Efficacy Studies for Sleep Disorders

- Aim is to assess the extent to which treatment normalizes:
  - Sleep
  - Neurological functions
  - Other impaired daytime functions
- Most research has focused on sleep as the primary outcome measure
- Treatment benefits for daytime functions are understudied

Treatment Efficacy

- Evidence from meta-analyses
  - Evidence from more than 50 clinical trials
  - Effect sizes for CBT are
    - sleep onset latency (SOL) = 0.88
    - # of awakenings (NA) = 0.53-0.63
    - duration of awakenings (DA) = 0.65
    - total sleep time (TST) = 0.42-0.49
    - sleep quality ratings (SQ)= 0.94
  - These are moderate to large effect sizes

Treatment efficacy - cont.

- Subjective SOL is reduced from 60-65 min. to 35 min.
- Duration of awakenings is reduced from 70 min to 38 min
- Number of awakenings is reduced from 2 to 1
- TST is increased from 6 hrs to 6.5 hrs

Empirically validated therapies

- A recent review found that the following are well established treatments
  - Stimulus control therapy
  - Progressive muscle relaxation therapy
  - paradoxical intention

- Recent evidence has allowed the upgrade of CBT from probably efficacious to well established

Comparative efficacy of treatments

- Stimulus control therapy and sleep restriction therapy are slightly more effective (50-60% improvement) than other single modality therapies (relaxation 40%; paradoxical intention 30%)
- Sleep hygiene education produces little impact on sleep
- Formal cognitive therapy has not been evaluated as a single modality tx. but when combined with other txs. results have been excellent.
- Dysfunctional cognitions at post tx. are correlated with improvement

Comparative efficacy of treatments - cont.

- Multi-component therapies which combine cognitive (cognitive restructuring) and behavioral (stimulus control, sleep restriction and sometimes relaxation) have become standard practice.
- The appeal of this approach is that it addresses several facets of insomnia at the same time.

Combined CBT and pharmacological therapy

- Studies indicate that drug therapy produces quicker results in the acute phase (1-2 weeks), but CBT is equally as effective in the short-term (6-8 weeks).
- Long-term results (6 months-2 years) have shown that improvements are sustained with CBT and improvements are lost when medicine is discontinued
- The long-term results for combined CBT+medicine have been mixed with some patients retain improvements while others return to baseline levels

