcome. Sleep diaries and actigraphy were used in 11 and 3 studies, respectively, assessing sleep parameters such as SOL, WASO, TST, TIB, and SE. Eleven studies assessed depression, with the Hospital Anxiety and Depression Scale (HADS) [69] (K=3) being the most frequently used, followed by the Beck Depression Inventory (BDI) [70] (K=2), the Patient Health Questionnaire (PHQ) [71] (K=2), and The Center for Epidemiologic Studies Depression Scale (CES-D) [72] (K=2). Nine studies assessed anxiety, with most (K=4) using the HADS, followed by the General Anxiety Disorder-7 (GAD-7) [73], and seven studies assessed fatigue, most frequently using the Multidimensional Fatigue Inventory (MFI) [74] (K=4). Fourteen studies reported follow-up data with time-to-follow-up ranging from nine to 52 weeks.

Table 1. Study characteristics

Study (country)	Participant character-ristics; insomnia type; sample type	Demo-graphic character er-istics (Mean age; % women)	N (eCBTI; ipCBTI) (total N)	eCBTI Treatment format; Delivery mode; Therapist contact; No. of sessions	ipCBTI Treat-ment format; No of sessions	Sleep out-comes	Secon-dary outcomes	Time to post; Time to FU (wks)	a) Study drop-out (eCBTI; ipCBTI) [a] b) Treatment drop-out (eCBTI; ipCBTI) [b]	No. of CBTI compo-nents (eCBTI; ipCBTI)	ROB-2: Low risk, some concerns, high risk
Currie et al., 2004 (Canada) [75]	Adults; Comorbid insomnia (abstinent alcoholics); Clinical	Mean age = 43.1; 30% women	28; 29 (57)	Individual; Self-help and telephone; Synchronous; 5 sessions	Individua l; 5 sessions	Insomnia severity; SQ; Sleep diary (SOL, WASO, TST, SE)	Depressi on	0; 26	a) 50%; 38% b) NR; NR	5; 5	Some concerns
Bastien, et al., 2004 (Canada) [76]	Adults; primary insomnia; Community	Mean age = 42.8; 62% women	14; 15 (29)	Individual; Telephone; Synchronous; 8 sessions	Individua l; 8 sessions	Insomnia severity; Sleep diary (SOL, WASO, TST, TIB, SE)	Anxiety; Depressi on	0; 26	a) 50%; 40% b) 0%; 0%	4; 4	High risk
Savard et al. 2014/2016 (Canada) [77, 78]	Adults; Comorbid Insomnia (breast cancer); Clinical	Mean age: 53.9; 100% women	80; 81 (161)	Individual; Video-based self-help with phone-support; Synchronous; 6 sessions	Individua l; 6 sessions	Insomnia severity; Sleep diary (SOL, WASO, TST, SE)	Fatigue; Anxiety, Depressi on	0; 52	a) 39%; 25% b) NR; NR	4; 4	High risk
Blom et al., 2015 (Sweden) [79]	Adults; Primary insomnia; Community	Mean age = 54.4, 48% women	24; 24 (48)	Individual; Web-based with written feedback; Asynchronou s; 8 sessions	Group; 8 sessions	Insomnia severity; Sleep diary (SOL, TST, SE)	Depressi on	0; 26	a) 38%; 29.2% b) 29%; 17%	5; 5	Some concerns
de Bruin et al.,	Adolescent s; Primary	Mean age =	39; 38 (77)	Individual; Web-based	Group; 6 sessions	Insomnia severity;	Anxiety; Depressi	0; 9-52	a) 56%; 53% b) 0; 0	5; 5	Some concerns

2015/2018 (The Netherlands) [80, 81]	insomnia; Community	15.5; 77% women		with written feedback and chat; Mixed; 6 sessions		Sleep diary and actigraphy (SOL; WASO; TST, TIB, SE)	on				
Lancee et al., 2016 (The Netherlands) [82]	Adults; Primary insomnia; Community	Mean age = 39.9; 80% women	30; 30 (60)	Individual; Web-based with e-mail feedback; Asynchronous; 6 sessions	Individual; 6 sessions	Insomnia Severity; Sleep diary (TST; SE)	Anxiety; Depression	4; 26	a) 30%; 13% b) 23%; 7%	5; 5	High risk
Taylor et al., 2017 (USA) [83]	Adults; Primary insomnia; Army personnel	Mean age = 32.7; 19% women	34; 33 (67)	Individual; Web-based (automated); None; 6 sessions	Individual; 6 sessions	Insomnia severity; Sleep diary and actigraphy (SOL, WASO, TST, SE)	-	0; NA	a) 21%; 9% b) 21%; 12%	5; 5	High risk
Franklin et al., 2018 (USA) [84]	Adults; Comorbid insomnia (PTSD); Clinical	Mean age = 53.8; 0% women	11; 7 (18)	Individual; Telephone; Synchronous; 6 sessions	Individual; 6 sessions	SQ	-	0; 13	a) 46%; 14% b) 18%; 0%	5; 5	High risk
Gieselmann et al., 2019 (Germany) [85]	Adults; Primary insomnia; Community	Mean age = 39.5; 52% women	23; 27 (50)	Individual; Chat; Synchronous; 3 sessions	Individual; 3 sessions	SQ; Sleep Diary and actigraphy (SOL, TST, SE)	Fatigue; Anxiety; Depression	0; 9	a) 9%; 33% b) NR; NR	2; 2	Some concerns
Gehrman et al., 2020 (USA) [86]	Adults; Comorbid insomnia (PTSD); Clinical	Mean age: 55.1, 10% women	49; 47 (96)	Group; Video conferencing; Synchronous; 6 sessions	Group; 6 sessions	Insomnia severity; SQ	-	2; 13	a) 20%; 13% b) 29%; 26%	5; 5	Some concerns
Arnedt et al., 2021 (USA) [87]	Adults; Primary insomnia; Community	Mean age = 47.2; 71% women	33; 32 (65)	Individual; Video conferencing; Synchronous; 6 sessions	Individual; 6 sessions	Insomnia severity; Sleep diary (SOL, WASO, TST, SE)	Fatigue; Anxiety; Depression	0; 13	a) NR; NR b) 6%; 3%	5; 5	Some concerns
Gehrman et al., 2021 (USA) [86]	Adults; Primary insomnia; Community	Mean age = 33.4; 63% women	21; 20 (41)	Individual; Video conferencing; Synchronous; 8 sessions	Individual; 8 sessions	Insomnia severity	Fatigue; Anxiety; Depression	3; 13	a) 0%; 5% b) 19%; 30%	5; 5	Some concerns
Kallestad et al., 2021 (Norway) [88]	Adults; Primary insomnia; Clinical	Mean age = 41.4; 75% women	49; 52 (101)	Individual; Web-based (automated); None; 6 sessions	Individual; 8 sessions	Insomnia severity; Sleep diary (SOL, WASO, TST, SE)	Fatigue	0; 26	a) 16%; 8% b) 12%; 0%	4; 4	Some concerns
Wong et al., 2021 (Hong Kong) [89]	Adolescents or older; Primary insomnia; Community	Mean age = 37.6; 64% women	70; 70 (140)	Individual; Web-based self-help; None; 4 sessions	Group; 1 session (workshop)	Insomnia severity	Anxiety; Depression	4; 12	a) 26%; 30% b) NR; 49%	5; 5	Some concerns
Chan et al., 2022 (China) [90]	Youths; Primary insomnia; Community	Mean age = 20.2; 69% women	45; 45 (90)	Individual; E-mail self-help; None; 8 sessions	Group; 8 sessions	Insomnia severity; SQ; Sleep diary (SOL, WASO, TST, TIB, SE)	Fatigue; Anxiety; Depression	1; 26	a) 47%; 22% b) 38%; 4%	5; 4	High risk

