Cognitive Behavioral Therapy for Patients with Primary Insomnia or Insomnia Associated Predominantly with Mixed Psychiatric Disorders: a Randomized Clinical Trial

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Objective: This study was conducted to evaluate the efficacy of cognitive behavioral therapy (CBT) against a sleep hygiene education control therapy in patients with primary or comorbid insomnia.

Design and Setting: Randomized, parallel-group, clinical trial conducted at a single Veterans Affairs medical center, with recruitment from March 2001 to June 2005.

Participants: Eighty-one adults (n = 11 women; mean age, 54.2 years) with chronic primary (n = 40) or comorbid insomnia associated predominantly with mixed psychiatric disorders (n = 41).

Interventions: Patients, screened via structured interviews and diagnostic polysomnography, were randomly assigned to receive CBT (sleep education, stimulus control, and time-in-bed restrictions; 20 patients with primary and 21 with comorbid insomnia), or sleep hygiene (SH: education about aspects of lifestyle and the bedroom environment that affect sleep; 20 patients with primary and 20 with comorbid insomnia). Outpatient treatment included 4 biweekly sessions with a posttreatment assessment and a follow-up conducted at 6 months.

Measures and Results: Participants completed actigraphy and sleep diaries for 2 weeks prior to therapy, during a 2-week posttreatment assessment, and during 2 weeks at follow-up. They also completed questionnaires measuring global insomnia symptoms, general sleep quality, and sleep-disruptive beliefs before treatment, immediately following treatment, and at the follow-up time point. Consistent with previous studies, CBT outperformed sleep hygiene across several study outcome measures for the sample as a whole. Statistical analyses showed no significant 3-way interaction of treatment group, time, and insomnia type for any of the sleep or questionnaire measures, suggesting the benefits of CBT over sleep hygiene were comparable for patients with primary insomnia and comorbid insomnia. Moreover, only 1 of several indexes of clinically notable improvement suggested a significantly better response to CBT by patients with primary insomnia, as compared with those with comorbid insomnia.

Conclusions: A fixed 4-session "dose" of CBT produced similar benefits for patients with primary and those with comorbid insomnia across most measures examined. Thus, CBT appears to be a viable psychological insomnia therapy both for those with primary insomnia and for groups composed mainly of patients with insomnia and nonpsychotic psychiatric conditions.

Keywords: Cognitive behavioral therapy (CBT), sleep hygiene therapy, primary insomnia, comorbid insomnia.

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CHRONIC INSOMNIA IS A SERIOUS FORM OF SLEEP DISTURBANCE ASSOCIATED WITH REDUCED QUALITY OF LIFE, INCREASED RISKS FOR SERIOUS PSYCHIATRIC illness, and enhanced healthcare utilization among millions worldwide.[1-3] Insomnia may present either as a primary sleep disorder or as a disorder comorbid with another sleep, medical, or psychiatric disorder or a combination thereof. Both primary insomnia (PI) and comorbid insomnia (CMI) are relatively common maladies, but CMI is more prevalent than PI in both clinical venues[4,5] and the general population at large.[6] Moreover, CMI may be more persistent and have even more serious consequences than PI. Recent data,[7] for example, show that insomnia sufferers with comorbid gastrointestinal problems, chronic pain, hypertension, or problems with breathing or urination report more chronic insomnia than do those without such conditions. Furthermore, when insomnia occurs comorbid with a psychiatric illness such as major depression, it complicates disease management and often remains as a residual symptom that enhances risk for both suicide and relapse.[8,9] In view of these considerations, patients who present with insomnia and particularly those with CMI warrant early and effective treatment.

Pharmacotherapy with benzodiazepine receptor agonists or sedating antidepressants currently remains the most common treatment offered to patients with insomnia.[10] However, cognitive behavioral therapy (CBT), designed to address sleep-disruptive beliefs and habits, has become an increasingly well-regarded insomnia treatment.[10] Results of meta-analyses (e.g., Smith, et al.[11]) and head-to-head comparisons[12] suggest CBT produces short-term sleep improvements that compare favorably to those achieved with various forms of pharmacotherapy. Furthermore, sleep improvements following CBT appear to endure long after treatment is completed,[13] and limited data suggest that patients prefer CBT over treatment with sleep medications.[14] Given such observations, CBT has become a popular alternative for insomnia management.

Most evidence supporting the efficacy of CBT comes from studies conducted with patients with PI, although there is some

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limited evidence supporting use of this treatment with CMI as well. Some uncontrolled case series or clinic-based studies have suggested the efficacy of CBT among patients with CMI and mixed psychiatric and medical conditions.[15] Other case series or quasi-experimental studies have suggested CBT may be efficacious for treating insomnia in such specific patient groups as those with chronic pain,[16] cancer,[17] posttraumatic stress disorder,[18] and clinical depression[19] and those with mixed serious mental disorders.[20] In addition, a number of small to moderately sized, single-site, randomized clinical trials have suggested that CBT is efficacious for patients with insomnia and comorbid chronic peripheral pain syndromes,[21] treated breast cancer,[22] fibromyalgia[23], mixed medical disorders,[24] mixed psychiatric and medical disorders,[25] and alcoholism.[26] Despite these findings, it is yet to be determined whether patients with PI or CMI show similar improvement from an equal and standard "dose" of CBT intervention. The current study tested the relative efficacy of CBT against a sleep hygiene control treatment (SH) in patients with PI and in a group of patients with CMI composed predominantly of individuals with mixed comorbid psychiatric disorders. The study hypotheses predicted that CBT would produce significantly greater short- and longer-term improvements in insomnia symptoms than would sleep hygiene in the sample as a whole. The data obtained were also examined to assess the relative efficacy of CBT in the PI and CMI groups considered separately.

METHOD

Design

This study used a randomized, parallel-group, experimental design. Participants were stratified by sex, age group (< 55 vs 55 years and older), current use of sleep medication (some vs none), initial insomnia severity (sleep diary mean total wake time < 90 minutes/night vs ≥ 90 minutes/night), and global insomnia diagnosis (PI vs CMI). They then were randomly assigned to treatments (CBT vs SH) and therapists (1 woman, 1 man). Participants were blind to the study hypotheses but were informed they would receive 1 of 2 nondrug treatments for insomnia. The Institutional Review Board of the Durham (NC) VA Medical Center reviewed and approved the study protocol before study enrollment began. A study coordinator met individually with volunteers prior to enrollment to inform them about nature of the study, describe study procedures, and obtain written informed consent. Study participants received a small amount of compensation for completing study measures (e.g., sleep diaries, questionnaires) and were reimbursed for their transportation expenses.

