Original Investigation

Cognitive Behavioral Therapy for Insomnia Comorbid With Psychiatric and Medical Conditions
A Meta-analysis

Jade Q. Wu, MA; Erica R. Appleman, MA; Robert D. Salazar, MA; Jason C. Ong, PhD

IMPORTANCE Cognitive behavioral therapy for insomnia (CBT-I) is the most prominent nonpharmacologic treatment for insomnia disorders. Although meta-analyses have examined primary insomnia, less is known about the comparative efficacy of CBT-I on comorbid insomnia.

OBJECTIVE To examine the efficacy of CBT-I for insomnia comorbid with psychiatric and/or medical conditions for (1) remission from insomnia; (2) self-reported sleep efficiency, sleep onset latency, wake after sleep onset, total sleep time, and subjective sleep quality; and (3) comorbid symptoms.

DATA SOURCES A systematic search was conducted on June 2, 2014, through PubMed, PsycINFO, the Cochrane Library, and manual searches. Search terms included (1) *CBT-I* or *CBT* or *cognitive behavioral* [and its variations] or *behavioral therapy* [and its variations] or *behavioral sleep medicine* or *stimulus control* or *sleep restriction* or *relaxation therapy* or *relaxation training* or *progressive muscle relaxation* or *paradoxical intention*; and (2) *insomnia* or *sleep disturbance*.

STUDY SELECTION Studies were included if they were randomized clinical trials with at least one CBT-I arm and had an adult population meeting diagnostic criteria for insomnia as well as a concomitant condition. Inclusion in final analyses (37 studies) was based on consensus between 3 authors' independent screenings.

DATA EXTRACTION AND SYNTHESIS Data were independently extracted by 2 authors and pooled using a random-effects model. Study quality was independently evaluated by 2 authors using the Cochrane risk of bias assessment tool.

MAIN OUTCOMES AND MEASURES A priori main outcomes (ie, clinical sleep and comorbid outcomes) were derived from sleep diary and other self-report measures.

RESULTS At posttreatment evaluation, 36.0% of patients who received CBT-I were in remission from insomnia compared with 16.9% of those in control or comparison conditions (pooled odds ratio, 3.28; 95% CI, 2.30-4.68; $P < .001$). Pretreatment and posttreatment controlled effect sizes were medium to large for most sleep parameters (sleep efficiency: Hedges $g = 0.91$ [95% CI, 0.74 to 1.08]; sleep onset latency: Hedges $g = 0.80$ [95% CI, 0.60 to 1.00]; wake after sleep onset: Hedges $g = 0.68$; sleep quality: Hedges $g = 0.84$; all $P < .001$), except total sleep time. Comorbid outcomes yielded a small effect size (Hedges $g = 0.39$ [95% CI, 0.60-0.98]; $P < .001$); improvements were greater in psychiatric than in medical populations (Hedges $g = 0.20$ [95% CI, 0.09-0.30]; χ^2 test for interaction = 12.30; $P < .001$).

CONCLUSIONS AND RELEVANCE Cognitive behavioral therapy for insomnia is efficacious for improving insomnia symptoms and sleep parameters for patients with comorbid insomnia. A small to medium positive effect was found across comorbid outcomes, with larger effects on psychiatric conditions compared with medical conditions. Large-scale studies with more rigorous designs to reduce detection and performance bias are needed to improve the quality of the evidence.

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Author Affiliations: Department of Psychological and Brain Sciences, Boston University, Boston, Massachusetts (Wu, Appleman, Salazar); Sleep Disorders Service and Research Center, Department of Behavioral Sciences, Rush University Medical Center, Chicago, Illinois (Ong).

Corresponding Author: Jason C. Ong, PhD, Sleep Disorders Service and Research Center, Department of Behavioral Sciences, Rush University Medical Center, 1653 W Congress Pkwy, Chicago, IL 60612 (jason_ong@rush.edu).

Cognitive behavioral therapy for insomnia (CBT-I) is a multicomponent treatment package that usually includes stimulus control, sleep restriction, and cognitive therapy (eTable 1 in the Supplement) and has emerged as the most prominent nonpharmacologic treatment for chronic insomnia.[1,2] Previous meta-analyses have found that CBT-I improves sleep parameters and sleep quality at post treatment[3-8] and follow-up[6] for adults and older adults.[5] Most of these studies selected individuals with primary insomnia, excluding patients with comorbid psychiatric and medical conditions. However, patients with insomnia who present to internists and primary care physicians are likely to report comorbid conditions associated with the sleep disturbance. Furthermore, insomnia was previously conceptualized as a symptom arising from the comorbid disorder and treatment was targeted at the underlying disorder. However, accumulating evidence[9,10] indicates that insomnia can have a distinct and independent trajectory from the comorbid disorder, thus indicating a need for separate treatment from the comorbid condition.

As a result of this paradigm shift, the literature on CBT-I for comorbid insomnia has flourished over the past decade. Randomized clinical trials have examined the efficacy of CBT-I on a range of comorbidities including cancer, chronic pain, depression, and posttraumatic stress disorder. Although reviews[11,12] have been conducted on CBT-I and comorbid psychiatric conditions, to our knowledge no meta-analysis has examined the effect of CBT-I on both psychiatric and medical conditions. Given the patient profile encountered in primary care and internal medicine, data on remission and treatment effects of CBT-I for comorbid insomnia could aid in treatment planning and referrals.

The purpose of this meta-analysis was to answer 2 research questions regarding the efficacy of CBT-I for comorbid insomnia populations: What is the efficacy of CBT-I on sleep outcomes and insomnia symptoms for comorbid insomnia? What is the efficacy of CBT-I on outcomes related to the comorbid condition? Given the heterogeneity in comorbid conditions and study design, exploratory analyses were conducted to examine potential moderators of treatment effects.

Methods

Initial Search

A systematic search was conducted June 2, 2014, in PubMed, PsycINFO, and the Cochrane Library from the first available date. The following sets of search terms were used: (1) *CBT-I* or *CBT* or *cognitive behavioral* [and its variations] or *behavioral therapy* [and its variations] or *behavioral sleep medicine* or *stimulus control* or *sleep restriction* or *relaxation therapy* or *relaxation training* or *progressive muscle relaxation* or *paradoxical intention*; and (2) *insomnia* or *sleep disturbance*. In addition, manual searches were conducted through reference lists of reviews and meta-analyses identified through the above systematic database searches.

Trial Selection

From the pool of studies identified by the database searches, published studies were selected if they met the inclusion criteria. First, the trial had CBT-I as a treatment arm, defined as a multicomponent intervention that includes at least one behavioral component plus a cognitive or relaxation therapy (eTable 1 in the Supplement), which is consistent with the standard recommendations for the treatment of insomnia disorders.[2] Second, the sample consisted of adults 18 years or older who met *Diagnostic and Statistical Manual of Mental Disorders* (Third Edition), *Diagnostic and Statistical Manual of Mental Disorders* (Fourth Edition), or *International Statistical Classification of Diseases and Related Health Problems, Tenth Revision* criteria for an insomnia disorder or established quantitative criteria for insomnia, and another well-characterized psychiatric disorder (ie, primary symptoms are mental) or medical condition (ie, primary symptoms are physical). Third, the trial had a randomized controlled design including at least one control or comparison group that did not receive CBT-I. Finally, the trial reported sufficient data for performing effect size (ES) calculations for primary variables of interest. Studies were excluded if the data reported in the trial represented a secondary analysis or were reported in another included trial, if the data were unpublished, or if an English version of the article was not available.

The selection process was conducted by 3 of us (J.Q.W., E.R.A., and R.D.S.), during which each of the studies identified as relevant through the initial search was independently evaluated for inclusion and exclusion criteria by at least 2 of 3 authors. Initial interrater agreement was 94%. All disagreements regarding a trial's eligibility were resolved through case-by-case discussion among raters.