Abbreviations: eCBTI: eHealth cognitive behavioral therapy for insomnia; ipCBTI: In-person-delivered CBTI; NA = not applicable; NR = Not reported; SQ = sleep quality; SOL = sleep onset latency; WASO = wake after sleep onset; TST =

total sleep time, TIB = Time in bed; SE = sleep efficiency (%) (TST/TiB×100). Notes: a) study drop-out: Proportion of participants lost to follow-up at the most distant time-point after baseline; b) treatment drop-out: Proportion of participants who dropped out of treatment (defined as completing fewer than 50% of treatment cores/sessions)

In all but one study, eCBTI was delivered individually. In most studies, eCBTI involved some degree of interaction with a treatment provider (K=10), with real-time, synchronous therapist contact being available in eight studies and asynchronous support, e.g., by e-mail, being offered in two studies. One study provided both synchronous and asynchronous therapist contact. In four studies, eCBTI was provided completely without interaction with a treatment provider, e.g., with a fully automated format. ipCBTI was primarily delivered individually (K=10), with five studies using a group format.

Risk of bias

The risk of bias in the individual studies is summarized in the Appendix, Figure A1. Ten studies (67%) were characterized as having some concerns regarding the overall risk of bias, and the remaining five studies (33%) were classified as having a high risk of bias overall. No studies were characterized as having a low risk of bias. The reasons for being categorized as having a high risk of bias stemmed primarily from “bias due to missing outcome data” due to the combination of high rates of missing outcome data and failure to include analyses correcting for this, e.g., sensitivity analyses. Bias raising “some concerns” primarily stemmed from “bias in the measurement of the outcome” due to the combination of using a self-reported outcome and non-blinding. Only few studies had attempted some element of blinding. Three studies [85, 87, 89] reported that participants were kept blind to study hypotheses, one study reported that treatment providers were kept blind to study hypotheses [85], and two studies reported that the data analyst was blinded to allocation status of the participants [88, 89]. In addition, bias raising “some concerns” stemmed from “bias in the selection of the reported result” due to inadequate preregistration of the analytical strategy.

Comparing intervention characteristics of ipCBTI and eCBTI

More participants had dropped out of eCBTI than ipCBTI at both post-intervention (19.5% vs. 9.7%)

and FU (32.6% vs. 25.9%). The differences, however, did not reach statistical significance (p= 0.09 and 0.33). No between-condition differences were found in the mean number of sessions (6.0 vs. 6.1; p=0.914), duration of the intervention (6.7 weeks vs. 6.6 weeks; p=0.828), and the number of CBTI components (4.5 vs. 4.6; p=0.828).

Within-group effects

As seen in Appendix, Table A3, statistically significant improvements from pre- to post-intervention and from pre-intervention to follow-up were observed for both ipCBTI and eCBTI for all self-reported sleep outcomes. At post-intervention, the effect sizes (Hedges' g) ranged from 0.27 (TST) to 1.97 (ISI) for ipCBTI and from0.23 (TST) to 1.36 (ISI) for eCBTI. Similarly, at FU, effect sizes ranged from 0.43 (TST) to 1.88 (ISI) for ipCBTI and from 0.39 (TST) to 1.41 (total sleep disturbance) to for eCBTI. For the few actigraphy-based sleep outcomes at post-intervention (K=3), only the results for SOL in the ipCBTI condition (g=0.53; mean difference= −11.5 min) reached statistical significance. At post-intervention, in the ipCBTI condition, ISI was, on average, improved by 9.0 points, the PSQI by 4.4 points, diary-based SE by 12.1%, and diary-based SOL, WASO, and TST by −20.9, −23.5, and +21.3 min, respectively. The comparable results for eCBTI were 7.1 points, 3.5 points, 10.3%, −19.6 min, −19.5 min, and +16.3 min. As also seen in Appendix, Table A3, the within-participant improvements in fatigue, anxiety, and depression were all statistically significant and similar for both delivery formats at post-intervention. Similar results were found for the secondary non-sleep outcomes at FU (data not shown).

Conventional superiority meta-analysis

As seen in Table 2, when analyzed with conventional superiority meta-analysis, the pooled differences between ipCBTI and eCBTI reached statistical significance in 11 out of 32 comparisons. The effects generally favored ipCBTI but were small, e.g., corresponding to a mean difference of 1.8 points on the ISI and 1.9% in SE. The pooled difference for total sleep disturbance corresponded to a small effect size (g = 0.32). The forest plots are shown in Figures 2 to 4, and Appendix, figures A2-

A11. Concerning the secondary non-sleep outcomes of fatigue, anxiety, and depression, no differences in the conventional superiority analyses reached statistical significance (Appendix, Table A4)

Equivalence meta-analysis

As shown in Table 2, the equivalence CI for total sleep disturbance was 0.14 to 0.49. As the 95%CI was included in the pre-specified equivalence interval for this outcome, the null-hypothesis of non-equivalence was rejected (p=0.042). As shown in Table 2, based on the pre-specified equivalence intervals for the various sleep outcomes, ipCBTI and eCBTI were statistically significantly equivalent for a total of 25 out of 32 calculations, and based on the pre-specified equivalence intervals, ipCBTI and eCBTI emerged as statistically significantly equivalent for all three secondary non-sleep outcomes at both time points (see Appendix, Table A4).

Figure 2. Forest plot of post-intervention differences (Hedges's g) between effects of eCBTI and ipCBTI on total sleep disturbance (red lines denote the equivalence margin)

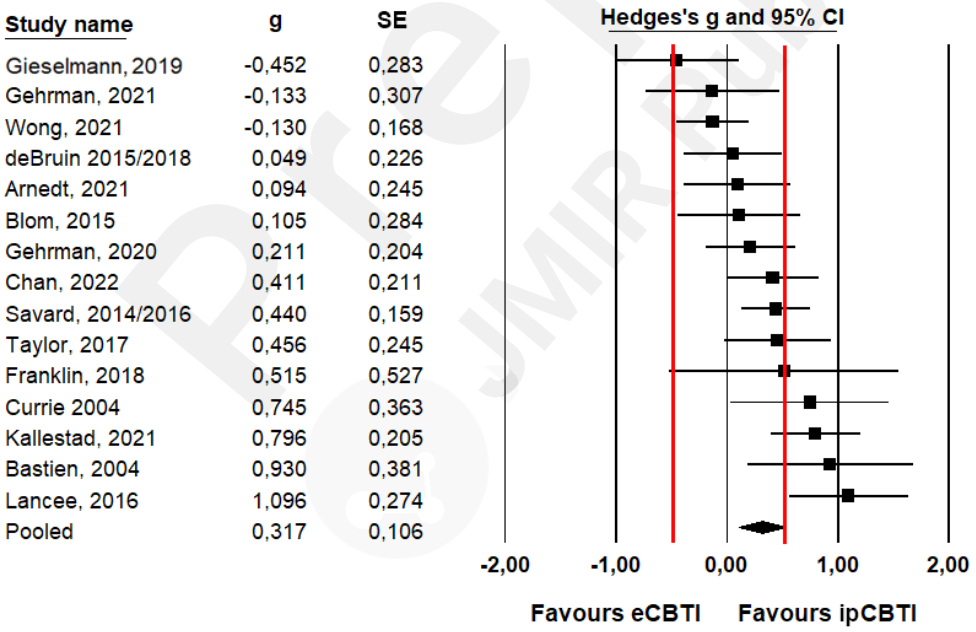


Figure 3: Forest plot of post-intervention mean differences (%) between effects of eCBTI and ipCBTI on sleep efficiency (SE) (red lines denote the equivalence margin)