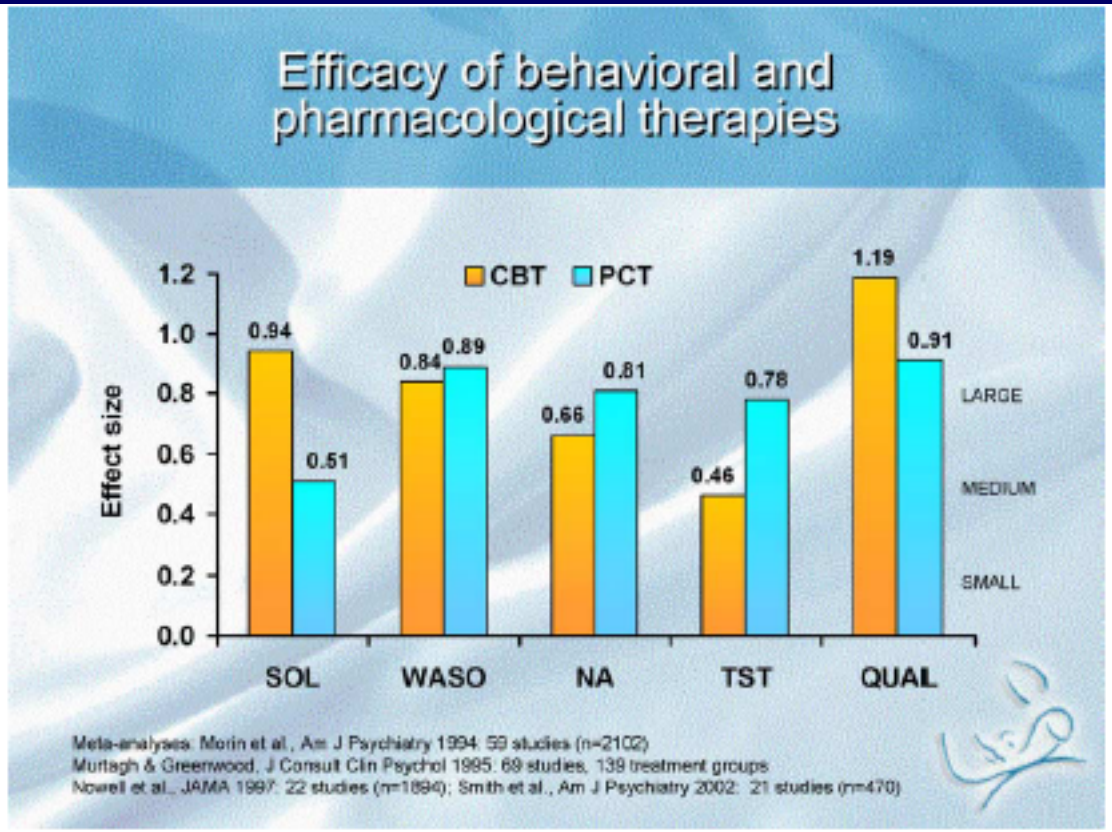


Fig. 1. Comparative efficacy of behavioral and pharmacological therapies on sleep parameters, as assessed in a number of meta-analyses [9,12–14]. SOL, sleep onset latency; WASO, wake after sleep onset; NA, night-time awakening; TST, total sleep time; QUAL, quality of life; CBT, cognitive behavioral therapy; PCT, pharmacotherapy.

Combined CBT and pharmacological therapy - cont.

- It is unclear why some individuals do not sustain tx benefits using the combined approach
- When combining CBT and medicine, recurrence of insomnia may occur when patients attribute therapeutic benefit to the drug alone and don't integrate self-management skills.

Efficacy vs. specificity of treatment

- Efficacy of CBT for insomnia has been established, but neither specificity nor the active mechanisms in the treatment have been.
- Few studies have included attention placebo conditions.
- The percentage of variance due to specific therapeutic components (i.e., restriction of time in bed), the measurement process (i.e., self-monitoring) or non-specific factors (i.e., therapist attention) is not known

Initial tx response vs. sustained efficacy

- A robust finding from research is that CBT provides stable changes in sleep patterns over time.
- Improvements in sleep latentcy and wake after sleep onset are well maintained over 1, 2 and 3 year periods.
- Total sleep time shows only modest improvement after initial treatment, but these gains are enhanced at follow-up

Treatment effectiveness and generalizability

- Treatment studies have focused on highly selected primary insomnia patient populations and it is important to know if these results would generalize to patients in primary care settings (effectiveness study).
- Recent studies in primary care setting have found results similar to those with more selected samples
- SOL was reduced from 61 to 28 min and 84% of hypnotic users remained drug-free at 1-year follow-up.

Treatment effectiveness and generalizability - cont.

- Another study found SOL reduction of 67 to 30 min, TST improvement of 298 to 351 min and sleep efficiency improvements of 59% to 77%. These results were maintained at 36 months.
- Additional clincal case series studies have found results similar to those in patients solicited for clinical trials.
- Absolute measures in the case series studies are usually worse than clinical trial participants, but changes in sleep measures are comparable.

Treatment of medicated patients

- Studies have demonstrated that medicated insomniacs can benefit from stimulus control and relaxation therapy although the treatment response is smaller.
- Reductions of hypnotic medication usage is also reported in these studies although these patients require systematic and supervised withdrawal from their medication.

Secondary insomnia

- Treatment of secondary insomnia has received little attention.
- Only one group study was conducted prior to 2000.
- More recently studies have been conducted with patients who have insomnia secondary to chronic pain, psychiatric, and medical conditions.
- These studies have shown that CBT, stimulus control and relaxation therapies improve the sleep of these patients. These treatments appear to be the least efficacious in psychiatric patients.

