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# **CLINICAL REVIEW**

# Efficacy of internet-delivered cognitive-behavioral therapy for insomnia — A systematic review and meta-analysis of randomized controlled trials



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#### SUMMARY

Cognitive-behavioral therapy for insomnia (CBT-I) has been shown efficacious, but the challenge remains to make it available and accessible in order to meet population needs. Delivering CBT-I over the internet (eCBT-I) may be one method to overcome this challenge. The objective of this meta-analysis was to evaluate the efficacy of eCBT-I and the moderating influence of various study characteristics. Two researchers independently searched key electronic databases (1991 to June 2015), selected eligible publications, extracted data, and evaluated methodological quality. Eleven randomized controlled trials examining a total of 1460 participants were included. Results showed that eCBT-I improved insomnia severity, sleep efficiency, subjective sleep quality, wake after sleep onset, sleep onset latency, total sleep time, and number of nocturnal awakenings at post-treatment, with effect sizes (Hedges's g) ranging from 0.21 to 1.09. The effects were comparable to those found for face-to-face CBT-I, and were generally maintained at 4—48 wk follow-up. Moderator analyses showed that longer treatment duration and higher degree of personal clinical support were associated with larger effect sizes, and that larger study dropout in the intervention group was associated with smaller effect sizes. In conclusion, internet-delivered CBT-I appears efficacious and can be considered a viable option in the treatment of insomnia.

#### Introduction

Insomnia is a common clinical condition with an annual prevalence of 10–20% [1] and approximately half (6%) with a chronic trajectory, i.e., persisting for more than 3 mo [2]. Chronic insomnia has been associated with a number of negative health outcomes, including obesity and metabolic dysregulation [3,4], hypertension and increased risk of myocardial infarction [5,6], increased susceptibility to infections [7], and depression [8]. While pharmacotherapy remains the most commonly used treatment option, hypnotics such as benzodiazepine receptor agonists are associated with side-effects, dependence, and tolerance over time. They are

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usually not curative, leading to long-term treatment over many years despite lack of safety and efficacy data beyond 1–2 y [9,10]. In contrast, cognitive-behavioral therapy for insomnia (CBT-I) has, in several meta-analyses, been found efficacious in improving sleep outcomes [11–13] with acute effects comparable or superior to those found for pharmacotherapy [14], and these effects have been maintained for up to 3 y [10]. While CBT-I has been shown efficacious and desired by many patients preferring non-pharmacological approaches [15,16], the challenge remains to make it available and accessible to meet population needs [17] due to the limited availability of trained therapists and the relatively high costs of CBT-I delivered face-to-face [18,19].

One method to overcome these challenges may be to provide CBT-I over the internet [20]. The first randomized controlled trial (RCT) evaluating internet-delivered CBT-I, published in 2004, compared a 5-wk internet-delivered sleep management program to a waiting list control in a sample with clinical insomnia [21]. The program, which was derived from existing CBT-I manuals [22,23].

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Abbrevia	ations	PRISMA	preferred reporting items for systematic reviews and meta-analyses
CBT	cognitive-behavioral therapy	PSQI	Pittsburgh sleep quality index
CBT-I	cognitive-behavioral therapy for insomnia	RCT	randomized controlled trial
DSM-IV	diagnostic and statistical manual of mental disorders,	SCI	sleep condition indicator
	fourth edition	SD/SE	standard deviation or standard error
DSM-5	diagnostic and statistical manual of mental disorders,	SE	sleep efficiency
	fifth edition	SOL	sleep onset latency
eCBT-I	internet-delivered CBT-I	SQ	subjective sleep quality
ES	effect size	TAU	treatment as usual
ISI	insomnia severity index	TIB	time in bed
ITT	intention to treat	TST	total sleep time
K	number of studies	WASO	wake after sleep onset
NA	number of nocturnal awakenings	WLC	wait list control
NNT	number needed to treat		

included sleep restriction [24], stimulus-control [25], sleep hygiene education [26], cognitive therapy [27], and relaxation techniques [28]. The results showed improvements in several sleep outcomes, including total sleep time (TST), wake after sleep onset (WASO), and sleep efficiency (SE). A meta-analysis published in 2012 [29] provided a quantitative review of four studies and reported statistically significant effects for subjective sleep quality (SQ), SE, sleep onset latency (SOL), number of nocturnal awakenings (NA), and insomnia severity (Cohen's d range: 0.41 to 0.86). While internet-delivered CBT-I appeared to be a promising approach to treating insomnia, the results were considered preliminary given the limited number of studies available at the time of the publication of the review. In addition, no data were provided on publication bias [30] or the robustness of results, i.e., the number of null-findings needed to bring the results to statistical non-significance [31], and only one study examined the effect at a follow-up [32].

Given the rapid development in the field of internet-delivered interventions, we conducted a new systematic review and metaanalysis with the aim of not only evaluating the efficacy of internet-delivered CBT-I, but also to assess long-term effects, robustness of results, and possible publication bias, and to explore the potential moderating effects of relevant study characteristics, including attrition, intervention duration, and the degree of personal clinical support provided during the intervention.

#### Methods

The study was conducted in accordance with the PRISMA recommendations for reporting systematic reviews and meta-analyses [33] and preregistered with PROSPERO [34], registration #: CRD42015020660.