Outcome Variables and Measures

Remission From Insomnia

Remission from insomnia was derived from 2 standard measures that are recommended as global measures of insomnia.[13] The Insomnia Severity Index (ISI) is a brief 7-item scale with a total score of less than 8 serving as a cut-off value for insomnia remission.[14] The Pittsburgh Sleep Quality Index (PSQI) is a 10-item scale with a total score of 5 or less serving as a cut-off for "good sleepers."[15]

Sleep Outcome Measures

Sleep parameters included sleep diary measures of sleep efficiency (SE), total sleep time (TST), sleep onset latency (SOL), and wake after sleep onset (WASO), as well as self-report measures of subjective sleep quality. These variables were chosen because they are clinically meaningful in the assessment of insomnia severity[13] and were the most commonly reported outcomes among included studies.

Comorbid Outcome Measures

Main outcomes identified in each study for the specified comorbid disorder were extracted as the comorbid outcome measure for the present meta-analysis. In cases in which disorder-specific outcomes (eg, kidney functioning) were not measured or reported, general outcomes of fatigue, depression, anxiety, and quality of life were substituted as comorbid outcomes.

Planned Analyses

A priori analyses were designed to produce (1) posttreatment remission rates and odds ratios (ORs); (2) baseline to posttreatment controlled treatment ESs for sleep and comorbid outcomes; (3) baseline to follow-up controlled treatment ESs for sleep outcomes and comorbid outcomes; and (4) moderating effects of type of comorbidity, length of treatment, publication year, sample size, and objective vs subjective measurements of sleep parameters on ESs.

Data Extraction

Two of us (J.Q.W., R.D.S.) identified target outcomes from each included trial and extracted numeric data. In the case of multiple control/comparison conditions, the most active nonpharmacologic condition was chosen. If an appropriate nonpharmacologic condition did not exist, the pharmacologic condition was chosen. Twenty-five percent of extracted data were independently entered by those 2 of us to spot-check for accuracy. If data necessary for effect size or remission rate calculations were not reported in the published article, corresponding authors were contacted with data requests, and the trial was excluded from analyses if the authors were unable to provide necessary data or did not respond after 3 contact attempts.

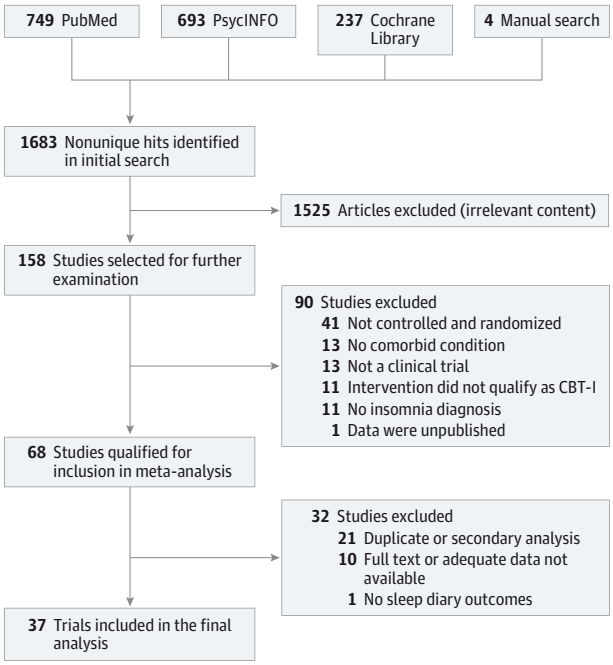
Quantitative Data Synthesis

A random-effects model was used to account for variance in design and outcome variables.[16,17] To compare rates of remission from insomnia between groups, we calculated pooled ORs. To evaluate the effects of CBT-I on sleep and comorbid symptoms, we calculated the pooled Hedges *g* value and its 95% CI. Consistent with convention, a conservative estimate of $r = 0.70$ was used as the pre-post correlation in the calculation if it was not reported.[18] Consistent with convention, an effect size of 0.2 was interpreted as small, 0.5 as medium, and 0.8 as large.[19] In trials with multiple measures of outcome variables (eg, PSQI and ISI), ES estimates were averaged across all measures. To explore the potential role of type of comorbidity and objective vs subjective measures of sleep parameters as moderators of treatment effects, we conducted separate subgroup analyses. Furthermore, we entered publication year, sample size, and treatment length into a metaregression model to evaluate their potential relative contributions to between-study variance.

Publication Bias and Study Quality

Several strategies were used to address potential publication bias: (1) conducting fail-safe *N* analyses[18,20] to assess the robustness of ESs; (2) inspecting funnel plots to assess overrepresentation of positive and negative studies; and (3) using the trim-and-fill method to adjust ESs accordingly.[21] Study quality was assessed independently by 2 of us (J.Q.W. and J.C.O.) using the Cochrane Collaboration's risk of bias assessment tool.[22] In each domain, studies were given a rating of low risk, high risk, or unclear risk. Consensus ratings were reached through discussion between these 2 of us. All analyses were performed using the software program Comprehensive Meta-Analysis, version 2.[23]

Figure 1. Selection Process for Trials Included in the Meta-analyses



The total number of trials is greater than the total number of studies (n = 37) because 1 study[24] included 2 trials (ie, 2 cognitive behavioral therapy for insomnia [CBT-I] conditions, each with an independent control/comparison condition).

Results

Trial Flow

The initial database and manual search identified 1683 nonunique hits that yielded 158 potential studies for further examination (**Figure 1**). Of these, 68 qualified for preliminary inclusion, but 21 were excluded because they were duplicates or reported secondary analyses of data already reported in another included trial. A further 10 studies could not be included because their full-text articles could not be obtained or the published article did not report adequate data needed for meta-analysis, and authors were unable to provide them. One other study was excluded because it did not report sleep diary or comorbid outcomes. Thus, the present meta-analysis extracted data from 36 published studies. Because one study[24] included multiple intervention and control conditions that allowed for analyses of 2 independent CBT-I interventions, each with an appropriate control condition, the final analyses reflect ESs from 37 randomized clinical trials.

Characteristics of analyzed trials are presented in the **Table**. They were published between 1996 and 2014. The 37 trials reported data from a total of 2189 participants. There was a range of comorbid disorders falling into 3 broad categories: psychiatric (n = 10)[25-34] medical (n = 26),[24,35-58] and mixed (n = 1).[9] The mean total sample size per trial was 59.16. Most trials included both male and female participants, with the exception of 8 trials that included only women with breast cancer