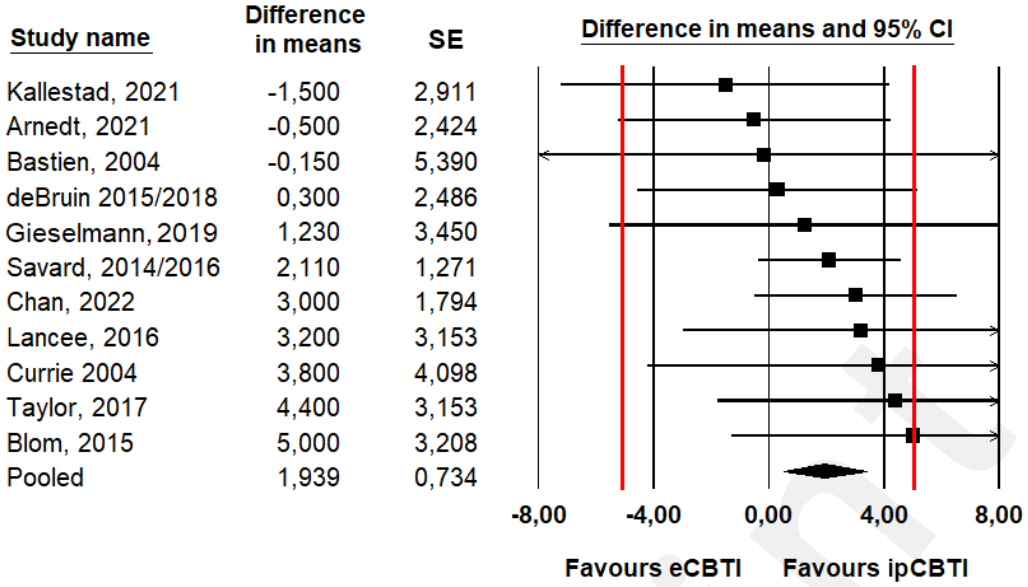
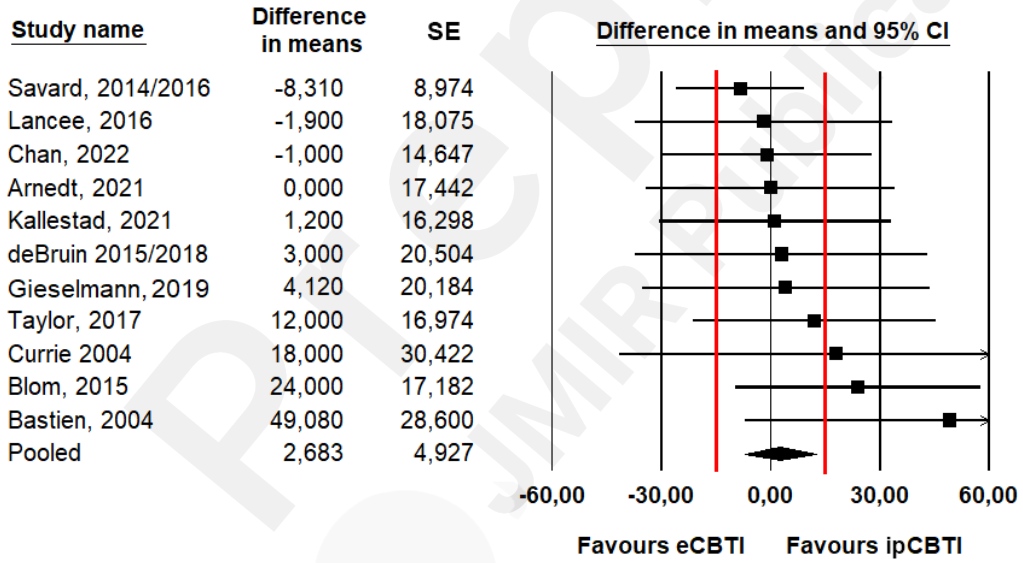


Figure 4: Forest plot of post-intervention mean differences (minutes) between effects of eCBTI and ipCBTI on total sleep time (TST) (red lines denote the equivalence margin)



Publication bias and outliers

Inspecting the funnel plot and Egger's test for total sleep disturbance, which included data from all included studies (K=15), did not indicate publication bias (Egger's test, p=.56) (see funnel plot in Appendix Figure A12). Considering effect sizes (ESs) beyond the pooled ES ±2 standard deviations (SDs) revealed no outliers.

Table 2. Results of meta-analysis of studies directly comparing the efficacy of in-person delivered cognitive behavioral therapy for insomnia (ipCBTI) and telehealth or digitally delivered CBTI (eCBTI), including tests of differences being different from zero and tests of statistical equivalence.

Comparison: ipCBTI vs eCBT	Heterogeneity				Pooled effect				Equivalence [f]	
	K [a]	N [b]	I^2	T^2	Effect [c]	95%CI	*P* [d]	95%PI [e]	MID	*P*
Self-reported sleep outcomes - Post-intervention										
Total sleep disturbance (Hedges' g)	15	1068	63.5	0.10	0.32	0.11;0.53	.003*	-0.41;1.04	0.5 SD[h]	.04*
ISI (mean difference, pts.)	11	897	70.0	2.35	-1.8	-2.9;-0.7	.002*	-5.48;1.92	2.6 pts[g]	.07
ISI (Hedges' g)	11	897	63.7	0.09	0.37	0.15;0.60	.001*	-0.35;1.10	0.5 SD[h]	0.13
PSQI (mean difference, pts.)	5	279	63.1	1.48	-0.9	-2.3;0.6	.23	-5.35;3.64	4.4 pts [i]	<.001*
PSQI (Hedges' g)	5	279	62.0	0.13	0.26	-0.15;0.67	.22	-1.06;1.58	0.5 SD [h]	.12
SE diary (mean difference, %)	11	779	00.0	0.00	1.9	0.5;3.4	.01*	N/A	5% [j]	<.001*
SE diary (Hedges' g)	11	779	00.0	0.00	0.17	0.03; 0.31	.02*	N/A	0.5 SD [h]	<.001*
SOL diary (mean difference, min)	10	719	00.0	0.00	-2.6	-6.5; 1.2	.18	N/A	10 min [k]	<.001*
SOL diary (Hedges' g)	10	719	2.0	0.00	0.07	-0.08;0.21	.39	-0.13;0.26	0.5 SD	<.001*
WASO diary (mean difference, min)	8	621	14.7	7.80	-2.5	-7.5;2-6	.34	-11.79;6.82	15 min [l]	<.001*
WASO (Hedges' g)	8	621	12.7	0.01	0.09	-0.08;0.26	.30	-0.21;0.39	0.5 SD [m]	<.001*
TST (mean difference, min)	11	779	00.0	0.00	-2.7	-12.3;7.0	.59	N/A	15 min [n]	.01*
TST (Hedges' g)	11	779	00.0	0.00	0.05	-0.09;0.19	.52	N/A	0.5 SD [m]	<.001*
Self-reported sleep outcomes - Follow-up										
Total sleep disturbance (Hedges' g)	14	988	58.1	0.08	0.24	0.04;0.45	.02*	-0.42;0.90	0.5 SD [h]	.01*
ISI (mean difference, pts.)	10	817	65.7	1.98	-1.3	-2.4;-0.2	.02*	-4.81;2.20	2.6 pts [g]	<.001*
ISI (Hedges' g)	10	817	61.4	0.08	0.27	0.04;0.50	.02*	-0.44;0.98	0.5 SD [h]	.03*
PSQI (mean difference, pts.)	5	279	55.8	1.20	-0.8	-2.1;0.6	.28	-4.87;3.37	4.4 pts [i]	<.001*
PSQI (Hedges' g)	5	279	53.8	0.09	0.21	-0.16;0.58	.27	-0.92;1.34	0.5 SD [h]	.06
SE diary (mean difference, %)	10	700	52.0	7.81	2.8	0.3;5.4	.03*	-4.26;9.92	5% [j]	.047*
SE diary (Hedges' g)	10	700	51.3	0.06	0.25	0.03;0.47	.03*	-0.38;0.88	0.5 SD [h]	.01*
SOL diary (mean difference, min)	9	640	9.0	4.46	-4.8	-9.3;-0.2	.04*	-12.14;2.65	10 min [k]	.01*
SOL diary (Hedges' g)	9	640	22.0	0.02	0.14	-0.04;0.32	.12	-0.23;0.52	0.5 SD	<.001*
WASO diary (mean difference, min)	7	542	37.1	24.2	0.6	-5.9;7.0	.87	-14.66;15.77	15 min [l]	<.001*
WASO diary (Hedges' g)	7	542	35.4	0.03	-0.02	-0.24;0.20	.86	-0.55;0.51	0.5 SD [m]	<.001*
TST	10	700	38.3	193.2	6.3	-8.2;20.9	.39	-29.98;42.66	15 min [n]	.12