#### Search strategy

A keyword-based search in the electronic databases of PubMed, PsycINFO, CINAHL, Scopus, Cochrane Central Registry of Controlled Trials (CENTRAL), and ClinicalTrials.gov was conducted using the following keywords: (insomnia OR sleep-disturbance) AND (intervention OR treatment OR therapy OR counseling OR CBT OR self-help) AND (eHealth OR internet\* OR web-based OR online OR digital OR computer\*). The search was conducted independently by two authors (MSL, MSO) for the period from 1991 (the year of the introduction of the World Wide Web) to June 2015. In addition, a backward search (snowballing) was conducted of reference lists of identified articles and earlier systematic reviews together with a

forward search (citation tracking) until no additional relevant articles were found.

#### Selection procedure and data extraction

Reports published in peer-reviewed journals were considered eligible for the present study. Study eligibility was assessed using the PICOS approach [35]. **Population**: a study population of adults (>18 yrs) with insomnia or self-reported sleep difficulties. Inter**vention**: a) a multi-component cognitive behavioral intervention for insomnia (CBT-I), including a combination of two or more elements typically considered part of CBT-I (sleep restriction, stimulus-control, cognitive therapy, sleep hygiene education, relaxation), b) delivered over the internet (eCBT-I). **Comparison**: participants randomized to at least one non-intervention control condition, e.g., wait list control. Outcomes: pre- and posttreatment data for both intervention and controls for one or more sleep-related outcomes, including the primary outcomes of insomnia severity, sleep efficiency (SE) and the secondary outcomes of sleep onset latency (SOL), wake after sleep onset (WASO), number of nocturnal awakenings (NA), total sleep time (TST), total time in bed (TIB), and subjective sleep quality (SQ). Study design: randomized controlled trial (RCT). Studies should report results as either pre-post means and SD/SE in all groups, change-scores in all groups, or effect sizes (e.g., Cohen's d, Eta<sup>2</sup>). Studies were excluded if they did not include a) an internet-based program, b) results on sleep-related outcomes, e.g., if the primary study focus was comorbid symptoms (fatigue, depression, pain), c) a non-intervention control group, e.g., non-inferiority trial comparing two interventions, or d) quantitative sleep data.

First, two of the authors (MSO, MSL) independently removed duplicates and screened the titles and abstracts of the identified references with the purpose of excluding irrelevant studies. Then full-texts of the remaining references were evaluated and ineligible reports excluded on the basis of the criteria described above and reasons for exclusion registered. Three authors (MSO, MSL, RZ) then discussed disagreements until a negotiated conclusion was reached.

#### Quality assessment

Methodological quality was assessed using eight modified items from the original Jadad scale [36], one item from the Cochrane assessment of bias tool [37], and three additional sleep-relevant study quality criteria. The resulting 12 quality criteria are: 1) randomization procedure clearly described, 2) allocation concealed

for researchers during the intervention, 3) clear description of withdrawals and study dropouts, 4) study objectives clearly defined, 5) outcome measures clearly defined, 6) inclusion and exclusion criteria clearly described, 7) sample size justified (e.g., power calculation), 8) statistical methods clearly described, 9) study report free of suggestion of selective outcome reporting (e.g., results for all included outcomes are described), 10) relevant and clearly defined sleep measures, 11) sleep intervention components and level of human involvement clearly described, and 12) a study population with verified sleep problems, e.g., based on diagnostic criteria for insomnia [38]. Scores were "0" (No), "1" (Partly/unclear), and "2" (Yes), yielding a total quality score range of 0-24. To obtain valid quality scores, the quality ratings were first conducted independently by three authors (MSO, MSL, RZ). Disagreements and uncertainties were then discussed among the three authors until a negotiated final score was reached for each study. Quality ratings were not used as weights when calculating aggregated effect sizes (ESs), as this is discouraged due to risk of inducing bias [39]. Instead, possible associations between ESs and specific design characteristics and study quality scores were explored with metaregression [40] (see below).

#### Heterogeneity

Heterogeneity was explored using Q and  $I^2$  statistics [41]. Due to generally low statistical power of heterogeneity tests, a more liberal p-value of  $\leq$ 0.10 was used to determine significant heterogeneity [42]. The  $I^2$  statistic is an estimate of the amount of variance in a pooled ES accounted for by heterogeneity in the sample of studies and is unaffected by the number of studies (K) [43]. An  $I^2$  value of 0% indicates no observed heterogeneity. Values of 25%, 50%, and 75% are considered low, moderate, and high, respectively.

# Computing effect sizes

Hedges's *g*, a variation of Cohen's *d* [44], correcting for possible bias due to small sample size [45] was used as the standardized effect size. ESs were computed using pre- and post-intervention means and their standard deviations or standard errors. Pooled ESs were weighted by the inverse standard error, taking into account the precision of each study. When available, the N used in the calculation was the N in the final analysis for each outcome. A random effects model was chosen for all analyses. A positive value was chosen to indicate an ES in the expected direction, e.g., increased TST and reduced SOL. If necessary, independence of results was ensured by averaging ESs across all outcomes or subgroups so that only one result per study was used for each quantitative data synthesis.

#### Publication bias

Publication bias, a widespread problem when conducting metaanalyses [30], was inspected with funnel plots and tested with Egger's test [46]. If the results were suggestive of publication bias, we calculated an adjusted ES using Duval and Tweedie's trim and fill method [47], which imputes ESs of missing studies and recalculates the ES accordingly. In case of statistically significant results, we calculated the failsafe number [31,48], i.e., the number of unpublished studies with null-findings that would reduce the result to statistical non-significance (p > 0.05), and evaluated the robustness of results by comparing the fail-safe number with the suggested criterion ( $K \times 5 + 10$ ) [31].