Table. Trial Characteristics

Source	Comorbid Condition	Participants[a]	Sleep Outcomes/ Measures	Comorbid Outcomes/ Measures	Type of CBT-I[b]	Comparison Condition	Study Quality
Psychiatric Conditions							
Arnedt et al,[25] 2011	Alcohol dependence	N = 17; 35% female; mean age, 46.2 y	SE, SOL, TST, sleep quality/ sleep diary, ISI	Alcohol use/ abstinent days (%), heavy drinking days (%), drinks per drinking day	CBT-I for alcohol dependence; 8 sessions; no follow-up data	Behavioral placebo treatment	Good
Currie et al,[26] 2004	Alcohol dependence	N = 60; 30% female; mean age, 43.3 y	SE, SOL, TST, sleep quality/ sleep diary, PSQI, SII	Depression/BDI	CBT-I; 5 sessions; 6-mo follow-up	Self-help with telephone support	Good
Edinger et al,[27] 2009	Mixed	N = 81; 14% female; mean age, 54.2 y	SE, SOL, TST, sleep quality/ sleep diary, actigraphy, PSQI, ISQ	None	CBT-I; 4 sessions; 6-mo follow-up	Sleep hygiene	Good
Manber et al,[28] 2008	MDD	N = 30; 61% female; mean age, 48.6 y	SE, TST, sleep quality/ sleep diary, actigraphy, ISI	Depression/HRSD	Escitalopram plus CBT-I; 7 sessions; no follow-up data	Escitalopram plus quasi desensitization	Good
Margolies et al,[29] 2013	PTSD	N = 40; 10% female; mean age, 37.7 y	SE, SOL, TST, sleep quality/ sleep diary, PSQI, ISI	Mood, PTSD symptom severity/POMS, PSQI-A, PTSD symptom severity	CBT-I; 4 sessions; no follow-up data	WLC	Good
Morgan et al,[30] 2004	Hypnotic dependence	N = 209; 67% female, mean age, 65.4 y	SOL, TST, sleep quality/ PSQI	Alcohol use/abstinent days per week	CBT-I; 6 sessions; no follow-up data	TAU	Good
Talbot et al,[31] 2014	PTSD	N = 45; 69% female; mean age, 37.2 y	SE, SOL, TST, sleep quality/ sleep diary, actigraphy, PSG, ISI	PTSD severity/ PCL, CAPS	CBT-I; 8 sessions; no follow-up data	WLC	Good
Ulmer et al,[32] 2011	PTSD	N = 22; 32% female; mean age, 46.0 y	SE, SOL, TST, sleep quality/ sleep diary, PSQI, ISI	PTSD severity/PCL-M	CBT-I plus imagery rehearsal; 6 sessions; no follow-up data	Usual care	Good
Wagley et al,[33] 2013	Residual depression	N = 30; 70% female; mean age, 45.1 y	Sleep quality/ PSQI	Overall functioning/ PHQ-9	Brief CBT-I; 2 sessions; 1-mo follow-up data	TAU	Good
Watanabe et al,[34] 2011	Residual depression	N = 37; 62% female; mean age, 50.5 y	Sleep quality/ PSQI, ISI	Depression/HRSD	Brief CBT-I; 4 sessions; 8-mo follow-up data	TAU	Good
Medical Conditions							
Currie et al,[35] 2000	Chronic pain	N = 60; 55% female; mean age, 45 y	SE, SOL, TST, sleep quality/ sleep diary, PSQI	Medication use, pain/medication quantification, pain severity	CBT-I; 7 sessions; 3-mo follow-up	WLC	Good
Chen et al,[36] 2011	Renal disease	N = 72; 58% female; mean age, 58 y	SE, SOL, TST, sleep quality/ sleep diary, PSQI	Depression, anxiety, fatigue/BAI, BDI, FSS	CBT-I; 6 sessions; no follow-up data	Sleep hygiene	Good
Dirksen and Epstein,[37] 2008	Breast cancer	N = 72; 100% female; mean age, 58 y	Sleep quality/ISI	Fatigue/POMS-F	CBT-I; 6 sessions; no follow-up data	Sleep hygiene	Good
Edinger et al,[38] 1996	PLMD	N = 16; 56% female; mean age, 66.1 y	SE, TST/ sleep diary, PSG	Apnea/Arousal Index, Movement Index	CBT-I; 4 sessions; no follow-up data	Clonazepam (0.5-1.5 mg)	Good
Edinger et al,[39] 2005	Fibromyalgia	N = 47; 96% female; mean age, 48.6 y	SE, SOL, TST, sleep quality/ sleep diary, actigraphy, ISQ	Pain/BPI, MPQ	CBT-I; 6 sessions; 6-mo follow-up	Sleep hygiene	Good
Epstein and Dirksen,[40] 2007	Breast cancer in remission	N = 72; 100% female; mean age, 55.2 y	SE, SOL, TST, sleep quality/ sleep diary, actigraphy	None	CBT-I; 6 sessions; no follow-up data	Sleep hygiene	Good
Espie et al,[41] 2008	Breast cancer	N = 150; 100% female; mean age, 61 y	SE, SOL, TST/ sleep diary, actigraphy	None	CBT-I; 5 sessions; 6-mo follow-up	TAU	Good

(continued)

Table. Trial Characteristics (continued)

Source	Comorbid Condition	Participants[a]	Sleep Outcomes/ Measures	Comorbid Outcomes/ Measures	Type of CBT-I[b]	Comparison Condition	Study Quality
Fiorentino et al,[42] 2009	Breast cancer	N = 14; 100% female; mean age, 61 y	Sleep quality/ PSQI, ISI	Fatigue, depression, quality of life/MFSI, MOS-SF-36, CES-D	CBT-I; 5 sessions; no follow-up data	TAU	Fair
Garland et al,[43] 2014	Cancer	N = 111; 72% female; mean age, 58.9 y	SE, SOL, TST/ sleep diary, actigraphy	Mood/POMS-SF	CBT-I; 8 sessions; 5-mo follow-up	Mindfulness-based stress reduction	Good
Guilleminault et al,[44] 2008	Obstructive sleep apnea	N = 30; 63% female; mean age, 31.4 y	SOL, TST/PSG	Apnea/AHI, RDI	CBT-I; 7 sessions; no follow-up data	OSA surgery	Good
Jansson-Fröjmark et al,[45] 2012	Hearing impairment	N = 32; 63% female; mean age, 55.8 y	TST, sleep quality/ sleep diary, ISI	Depression, anxiety/HADS, WSAS	CBT-I; 7 sessions; 5-mo follow-up	WLC	Good
Jungquist et al,[46] 2010	Chronic pain	N = 28; 78% female; mean age, 48.7 y	SE, SOL, TST, sleep quality/ sleep diary, ISI	Pain/MPI, PDI, Average Daily Pain	CBT-I; 8 sessions; no follow-up data	Contact/ measurement control	Good
Kapella et al,[47] 2011	COPD	N = 18; 44% female; mean age, 63 y	SE, SOL, TST, sleep quality/ sleep diary, actigraphy, PSQI, SII	Fatigue/CRQ-F; POMS-F	CBT-I; 6 sessions; no follow-up data	Wellness education	Good
Martínez et al,[48] 2014	Fibromyalgia	N = 64; 100% female; mean age, 47.6 y	Sleep quality/ PSQI	Fatigue, pain/MFI, MPQ, PCS	CBT-I; 6 sessions; 6-mo follow-up	Sleep hygiene	Good
Matthews et al,[49] 2014	Breast cancer	N = 56; 100% female; mean age, 52 y	SE, SOL, TST, sleep quality/ sleep diary	Fatigue/PFS	CBT-I; 6 sessions; 6-mo follow-up	Behavioral placebo treatment	Good
Miró et al,[50] 2011	Fibromyalgia	N = 40; 100% female; mean age, 46.5 y	Sleep quality/ PSQI	Pain	CBT-I; 6 sessions; no follow-up data	Sleep hygiene	Good
Morgan et al,[51] 2012	Chronic diseases	N = 193; 66% female; mean age, 66.7 y	Sleep quality/ PSQI, ISI	Fatigue/FSS	Self-help CBT-I with telephone hotline; no formal sessions	TAU	Good
Pigeon et al,[24] 2012-1[c]	Chronic pain	N = 10; 33% female; mean age, 50.7 y	SE, TST, sleep quality/ sleep diary, ISI	Pain/MPI, PDI	CBT-I; 10 sessions; no follow-up data	WLC	Good
Pigeon et al,[24] 2012-2[c]	Chronic pain	N = 11; 33% female; mean age, 50.7 y	SE, TST, sleep quality/ sleep diary, ISI	Pain/MPI, PDI	CBT-I/P (insomnia/pain); 10 sessions; no follow-up	CBT-P (pain)	Good
Ritterband et al,[52] 2012	Cancer	N = 28; 86% female; mean age, 56.7 y	SE, SOL, TST, sleep quality/ sleep diary	Fatigue/MFSI-SF	CBT-I; 6 sessions; no follow-up data	WLC	Good
Rios Romenets et al,[53] 2013	Parkinson disease	N = 12; 25% female; mean age, 64.9 y	Sleep quality/ PSQI, ISI, PDSS, SCOPA-night	None	CBT-I + light therapy/ 6 sessions, no follow-up data	Doxepin (10 mg)	Poor
Rybarczyk et al,[54] 2002	Multiple medical conditions	N = 25; 56% female; mean age, 66 y	SE, SOL, TST, sleep quality/ sleep diary, actigraphy, PSQI	None	CBT-I; 8 sessions; 4-mo follow-up	Audiotape relaxation training	Good
Rybarczyk et al,[55] 2005	Osteoarthritis, coronary artery disease, pulmonary disease	N = 92; 67% female; mean age, 69 y	SE, SOL, TST, sleep quality/ sleep diary, PSQI, SII	Mood, pain, functional interference/POMS, SF-MPQ, SIP	CBT-I; 8 sessions; no follow-up data	Stress management and wellness	Good
Savard et al,[56] 2005	Breast cancer	N = 57; 100% female; mean age, 54.1 y	SE, SOL, TST, sleep quality/ sleep diary, ISI	None	CBT-I; 8 sessions; no follow-up data	WLC	Good
Tang et al,[57] 2012	Chronic pain	N = 20; 90% female; mean age, 48.5 y	SE, SOL, TST, sleep quality/ sleep diary, ISI	Pain/BPI, BPI-PPI	CBT-I plus CBT for chronic pain; 4 sessions; no follow-up data	Symptom monitoring	Good
Vitiello et al,[58] 2013	Osteoarthritis	N = 244; 80% female; mean age, 73.1 y	Sleep quality/ PSQI, ISI	Pain severity/CPS	CBT-PI (pain and insomnia); 6 sessions; no follow-up data	CBT-P (pain)	Good