PARTICIPANTS

Recruitment occurred between March 2001 and June 2005 through posted announcements, dissemination of study information to physician providers, targeted recruitment letters mailed to Veterans Administration (VA) outpatients with insomnia diagnoses or histories of sleep medication use, and periodic operation of a study information table in the VA medical center where the study was conducted. Patient volunteers were considered for inclusion if they (1) met research diagnostic criteria for insomnia disorder,[27] (2) had a mean total wake time (sleep onset + wake after onset) of more than 60 minutes per night during a screening week of sleep-diary monitoring, (3) provided informed consent, and (4) had concurrence for enrollment from their primary care physician. Excluded from the study were those who (1) were terminally ill, (2) had a highly unstable medical or psychiatric condition (i.e., a condition requiring hospitalization imminently or within 3 months prior to study enrollment), (3) were suicidal, (4) had acute pain or poorly managed chronic pain syndromes that they viewed as a primary cause of their insomnia, 4) were not mentally competent (i.e., score < 27 on the Mini-Mental Status Exam), or (5) showed evidence of clinically significant sleep apnea or periodic limb movement disorder on a qualifying polysomnogram. These selection criteria allowed enrollment of patients with PI as well as those with CMI who had relatively stable/treated comorbid mental or medical conditions.

Patient volunteers underwent telephone or brief face-to-face screening, and those passing this stage completed structured interviews, sleep-diary monitoring (1 week), and screening polysomnography. The interviews were conducted by a clinical psychologist using the Structured Interview for Psychiatric Disorders, Patient Version (SCID-P)[28] and the Duke Structured Interview for Sleep Disorders (DSISD), an instrument developed by our lab that has shown satisfactory reliability/validity for insomnia diagnoses.[29,30] Based on these structured interviews, those patients enrolled were assigned a diagnosis of PI or CMI. Those diagnosed with PI met research diagnostic criteria (RDC) and DSM-IV-TR[31] criteria for primary insomnia and had no active concurrent Axis I psychiatric diagnosis and no findings on a structured sleep interview suggesting a medical or medication cause for their insomnia. Those assigned a CMI diagnosis met RDC criteria for insomnia disorder and had findings on a structured sleep interview suggesting that their insomnia was at least partially the result of a concurrent active psychiatric or medical problem. Eighty-one volunteers qualified, underwent pretreatment assessment, and subsequently were randomly assigned to the treatment and therapist arms of the study using the minimization method[32] to ensure overall balance on the pretreatment stratification variables. Forty of these patients met study criteria for PI, whereas the remaining 41 met the study definition of CMI. The CMI group comprised 18 patients with comorbid combat-related posttraumatic stress disorder, 16 with comorbid mood disorder (major depression or dysthymia), 3 with substance-induced insomnia, 3 whose insomnia was associated with a chronic pain syndrome (e.g., low back pain) and 1 with a combination of gastroesophogeal reflux disease and anxiety disorder not otherwise specified. Prestudy power calculations (with standard deviation based on pilot data) showed that the enrolled sample size was sufficient to detect pretreatment–posttreatment differences in sleep efficiency of 5.2% between the CBT and SH arms. Figure 1 shows the participant flow, whereas Table 1 presents descriptive data for the whole sample and each treatment group. A significantly ($P = 0.01$) higher percentage of those with CMI (61.0%) reported sleep-medication use upon study entry than did those in the PI group (32.5%). Otherwise, the treatment conditions and insomnia diagnosis subgroups seemed reasonably comparable

Table 1—Demographic Characteristics of Study Sample

Characteristic	CBT		SH		Total
	PI	CMI	PI	CMI	Sample
	N = 20	N = 21	N = 20	N = 20	N = 81
Age – Years: Mean (SD)	56.9 (16.3)	52.0 (11.1)	55.0 (15.9)	53.0 (11.5)	54.2 (13.7)
Employed full time	10	5	6	7	28
Gender: male	18	17	17	18	70
Medication use (for randomization)	6	12	7	13	38
Race – white	10	12	12	13	47
Currently married[1]	13	14	10	17	54
Nature of sleep complaint[2]					
Sleep onset	3	4	2	2	11
Sleep maintenance	8	6	7	7	28
Sleep onset and maintenance	7	6	7	10	30
Other	2	5	2	0	9
Therapist assignment					
Male Therapist: total (M,F)	12 (11,1)	9 (7,2)	10 (9,1)	10 (9,1)	41 (36,5)
Female Therapist: total (M,F)	8 (7,1)	12 (10,2)	10 (8,2)	10 (9,1)	40 (34,6)
Body mass index: Mean (SD)[3]	27.4 (4.4)	26.9 (4.3)	29.2 (5.1)	28.0 (5.0)	27.8 (4.7)
Self-report medical comorbidities: mean(SD)[4]	3.3 (2.4)	3.6 (2.4)	4.4 (2.7)	3.7 (2.1)	3.7 (2.4)
Self-report psych comorbidities: Median (IQR)[4]	1.0 (1.0)	2.0 (3.0)	0.0 (1.5)	2.5 (2.0)	1.0 (2.0)
Duration of sleep complaint[5] – years: Median (IQR)	11.0 (13.0)	12.0 (18.0)	8.0 (11.0)	10.0 (10.0)	10.0 (11.0)

[1]One subject (randomized to CBT and has primary insomnia) did not have a response for marital status; [2]3 participants did not have a response for nature of sleep complaint. All 3 were randomized to SH, (2 have primary insomnia, 1 comorbid insomnia); [3]3 missing BMI; [4]The medical/psychiatric comorbidities listed here were taken from a self-report sleep history questionnaire completed by participants during screening. These data were considered in deriving final insomnia diagnoses but were not equivalent to the final insomnia diagnoses assigned. The final insomnia diagnoses were based on a range of data from PSG, questionnaire responses and structured interviews; [5]8 participants did not have a response for duration of sleep complaint. Six participants randomized to CBT (4 have primary insomnia, 2 comorbid insomnia) and 2 randomized to SH (1 has primary insomnia, 1 has comorbid insomnia); SD = standard deviation; IQR = interquartile range.

in regard to the demographic characteristics listed in Table 1, so no statistical tests were conducted to compare the subgroups in regard to the remaining demographic variables.