#### Analytical strategy

An *a priori* statistical power analysis [49] indicated that to detect a small statistically significant ES (0.30), smaller than the average ES (0.42) found across all outcomes in a previous meta-analysis [29], with an alpha of 5%, a statistical power of 80%, and an average sample size of 75, as found in the previous meta-analysis, would require eight studies using a random effects model.

Pooled ESs for all individual sleep outcomes (insomnia severity, SE, SOL, NA, WASO, TST, TIB, SQ) reported in a sufficient number of studies (K > 2) were calculated separately. If more than one post-treatment or follow-up assessment time point was included, the time points closest in time to post-treatment were chosen. The influence of possible outliers was analyzed by examining ESs below or above two standard deviations from the pooled ES and Winsorizing the ESs by replacing outliers with the value of the lower or upper value of the range [50].

When available for >3 studies, the following possible moderators of the effects on primary outcome ESs were explored with meta-regression: a) insomnia duration, b) intervention duration, c) post-treatment assessment time, d) time to follow-up, e) study quality score, f) study dropout in eCBT-I, g) study dropout in control group, h) number of CBT-I components used, i) whether a specific CBT-I component was included, and j) the degree of personal contact/support provided  $(0-2, "0" = \text{fully automated}; "1" = \text{possibility of contacting staff and receiving individualized clinical support; "2" = \text{personal contact as an integral part of the intervention).}$ 

Finally, we calculated the average improvements and 95% confidence intervals of sleep-outcomes in minutes. We also calculated the average number needed to treat (NNT) based on number of participants in each group reported to show improvement at post-treatment [51] or estimated from the ES using the formula suggested by Kraemer and Kupfer [52]. The main analyses were conducted using Comprehensive Meta-Analysis, version 3.3 [53].

#### Results

The study selection process with reasons for exclusion is described in Fig. 1. Eleven individual research papers describing the results of 11 independent randomized controlled trials published between 2004 and 2015 were included and subjected to meta-analytic evaluation. See Supplementary data, Table S1 for further details of excluded studies.

#### Study characteristics

As seen in Table 1, the 11 studies had recruited a total of 1460 participants, and presented complete data for 1131 participants with a mean study sample size of 102.8 (range: 26-349). All but one study [54] included participants with clinical insomnia based on DSM-IV or DSM-5 criteria. Mean duration of insomnia was 9.6 y (K = 5).

The eCBT-Is employed in all studies were multicomponent interventions including behavioral, educational, and cognitive techniques used in traditional CBT-I [22]. The techniques included: 1) stimulus-control [25], i.e., instructions aimed at strengthening the association between the bed or bedroom, bedtime, and sleep (K = 11), 2) sleep hygiene education [26], which focuses on the lifestyle and environmental factors related to sleep (e.g., avoiding caffeine and alcohol before bedtime and increasing exercise) (K = 11), 3) cognitive therapy [27] aimed at changing unhelpful

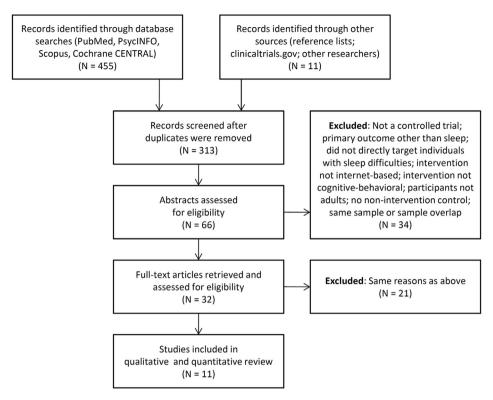


Fig. 1. PRISMA study inclusion flowchart.

sleep-related thoughts (e.g., worry about the consequences of sleep loss) and beliefs (e.g., the necessity for 8 h of sleep to maintain health) (K = 11), 4) sleep restriction [24] aimed at regulating the sleep-wake schedule and reducing the proportion of the time spent in bed awake (K = 10), and 5) relaxation techniques [28,55] aimed at improving the preconditions for sleep by reducing anxiety and pre-sleep arousal (K = 8 (optional in 2/8 studies)). The degree of human involvement also varied with four studies providing only automated prompting and feedback, three studies providing the option of contacting staff and receiving individualized support, three studies providing personal contact as an integral part of the intervention, and one study examining two conditions with and without telephone support. The average duration of eCBT-I was 5.5 wk (range:2–9 wk). See Table S2 for details.

No single outcome measure was reported across all 11 studies. Eight studies reported data on a relevant insomnia severity measure, including the insomnia severity index (ISI) [56] (K = 6), the sleep condition indicator (SCI) [57] (K = 1), or sleep-50 [58] (K = 1). Ten of the 11 studies reported data on SE. Secondary sleep outcomes were: SOL (K = 10), TST (K = 10), SQ (K = 8), WASO (K = 7), NA (K = 6), and TIB (K = 4). See Table S3 for details. Mean post-treatment assessment time was 2 wk after intervention completion (range: 0–6 wk). Five studies included follow-up data for both eCBT-I and controls, with follow-up assessment times ranging from 4 to 48 wk. On average, study dropout was 24.7% (range:0.0–41.3%) in the eCBT-I group and 13.2% (range:0.0–33.9%) in the control group.