ORIGINAL CONTRIBUTION

Cognitive Behavioral Therapy for Treatment of Chronic Primary Insomnia

A Randomized Controlled Trial

Jack D. Edinger, PhD
William K. Wohlgemuth, PhD
Rodney A. Radtke, MD
Gail R. Marsh, PhD
Ruth E. Quillian, PhD

Context Use of nonpharmacological behavioral therapy has been suggested for treatment of chronic primary insomnia, but well-blinded, placebo-controlled trials demonstrating effective behavioral therapy for sleep-maintenance insomnia are lacking.

Objective To test the efficacy of a hybrid cognitive behavioral therapy (CBT) compared with both a first-generation behavioral treatment and a placebo therapy for treating primary sleep-maintenance insomnia.

Design and Setting Randomized, double-blind, placebo-controlled clinical trial conducted at a single academic medical center, with recruitment from January 1995 to July 1997.

Patients Seventy-five adults (n=35 women; mean age, 55.3 years) with chronic primary sleep-maintenance insomnia (mean duration of symptoms, 13.6 years).

Interventions Patients were randomly assigned to receive CBT (sleep education, stimulus control, and time-in-bed restrictions; n=25), progressive muscle relaxation training (RT; n=25), or a quasi-desensitization (placebo) treatment (n=25). Outpatient treatment lasted 6 weeks, with follow-up conducted at 6 months.

Main Outcome Measures Objective (polysomnography) and subjective (sleep log) measures of total sleep time, middle and terminal wake time after sleep onset (WASO), and sleep efficiency; questionnaire measures of global insomnia symptoms, sleep-related self-efficacy, and mood.

Results Cognitive behavioral therapy produced larger improvements across the majority of outcome measures than did RT or placebo treatment. For example, sleep logs showed that CBT-treated patients achieved an average 54% reduction in their WASO whereas RT-treated and placebo-treated patients, respectively, achieved only 16% and 12% reductions in this measure. Recipients of CBT also showed a greater normalization of sleep and subjective symptoms than did the other groups with an average sleep time of more than 6 hours, middle WASO of 26.6 minutes, and sleep efficiency of 85.1%. In contrast, RT-treated patients continued to report a middle WASO of 43.3 minutes and sleep efficiency of 78.8%.

Conclusions Our results suggest that CBT represents a viable intervention for primary sleep-maintenance insomnia. This treatment leads to clinically significant sleep improvements within 6 weeks and these improvements appear to endure through 6 months of follow-up.

JAMA. 2001;285:1856-1864 www.jama.com

PERSISTENT PRIMARY INSOMNIA (PPI), a sleep disorder that predicts clinical depression and enhanced health care use, affects up to 5% of the general population and about 20% of those insomnia patients seen clinically.[1-13] Currently, sedative hypnotics or antidepressant drugs remain the most common treatments offered PPI patients.[3,12,16] However, numerous adverse effects encumber traditional hypnotics (eg, benzodiazepines), and evidence supporting the long-term efficacy/safety of antidepressants among nondepressed insomnia patients is currently lacking.[16-20] Moreover, these agents provide only symptomatic relief since they fail to address underlying mechanisms that sustain PPI. Consequently, patients commonly show a full return of their insomnia symptoms on termination of these treatments.[12,13,16-20]

Alternative, behavioral interventions, which target presumed perpetuating mechanisms of patients with PPI, have shown much more durable improvements following treatment. First-generation behavioral therapies, designed to correct sleep-disruptive habits (eg, stimulus control) or reduce bedtime arousal (eg, relaxation training [RT]), have proven very effective for treating sleep onset problems, but their results among the larger PPI subgroup reporting sleep maintenance complaints have been mixed.[21-28] However,

Author Affiliations: VA Medical Center (Dr Edinger) and Duke University Medical Centers (Drs Edinger, Wohlgemuth, Radtke, Marsh, and Quillian), Durham, NC.
Corresponding Author and Reprints: Jack D. Edinger, PhD, Psychology Service (116B), VA Medical Center, 508 Fulton St, Durham, NC 27705 (e-mail: jack.edinger@duke.edu).