MEASURES

Polysomnography

Study candidates completed a screening polysomnogram conducted in a private hospital room or affiliated hotel boarding facility. All polysomnograms were conducted using a 32-channel Safiro™ digital recording device (Compumedics USA, Inc., Fridley, MN). The monitoring montage consisted of 2 electroencephalography channels (C_3-M_2, Oz-Cz), 1 chin electromyography channel, 2 electrooculography channels (left eye-M_1, right eye-M_2), 1 channel of airflow (nasal-oral thermistor), 2 channels of respiratory effort (thoracic and abdominal impedance), 1 channel of pulse oximetry (taken from the index finger), 2 anterior tibialis electromyography channels (right and left legs) and 1 channel to monitor body position. An experienced sleep disorders clinician scored all polysomnograms using standard criteria/methods for sleep-stage assignment and quantification of sleep disordered breathing events, periodic limb movements, and electroencephalographic arousals.[33-36] An apnea-hypopnea index of greater than 15 or a periodic limb movement arousal index of greater than 15 resulting from this scoring led to study exclusion.

Actigraphy

Mini-Mitter Actiwatch® actigraphs (Mini-Mitter Co., Inc., Sun River, OR) were used to derive objective estimates of sleep parameters throughout 2-week monitoring periods during a pretreatment baseline assessment, immediately following the 8-week treatment phase, and during a 6-month follow-up. The Actiwatch model contains a calibrated accelerometer, an event marker, and 32-K memory storage apparatus housed in a casing that, in size and shape, resembles a wristwatch. The Actiwatch is designed to interface with a PC computer via a specially designed Reader/Interface unit. PC Windows-style software accompanies the Actiwatch and is used to program the recording unit, download data into storage, and engage a scoring algorithm that provides estimates of various sleep parameters. The specific measures derived using this software included time in bed (TIB: i.e., total time expressed in minutes between lights out indicated by Actiwatch event marker and final morning rising time), minutes of total sleep time (TST) each night, sleep onset latency (SOL: i.e., time between lights out indicated by Actiwatch event marker and onset of sleep in minutes), wake time after sleep onset (WASO: i.e., total minutes of wakefulness between first sleep onset and the morning rising time), and sleep efficiency (SE: i.e., [TST ÷ TIB] x 100%). Previous findings in our lab[37] showed moderate to high correlations between Actiwatch and polysomnography

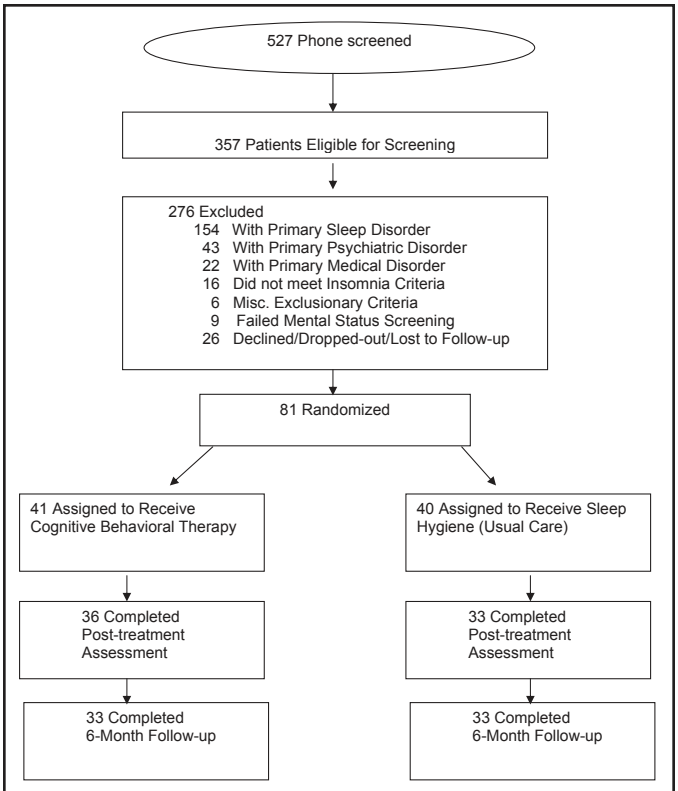

Figure 1—Study Flow Chart

measures of TST (r = 0.68), SOL (r = 0.87), WASO (r = 0.69), TWT (r = 0.74), and SE (r = 0.67).

Electronic Sleep Diary

Along with the objective monitoring, subjective sleep estimates of TIB, TST, SOL, WASO, and SE were obtained from most participants using a specially programmed hand-held computer. However, a small number of patients who showed difficulty using the electronic diary were provided paper diaries to complete at all study time points when diary monitoring was required. The electronic diary consisted of a Palm Pilot®-style personal data assistant containing an interactive program that automates the collection of subjective sleep data. The program, developed by our lab using Satellite Forms© software (Thacker Network Technologies, Inc, Lacombe, Alberta), presented questions about each night's bedtime, SOL, number and length of nocturnal awakenings, time of final awaking, and rising time. Also, the program solicited respondents' ratings (made on a 10-point scale) of the quality of each night's sleep and how rested they feel upon arising. At the end of the entries for 1 day, the program automatically recorded a time stamp to verify the time and date data were entered. For the purposes of deriving the sleep-diary measures, SOL was defined as the estimated time between "lights out" and the onset of sleep. Otherwise, the definitions used for the diary-derived sleep measures were similar to those used for the actigraphy measures. Our research[37] has shown moderate to high correlations between the electronic diary and polysomnography TST (r = 0.73), SOL (r = 0.48), WASO (r = 0.76), TWT (r = 0.73), and SE (r = 0.66).

Outcome Questionnaires

Participants completed a computer-administered questionnaire battery on 1 occasion during the baseline period, a second time immediately following treatment, and again at the 6-month follow-up. The primary outcomes of interest were obtained from the following questionnaires included in this battery.