The two raters agreed on 110 (83.3%) of the 132 individual study quality ratings, and the between-rater total score correlation was 0.91 (p = 0.001). Disagreements were discussed in depth among three authors (MSO, MSL, RZ) and a final rating was negotiated. The mean final total quality rating was 19.4 (SD = 2.5; range:16–23). The primary methodological limitations were that the allocation

was not sufficiently concealed to researchers (K=11), and that studies had not based sample size on statistical power calculations (K=6). See Table S4 for details.

#### Post-treatment effects

As seen in Table 2 and Fig. 2, statistically significant effects of eCBT-I were found for post-treatment results for both primary outcomes, insomnia severity and SE, and for five of the six secondary sleep outcomes, SOL, WASO, NA, TST, and SQ. Only the ES for TIB did not reach statistical significance. The effect sizes ranged from small (NA = 0.21) to large (insomnia severity = 1.03). Furthermore, most results appeared robust, with failsafe numbers exceeding the criterion for insomnia severity, SE, SOL, WASO, and SQ. For NA and TST, failsafe numbers did not exceed the criterion, indicating somewhat less robust results.

Although Egger's test of asymmetry in the distribution of ESs did not reach statistical significance for all outcomes (p: 0.01–0.91), a visual inspection of the funnel plots revealed some asymmetry suggesting the possibility of publication bias in the direction of larger, positive ESs for the outcomes of insomnia severity, SE, SOL, NA, TST, and SQ. See Figs. S1.1–1.8. As seen in Table 2, when imputing "missing studies", thereby adjusting the ESs [47], all results, except for NA, remained statistically significant. The analyses revealed high heterogeneity for insomnia severity - and low-to-moderate for SE, WASO, and SQ.

When searching for possible outliers above or below two standard deviations from the pooled ESs for insomnia severity (range: 0.22-2.05) and SE (-0.36-1.52), one study [54] fell outside of this range for SE (g=-0.59). The ES for this study was Winsorized [50] by replacing it with the lower value of the range (-0.36), thereby retaining the study with an attenuated influence. Reanalyzing with the Winsorized effect size revealed an effect of similar magnitude (g=0.60).

 Table 1

 Included studies: randomized controlled trials of internet-delivered cognitive-behavioral therapy for insomnia (eCBT-I).

Authors	Year	N	Participant charac- teristics	Mean insomnia duration (y)	Randomized		Completers <sup>a</sup>		Dropout		Ctrl	eCBT-I	Post-treatm.		Quality
					eCBT-I (N)	Ctrl (N)	eCBT-I (N)	Ctrl (N)	eCBT-I (%)	Ctrl (%)	cond.	duration (wk)	Asessment (wk)	time (wk)	score: 0–24 <sup>b</sup>
Ström et al. [21]	2004	109	Adults with insomnia	10.6	54	55	30	51	40.7	7.3	WLC	5	2		16
Suzuki et al. [54]	2008	43	Adult workers	n.r.	21	22	12	18	42.9	18.2	WLC	2	3		16
Ritterband et al. [61]	2009	45	Adults with insomnia	10.6	22	23	21	22	4.5	4.3	WLC	9	2		20
Vincent & Lewyecky	2009	118	Adults with chronic insomnia	(>6 mo)	59	59	40	39	32.2	33.9	WLC	5	0	4	21
Ritterband et al. [60]	2012	28	Cancer patients with insomnia	6.4	14	14	14	14	0.0	0.0	WLC	9	2		17
Lancee et al. [72]	2012	418 <sup>c</sup>	Adults with insomnia	n.r.	216	202	167	182	22.7	8.9	WLC	6	4	48	22
Espie et al.	2012	109 <sup>d</sup>	Adults with insomnia	(46.3% > 11 y)	55	54	43	47	21.8	13.0	TAU	6	0	8	23
Van Straten et al. [73]	2014	118	Adults with insomnia	11.8	59	59	43	55	27.1	6.8	WLC	6	6		20
Ho et al. [74]	2014	312 <sup>e</sup>	Adults with insomnia	8.5	207	105	119	70	42.5	33.3	WLC	6	0	4	22
Thiart et al. [75]	2015	128	Teachers with insomnia	n.r.	64	64	56	62	12.5	3.1	WLC	6	2	18	19
Pillai et al.	2015	32	Adults with insomnia	n.r.	19	13	15 <sup>f</sup>	11 <sup>f</sup>	21.1	15.4	AC	6	1		17
Total		1460			790	670	560	571							
Mean (SD)		133 (123)		9.6 (2.1)	71.8 (71.6)	60.9 (54.2)	50.9 (48.9)	51.9 (47.7)	24.7 (15.1)	13.2 (11.4)	WLC = 81.8%	5.5 (1.2)	2.0 (1.8)	16.4 (18.6)	19.5 (2.7)

Abbreviations: AC: active control, e.g., educational booklet/e-mails; Ctrl: Controls; n.r.: not reported; TAU: treatment as usual; WLC: wait list control.

- <sup>c</sup> Three conditions: eCBT-I, paper and pencil CBT-I, and WLC. Only eCBT-I and WLC included.
- d Three conditions: eCBT-I, imagery relief therapy, TAU. Only eCBT-I and TAU included.
- <sup>e</sup> Three conditions: eCBT-I, eCBT-I + telephone support, and waitlist controls. All included.
- $^{\rm f}$  Completers include 2  $\times$  2 outliers (>3 SD) excluded from analysis.