(continued)

Table. Trial Characteristics (continued)

Source	Comorbid Condition	Participants[a]	Sleep Outcomes/ Measures	Comorbid Outcomes/ Measures	Type of CBT-I[b]	Comparison Condition	Study Quality
Psychiatric and Medical Conditions							
Lichstein et al,[9] 2000	Mixed conditions	N = 44; 48% female; mean age, 68.5 y	SE, SOL, TST, sleep quality/sleep diary	Depression, anxiety/GDS, STAI	Stimulus control, relaxation, sleep hygiene; 4 sessions; 3-mo follow-up	Delayed treatment	Fair

Abbreviations: AHI, Apnea-Hypopnea Index; CBT-I, cognitive behavioral treatment for insomnia; BDI, Beck Depression Inventory; BPI, Brief Pain Inventory; BPI-PPI, BPI-Present Pain Intensity; CAPS, Clinician-Administered Posttraumatic Stress Disorder (PTSD) Scale; CBT-P, CBT for pain; CBT-PI, CBT for pain and insomnia; CES-D, Center for Epidemiological Studies Depression Scale; COPD, chronic obstructive pulmonary disease; CPS, Chronic Pain Scale; CRQ-F, Chronic Respiratory Disease Questionnaire Fatigue Scale; FSS, Fatigue Severity Scale; GDS, Geriatric Depression Scale; HRSD, Hamilton Rating Scale for Depression; ISI, Insomnia Severity Index; ISQ, Insomnia Symptom Questionnaire; MDD, major depressive disorder; MFI, Multidimensional Fatigue Inventory; MFSI-SF, Multidimensional Fatigue Inventory–Short Form; MOS-SF-36; Medical Outcomes Study–Short-Form-36; MPI, Multidimensional Pain Inventory; MPQ, McGill Pain Questionnaire; OSA, obstructive sleep apnea; PCL, PTSD Checklist; PCL-M, PTSD Checklist–Military Version; PCS, Pain Catastrophizing Scale; PDI, Pain Disability Index; PDSS, Parkinson Disease Sleep Scale; PFS, Piper Fatigue Scale; PHQ-9, Patient Health Questionnaire; PLMD, periodic limb movement disorder; POMS, Profile of Mood States; POMS-F, POMS-Fatigue; POMS-SF, POMS–Short-Form; PSG, polysomnography; PSQI, Pittsburgh Sleep Quality Index; PSQI-A, PSQI–Addendum for PTSD; RDI, Respiratory Disturbance Index; SCOPA-night, Scales for Outcomes in Parkinson disease–night-time sleep; SE, sleep efficiency; SF-MPQ, Short-Form McGill Pain Questionnaire; SII, Sleep Impairment Index; SIP, SIP, Sickness Impact Profile; SOL, sleep onset latency; STAI, State-Trait Anxiety Inventory; TAU, treatment as usual; TST, total sleep time; WLC, waiting list control; WSAS, Work and Social Adjustment Scale.

[a] Total number is based on total participants in the treatment/control conditions included in analyses.

[b] Follow-up length is indicated only for trials with adequate follow-up data for both CBT-I and control/comparison groups for calculation of controlled effect sizes.

[c] Mean age and percentage of women were estimated based on pooled sample for both trials.

or fibromyalgia.[37,40-42,48-50,56] Trials used a range of control or comparison groups, including waiting list control or delayed treatment or symptom monitoring (10), treatment as usual (7), sleep hygiene education (7), and other active behavioral comparison conditions (13), such as behavioral placebo treatment, pharmacotherapy, mindfulness-based stress reduction, surgery, and relaxation training. Twenty-six trials* used the ISI and/or PSQI, and of these, only 4 failed to provide data on remission.[34,36,50,54] The most common assessment methods for the quantitative sleep parameters were sleep diaries/logs and, for subjective sleep quality, the PSQI and ISI (Table). Ten trials reported SE, SOL and WASO as measured by actigraphy or polysomnography, which did not produce sufficient objective sleep data for quantitative synthesis.

Study Quality

Overall, the quality of studies was moderate to high, and we judged them to have generally low risk of bias in most domains (eTable 2 in the Supplement). High risk in performance bias (42.1%) and detection bias (57.9%) were observed. The potential for bias in these domains was the result of having a waiting list or treatment as usual control condition and unblinded participants, therapists, and assessors. Overall, only 3 studies[9,42,53] received a high-risk rating in more than 2 domains.

Quantitative Data Synthesis

Insomnia Remission

Twenty-two trials† reported or provided ISI or PSQI at post treatment, allowing calculation of remission rates based on a total of 482 control patients and 539 patients who underwent CBT-I (**Figure 2**). Of patients receiving CBT-I, 36.0% reached remission status, compared with 16.9% of those in control/comparison conditions. Meta-analysis yielded a pooled OR of 3.28 (95% CI, 2.30-4.68; $P < .001$). The fail-safe N was a robust 280. The funnel plot of log OR and standard error was asymmetrical toward the right, indicating potential publication bias. The newly imputed OR was 2.61.

Sleep Efficiency

Twenty-four trials‡ reported SE using sleep diaries (**Figure 3**). The random effects meta-analysis yielded a pooled Hedges $g = 0.91$ (95% CI, 0.74 to 1.08; $z = 10.32$; $P < .001$). With an α level of .01, the fail-safe N for the SE analysis was 1028 ($z = 12.98$), indicating that 1028 trials with ESs of zero would be needed to nullify these results. The above pooled ES is thus considered statistically robust. The funnel plot revealed potential publication bias; the trim-and-fill analysis[21] determined that 1 trial would have to fall to the right of the mean to render the plot symmetrical, and the newly imputed ES after adjusting for asymmetry was Hedges $g = 0.93$ (95% CI, 0.76-1.10).