Insomnia Symptom Questionnaire

The Insomnia Symptom Questionnaire (ISQ), originally developed by Spielman et al.,[38] was included in this trial to detect improvements in global insomnia symptoms. It includes 13 items that assess various sleep-related and daytime complaints and symptoms of insomnia. The computerized version of this instrument used herein presented each item on the computer screen separately along with a 100-mm horizontal line labeled "Never" at its left extreme and "Always" at its right extreme. Respondents indicated their responses by using the computer mouse to designate the point on 100-mm analog scale for each item. The distance from the left end of the line to the mouse response reflected the item's score, and the mean score across all questionnaire items represented the respondent's overall score for that instrument. Previous research has shown that the ISQ has reasonably good internal consistency (Cronbach $\alpha = 0.73$)[39] and good sensitivity for detecting improvements in insomnia symptoms resulting from cognitive and behavioral insomnia therapies.[38-40]

Pittsburgh Sleep Quality Index

The Pittsburgh Sleep Quality Index (PSQI) was included in the questionnaire battery to detect changes in global sleep quality resulting from treatment. This well-validated[41] instrument is composed of 4 open-ended questions and 19 self-rated items (0-3 scale) assessing sleep quality or disturbances and symptoms of various primary sleep disorders over a 1-month interval. Specific domains of focus include sleep latency, duration, efficiency, and quality; other sleep disturbances; medication use; and daytime dysfunction. For the purposes of this study, standard scoring methods[41] were used to derive a global or summary sleep-quality score across all items for each participant at each study time point (baseline, posttreatment, follow-up). Research has also shown the global PSQI score is useful for detecting treatment-related improvements among subgroups with either PI or CMI.[18,42] It should also be noted that a recently published consensus statement recommended use of the PSQI in all treatment-outcome studies to facilitate standard insomnia research practice.[43]

Dysfunctional Attitudes and Beliefs About Sleep Scale

We included an abbreviated 14-item version of the Dysfunctional Attitudes and Beliefs About Sleep Scale (DBAS) in our battery to assess important changes in sleep-related cognitions or beliefs resulting from treatment. The specific 14 items chosen for use here were derived from a previous factor-analysis study showing that these items comprise 4 subscales that account for most of the test variance in the larger 30-item instru-

ment.[44] Like the computerized ISQ, each DBAS item appeared on the computer screen separately along with a 100-mm horizontal line labeled "strongly disagree" at its left extreme and "strongly agree" at its right extreme. Respondents used the computer mouse to designate the point on the 100-mm analog scale for each item, indicating their responses. The distance from the left end of the line to the mouse response reflected the score of the item, and the mean score across all questionnaire items represented the respondent's overall score for that instrument. Both the full and abbreviated versions of the DBAS have good internal consistency[39,45,46] and have proven sensitivity for detecting treatment-related changes resulting from cognitive or behavioral interventions.[45,47]

Therapy Evaluation Questionnaire

Treatment credibility was assessed via responses (Likert ratings) to the 7-item Therapy Evaluation Questionnaire (TEQ).[48] The first 5 questions of the TEQ assess perceived logic of and confidence in a treatment, willingness to repeat the treatment, and likelihood the treatment will help others. The final 2 items assess therapist warmth and competence. Our previous research[39] with this instrument showed that the TEQ has high internal consistency (Cronbach $\alpha = 0.79$). Participants completed the initial 5 TEQ items after their first treatment session and all 7 items after their last session. Because differential treatment effects were expected to affect responses to treatment-credibility items during the second TEQ administration, only the analyses of responses to the last 2 TEQ items assessing the therapeutic relationship were considered for the end-of-treatment assessment.

THERAPISTS AND TREATMENTS

One female and one male licensed clinical psychologist with 5 and 19 years experience conducting behavioral insomnia therapy served as therapists and delivered CBT and SH treatments guided by a study treatment manual. These therapists provided their assigned participants 4 biweekly, 30- to 60-minute individual sessions of their respective treatments (CBT or SH). The SH condition was included as a treatment control because this form of intervention is commonly used as a component of a multicomponent behavioral insomnia therapy, yet available data suggest it is not an effective insomnia intervention when used as a stand-alone treatment.[13] Moreover, our previous work[40] has shown that patients rate CBT and SH as equally credible insomnia therapies. In the current trial, attempts were made to match the therapist support or contact afforded to participants in each treatment condition and to require similar amounts of out of therapy "homework" between treatment sessions.

During CBT, the therapist first presented a standardized audiocassette cognitive therapy module designed to correct patients' misconceptions about sleep requirements and the effects of aging, circadian rhythms, and sleep loss on sleep/wake functioning. The therapist then reviewed a set of modified stimulus-control instructions designed to accommodate their integration with sleep-restriction strategies. Specifically, this regimen included instructions to (a) establish a standard wake-up time, (b) get out of bed during extended awakenings, (c) avoid sleep-incompatible behaviors in the bed or bedroom, and (d) eliminate daytime napping. Additionally, the therapist provided an initial TIB prescription equal to the patient's average sleep time (from baseline diaries) plus 30 minutes (i.e., normal sleep latency and brief awakenings). With an agreed-upon rising time established, this prescription designated the earliest retiring time allowed each night. The patient was instructed to retire at this designated retiring time or later in response to feeling sleepy. At the end of the session, the patient was given a pamphlet reiterating the stimulus-control and sleep-restriction instructions and told to follow these between sessions. Sessions 2 through 4 entailed reviewing instructions and adjusting TIB. TIB was (1) increased by 15 minutes each week the patient showed a mean SE of 85% or higher but reported continued daytime sleepiness and (2) decreased by 15 minutes each week the patient showed a mean SE of less than 80%. Otherwise, TIB was held constant.

Participants in the SH group received 4 biweekly treatment sessions that were similar in length to those provided to CBT assignees. During the initial SH session, the therapist first presented an audiocassette recording that reviewed general information about sleep stages, normal sleep architecture, and sleep cycles. The therapist then presented a series of recommendations, including eliminating caffeine and alcohol in the evening, engaging in moderate exercise, having a light snack before bed, and keeping the bedroom dark and at a comfortable temperature. These recommendations were applied to the participant's own circumstances in detail, such as planning a particular snack or scheduling regular times during the week for walking or other exercise. As was the case for the CBT intervention, the patient was given a pamphlet reiterating the list of SH instructions and told to follow these between sessions. During the remaining 3 SH sessions, the therapist reviewed generic SH recommendations and engaged the patient in problem solving to address any treatment adherence problems.

Treatment Adherence

At the conclusion of treatment, each participant was asked to complete a brief questionnaire to assess treatment adherence and the usefulness of the CBT or SH treatment recommendations received. Those in the CBT group were asked how many days per week they enacted each of 6 core elements of the CBT regimen (i.e., standard rise time, avoidance of naps, not worrying in bed, use of the bed only for sleeping, adherence to TIB prescription, getting out of bed when unable to sleep), and they were asked to rate the usefulness (0 = not at all; 10 = a great deal) of each of these strategies. Those in the SH group were asked for similar information about 6 core elements of the SH recommendations (i.e., limit caffeine, avoid alcohol before bed, keep bedroom quiet and dark, daily exercise, bedtime snack, keep bedroom at comfortable temperature). Participants' adherence responses across the 6 items were averaged and used as an index of average adherence to key treatment recommendations, whereas their ratings of usefulness were averaged and used to compare the perceived utility of the 2 interventions. We also assessed CBT adherence using sleep-diary measures of within-subject standard deviations for nightly TIB and daily rising times during baseline and during the posttreatment phase. Because CBT recipients were expected to show more marked

baseline-to-posttreatment decreases in their TIB and rising time variability than the SH recipients, these variability indexes provided an additional measure of adherence.