#### Effects at follow-up

When examining ESs at follow-up (K = 5), statistically significant pooled ESs were found for insomnia severity (g=0.68; p<0.001), SE (0.57; p=0.009), and SQ (0.58; p=0.003). The results for insomnia severity and SE were robust (failsafe numbers > criterion). The results for SOL, WASO, and TST did not reach statistical significance (p=0.06-0.08). When adjusting for possible publication bias, the ES for SQ no longer reached statistical significance. Heterogeneity was generally high with heterogeneity tests reaching statistical significance for all but one ES (TST). See Table S5 for details.

# Practical significance

Compared to changes in controls, eCBT-I participants on average spent 16.8 min less falling asleep, 16.6 min less on nocturnal awakenings, had 20.6 min longer total sleep, and experienced a 6.7% increase in SE. For the eight studies presenting data allowing for the calculation of NNT, the average NNT for insomnia severity was 2.2. See Table S6 for details. The ES for insomnia severity was statistically significantly correlated with NA (r = 0.98, p = 0.02). The correlations with the remaining sleep outcomes did not reach statistical significance (r:0.01–0.74; p:0.06–1.00). The ES for SE was associated with the ES for TST (r = 0.81; p < 0.01; K = 9), but not TIB (r = 0.09; p = 0.91; K = 4). The ESs and 95%CIs for eCBT-I were compared with ESs reported in two recent meta-analyses of face-

to-face delivered CBT-I [13] and group-based CBT-I [59]. As seen in Fig. S2, all confidence intervals overlapped, suggesting that the effect of eCBT-I does not differ from that obtained in traditionally delivered formats.

#### Moderator effects

As seen in Table 3, we found several moderating effects of various study characteristics on the effects of eCBT-I on the primary outcomes (insomnia severity and SE). Treatment duration, degree of personal support, and insomnia duration were generally associated with larger ESs, whereas study dropout in eCBT-I and the inclusion of a relaxation component were associated with smaller ESs. Longer treatment duration was significantly associated with lower study dropout rates (r: -0.84; p < 0.001), and we therefore adjusted for the other factor when examining the role of each factor. Results generally persisted when adjusting for treatment duration but generally failed to reach statistical significance after adjusting for study dropout.

#### Discussion

The statistically significant effects found in the present study were generally larger (0.21–1.03) than those reported in an earlier meta-analysis (0.18–0.86) [29], which combined ESs of four studies [21,32,60,61]. Thus, eCBT-I appears a viable alternative to traditional, face-to-face delivered insomnia treatment. It should be

<sup>&</sup>lt;sup>a</sup> Discrepancies between N in Tables 1–3 are due to larger N's in intention to treat (ITT) analyses in some studies. Completers indicate participants who completed post-assessment. Number may not correspond to those who have completed the intervention.

<sup>&</sup>lt;sup>b</sup> A 12 item quality score based on eight items from the Jadad scale [36], one item from the Cochrane instrument for assessing reporting bias [41], and three additional sleep intervention-specific items. Rating: "0" (no), "1" (partly/unclear), "2" (yes).

 Table 2

 Pooled post-treatment effects of internet-delivered cognitive behavioral therapy for insomnia (eCBT-I).

Outcome	Sample size		Heterogeneity <sup>b</sup>			Global effect sizes			Failsafe N <sup>d</sup>	Criterion <sup>e</sup>	
	K	Nª	Q	df	р	$I^2$	Hedges's g <sup>c</sup>	95% CI	p <sup>h</sup>		
Primary outcomes											
Insomnia severity <sup>f</sup>	8	1071	40.7	7	<0.001	82.8	1.09	0.74-1.45	<0.001	386	50
Adjusted for publication bias <sup>g</sup>	(9)						0.89	0.53 - 1.25			
Sleep efficiency (SE)	10	1220	28.5	9	0.001	68.4	0.58	0.36-0.81	< 0.001	202	65
Adjusted for publication bias	(11)						0.49	0.27 - 0.71			
Secondary outcomes											
Sleep onset latency (SOL)	10	1114	8.6	9	0.471	0.0	0.41	0.29-0.53	<0.001	107	60
Adjusted for publication bias	(14)						0.34	0.20 - 0.48			
Wake after sleep onset (WASO)	7	944	11.6	6	0.070	48.5	0.45	0.25 - 0.66	< 0.001	65	45
No. of nocturnal awakenings (NA)	6	640	5.1	5	0.400	2.5	0.21	0.05 - 0.37	0.011	10	40
Adjusted for publication bias	(9)						0.13	-0.05 - 0.31	Ns <sup>i</sup>		
Total sleep time (TST)	10	1114	9.5	9	0.391	5.4	0.29	0.17 - 0.42	< 0.001	43	60
Adjusted for publication bias	(12)						0.24	0.10 - 0.38			
Time in bed (TIB)	4	464	1.5	3	0.681	0.0	0.17	-0.02 - 0.08	0.075		
Subjective sleep quality (SQ)	8	801	10.7	7	0.153	34.5	0.49	0.30 - 0.68	< 0.001	78	50
Adjusted for publication bias	(10)						0.40	0.18 - 0.61			