Sleep Onset Latency

Twenty trials reported SOL,§ yielding a pooled Hedges $g = 0.80$ (95% CI, 0.60 to 1.00; $z = 7.79$, $P < .001$). The fail-safe N was a statistically robust 614 ($z = 11.03$). Trim and fill analysis[21] indicated no publication bias.

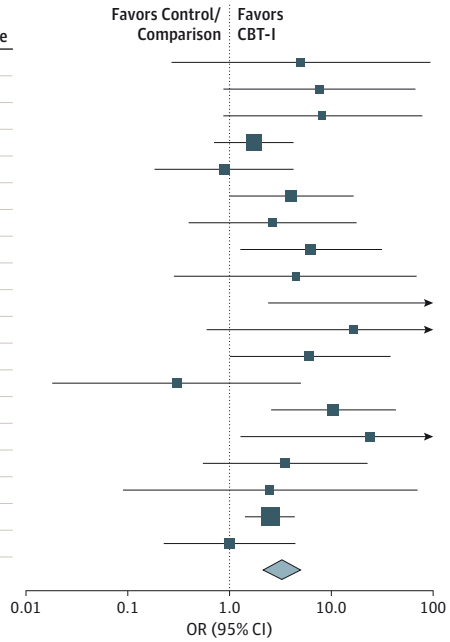
Wake After Sleep Onset

Eighteen trials|| reported WASO, yielding a pooled Hedges $g = 0.68$ (95% CI, 0.60-0.98; $z = 8.08$; $P < .001$), with a statistically robust fail-safe N of 333 ($z = 11.22$). The funnel plot was symmetrical, indicating no publication bias.

*References 24-37, 42, 45-48, 50, 51, 53-58
†References 24-33, 35, 37, 45, 47, 51-53, 55-58
‡References 9, 24-29, 31, 32, 35, 36, 38-40, 43, 46, 47, 49, 52, 54-57
§References 9, 25-27, 29-32, 35, 36, 39-41, 43, 44, 46, 47, 49, 52, 54-57
|| References 9, 25-27, 29, 31, 32, 35, 39, 40, 42-44, 46, 47, 52, 54, 55, 57

Figure 2. Remission From Insomnia at Posttreatment

Source	OR	Statistics for Each Study			
		OR	95% CI	*z* Value	*P* Value
Alcohol dependence: Arnedt et al,[25] 2011	ISI	5.00	0.27-91.52	1.09	.28
Chronic pain: Currie et al,[40] 2000	PSQI	7.56	0.87-65.87	1.83	.07
Alcohol dependence: Currie et al,[26] 2004	PSQI	8.14	0.88-75.48	1.85	.06
Breast cancer: Dirksen and Epstein,[37] 2008	ISI	1.73	0.71-4.17	1.21	.22
Mixed psychiatric: Edinger et al,[27] 2009	PSQI	0.88	0.19-4.16	−0.16	.87
Hearing impairment: Jansson-Frajmark,[45] 2012	ISI	3.96	0.97-16.27	1.91	.06
COPD: Kapella et al,[47] 2011	PSQI	2.63	0.39-17.46	1.00	.32
Depression: Manber et al,[28] 2008	ISI	6.26	1.27-30.80	2.26	.02
PTSD: Margolies et al,[29] 2013	Combined	4.45	0.29-67.55	1.07	.28
Chronic pain: Pigeon et al,[24] 2012-1	ISI	143.00	2.42-8467.01	2.38	.02
Chronic pain: Pigeon et al,[24] 2012-2	ISI	16.20	0.59-441.68	1.65	.10
Cancer: Ritterband et al,[52] 2012	ISI	6.00	0.97-37.30	1.92	.05
PD: Rios Romenets et al,[53] 2013	ISI	0.30	0.02-4.91	−0.84	.40
Breast cancer: Savard et al,[56] 2005	ISI	10.38	2.55-42.33	3.26	<.001
PTSD: Talbot et al,[31] 2014	ISI	23.57	1.29-430.80	2.13	.03
Chronic pain: Tang et al,[57] 2012	ISI	3.50	0.55-22.30	1.33	.18
PTSD: Ulmer et al,[32] 2011	ISI	2.48	0.09-68.14	0.54	.59
Osteoarthritis: Vitiello et al,[58] 2013	Combined	1.00	1.43-4.30	3.22	<.001
Depression: Wagley et al,[33] 2012	PSQI	3.17	0.23-4.37	0.00	>.99
			2.09-4.83	5.40	<.001



Variation in data marker size indicates relative weighting by sample size. CBT-I indicates cognitive behavioral therapy for insomnia; COPD, chronic obstructive pulmonary disease; ISI, Insomnia Severity Index; PD, Parkinson disease; PSQI, Pittsburgh Sleep Quality Index; and PTSD, posttraumatic stress disorder.

Total Sleep Time

Twenty-five trials# reported TST, with a pooled Hedges *g* = 0.19 (95% CI, 0.06-0.31; *z* = 2.92; *P* = .003). However, the fail-safe *N* of 55 (*z* = 3.50) was less than 5k +10, where k is the number of observed trials; the above pooled ES is not considered statistically robust. Therefore, TST was excluded from further moderator analyses.

Sleep Quality

Thirty-four trials** reported on subjective sleep quality (eFigure in the Supplement), yielding a pooled Hedges *g* = 0.84 (95% CI, 0.69-1.00; *z* = 10.42; *P* < .001), with a statistically robust fail-safe *N* of 2206 (*z* = 15.91). Trim and fill analysis[21] indicated no publication bias.

Comorbid Condition Outcomes

Thirty-one trials†† reported clinical outcomes for the target comorbid disorder using psychometrically validated self-report instruments and standard medical outcome measures (**Figure 4**), yielding a pooled Hedges *g* = 0.39 (95% CI, 0.25-0.53; *z* = 5.51; *P* < .001). The fail-safe *N* for the sleep quality analysis was a statistically robust 409 (*z* = 7.38). Trim and fill analysis[21] determined that 13 trials would have to fall to the left of the mean to render the plot symmetrical, indicating potential publication bias; the newly imputed ES after adjusting for asymmetry was Hedges *g* = 0.16 (95% CI, 0.01-0.32).

Follow-up Outcomes

Thirteen trials‡‡ reported follow-up outcomes for both CBT-I and control/comparison groups, with follow-up time points ranging from 3 to 12 months post intervention. Of these, only 8 trials[9,26,27,35,39,43,49,54] reported SE outcomes at follow-up to yield a medium ES (Hedges *g* = 0.61; 95% CI, 0.39-0.82; *z* = 5.61; *P* < .001, fail-safe *N* = 58; *z* = 7.42). Adjusted Hedges *g* was 0.52 (95% CI, 0.33-0.72) with trim-and-fill analysis.[21] Twelve trials§§ reported sleep quality at follow-up outcomes to yield a medium to large ES (Hedges *g* = 0.70; 95% CI, 0.25-0.52; *z* = 5.61; *P* < .001, fail-safe *N* = 161; *z* = 7.42). Trim-and-fill analysis[21] indicated an adjusted Hedges *g* = 0.55, 95% CI [0.30 to 0.81]. Follow-up outcomes were reported in 10 trials for TST, || || 8 for SOL,[9,26,27,34,35,39,43,54] and 7 for WASO.[9,27,35,39,42,43,54] There was not enough power to produce statistically robust pooled ESs (fail-safe *N* values <36) for these outcomes.