RESULTS

Treatment Attendance and Follow-up

Thirty-six (16 PI, 20 CMI) of the 41 patients assigned to CBT and 33 (18 PI, 15 CMI) assigned to SH treatment completed treatment and the posttreatment assessment. Of these patients, 33 (16 PI, 17 CMI) in the CBT group and 33 (18 PI, 15 CMI) in the SH group also completed the 6-month follow-up. Thus, less than 20% of the enrolled sample was lost to attrition by the follow-up time point. A higher percentage of patients with PI completed the study as compared with patients with CMI (85% vs 78%). In addition, patients who completed the study were older (55 vs 52 years), had more self-reported medical comorbidity, were less likely to be employed full time, and were more likely to use sleep medications at baseline. Given these observations, information about participant's insomnia type, age, employment status, and use of sleep medications was considered in our imputation of missing data, as discussed later herein.

Treatment Credibility and Adherence

Enrollees completed the TEQ after the initial treatment session (n = 71) and after treatment was completed (n = 68). Treatment adherence and usefulness assessments were also collected after treatment (n = 67). Wilcoxon rank sum statistics were used to analyze differences between randomization groups. Treatment groups did not statistically differ on TEQ items assessed after the initial visit (P values ranging from 0.08 to 0.73). At posttreatment, the treatment groups did not differ significantly in their ratings of TEQ items 6 and 7 that, respectively, measured therapist competence (P = 0.68) and therapist warmth (P = 0.66) displayed throughout treatment.

Self-ratings of treatment adherence showed patients in the CBT group reported adhering to 6 core elements of their treatment an average of 6.23 days per week, compared with the 5.80 days per week reported by the SH group ($t_{62} = 2.21$, P = 0.03). The CBT group also reported higher average usefulness scores, compared with those in the SH group (difference in means = 1.44, $t_{64} = 2.34$, P = 0.02). Controlling for baseline, posttreatment sleep-diary data showed the CBT group had significantly less variability in their TIB ($F_{1, 61} = 7.73$, P = 0.01) and rising times ($F_{1, 60} = 9.41$, P = 0.003) than did the SH group. These findings suggest adherence to key therapy recommendations by CBT assignees and also document the expected CBT and SH group differences in treatment enactment.

Treatment Purity

All therapy sessions were tape recorded, and a randomly selected subset (24 CBT and 23 SH) were selected for scrutiny. Using a checklist designed for this project, a judge blinded to the intended therapy recorded on each tape reviewed these recordings and identified treatment-specific instructions presented therein. The checklist included at total of 6 distinctive treatment-appropriate instructions for each of the 2 treatments. From this review, the judge observed a mean (SD) of 4.75 (1.57) appropriate instructions during the CBT sessions and 5.0 (1.04) appropriate instructions during SH sessions; these means were not statistically different (Wilcoxon rank sum test, Z = 0.03, P = 0.97). Furthermore, all sessions were rated 100% pure; none of the sessions contained elements from more than 1 treatment.

Analyses of Sleep Data

Descriptive and inferential statistics for the sleep measures taken from sleep diaries and actigraphy were computed using SAS 9.1 statistical software.[49] An α of 0.05 (2 tailed) was used to assign significance for all inferential tests. Linear mixed models, using the SAS PROC MIXED procedure, were used to analyze each sleep measure. Linear mixed models offer more flexibility than repeated-measures analysis of variance models in that participants with incomplete follow-up (i.e., unbalanced) data are not removed from the analysis, and the correlation between repeated measures is not assumed to be equal for all time points.[50] We constructed 2 types of linear mixed models. The fixed effects in the primary analyses included treatment group (CBT vs SH), time (pretreatment, posttreatment, and 6-month follow-up), and the 2-way interaction of treatment and time. Secondarily, we also examined the treatment effect within insomnia type. The fixed effects in these models included treatment group (CBT vs SH), time (pretreatment, posttreatment, and 6-month follow-up), insomnia type (PI vs CMI), all 2-way interactions, and the 3-way interaction of treatment group, time, and insomnia type. For all models, an unstructured covariance matrix was fit to account for the correlation of patients' repeated measures over time. Participants who failed to complete sleep diary and actigraphy (n = 6) monitoring at baseline, after treatment, and 6-month follow-up were dropped from these analyses. All remaining sleep data, including those from participants who subsequently discontinued the study, were used for the longitudinal analyses (n = 75 participants).

Patients who discontinued the study differed on baseline characteristics, as compared with those who completed the study, so a multiple imputation procedure, as described by Rubin,[51] was employed to estimate missing values. The imputation model included predictors of dropout mentioned above (e.g., age, employment status, insomnia subtype), in addition to treatment group, and the sleep outcomes at screening, baseline, after treatment and 6-month follow-up. PROC MI in SAS was used to generate m = 5 imputed datasets via a Bayesian simulation technique called Markov chain Monte Carlo.[52] The same linear mixed model mentioned above was fit to each of these data sets, and the m-sets of parameter estimates and standard errors were combined using the Rubin rules for multiple imputation (using PROC MIANALYZE in SAS). More information on this general analytic approach can be found elsewhere.[53,54] For each measure, a treatment effect size (ES) was calculated by combining the difference of means for each group and time point (i.e., baseline versus posttreatment and baseline versus follow-up) across the multiply imputed datasets; the CBT-SH mean difference was then divided by the overall baseline standard deviation.