- <sup>a</sup> Discrepancies between N in Tables 1–3 due to larger N noted for some studies due to intention to treat (ITT) analysis.
- <sup>b</sup> Q-statistic: *p*-values<0.1 taken to suggest heterogeneity. I<sup>2</sup> statistic: 0% (no heterogeneity), 25% (low heterogeneity), 50% (moderate heterogeneity), 75% (high heterogeneity).
- <sup>c</sup> ES = Hedges g. A positive value indicates an effect size in the hypothesized direction. All ES's were combined using a random effects model. Conventions: small (0.2); medium (0.5); Large (0.8) [44].
  - <sup>d</sup> Failsafe N = number of non-significant studies that would bring the p-value to non-significant (p > 0.05).
  - <sup>e</sup> A Failsafe N exceeding the criterion  $(5 \times k + 10)$  indicates a robust result [31].
- f Insomnia severity = ISI (insomnia severity index), SCI (sleep condition indicator), or sleep-50 (two studies using the Pittsburgh sleep quality index (PSQI) were not included).
- <sup>g</sup> If analyses indicated possible publication bias, missing studies were imputed and an adjusted effect size (ES) calculated (italics) [47]. (K) indicates number of published studies + number of imputed studies.
- h Statistically significant results shown in bold.
- i Ns = statistically non-significant.

noted that reducing TIB is not a specific goal of CBT-I, but rather an intermediate mechanism used in sleep restriction [24] with the aim of improving SE. Therefore, the lack of effect on TIB in either of the two meta-analyses is not unexpected. In addition, the ESs found in our updated meta-analysis were generally robust with large failsafe numbers exceeding the criterion [31]. For example, to reduce the

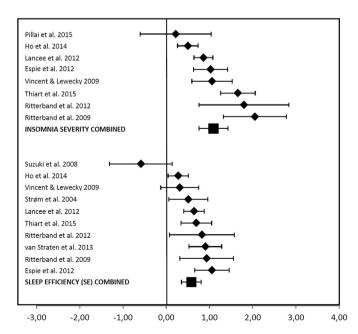


Fig. 2. Forest plot of post-treatment effect sizes for insomnia severity and sleep efficiency (SE).

effects of eCBT-I on insomnia severity and SE, it would require more than 386 and 202 unpublished null-findings, respectively, to reach statistical non-significance. In the present study, we also examined the durability of the effects over time in five studies and found the effects to be maintained and robust for both primary outcomes.

Participants in eCBT-I on average spent 20.6 min less falling asleep, 25.5 min less awake during the night, and slept 37.5 min longer after the intervention. These changes are comparable to the improvements after both face-to-face delivered CBT-I (23.3, 38.4, 19.6) and pharmacotherapy (14.5, 25.6, 40.5) reported in a meta-analysis of studies comparing CBT-I with pharmacotherapy [14]. Furthermore, when we compared the ESs and their confidence intervals found in our study with those reported in two recent meta-analyses of face-to-face delivered [13] and group-based CBT-I [59], none of the ESs for eCBT-I differed significantly from the ESs reported for the other delivery formats. Due to few available non-inferiority trials directly comparing different treatments with notreatment controls, these comparisons should be interpreted cautiously.

#### Moderators

Several of the study characteristics examined emerged as statistically significant moderators of the effect of eCBT-I on the two primary outcomes. *Treatment duration* varied considerably across studies (2–9 wk) with longer duration associated with larger effects. This finding is in concordance with other studies, e.g., as reported in a recent meta-analysis of 44 studies on CBT for anxiety disorders [62]. *Attrition* has been suggested to be a potential problem, especially in internet-delivered interventions, showing study non-completion rates ranging from 43% to 99% [63]. We

 Table 3

 Moderators of effects on the primary outcomes at post-treatment and follow-up of insomnia severity and sleep efficiency: results of meta-regression analyses.

Moderator	Dependent variable (post-treatment) <sup>a</sup>	K	Beta <sup>b</sup>	95%CI	P (two-tailed)e
Study quality score (0–24)	Insomnia severity <sup>c</sup>	8	-0.08	-0.25-0.10	0.38
	Sleep efficiency (SE)	10	0.06	-0.04 - 0.15	0.23
Treatment duration (weeks)	Insomnia severity	8	0.29	0.03-0.54	0.028
	-adj. for dropout in eCBT-I	8	0.06	-0.18 - 0.29	0.644
	Sleep efficiency (SE)	10	0.19	0.06-0.31	0.004
	-adj. for dropout in eCBT-I	10	0.09	-0.05 - 0.23	0.198
Dropout in eCBT-I group (%)	Insomnia severity	8	-0.03	-0.05 to $-0.02$	<0.0001
	-adj. for treatment duration	8	-0.03	-0.05 to $-0.01$	0.0006
	-adj. for dropout in control	8	-0.06	-0.09 to $-0.03$	0.0002
	Sleep efficiency (SE)	10	-0.02	-0.03 to $-0.01$	0.0002
	-adj. for treatment duration	10	-0.01	-0.03 to $-0.00$	0.020
	-adj. for dropout in control	10	-0.01	-0.03 - 0.00	0.10
Insomnia duration (y)	Sleep efficiency (SE)	5	0.12	0.01-0.24	0.035
	-adj. for treatment duration	5	0.16	0.04-0.28	0.010
	-adj. for dropout in eCBT-I	5	0.11	-0.01 - 0.22	0.062
Post-treatment assessment	Insomnia severity	8	0.11	-0.14 - 0.35	0.40
time (wk)	Sleep efficiency (SE)	10	0.03	-0.07 - 0.14	0.49
Number of CBT-I	Insomnia severity	8	-0.69	-1.44 - 0.06	0.07
components	Sleep efficiency (SE)	10	0.08	-0.36 - 0.51	0.73
Relaxation component	Insomnia severity	8	-1.00	-1.42 to $-0.57$	0.0001
(Yes/no) (reference = 0)	-adj. for treatment duration	8	-0.97	-1.49 to $-0.44$	0.0003
	-adj. for dropout in eCBT-I	8	-0.65	-1.11 - 0.18	0.007
	Sleep efficiency (SE)	10	-0.27	-0.76 - 0.21	0.27
Degree of personal	Insomnia severity	7	0.01	-0.45 - 0.50	0.98
support $(0-2)^d$	-adj. for dropout in eCBT-I	7	0.14	-0.15 - 0.43	0.34
	Sleep efficiency (SE)	9	0.25	0.04 - 0.45	0.019
	-adj. for dropout in eCBT-I	9	0.24	0.03-0.44	0.024
Moderator	Dependent variable (follow-up)	K	Beta	95%CI	P (two-tailed)
Time to follow-up (wk)	Insomnia severity	5	-0.01	-0.03 - 0.01	0.46
	Sleep efficiency (SE)	4	-0.01	-0.03 - 0.01	0.50
Study quality score (0-24)	Insomnia severity	5	-0.22	-0.46 - 0.01	0.06
	Sleep efficiency (SE)	4	0.42	-0.04 - 0.89	0.09
Degree of personal support (0–2)	Insomnia severity	4	0.87	0.42-1.33	0.0002