Moderator Analyses

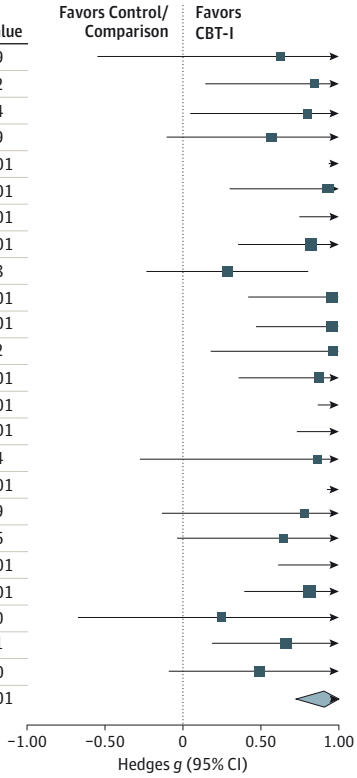
Psychiatric vs Medical Comorbidity

Nine studies of insomnia comorbid with psychiatric disorders[25,26,28-34] (Hedges *g* = 0.76; 95% CI, 0.46-1.05) yielded a larger pooled ES on comorbid outcomes than did 21 studies of insomnia comorbid with medical conditions[24,35-39,42-52,55,57,58] (Hedges *g* = 0.20; 95% CI, 0.09-0.30; χ^2 test for interaction = 12.30; *P* < .001), suggesting that psychiatric symptoms comorbid with insomnia may be more responsive to CBT-I than

#References 9, 24-32, 35, 36, 38-41, 43-47, 49, 52, 54-57
**References 9, 24-37, 39, 40, 42, 43, 45-58
††References 9, 24-26, 28-39, 42-52, 55, 57, 58
‡‡References 9, 26, 27, 33-35, 39, 41, 43, 45, 48, 49, 54
§§References 9, 26, 27, 33-35, 39, 43, 45, 48, 49, 54
|| || References 9, 26, 27, 35, 39, 41, 43, 45, 49, 54

Figure 3. Sleep Efficiency (SE)–Controlled Effect Sizes From Baseline to Posttreatment

Source	Hedges g	95% CI	Standard Error	Variance	z Value	P Value
Alcohol dependence: Arnedt et al,[25] 2011	0.63	−0.54 to 1.81	0.60	0.36	1.06	.29
Alcohol dependence: Currie et al,[26] 2004	0.85	0.15 to 1.54	0.36	0.13	2.38	.02
Depression: Manbar et al,[28] 2008	0.80	0.05 to 1.55	0.38	0.15	2.08	.04
Mixed psychiatric: Edinger et al,[27] 2009	0.57	−0.10 to 1.24	0.34	0.12	1.68	.09
PTSD: Margolies et al,[29] 2013	1.97	1.20 to 2.75	0.40	0.16	4.98	<.001
PTSD: Talbot et al,[31] 2014	0.93	0.30 to 1.56	0.32	0.10	2.90	<.001
PTSD: Ulmer et al,[32] 2011	1.74	0.76 to 2.72	0.50	0.25	3.47	<.001
Breast cancer: Epstein and Dirksen,[40] 2007	0.82	0.35 to 1.30	0.24	0.06	3.39	<.001
Breast cancer: Matthews et al,[36] 2014	0.29	−0.23 to 0.81	0.27	0.07	1.09	.28
Breast cancer: Savard al,[56] 2005	0.96	0.42 to 1.51	0.28	0.08	3.48	<.001
Cancer: Garland et al,[43] 2014	0.96	0.47 to 1.45	0.25	0.06	3.87	<.001
Cancer: Ritterband et al,[52] 2012	0.97	0.18 to 1.76	0.40	0.16	2.40	.02
Chronic pain: Currie et al,[35] 2000	0.87	0.35 to 1.40	0.27	0.07	3.27	<.001
Chronic pain: Jungquist et al,[46] 2010	1.77	0.88 to 2.67	0.46	0.21	3.87	<.001
Chronic pain: Pigeon et al,[24] 2012-1	2.24	0.74 to 3.75	0.77	0.59	2.92	<.001
Chronic pain: Pigeon et al,[24] 2012-2	0.87	−0.28 to 2.01	0.58	0.34	1.48	.14
Chronic pain: Tang et al,[57] 2012	1.96	0.92 to 3.00	0.53	0.28	3.71	<.001
COPD: Kapella et al,[47] 2011	0.78	−0.13 to 1.70	0.47	0.22	1.67	.09
Fibromyalgia: Edinger et al,[39] 2005	0.65	−0.03 to 1.34	0.35	0.12	1.87	.06
Mixed medical: Rybarczyk et al,[54] 2002	1.52	0.61 to 2.43	0.46	0.21	3.28	<.001
Mixed medical: Rybarczyk et al,[55] 2005	0.81	0.39 to 1.24	0.22	0.05	3.78	<.001
PLMD: Edinger et al,[38] 1996	0.25	−0.68 to 1.18	0.47	0.23	0.53	.60
Renal disease: Chen et al,[36] 2011	0.66	0.19 to 1.13	0.24	0.06	2.76	.01
Mixed psych/medical: Lichstein et al,[9] 2000	0.49	−0.10 to 1.08	0.30	0.09	1.64	.10
Total	0.91	0.74 to 1.08	0.09	0.01	10.32	<.001



All outcomes were derived from sleep diaries. Variation in data marker size indicates relative weighting by sample size. CBT-I indicates cognitive behavioral therapy for insomnia; COPD, chronic obstructive pulmonary disease; PD, Parkinson disease; PLMD, periodic limb movement disorder; and PTSD, posttraumatic stress disorder.

are medical symptoms. However, there were no significant differences between the 2 types of comorbid populations in terms of sleep outcomes (χ^2 test for interactions <1.32; all $P > .31$). In other words, the positive response to CBT-I on insomnia symptoms does not appear to be moderated by the type of comorbid condition.

Objective vs Subjective Measure of Sleep Parameters

Ten trials## reported actigraphy and/or polysomnography measures of SE, SOL, and/or WASO. Owing to a lack of power, statistically robust pooled ESs could not be produced (ie, fail-safe *N* values ≤29). Preliminary findings indicated statistically nonsignificant ESs in the small to medium range for SE (n = 10; Hedges $g = 0.12$; 95% CI, −0.30 to 0.27; $P = .12$), SOL (n = 7; Hedges $g = 0.46$, 95% CI, 0.18 to 0.74; $P = .01$), and WASO (n = 8; Hedges $g = 0.53$; 95% CI, 0.07 to 1.00; $P = .02$).

Publication Year, Sample Size, and Treatment Length

With an α level of .01, omnibus tests did not reach statistical significance ($Q < 8.95_3$; $P > .03$); together, publication year, sample size, and treatment length contributed 9% or less of the between-study variance to sleep and comorbid outcomes. However, holding other covariates constant, increase in the number of sessions predicted slightly larger improvement in sleep quality ($\beta = 0.13$; $z = 2.62$; $P < .01$). Publication year and sample size did not independently predict sleep/comorbid parameter ESs ($|\beta|$s <.02, all $P > .29$).