(mean difference, min)										
TST (Hedges' g)	10	700	36.9	0.03	0.08	-0.11; 0.28	.40	-0.40;0.57	0.5 SD [m]	<.001*
Actigraphy-based sleep outcomes – post-intervention										
SE actigraphy (mean difference, %)	3	194	00.0	0.00	-0.8	-2.9;1.3	.47	N/A	5% [j]	<.001*
SE actigraphy (Hedges' g)	3	194	00.0	0.00	-0.09	-0.37;0.19	.53	-1.91;1.73	0.5 SD [h]	.002*
SOL actigraphy (mean difference, min)	3	194	00.0	0.00	-2.6	-8.9;3.6	.41	-43.07;37.83	10 min [k]	.01*
SOL actigraphy (Hedges' g)	3	194	00.0	0.00	0.14	-0.14;0.42	.32	-1.68;1.96	0.5 SD [h]	.01*
TST actigraphy (mean difference, min)	3	194	2.8	7.04	-16.9	-34.6;0.8	.06	-136.2;102.4	15 min [n]	.42
TST actigraphy (Hedges' g)	3	194	31.2	0.03	-0.24	-0.58;0.10	.17	-3.33; 2.87	0.5 SD [h]	.09

Abbreviations and explanations: ipCBTI: In-person delivered cognitive-behavioral therapy for insomnia; eCBTI: eHealth CBTI; Post: post-intervention; FU: Follow-up; Sleep disturbance (All): combined self-report sleep outcomes, e.g., ISI, PSQI, HSDQ; ISI: Insomnia Severity Index; PSQI: Pittsburgh Sleep Quality Index; HSDQ: Holland Sleep Disorder Questionnaire; SE: Sleep Efficiency (%) ((TST/TiB (time in bed))×100); SOL: Sleep Onset Latency (minutes); WASO: Wake after sleep onset (minutes); TST: Total sleep time (minutes); Diary: Sleep parameters based on sleep diaries, e.g., The Consensus Sleep Diary [91]; Actigraphy: Sleep parameters based on actigraphy; MID = Minimal Important Difference (or Clinical Significance Threshold) (see e.g., [54]).
Notes: a) K = number of studies; b) N= total number of participants; c) Analyses were conducted for outcomes with K ≥ 3 for mean differences (%, minutes) and SMD (Hedges's g: Standardized Mean Difference adjusted for small sample bias) [53], with positive values of Hedges's g indicating difference of effects in favor of ipCBTI compared to eCBTI; d) P-values (two-tailed): Statistically significant ($P< 0.05$) marked with *; e) 95% prediction interval, i.e., the interval in which 95% of future observations from the same family of studies will fall [61]; f) Test of equivalence: tests whether the confidence interval (CI) falls within an equivalence interval. The equivalence test is based on the largest *p*-value from two one-sided tests [44]. P-values marked with ***** indicate equivalence. The tests are based on the following definitions of minimal important differences (MIDs): g) 2.6 point difference on the ISI, corresponding to 0.5 × the SD found in the original validation study (SD=4.2) [48] (average ISI baseline SD across studies in the present review = 4.1; h) SMD = 0.50, suggested by [54]; i) 4.4 point difference on the PSQI suggested by [55]; j) 5% difference suggested by [54]; k) 10 minute difference in SOL suggested by [54]; l) 15 minute difference in WASO suggested by [54]; m) When no available MIDs are available, we have chosen 0.5 SD as suggested by [58]; n) 15 min difference in TST suggested by [54].

Heterogeneity and moderator analyses

As seen in Table 2, heterogeneity analyses suggested varying proportions of the variance in post-intervention effects stem from between-study differences beyond random error. The I^2 values were highest for the questionnaire-based sleep outcomes (62.0% to 70.0%) and generally lower for the sleep diary and actigraphy-based outcomes (0.0% to 31.2%). The data also suggested relatively high levels of heterogeneity for outcomes at follow-up. As shown in Table 3, when exploring possible explanations for the heterogeneity with meta-regression, two of the eleven analyzed moderators reached statistical significance. Differences between the proportions of drop-outs in the eCBTI and ipCBTI moderated the between-group effects, with larger drop-out in eCBTI compared with ipCBTI

being associated with larger differences in favor of ipCBTI at both post-intervention and FU, explaining 50% and 74% of the variation, respectively. Longer overall treatment duration was associated with larger differences in favor of ipCBTI compared with eCBTI at both time points. No statistically significant effects were found for the remaining moderators analyzed.

Results of supplementary Bayesian analyses

As seen in Appendix Table A5, the Bayesian meta-analyses favored the alternative hypothesis of equivalence, i.e., a zero difference between ipCBTI and eCBTI, for 4 out of 6 sleep outcomes at post-intervention. The Bayes factors (BFs), i.e., the probabilities of the alternative hypotheses relative to the null hypotheses, ranged from 1.7 (PSQI) to 9.9 (TST), indicating that a zero difference between ipCBTI and eCBTI is 1.7 to 9.9 times more likely than a non-zero difference. The level of the evidence [92] ranged from anecdotal (BF: 1-3) for PSQI to moderate (3-10) for SOL, WASO, and TST. A zero and non-zero difference for SE appeared equally likely (BF=1.2). ISI was the only outcome for which the current evidence clearly favored a non-zero difference, with this result being 10.5 times more likely than the null-hypothesis. Concerning heterogeneity, the data provided strong (BF=13.0) and anecdotal evidence (BF=2.3) for heterogeneous ISI and PSQI effect sizes, respectively. Non-heterogeneity was slightly more likely for the remaining outcomes (BF=1.9 to 3.5).

Table 3. Results of moderator analyses based on standardized mean differences (Hedges' g) in total self-reported sleep disturbance outcomes between ipCBTI and eCBTI at post-intervention and follow-up.