<sup>&</sup>lt;sup>a</sup> If a statistical significant moderator effect was found, additional analyses (shown in italics) were conducted adjusting for other relevant moderators, for which statistical significant effects for the same dependent variable were found and which could theoretically confound the result (e.g., dropout could be affected by treatment duration).

found an average study dropout rate in eCBT-I of 24.7%, which could bias the effect. This was supported by our results showing larger study dropout rates being associated with smaller effects. It should be emphasized that attrition was generally measured as the proportion of participants who failed to complete post-assessments, which may not necessarily correspond to the number who did not complete the interventions, and was only explicitly reported in a few studies. Participants in eHealth research may not be as accountable to the researchers for completing post-treatment assessments as they might be if they had met face-to-face. Future studies on eCBT-I could focus on this distinction. Finally, it should also be noted that attrition is not limited to internet-delivered interventions, with a meta-analysis of face-to-face delivered CBT-I reporting dropout rates in CBT-I from 0.0% to 33% [13].

Treatment duration and attrition could be linked, with longer treatment duration expected to be associated with larger study dropout during the course of treatment. Unexpectedly, we found a strong inverse correlation (-0.84) with lower study dropout rates in studies with longer treatment duration. One possibility is that participants in interventions of longer duration may be more patient with respect to experiencing improvement in their insomnia. When we adjusted for study dropout, treatment duration ceased to be a statistical significant moderator of effects on both insomnia severity and SE. In contrast, the moderating effects of study dropout were generally maintained when adjusting for treatment duration,

suggesting study dropout to be a key effect moderator at least partly explaining the other moderator effects found.

When examining the role of the individual *CBT-I components*, almost all studies included the common CBT-I components, and — most likely due to the lack of variance — no moderating effect of the number of CBT-I components reached statistical significance. Relaxation was the only component which showed some variation, and the inclusion of relaxation was associated with *smaller* ESs for insomnia severity. This was unexpected as previous studies have found relaxation alone to be effective in improving sleep quality [64]. An explanation could be that the studies without relaxation had considerably lower study dropout rates. However, although the association was reduced when adjusting for study dropout, it remained statistically significant, which could be due to confounding by other unknown between-study differences.

Many assume that the *degree of personal clinical support* is of importance to the efficacy of internet-delivered interventions [65]. This assumption was supported by our results showing that higher degree of personal support was associated with a larger effect size for SE at post-treatment and for insomnia severity at follow-up. A possible mechanism is that personal support may increase adherence. Although the reported data on treatment adherence were insufficient and difficult to compare, study dropout could serve as a proxy for adherence. Personal support and study dropout were uncorrelated and the results were

Maximum likelihood method.

<sup>&</sup>lt;sup>c</sup> Insomnia severity = ISI (insomnia severity index), SCI (sleep condition indicator), or sleep-50 (two studies using the Pittsburgh sleep quality index (PSQI) were not included).

<sup>&</sup>lt;sup>d</sup> One study [74] which had included two conditions with and without telephone support was excluded.

<sup>&</sup>lt;sup>e</sup> Statistically significant results shown in bold.

unchanged when we adjusted for study dropout. The limited number of studies suggests a cautious interpretation, and it is also possible that this result is due to an apparent need of less robust interventions to be supplemented by human assistance. Some studies indicate that fully automated systems can be quite effective (e.g., [60,61]), but these incorporate considerably more interactive and tailored elements. A related question not explored here, however, is the issue of cost, If personal clinical support is deemed important for improvements in efficacy for these types of interventions, it is critical to consider at what cost. Adding human support can substantially increase costs for dissemination and reduce scalability. Determining who might benefit from fully automated interventions compared to those who might require additional support may help improve efficiencies and reduce overall costs. This would also allow for more thoughtful discussions on the topic of support rather than blanket statements suggesting that it is a requirement for successful outcomes.

Finally, it could be relevant to explore the associations between the effect on insomnia and changes in the sleep-specific variables. The ES for insomnia severity was higher (g=1.09) than for SE (0.58), and although the correlation between the ESs for insomnia severity was large (r=0.62), it only approached statistical significance (p=0.06). The non-significant result is likely due to the limited number of studies in the analysis (K=7), and SE may still be a key sleep outcome in the management of insomnia [22]. This is supported by previous findings showing that improved SE is good predictor of the primary target for sleep intervention: improvement in insomnia [66].