Table 2—Predicted Means, Standard Error (SE) Values and Treatment Effect Sizes for Sleep Measures Across Study Time Points for PI (n = 37) and CMI (n = 38) Groups

Measures	primary insomnia					comorbid insomnia				
	CBT Group Predicted		SH Group Predicted		Effect	CBT Group Predicted		SH Group Predicted		Effect
	Mean	SE	Mean	SE	Size†	Mean	SE	Mean	SE	Size†
Total sleep time-min										
Sleep Diaries										
Baseline	338.1	18.9	345.1	19.4		333.2	18.4	379.7	20.5	
Post-treatment	371.6	21.7	365.1	20.1	0.17	344.5	20.2	386.4	23.3	0.05
6-month follow-up	397.2	18.6	397.7	17.8	0.08	340.8	18.2	395.0	20.0	-0.09
Actigraphy										
Baseline	327.9	19.9	334.5	20.4		367.1	19.6	374.4	20.8	
Post-treatment	326.9	23.8	341.2	21.9	-0.09	330.9	23.0	349.0	25.3	-0.13
6-month follow-up	344.8	18.8	362.5	17.9	-0.13	319.5	18.7	334.0	23.6	-0.09
Sleep Latency-min										
Sleep Diaries										
Baseline	43.1	6.9	38.1	7.1		52.3	6.7	36.4	7.5	
Post-treatment	23.3	4.5	27.8	4.4	-0.31	28.1	4.5	31.5	4.6	-0.64
6-month follow-up	28.3	5.0	22.4	5.1	0.03	32.7	5.4	25.1	5.4	-0.28
Actigraphy										
Baseline	17.7	3.9	22.1	4.0		21.2	3.8	19.3	4.1	
Post-treatment	13.8	3.2	18.1	3.0	0.01	17.3	3.1	20.8	3.3	-0.33
6-month follow-up	14.3	3.5	14.4	3.6	-0.25	24.1	3.8	20.6	4.8	0.09
Wake after onset-min										
Sleep Diaries										
Baseline	66.0	9.6	76.2	9.9		73.2	9.4	65.2	10.2	
Post-treatment	30.0	7.4	49.3	6.6	-0.22	35.9	6.5	44.5	6.9	-0.40
6-month follow-up	34.7	6.8	48.2	6.4	-0.08	39.1	6.3	41.3	6.7	-0.24
Actigraphy										
Baseline	83.3	8.4	61.8	8.6		65.7	8.2	60.6	8.7	
Post-treatment	59.9	7.1	62.5	6.4	-0.50	60.9	6.3	56.3	8.5	-0.03
6-month follow-up	70.3	6.3	66.9	5.9	-0.38	53.1	6.3	61.7	7.0	-0.65
Sleep Efficiency -%										
Sleep Diaries										
Baseline	74.7	2.7	74.9	2.8		72.4	2.7	78.9	3.0	
Post-treatment	86.8	3.1	82.2	2.4	0.38	82.7	2.4	83.0	2.7	0.53
6-month follow-up	86.0	2.2	84.9	2.1	0.10	81.6	2.2	85.7	2.2	0.21
Actigraphy										
Baseline	74.8	2.8	80.1	2.9		79.6	3.0	81.7	2.9	
Post-treatment	80.6	2.8	79.0	2.6	0.47	79.7	2.6	80.5	3.0	0.15
6-month follow-up	79.9	2.1	81.8	2.0	0.23	80.1	2.2	79.2	3.2	0.34

† Effect sizes retained + and – signs to indicate the direction of the CBT - SH differences.
Baseline standard deviations for each insomnia type were used to calculate effect sizes.

Statistical analyses showed significant treatment x time interactions that favored CBT over SH for the sample as a whole. CBT produced significantly greater pretreatment-to-posttreatment improvements in diary measures of SOL ($t = -2.82$, $P = 0.005$; ES = -0.48) and SE ($t = 2.00$, $P = 0.05$; ES = 0.46) than did SH. CBT recipients also showed significantly greater reductions in actigraphy measures of WASO ($t = -2.50$, $P = 0.02$; ES = -0.43) from the pretherapy assessment to the 6-month follow-up than did SH-treated patients. The effect sizes for all of these significant CBT versus SH group comparisons fell in the "medium" range. Statistical analyses also showed significant main effects for time across several of the sleep outcome measures. Posthoc testing showed the study sample, as a whole, achieved significant pretreatment-to-posttreatment reductions in their diary WASO ($P < 0.001$) and a concurrent significant increase ($P = 0.02$) in their diary TST. Moreover, study patients showed an additional significant mean increase ($P = 0.02$) in their diary TST between the posttreatment and 6-month follow-up.

In contrast with the above findings, results for the 3-way interaction of treatment group, time, and insomnia type were nonsignificant for all of the diary and actigraphy measures. This finding implies that the above-noted relative benefits of CBT over SH were not significantly greater in 1 of the 2 diagnostic subgroups (PI or CMI). Table 2 shows the means, standard error terms, and the CBT-versus-SH treatment effect sizes for the sleep measures within the PI and CMI subgroups. Because the above analyses showed significant CBT versus SH effects for diary measures of SOL and SE at the posttreatment assessment and actigraphic WASO at follow-up, it seems most pertinent to focus on these effects across the PI and CMI groups. Within

both diagnostic subgroups, the treatment effect sizes for the CBT versus SH comparison were in the small to medium range at posttreatment for diary measures of SOL and SE. Likewise, both diagnostic groups showed small to medium CBT versus SH treatment effect sizes for actigraphic WASO at follow-up. In general, these data imply relatively comparable benefits of CBT for the PI and CMI samples.

Outcome Questionnaires

Procedures used for statistical analyses and management of missing data with the outcome questionnaires were similar to those employed in the analyses of the sleep measures. Inasmuch as baseline questionnaire data were obtained from the entire study sample (N = 81), all participants were included in the questionnaire data analyses. Table 3 shows the means, standard error terms, and CBT-versus-SH treatment effect sizes for the questionnaire data in the total sample and within the PI and CMI groups considered separately. Analyses conducted with the total study sample showed that the CBT intervention produced significantly greater short-term (P = 0.03) and long-term (P = 0.02) reductions in insomnia symptoms (ISQ scores) than did the SH treatment. In addition, CBT recipients showed significantly (P = 0.04) greater short-term reductions in unhelpful beliefs about sleep (DBAS scores). These comparisons each suggested a "medium" treatment effect size for CBT relative to SH.

As was the case for the sleep measures, none of the 3-way interactions of treatment group, time, and insomnia type were significant in the analyses of the questionnaire data. It is perhaps worth noting that the CBT-versus-SH treatment effect sizes for the ISQ measure were in the large range for the PI group, whereas they fell in the medium range for the CMI group. Nonetheless, the lack of any 3-way interaction effects limits the inferences that can be drawn from this observation. Overall, these findings suggest that the relative benefits of CBT over SH for improving global insomnia symptoms, subjective sleep quality, and disruptive sleep-related beliefs were not significantly greater in 1 of the 2 diagnostic subgroups (PI or CMI).