Moderator	Time-point [a]	K [b]	Slope [c]	95%CI	*P* [d]	R^2
Mean sample age	Post	14	0.01	-0.01; 0.02	.55	.04
	FU	12	-0.01	-0.02; 0.01	.34	.18
Percent women	Post	15	0.00	-0.01; 0.01	.71	.03
	FU	13	0.00	-0.00; 0.01	.40	.07
Comorbid insomnia (ref. primary)	Post	15	0.16	-0.31;0.62	.51	.04
	FU	15	0.12	-0.31;0.56	.58	.06
Study drop-out (%)	Post	13	0.00	-0.02; 0.03	.78	.00
	FU	13	0.00	-0.01; 0.01	.68	.10
eCBTI-ipCBTI dropout difference (%) [e]	Post	13	0.02	0.00; 0.03	**.02**	.50

	FU	13	0.02	0.01; 0.03	**.004**	.74
eCBTI therapist contact (ref. none)	Post	15	-0.07	-0.51; 0.36	.74	.01
	FU	14	0.16	-0.28; 0.59	.48	.11
Number of treatment sessions	Post	15	0.10	-0.03; 0.24	.14	.26
	FU	14	0.11	-0.03; 0.25	.13	.32
Treatment duration (weeks)	Post	15	0.18	0.09; 0.26	**<.001**	.93
	FU	14	0.16	0.08; 0.24	**<.001**	.94
Number of eCBTI components	Post	15	0.11	-0.15; 0.37	.41	.03
	FU	14	0.18	-0.06; 0.42	.14	.15
Number of ipCBTI components	Post	15	0.09	-0.16; 0.35	.47	.02
	FU	14	0.17	-0.07; 0.41	.18	.11
Time to follow-up (weeks)	FU	14	0.01	-0.00; 0.02	.07	.34

Notes: a) Post = post-intervention; FU = follow-up; b) K = number of studies in the analysis; c) Meta-regression (maximum likelihood method), conducted when K ≥ 10; d) Two-tailed p-value, significant (p< .05) highlighted in **bold**; e) Difference in drop-out (%) between conditions (eCBTI drop-out minus ipCBTI drop-out) Positive values correspond to larger drop-out in eCBTI compared to ipCBTI. Combined self-reported sleep quality outcomes include measures of insomnia severity (ISI) and sleep quality (PSQI).

Discussion

Sleep outcomes

When pooling the results of the 15 unique randomized trials directly comparing eCBTIs with ipCBTIs using conventional meta-analysis, the observed differences generally favored ipCBTI. Specifically, the post-intervention results revealed statistically significant advantages for ipCBTI across several dimensions, including overall sleep disturbance (encompassing both insomnia severity and sleep quality), insomnia severity assessed independently, and SE. While ipCBTI was statistically significantly superior to eCBTI for these outcomes, the magnitudes of these differences were modest, corresponding to small effect sizes (Hedges's g) and small mean, non-standardized differences. For example, concerning the latter, the pooled mean differences in favor of ipCBTI for insomnia severity and SE were only 1.8 points (on the ISI) and 1.9%, respectively. Furthermore, for total sleep disturbance and SE, the confidence intervals fell within the suggested equivalence margins of ±0.5 SD and ±5%) [54].

Regarding the remaining self-reported sleep outcomes at post-intervention, none yielded statistically significantly superior results in favor of either delivery type. Furthermore, with the exception of

Hedges's g for the PSQI, all remaining analyses showed the two delivery types to be statistically significantly equivalent, i.e., that the confidence intervals of the pooled effect parameter fell within the suggested equivalence margin for that parameter. The same general pattern was observed for the results obtained at the (on average) 21-week follow-up. Based on the available data, eCBTI and ipCBTI were statistically significantly equivalent for almost all self-reported sleep outcomes, except for the effect size for sleep quality assessed with the PSQI and the mean difference in minutes for TST.

While equivalence indicates similar efficacy, if one only examines the between-group differences, it cannot be determined whether the equivalence stems from similar small or similar large improvements in both conditions. We, therefore, also calculated the within-group effects for each delivery format. The results revealed that both ipCBTI and eCBTI were associated with statistically significant within-condition improvements in all self-reported outcomes at both post-intervention and follow-up. The largest effects were seen in both conditions for total sleep disturbance, insomnia severity, sleep quality, and SE. Small-to-medium effects were observed for the remaining self-reported sleep outcomes. It may thus be concluded that both delivery formats appear efficacious, displaying improvements at post-intervention corresponding to 9 and 7-point reductions on the ISI, 12% and 10% improvements in SE, 21 and 20 minutes reductions in SOL, 24 and 20 minutes reductions in WASO, and 21 to 16 minutes increased TST for ipCBTI and eCBTI, respectively. These effects are all clinically relevant and well beyond the suggested MIDs and MICs for these outcomes, i.e., a 6-point within-person change on the ISI [56] and 10, 15, and 15 minutes for SOL, WASO, and TST, respectively [54]. In addition, these clinically relevant, positive improvements were sustained over time, supporting previous findings that CBTI, regardless of the delivery format, yields robust long-term effects[28].

Only three studies had assessed sleep objectively, i.e., with actigraphy. Despite the small number of studies, the results for SE and SOL showed the two delivery formats to be statistically significantly

equivalent. In contrast, the results for actigraphy-assessed TST appeared to be in favor of eCBTI, with the eCBTI resulting in increased TST and ipCBTI in reduced TST. However, neither the conventional nor the equivalence analyses reached statistical significance. When examining the within-group effects, statistically significant improvements were seen for actigraphy-based SOL in the ipCBTI group. The remaining effects for TST and SE failed to reach statistical significance. Such discrepancies between effects on self-reported and objectively assessed sleep outcomes, especially concerning estimates of sleep duration, are a well-recognized issue in sleep research and clinical practice [93].

Non-sleep outcomes

It is well-known that insomnia can lead to various physical and mental symptoms, including increased levels of fatigue [94], and that it is a significant predictor of later onset of mental disorders such as depression and anxiety [8]. We, therefore, also explored the effects on the secondary non-sleep outcomes of fatigue, anxiety, and depression. The two delivery formats of CBTI were statistically significantly equivalent in their effects on these symptoms, and both yielded statistically significant medium-to-large within-condition improvements of almost identical magnitude in all three outcomes. Our results thus add to the more general findings that CBTI may not only improve insomnia itself but also associated psychological and physical symptoms such as depression, anxiety, and fatigue [95-97], with our findings indicating that both delivery formats appear equally efficacious in reducing these symptoms.

Heterogeneity and its sources

When exploring possible heterogeneity of the post-intervention effects, the relatively large I^2 statistics observed for both insomnia severity and sleep quality and the combined outcome of total sleep disturbance indicate that a considerable proportion of the variance is due to systematic differences between the study characteristics. In contrast, the differences in effects on sleep diary outcomes displayed little or no signs of heterogeneity. When we investigated possible sources of

heterogeneity for the combined total sleep disturbance outcome, two study characteristics emerged as statistically significant moderators at both post-intervention and follow-up.