#### Strengths and limitations

Our meta-analysis has several strengths. First, the studies included in the analysis should be commended for being generally of high quality, in that they all reported the necessary data to calculate ESs, provided relatively detailed data on attrition, clearly described the eCBT-I components employed in the intervention, and used well-articulated and relevant sleep outcomes at pre- and post-treatment. Furthermore, some studies also provided follow-up data. These study characteristics allowed us not only to calculate pooled ESs, but also to explore the possible role of various moderators. Finally, we have explored the possibility of publication bias, and, when indications were found, adjusted ESs accordingly.

There are, however, factors that may limit the interpretability of the results. One issue is the moderate to high heterogeneity found in the present study, suggesting systematic between-study differences rather than variation due to random sampling error [41]. Statistical heterogeneity should not necessarily be interpreted as a limitation or flaw, neither in the individual studies nor in the meta-analytic process. Instead, as shown in our moderator analyses, it should be seen as an indication that the ESs may be influenced by possible between-study variations in the ESs due to between-study variability in treatment duration, study dropout rates, and other intervention characteristics. It should also be noted that statistical heterogeneity is only a correlate - and sometimes only a weak correlate – of clinical and pragmatic heterogeneity [67]. Specifically, one study [54] appeared to be an outlier and differed from the remaining studies mainly by not selecting participants based on whether they had a clinical diagnosis of insomnia. However, when Winsorizing [50] the ES for this study, the pooled effect was of similar magnitude.

There were also signs of possible *publication bias* in the direction of larger and positive ESs. Publication bias is a widespread problem when conducting meta-analyses [68] and may result in overestimating the effects found. While we addressed this possibility by imputing "missing studies" and adjusting ESs accordingly, we

cannot be certain about the degree of publication bias in our meta-analysis. First, not all statistical tests for funnel plot asymmetry reached statistical significance. Second, the precision of statistical tests for publication bias depends on certain conditions, e.g., a sufficient number of studies ( $\geq 10$ ) and moderate-to-low heterogeneity (<50%) [30]. While the number of studies was sufficient for most ESs, the heterogeneity was greater than 50% for both primary outcomes, and the degree of publication bias should therefore be interpreted with caution.

It should also be noted that there was some variation in the outcome measures used and/or reported. None of the outcomes were reported in all 11 studies. Only eight studies included a relevant measure of insomnia severity, e.g., the ISI; and, although the primary outcome of SE was reported in 10 of the 11 studies, some of the individual sleep diary components used to calculate SE were less frequently reported. To increase comparability of studies, researchers are encouraged to use and report both a relevant measure of insomnia severity and all standard sleep outcomes. Finally, due to the few studies in some moderator analyses, especially for the follow-up data, the subsequent risk of type-2 error calls for caution in the interpretation of these results.

#### **Conclusions**

Taken together, the results of our meta-analysis of 11 randomized controlled trials of internet-delivered CBT for insomnia indicated statistically significant and robust effects on insomnia severity and various sleep-related outcomes that translate into clinically relevant changes comparable to those found for both faceto-face delivered CBT-I and pharmacotherapy. Although only a few studies included follow-up assessments, our results also indicate that effects are maintained over time. Future research is advised to focus on non-inferiority trials directly comparing internetdelivered CBT-I with both face-to-face delivered CBT-I (e.g., as done in [69]) and pharmacotherapy. Dismantling studies investigating the relative effect of various CBT-I components (e.g., as partly done in [70]) are also needed, together with studies examining the additional effect of personal support while considering the costs and consequences for dissemination and implementation. Given the robust effects, dissemination studies are needed to evaluate internet-delivered CBT-I in daily clinical practice. Finally, while it is increasingly popular to deliver treatment over the internet, other delivery modalities may still be useful for those interested in other self-help approaches [71].

# **Practice points**

- The current literature supports the use of internetdelivered cognitive-behavioral therapy for treatment of insomnia.
- Effect sizes (Hedges's g) at post-treatment (0-6 wk) are
   1.09 (insomnia severity), 0.58 (SE), 0.49 (SQ), 0.45 (WASO), 0.41 (SOL), 0.29 (TST), and 0.21 (NA).
- 3) At post-treatment, participants who had received eCBT-l slept 37.5 min longer, spent 25.5 min less awake during the night, and spent 20.6 min less awake before falling asleen.
- Effects are maintained at long-term follow-up (4-48 wk), but the number of studies with follow-up data is limited.
- 5) Longer treatment duration and higher degree of personal clinical support are associated with larger effect sizes, and larger study dropout rates in the intervention group are associated with smaller effect sizes.

#### Research agenda

Future studies may include:

- 1) Long-term follow-up.
- Non-inferiority trials comparing internet-delivered CBT-I with face-to-face CBT-I, pharmacotherapy, and nonintervention controls.
- Dismantling studies examining the contribution of the individual CBT-I components and of the degree of personal clinical support to the effect of internet-delivered CBT-I.
- 4) Dissemination studies examining the effectiveness of internet-delivered CBT-I in clinical settings, e.g., in primary health care.

#### **Conflicts of interest statement**

Dr. Ritterband has equity ownership in BeHealth Solutions, LLC, a company developing and making available products related to the research reported in this publication. Specifically, BeHealth Solutions, LLC, has licensed the SHUTi program and the software platform on which it was built from the University of Virginia. The company had no role in preparing this manuscript. The terms of this arrangement have been reviewed and approved by the University of Virginia in accordance with its conflict of interest policy.

#### Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.smrv.2015.10.004.

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