Tests of Clinical Significance

In addition to these analyses, we conducted analyses in which we compared the proportions of patients in each subgroup that achieved several commonly used or recommended benchmarks connoting clinically significant improvement. One such benchmark is that of achieving "normative values" of the target sleep outcome measures after receiving treatment. What constitutes normal SOL or WASO has been debated, but recent reports[55,56] suggest values < 31 minutes of SOL and WASO as supportable cutoffs for insomnia in groups similar in age to our study sample. Lichstein et al.[55] originally suggested that SOL or WASO less than 31 minutes occurring 3 or more times per week indicated normal sleep. However, we[56] found that mean SOL or WASO values longer than 31 minutes across 2 weeks of diary monitoring discriminated normal sleepers from insomnia sufferers. Hence, we used mean diary values of less than 31 minutes of SOL and WASO as diary benchmarks for normative sleep patterns at the posttreatment assessment. A second common benchmark used is that of achieving a normal score connoting insomnia remission on a global symptom questionnaire such as the PSQI. A PSQI score of less than 5 is a well-validated cutoff for normal sleep quality; this cutoff has shown to have high sensitivity and specificity for discriminating normal sleepers from insomnia sufferers.[41] Thus, we chose this PSQI cutoff as an additional benchmark for assessing the clinical significance of our study participants' improvements. We then conducted a series of frequency-table and logistic-regression analyses to compare the proportions of each group meeting these various milestones at the posttreatment time point.

A review of pretherapy data showed that more than 40% of the sample had a mean diary SOL of less than 31 minutes per night at baseline. Hence, this milestone was dropped from consideration. Group comparisons for the other 2 milestones are shown in Figure 2. Frequency-table analyses (note that numbers and percentages are averaged across the 5 multiply imputed datasets) showed that, among those who had mean WASO scores greater 31 minutes at baseline (n = 65), 10 of 16 (60%) of the CBT-treated patients with PI, 7 of 18 (36.7%) of the CBT-treated patients with CMI, 4 of 16 (25%) in the SH-treated PI group, and 3 of 15 (17.3%) of the patients with CMI receiving SH had posttherapy mean WASO values in the normal range (i.e., < 31 minutes/night). The statistical test of differences among the 4 subgroups for achieving this benchmark fell short of significance (P = 0.13). However, the combined group of patients with PI and CMI receiving CBT showed a significantly greater likelihood (odds ratio = 3.37; 95% confidence interval = 1.06 to 10.77; P = 0.04) of achieving this milestone than did the entire group of SH recipients. Tabulations using our second benchmark showed 14 of the 19 (75.8%) CBT-treated patients with PI, 4 of the 21 (19%) CBT-treated patients with CMI, 5 of the 20 (27%) SH-treated PI group, and 4 of 19 (22%) SH-treated patients with CMI who had baseline PSQI scores greater than 5 reached a normal posttherapy PSQI score (P = 0.004). Additional analyses showed that the combined group of CBT-treated patients with PI and CMI did not show a significantly greater likelihood (odds ratio = 2.61; 95% confidence interval = 0.96 to 7.07; P = 0.06) of achieving PSQI-defined normal sleep quality than did the combined SH-treated group. Thus, patients with PI treated with CBT generally showed the best chances of achieving subjectively normal sleep quality by the end of treatment, at least as reflected by the PSQI.

DISCUSSION

CBT produced its largest effects across several measures of nocturnal wakefulness. Our mixed-model analyses showed that pretherapy-to-posttherapy comparisons of SOL and SE taken from sleep dairies favored CBT over the SH intervention. Although actigraphy suggested CBT produced somewhat more modest relative objective sleep improvements, CBT recipients did achieve significantly greater long-tem improvements in measures of WASO taken from actigraphy than did SH-treated patients. CBT-treated patients also showed greater short-term reductions in their sleep-interfering beliefs (DBAS scores) and greater short- and long-term reductions in their insomnia symptoms (ISQ scores) than did SH recipients. Finally, the CBT-treated group showed a greater propensity to achieve normative

Table 3—Predicted Means, Standard Error (SE) Values, and CBT vs. SH Effect Sizes for Questionnaires in the Total Sample (N = 81) and in the PI (n = 40) and CMI (n = 41) Subgroups

MEASURES	CBT Group Predicted		SH Group Predicted		Effect Size†
	Mean	SE	Mean	SE	
TOTAL SAMPLE					
ISQ total score					
Baseline	47.9	3.0	40.9	3.0	
Post-treatment	26.5	3.2	29.7	3.3	-0.53
6-month follow-up	25.4	3.6	29.6	3.8	-0.58
PSQI global score					
Baseline	12.4	0.5	11.8	0.6	
Post-treatment	7.1	0.7	7.8	0.7	-0.37
6-month follow-up	8.0	0.8	7.6	0.8	-0.04
DBAS					
Baseline	42.5	3.1	40.3	3.1	
Post-treatment	30.1	3.4	38.1	3.3	-0.52
6-month follow-up	30.8	3.7	35.5	3.6	-0.35
PI GROUP					
ISQ total score					
Baseline	45.6	4.2	36.1	4.2	
Post-treatment	23.5	4.7	27.6	4.6	-0.75
6-month follow-up	17.8	5.0	24.1	4.6	-0.87
PSQI global score					
Baseline	11.0	0.8	11.6	0.8	
Post-treatment	5.7	1.0	7.9	0.9	-0.51
6-month follow-up	5.9	1.2	7.7	1.1	-0.36
DBAS					
Baseline	37.0	4.3	33.7	4.3	
Post-treatment	28.7	5.2	29.4	4.6	-0.20
6-month follow-up	24.1	5.4	29.0	4.7	-0.40
CMI GROUP					
ISQ total score					
Baseline	50.0	4.1	45.8	4.2	
Post-treatment	29.4	4.3	31.8	5.0	-0.34
6-month follow-up	32.6	4.6	35.0	5.5	-0.34
PSQI global score					
Baseline	13.7	0.7	12.0	0.8	
Post-treatment	8.4	0.9	7.7	1.0	-0.26
6-month follow-up	10.1	1.0	7.5	1.2	0.23
DBAS					
Baseline	47.8	4.2	46.9	4.3	
Post-treatment	31.4	4.4	46.9	4.6	-0.95
6-month follow-up	37.2	4.6	42.0	5.1	-0.33

Note : The means and SE values are from the multiply imputed datasets.
† Effect sizes retained + and – signs to indicate the direction of the CBT - SH differences.

subjective values of WASO by the end of treatment than did those in the SH group. These findings are consistent with our previous reports[39,40] and support the relative efficacy of CBT within the current sample as a whole.