First, larger drop-out rates in the eCBTI conditions compared to ipCBTI were significantly associated with larger differences in favor of ipCBTI in effect on total sleep disturbance. At post-intervention, on average, twice as many participants in eCBTI had dropped out compared to ipCBTI. While we do not know the reasons for the larger drop-out rates in eCBTI, this factor, which explained between 50% and 74% of the variance in between-condition difference in effect, could represent an important, potentially modifiable factor that needs to be addressed if the efficacy of eCBTI is to be further increased. While the research on adherence to electronically adapted interventions for insomnia is still limited, studies in this [98] and other clinical populations suggest that common factors influencing drop-out and adherence across such interventions include engagement and motivation, technical issues and usability, and demographic factors such as age, educational level, and digital literacy [99, 100]. Second, while there was no difference in the mean duration of the two delivery formats, intervention with longer duration favored ipCBTI. The moderating effect of intervention duration persisted when adjusting for study drop-out. We have no clear explanation for this finding, but longer treatment duration may allow for increased trust and improved therapeutic alliance in personally delivered CBTI, which, in turn, will increase the effect.

None of the remaining moderators analyzed reached statistical significance, including demographic characteristics such as mean sample age and percent women in the sample, study characteristics such as time to follow-up, and treatment characteristics such as therapist contact versus no contact, number of treatment sessions, and number of CBTI components. Some of the non-significant results could be viewed as surprising. For example, one might have expected larger differences between ipCBTI and fully automated eCBTI than between ipCBTI and eCBTI with some degree of therapist contact. One would also have expected age to play a role, e.g., that older sample age would be associated with larger between-condition differences. Possible reasons for non-significant findings

could be insufficient between-study variation, e.g., in sample age, and inadequate statistical power due to the relatively small number of studies. Further research is needed to identify the common and different factors associated with increased efficacy of the two delivery formats.

Limitations

Our findings should be interpreted cautiously for several reasons.

First, the interpretability is challenged by between-study heterogeneity, e.g., by considerable between-study differences in eCBTI formats, with some eCBTIs delivered with direct therapist contact by telephone or video-conferencing, some delivered on the web with asynchronous therapist contact, e.g., through e-mail, and others offered as fully automated programs. While we attempted to explore the possible moderating role of such variations and found no indication of a moderating effect of the degree of therapist contact involved, the relatively small number of studies may have limited our ability to identify the influence of such characteristics.

Second, as demonstrated by the results of the Bayesian analyses, the small number of studies restricts the strength of the evidence. While the currently available evidence favored equivalent effects for four out of six outcomes (sleep quality, SOL, WASO, and TST), the level of evidence was weak (i.e., anecdotal) to moderate. The evidence for SE was inconclusive, and while the level of evidence for a non-zero difference in favor of ipCBTI was characterized as "strong," the BF was only just above the lower limit (i.e., ≥ 10) [92].

Third, interpreting the differences between eCBTI and ipCBTI as equivalent or non-equivalent clearly depends on the chosen equivalence margins. While we chose the minimal important differences (MIDs) suggested in the literature, e.g., 2.6 points, 4.4 points, 5%, 10 minutes, 15 minutes, and 15 minutes for ISI, PSQI, SE, SOL, WASO, and TST, respectively [48, 54, 55], specific MIDs have not been identified for all of the corresponding effect sizes. While we here used the 0.5 SD suggested in the literature [54, 58], the clinical relevance of this value has yet to be established for several of the sleep outcomes investigated in the present study.

Finally, assessed with the revised Cochrane risk of bias tool [51], one-third of the studies were characterized as having an overall "high risk" of bias, and the remaining two-thirds were characterized as having "some concerns." Among the main reasons for these categorizations were high rates of missing outcome data and the use of self-reported outcomes. These issues cannot easily be amended. For example, it is not too surprising that behavioral interventions, in general, and eHealth interventions, in particular, have higher drop-out rates than pharmacological trials. In addition, while sleep characteristics such as SOL, WASO, and TST can be assessed with both self-report and objective measures, insomnia is inherently a subjective outcome, which can only be evaluated with self-report. Furthermore, ensuring blinding is another factor that is difficult to obtain with behavioral interventions, and not possible when comparing in-person and electronically delivered interventions. Other reasons for the risk of bias assessments can be addressed more easily, including the failure to include sensitivity analyses correcting for missing outcome data and insufficient preregistering of analytical plans.

Conclusions

This, to our knowledge, first systematic review and meta-analysis of randomized head-to-head comparisons of eHealth CBTI and in-person delivered CBTI suggests that while the effects tended to be in favor of the latter, the mean differences were generally of small magnitudes, with several approaching zero. Furthermore, the two CBTI delivery formats were statistically significantly equivalent for most outcomes examined. Statistically significant equivalence means that the confidence intervals of the differences fell within the pre-specified equivalence margins, with the latter being based on the minimal clinically relevant differences suggested in the literature for each of the outcomes in question. Importantly, when examining the within-condition effects, both delivery formats yielded large and clinically relevant effects on most outcomes, including the non-sleep outcomes of fatigue, anxiety, and depression. Although the results should be interpreted cautiously due to the currently limited evidence base, they support eHealth CBTI, including fully automated

programs, as clinically relevant alternatives to CBTI delivered in person. These results are promising for people with insomnia, given the challenges of meeting population needs with conventional treatment formats.

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Conflicts of interest

None declared

Multimedia Appendix 1

Supplementary information: Tables A1-A5; Figures A1-A12
[URL File name]

Legends to figures

Figure 1. Study selection flowchart

Figure 2. Forest plot of post-intervention differences (Hedges's g) between effects of eCBTI and ipCBTI on total sleep disturbance

Figure 3: Forest plot of post-intervention mean differences (%) between effects of eCBTI and ipCBTI on sleep efficiency (SE)

Figure 4: Forest plot of post-intervention mean differences (minutes) between effects of eCBTI and ipCBTI on total sleep time (TST)