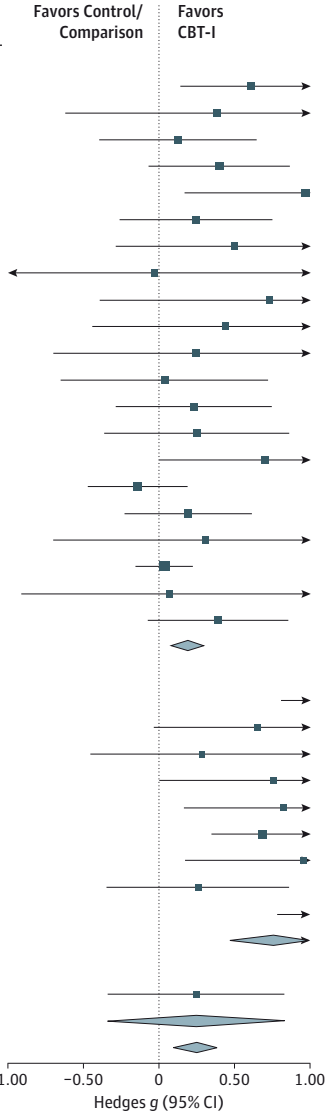
##References 27, 28, 31, 39-41, 43, 44, 47, 54

Discussion

The present meta-analysis examined the efficacy of CBT-I across 37 randomized clinical trials that included 2189 patients with insomnia comorbid with psychiatric and medical conditions. Overall, our findings indicate that CBT-I has positive effects on reducing insomnia symptoms and sleep disturbances in comorbid insomnia. At posttreatment evaluation, 35.6% of the patients who received CBT-I were in remission from insomnia, compared with 17.4% of those in control or comparison conditions. Pre-post controlled ESs were medium to large for most sleep parameters, including improvements in SE and subjective sleep quality and reductions in SOL and WASO, with the range from Hedges *g* being 0.67 to 0.88. These ESs are similar to those found in meta-analyses of primary insomnia trials[6-8] and collectively support the efficacy of CBT-I in reducing insomnia symptoms and improving sleep parameters across primary and comorbid insomnia disorders. In addition, the treatment effects remained in the medium range for SE and sleep quality at follow-up, indicating

Figure 4. Comorbid Outcomes–Controlled Effect Sizes From Baseline to Posttreatment

Source by Comorbid Diagnosis Type	Measure	Hedges *g*	Standard Error	Variance	95% CI	*z* Value	*P* Value
Medical							
Breast cancer: Dirksen and Epstein,[38] 2008	POMS-F	0.61	0.24	0.06	0.14 to 1.08	2.56	.01
Breast cancer: Fiorentino et al,[42] 2009	Combined	0.39	0.51	0.26	−0.62 to 1.39	0.76	.45
Breast cancer: Matthews et al,[49] 2014	PFS	0.13	0.26	0.07	−0.39 to 0.65	0.48	.63
Cancer: Garland et al,[43] 2014	POMS-SF	0.40	0.24	0.06	−0.06 to 0.87	1.70	.09
Cancer: Ritterband et al,[52] 2012	MFSI-SF	0.96	0.40	0.16	0.18 to 1.75	2.40	.02
Chronic pain: Currie et al,[35] 2000	Combined	0.25	0.26	0.07	−0.25 to 0.75	0.97	.33
Chronic pain: Jungquist et al,[46] 2010	Combined	0.50	0.40	0.16	−0.28 to 1.28	1.26	.21
Chronic pain: Pigeon et al,[24] 2012-1	Combined	−0.03	0.59	0.34	−1.18 to 1.12	−0.05	.96
Chronic pain: Pigeon et al,[24] 2012-2	Combined	0.74	0.58	0.33	−0.39 to 1.87	1.28	.20
Chronic pain: Tang et al,[57] 2012	Combined	0.44	0.45	0.20	−0.43 to 1.32	0.99	.32
COPD: Kapella et al,[47] 2011	Combined	0.25	0.48	0.23	−0.69 to 1.19	0.52	.61
Fibromyalgia: Edinger et al,[39] 2005	Combined	0.04	0.35	0.12	−0.65 to 0.73	0.11	.91
Fibromyalgia: Martinez et al,[48] 2014	Combined	0.23	0.26	0.07	−0.28 to 0.75	0.89	.38
Fibromyalgia: Miro et al,[50] 2011	MPQ	0.25	0.31	0.10	−0.36 to 0.86	0.81	.42
Hearing impairment: Jansson-Frajmark,[45] 2012	Combined	0.70	0.36	0.13	0.00 to 1.40	1.97	.05
Mixed chronic diseases: Morgan et al,[51] 2012	FSS	−0.14	0.17	0.03	−0.47 to 0.19	−0.83	.41
Mixed medical: Rybarczyk et al,[55] 2005	Combined	0.21	0.21	0.05	−0.20 to 0.63	1.00	.32
OSA: Guilleminault et al,[44] 2008	Combined	0.31	0.51	0.26	−0.70 to 1.31	0.60	.55
Osteoarthritis: Vitiello et al,[58] 2013	CPS	0.04	0.10	0.01	−0.15 to 0.23	0.41	.68
PLMD: Edinger et al,[38] 1996	Combined	0.07	0.50	0.25	−0.91 to 1.05	0.14	.89
Renal disease: Chen et al,[36] 2011	Combined	0.40	0.24	0.06	−0.07 to 0.86	1.68	.09
Subtotal		0.19	0.06	0.00	0.09 to 0.30	3.53	<.001
Psychiatric							
Alcohol dependence: Arnedt et al,[25] 2011	Combined	2.48	0.85	0.72	0.82 to 4.15	2.92	.003
Alcohol dependence: Currie et al,[26] 2004	BDI	0.66	0.35	0.12	−0.03 to 1.34	1.88	.06
Depression: Manber et al,[28] 2008	HRSD	0.29	0.38	0.14	−0.45 to 1.02	0.77	.44
Depression: Wagley et al,[33] 2013	PHQ-9	0.76	0.39	0.15	−0.00 to 1.52	1.95	.05
Depression: Watanabe et al,[34] 2011	HRSD	0.83	0.34	0.11	0.17 to 1.49	2.46	.01
Hypnotic dependence: Morgan et al,[30] 2004	Abstinent d/wk	0.69	0.17	0.03	0.35 to 1.03	4.02	<.001
PTSD: Margolies et al,[29] 2013	Combined	0.96	0.40	0.16	0.18 to 1.74	2.40	.02
PTSD: Talbot et al,[31] 2014	Combined	0.26	0.31	0.09	−0.34 to 0.86	0.85	.40
PTSD: Ulmer et al,[32] 2011	PCL-M	1.89	0.56	0.32	0.79 to 3.00	3.36	.001
Subtotal		0.76	0.15	0.02	0.46 to 1.05	5.03	<.001
Mixed							
Mixed psych and medical: Lichstein et al,[9] 2000	Combined	0.25	0.30	0.09	−0.33 to 0.84	0.84	.40
Subtotal		0.25	0.30	0.09	−0.33 to 0.84	0.84	.40
Total		0.26	0.05	0.00	0.16 to 0.36	5.12	<.001



Variation in data marker size indicates relative weighting by sample size.
BDI indicates Beck Depression Inventory; CBT-I, cognitive behavioral therapy for insomnia; COPD, chronic obstructive pulmonary disease; CPS, Chronic Pain Scale; FSS, Fatigue Severity Scale; HRSD, Hamilton Rating Scale for Depression; MFSI-SF, Multidimensional Fatigue Inventory–Short Form; MPQ, McGill Pain Questionnaire; OSA, obstructive sleep apnea; PCL-M, PTSD Checklist–Military Version; PFS, Piper Fatigue Scale; PHQ-9, Patient Health Questionnaire; PLMD, periodic limb movement disorder; POMS-SF, POMS–Short-Form; and PTSD, posttraumatic stress disorder.

that the benefits of CBT-I are generally maintained 3 to 12 months after completing treatment. Consistent with one previous review,[6] CBT-I did not yield significant effects on TST at posttreatment evaluation.