It should be noted that our mixed-model analyses showed that none of the 3-way interactions of treatment group, time, and insomnia type was statistically significant. Furthermore, CBT-treated patients with PI did not show a significantly greater propensity to achieve normative values of WASO by post-treatment than did patients with CMI treated with CBT. Such results imply that the relative benefits of CBT over SH were not significantly greater for the PI group than they were for the CMI group, at least across the majority of sleep and symptom measures we considered. These findings complement the growing number of reports suggesting that CBT represents a viable insomnia therapy for patients who present with comorbid medi-

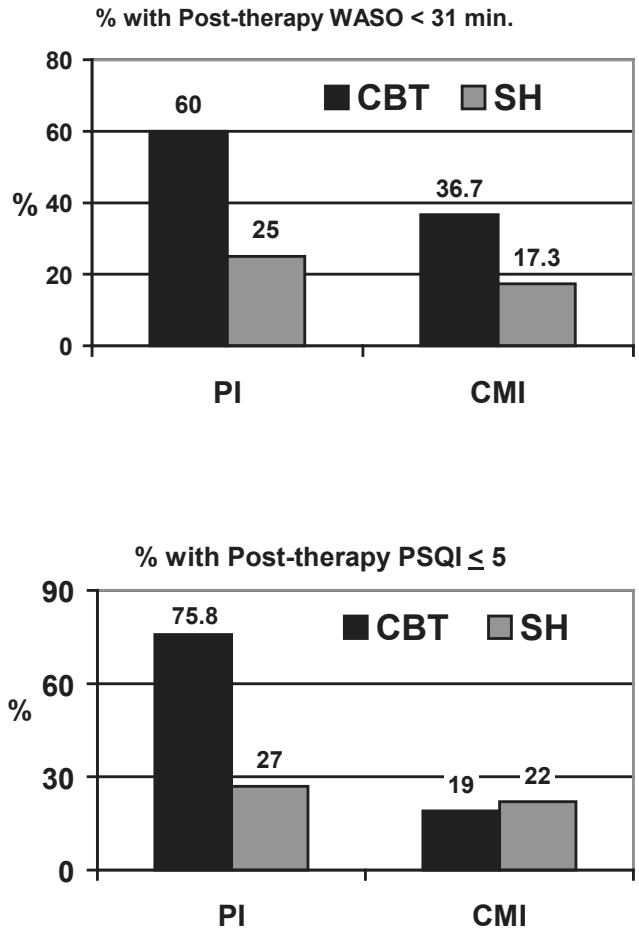

Figure 2—Proportions of Participants in Each Subgroup Achieving Clinical Benchmarks of Improvement
Note: The analysis for the first indicator of clinical significance, WASO < 31 minutes, included 65 of the 81 study participants; 10 participants who had a baseline WASO < 31 minutes and 6 participants with missing baseline data were excluded. The analysis for the second indicator of clinical significance, PSQI score ≤ 5, included 79 of the 81 study participants; 2 participants who had a baseline PSQI score ≤ 5 were excluded. CBT = Cognitive Behavioral Therapy; SH = Sleep Hygiene; PI = primary insomnia; CMI = comorbid insomnia.

cal and psychiatric conditions.[15-24,26] However, this is the first randomized trial in which patients with PI and CMI were compared side by side in regard to their responses to a standard fixed "dose" of CBT. Therefore, the results of this study speak more directly to the relative efficacy of CBT for treating insomnia in PI and CMI groups. In general, our results encourage the use of CBT models developed for treating both PI and those insomnia sufferers who present with the types of psychiatric comorbidities included in our CMI sample.

Only 1 of our many analyses suggested a differential response of patients with PI and patients with CMI to CBT. This analysis compared the CBT and SH responses of our subgroups using our PSQI benchmark of clinical improvement. As noted, more than 75% of the PI group treated with CBT reported normal sleep quality on the PSQI by posttreatment, compared with roughly 1 out of every 5 in the CBT-treated CMI subgroup. These findings imply that CBT may be more likely to return sleep-quality perceptions into the normative range among patients with PI than it is among patients with CMI. We[57] recently showed that the 4-session CBT dose used herein proved optimal for treating patients with PI. Yet, it is possible that this treatment dose is insufficient for improving sleep-quality perceptions in patients with more complex disorders, such as our CMI group comprised largely of patients with comorbid depression and posttraumatic stress disorder. As noted by Smith et al.,[58] some patients with CMI may require more specifically tailored CBT protocols that address aspects of their comorbid conditions. Perhaps protocols involving joint insomnia and comorbid-disorder treatment, as recently described for depressed patients, may prove optimal in this regard.[59] It should also be noted that the PSQI assesses such symptoms as bad dreams, pain, and nocturia, in addition to insomnia. As such, our differential findings on this measure could have been due more to our CMI patients' comorbid conditions than to their sleep difficulties, per se. Finally, it is possible that some medications (e.g., selective serotonin uptake inhibitors) taken by patients with CMI during the study could have contributed to insomnia, reduced the effect of CBT, or both. It is also possible that the greater propensity for the CMI group to be using hypnotics upon study entry could have dampened their CBT response, as measured by the PSQI. However, the data in Table 2 show that the PI and CMI groups had fairly comparable levels of subjective and objective sleep disturbance at baseline. Nonetheless, further research will be needed to investigate these possibilities.

Admittedly, this trial had a number of limitations that should be mentioned. First, this study would have benefited by a larger, more diverse, study sample, particularly since our CMI group was comprised mainly of patients with comorbid depression or combat-related posttraumatic stress disorder. Hence, results reported herein cannot necessarily be generalized to other patients with CMI. In hindsight, it may have been useful to include an outcome measure, such as the Insomnia Severity Index,[60] in this trial to ascertain if PI and CMI groups have significantly different treatment response and insomnia remission rates with CBT intervention. Furthermore, since polysomnography has typically been used to assess objective treatment outcomes in studies testing pharmacologic treatments for insomnia, the absence of such assessment in this study limits comparisons of our results with those obtained from tests of various currently available sleep medications. Finally, this study only tested effects of behavioral treatments, so it is not known how well approaches that combine CBT with selected hypnotic medications might perform with patients with CMI. Future studies of this nature, thus, may benefit by use of larger samples, polysomnographic assessment of outcomes, a more comprehensive assessment of the range of sleep and wake symptoms that characterize the insomnia disorder,[27] tests of specially tailored CBT for CMI sufferers, and evaluation of CBT and medication combinations. Nonetheless, our results deserve serious consideration and suggest that CBT models originally developed for PI may provide some benefits for CMI.

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