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Abbreviations

BDI: Beck Depression Inventory

BF: Bayes factor

CBTI: Cognitive behavioral therapy for insomnia

CES-D: Center for Epidemiologic Studies Depression Scale

CI: Confidence interval

eCBTI: electronically delivered (eHealth) CBTI

EMA: Early morning awakening

ES: Effect size

FDA: Food and Drug Administration

FU: Follow-up

GAD-7: General Anxiety Disorder-7

HADS: Hospital Anxiety and Depression Scale

ipCBTI: in-person delivered CBTI

ISI: Insomnia Severity Index

K: Number of studies

MFI: Multidimensional Fatigue Inventor

MID: Minimal important difference

PHQ: Patient Health Questionnaire

PICO: Population, Intervention, Comparison, Outcome

PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analysis

PROSPERO: International Prospective Register of Systematic Reviews

PSG: Polysomnography

PSQI: Pittsburgh Sleep Quality Index

RCT: Randomized controlled trial

RoB 2: Revised Cochrane Risk of Bias tool

SD: Standard deviation

SE: Sleep efficiency

SE: Standard error

SOL: Sleep onset latency

TiB: Time in bed

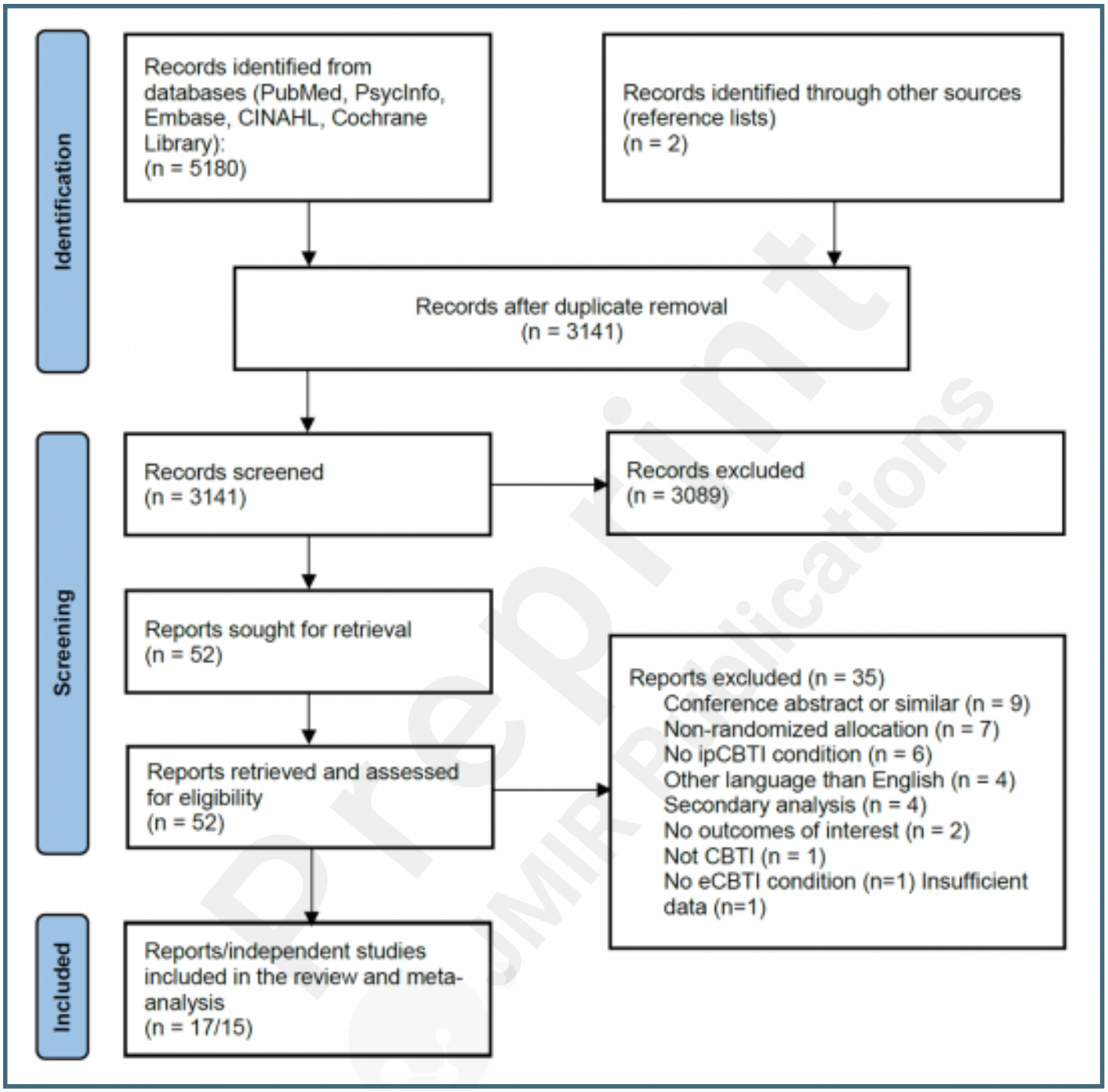
TST: Total sleep time

WASO: Wake after sleep onset

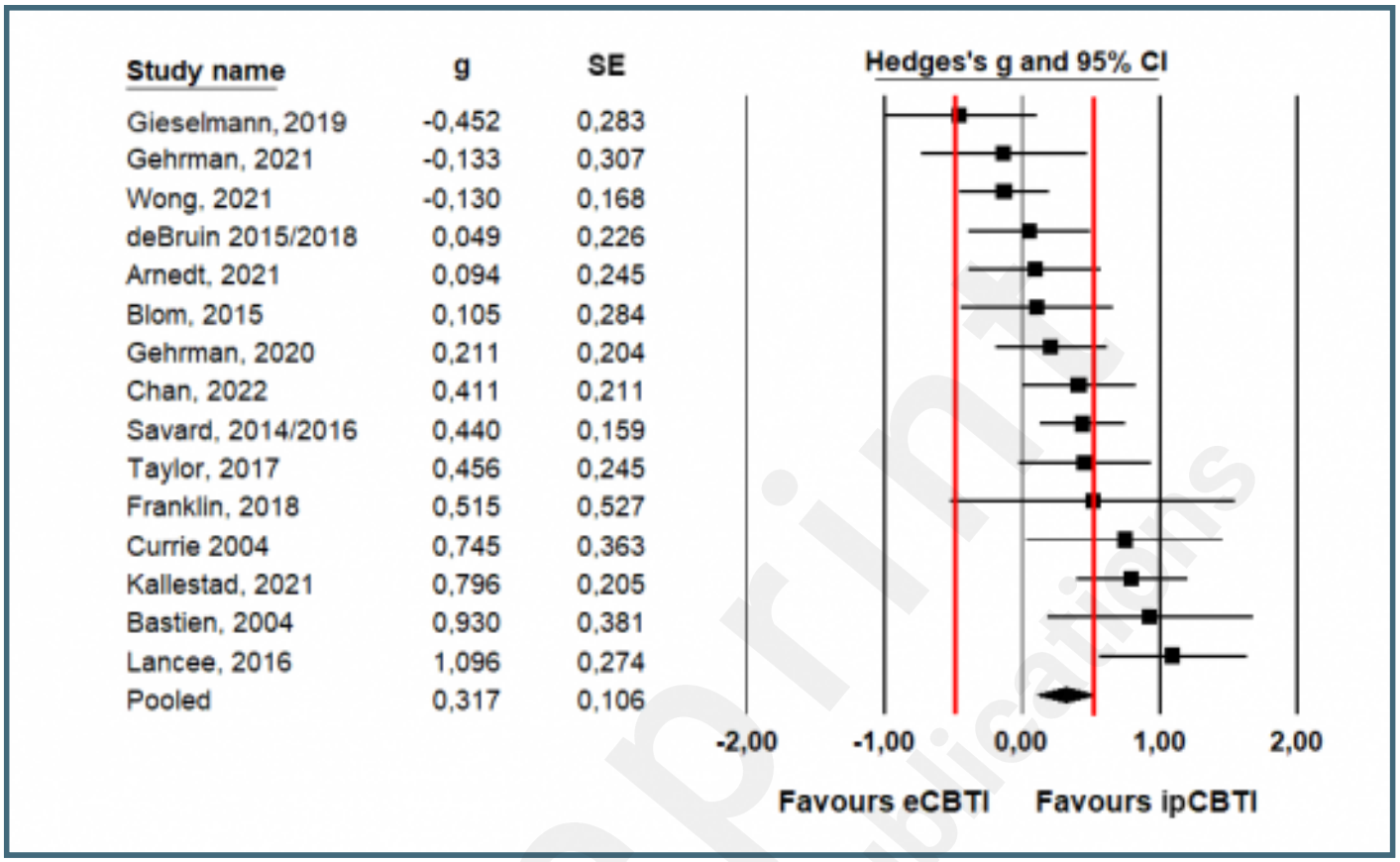
Supplementary Files

Figures

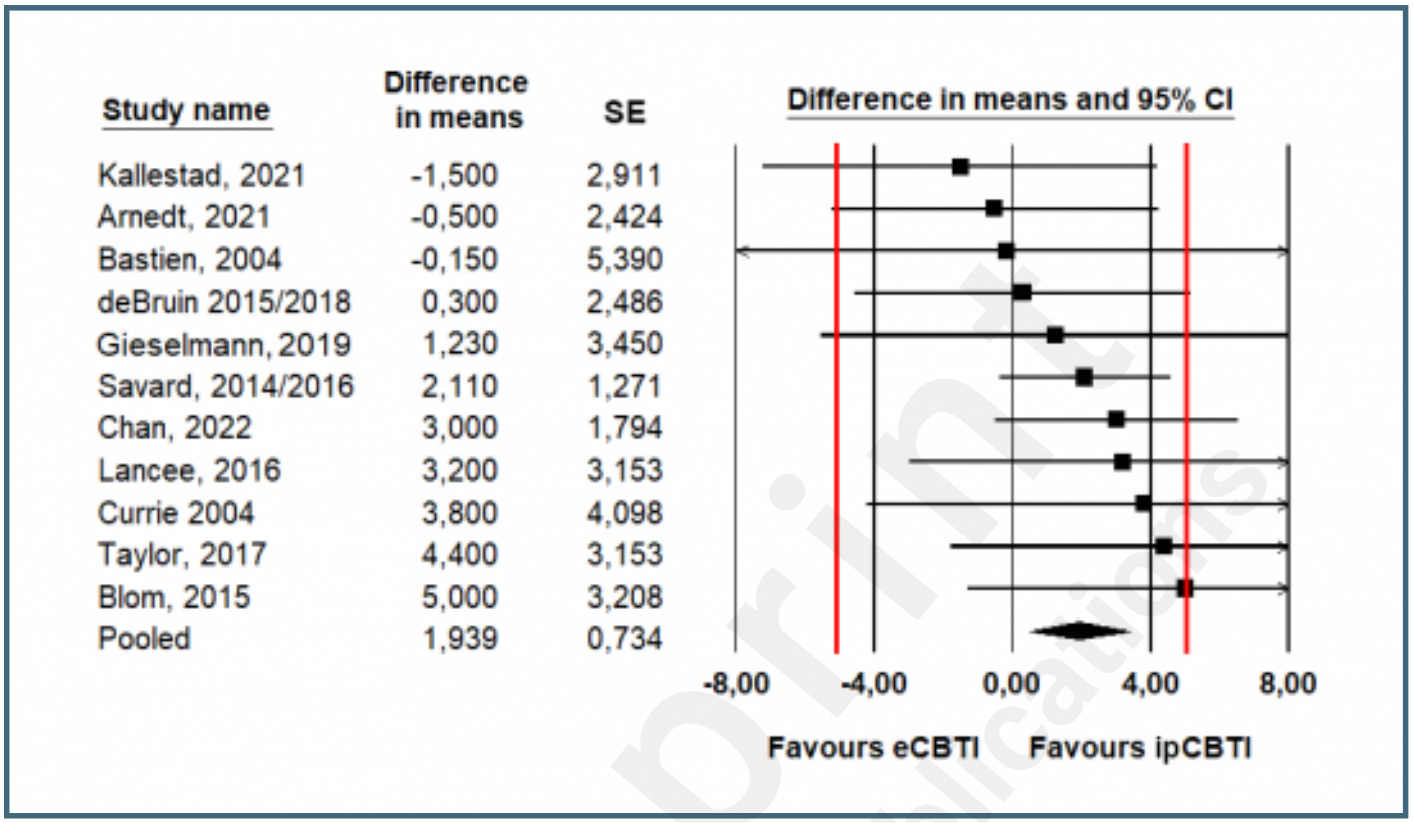
Study selection flowchart.



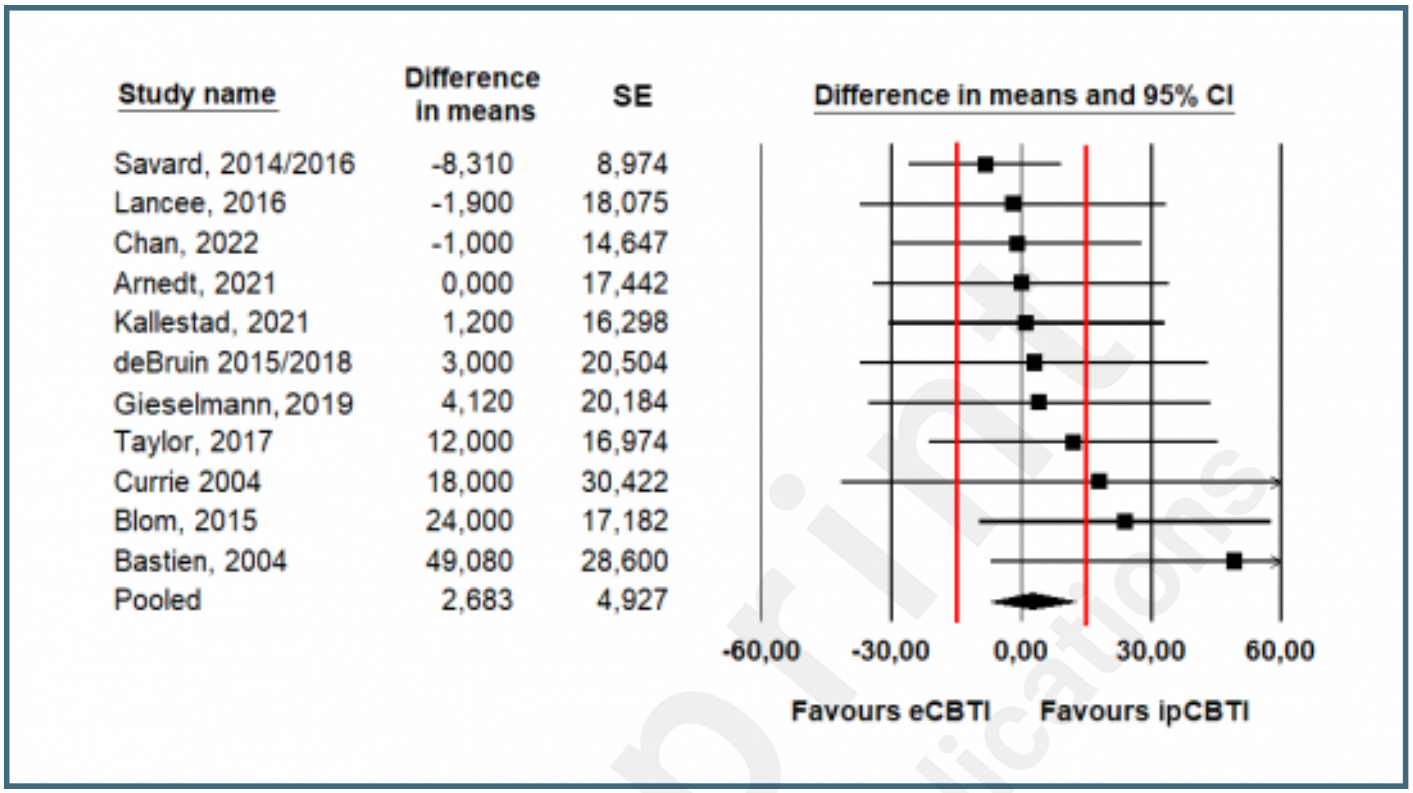
Forest plot of post-intervention differences (Hedges's g) between effects of eCBTI and ipCBTI on total sleep disturbance.



Forest plot of post-intervention mean differences (%) between effects of eCBTI and ipCBTI on sleep efficiency (SE).



Forest plot of post-intervention mean differences (minutes) between effects of eCBTI and ipCBTI on total sleep time (TST).



Multimedia Appendixes

Efficacy of eHealth vs. in-person cognitive-behavioral therapy for insomnia: A systematic review and meta-analysis of equivalence.
URL: http://asset.jmir.pub/assets/ce2bf219a244d240b76716e3900a6cda.pdf