Cognitive and behavioral therapy for insomnia also had positive effects on comorbid outcomes, including condition-specific clinical indices and general measures of mood and functioning, yielding a small to medium pooled ES of Hedges *g* = 0.39. The extent of improvement in comorbid symptoms was moderated by the type of comorbidity such that patients with psychiatric disorders demonstrated significantly larger changes (Hedges *g* = 0.76) compared with those with medical conditions (Hedges *g* = 0.20). There were no significant differences between the 2 populations in terms of improvements on sleep indices. These findings indicate that CBT-I has positive effects on sleep across comorbid conditions, but it has stronger effects on comorbid symptoms in psychiatric conditions compared with comorbid symptoms in medical conditions, leading to 2 possible hypotheses. First, sleep disturbance may be more strongly associated with cognitive-emotional symptoms than with physical symptoms. Therefore, reducing sleep disturbance would have a stronger effect on psychiatric illness, especially given the inclusion of sleep disturbance among the symptoms of posttraumatic stress disorder and mood disorders, 2 common psychiatric comorbidities. Second, greater improvements in psychiatric symptoms may be

due to common factors, which have been hypothesized to account for a proportion of the variance across different forms of psychotherapy.[59] For example, it is possible that patients with comorbid psychiatric symptoms benefit globally from elements of cognitive therapy contained in CBT-I, which have been shown to be effective for anxiety,[60] depression,[61] and quality of life in general.[62]

The trials reviewed in the present meta-analysis were of generally good quality and had low risk of bias. Approximately 90% of the trials were found to have a high risk for bias in 2 domains or fewer. However, we found large discrepancies on detection and performance bias. Specifically, few trials described efforts to use blinded assessors to collect self-report data or to score objective measures (polysomnography or actigraphy). Although self-reported sleep logs and global measures of insomnia severity are considered standard assessments for insomnia,[13,63] methods for collecting and scoring these data to minimize potential bias have not been specified. Mobilizing resources to reduce detection and performance bias in future randomized clinical trials on insomnia disorders could improve the methodologic rigor of this literature. In addition, the mean sample size of the studies was only 59 participants, indicating that the trials reviewed were mostly small-scale pilot studies. Overall, the literature on comorbid insomnia is still maturing and more rigorous, large-scale studies are needed to yield more stable and consistent effect sizes.

Several limitations should be noted with regards to our findings. First, there were only 10 trials that reported objective measures of sleep and rest-activity at both pretreatment and posttreatment (Table). As a result, independent ESs for each method could not be meaningfully produced; thus, the effects of CBT-I on objective measures of sleep remain inconclusive. Second, there were insufficient studies reporting TST at follow-up to examine the long-term effect of CBT-I on TST. Third, the full range of psychiatric and medical conditions is not represented in these studies, and the outcome measures on the comorbid condition were heterogeneous. In some studies, the outcome was specific to the comorbid condition, such as the percentage of abstinent days in the context of substance dependence[25]; in other studies, the outcome was a sequela of the comorbid condition or treatment of the comorbid condition, such as fatigue in the context of breast cancer.[37,49,52] As a result, we were unable to specify the direction of the association between insomnia and the comorbid condition.

Conclusions

Our findings indicate that CBT-I can improve insomnia symptoms and sleep parameters when insomnia is comorbid with medical and psychiatric conditions. Furthermore, CBT-I can affect symptoms associated with the comorbid condition, with stronger effects observed in psychiatric conditions compared with medical conditions. These findings provide empirical support for the recommendation of using CBT-I as the treatment of choice for comorbid insomnia disorders.[1,2] Given that insomnia disorders are highly prevalent in primary care settings,[64,65] health care professionals in these settings should regularly assess for sleep disturbances in the context of comorbid conditions and efforts should be directed at adapting CBT-I to the time constraints in this setting. For example, a brief behavioral therapy for insomnia delivered by a trained nurse has demonstrated efficacy in primary care[66] and can serve as a model for implementing CBT-I in this setting.

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Study concept and design: Wu.
Acquisition, analysis, or interpretation of data: All authors.
Drafting of the manuscript: Wu, Ong.
Critical revision of the manuscript for important intellectual content: All authors.
Statistical analysis: Wu.
Administrative, technical, or material support: Wu, Appleman, Salazar, Ong.
Study supervision: Ong.

Conflict of Interest Disclosures: Dr Ong serves as a consultant to Sleepio, Inc. This activity is not related to the present study. No other conflicts are reported.

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Invited Commentary

Treating Insomnia Disorder in the Context of Medical and Psychiatric Comorbidities

Michael A. Grandner, PhD, MTR; Michael L. Perlis, PhD

Insomnia is a common condition. It is estimated that approximately 30% of the population experiences some symptom of insomnia, and approximately 5% to 15% of these individuals are likely to meet criteria for an insomnia disorder.[1] Traditionally, insomnia was considered as either a primary disorder or secondary to another medical or psychiatric condition. During the past 2 decades, multiple lines of evidence have converged to support the proposition that insomnia, regardless of concurrent medical and/or psychiatric illness, is an independent disorder and should be treated accordingly.[2] Partially in response, insomnia is now formally classified in the *Diagnostic and Statistical Manual of Mental Disorders* (Fifth Edition) as a separate disorder, and the diagnosis of insomnia secondary to another condition was removed. Numerous studies have shown that targeted treatment for insomnia is effective in the context of other conditions. The success of cognitive behavioral therapy for insomnia (CBT-I) with secondary or comorbid insomnia strongly suggests that, although insomnia may be precipitated by psychiatric and/or medical illness, it is likely perpetuated by the same factors that are responsible for primary (chronic) insomnia.[2] The application of CBT-I in patients with comorbid insomnia also had one significant and unexpected outcome: treatment gains were evident for the so-called *parent disorder*. For example, CBT-I in patients with depression led to 29% lower depression ratings vs medication alone.[3]

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Given that numerous studies have found that CBT-I produces significant treatment outcomes in insomnia comorbid with such disorders as depression, chronic pain, and cancer (and often with outcomes that equal or exceed the norms with uncomplicated insomnia), the time seems ripe to take stock of such findings within the framework of a proper meta-analysis. The investigation in this issue of *JAMA Internal Medicine* by Wu and colleagues[4] does precisely this.

Cognitive-behavioral therapy for insomnia generally includes several components, such as sleep restriction therapy (aligning sleep opportunity with sleep ability to maximize sleep efficiency), stimulus control therapy (maximizing the stimulus value of the bed and bedroom for sleep), sleep hygiene (alleviating obvious barriers to sleep), cognitive therapy (addressing nighttime ruminations, worries, and fears), and sometimes relaxation interventions (reducing physiologic arousal).[5] Prior meta-analyses[6] have shown that CBT-I is an efficacious treatment for reducing sleep latency, wake time after sleep onset, and early morning awakenings, as well as increasing sleep efficiency. Furthermore, comparative meta-analyses[7] have shown that CBT-I performs at least as well as pharmacotherapy or even slightly better in the short term, with superior results in the long term. Based on these and other findings, CBT-I has been adopted as a recommended first-line treatment for insomnia by the American Academy of Sleep Medicine.

The study by Wu and colleagues[4] examined available clinical trials that evaluated CBT-I for insomnia in the context of other conditions. Studies were found that examined insomnia treatment in the context of substance abuse, renal disease, chronic pain, cancer, depression, posttraumatic stress disorder, and other conditions. Overall, this study found that CBT-I was associated with an increased likelihood of remission from insomnia (odds ratio, 3.28; 95% CI, 2.30-4.68; $P < .001$). In addition, positive findings were seen for improvements in sleep efficiency and overall sleep quality. Positive findings were also seen for the comorbid condition in general, such that CBT-I improved noninsomnia outcomes as well. There was a significant interaction: effects on psychiatric comorbid conditions were more robust than were effects for nonpsychiatric comorbidities. The meta-analysis showed that not only was CBT-I effective in the face of comorbid conditions, but the effects were relatively large (although slightly smaller than might be seen in primary insomnia).

The study had a few limitations that suggest directions for future research. First, the meta-analysis focused on remission and did not summarize outcomes with respect to treatment response. Second, the study could have placed more focus on the benefits of CBT-I for the comorbid condition. As noted above, there are several studies in the literature showing that treatment of comorbid insomnia not only improves the insomnia but also improves severity and/or tolerance of symptoms of the comorbid condition (eg, produces treat-