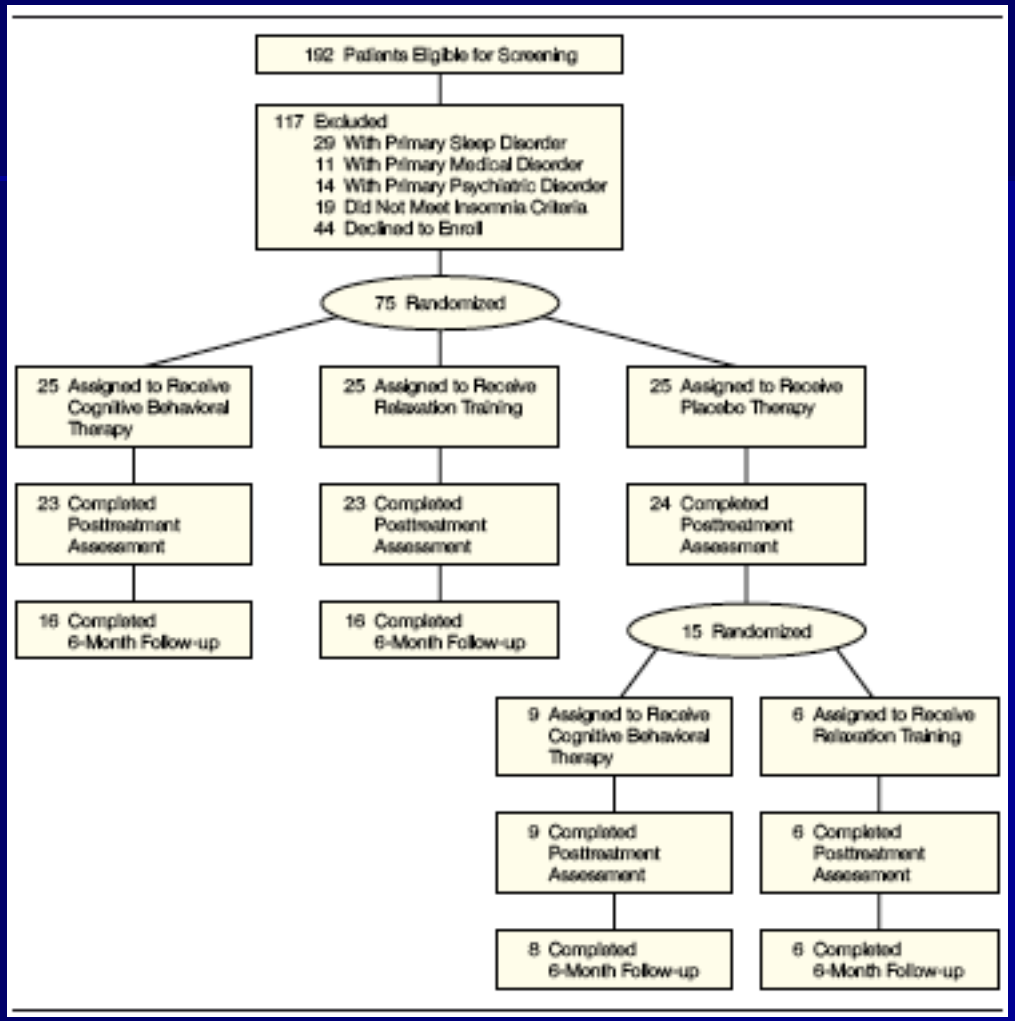

192 Patients Eligible for Screening
117 Excluded
29 With Primary Sleep Disorder
11 With Primary Medical Disorder
14 With Primary Psychiatric Disorder
19 Did Not Meet Insomnia Criteria
44 Declined to Enroll
75 Randomized
25 Assigned to Receive Cognitive Behavioral Therapy
25 Assigned to Receive Relaxation Training
25 Assigned to Receive Placebo Therapy
23 Completed Posttreatment Assessment
23 Completed Posttreatment Assessment
24 Completed Posttreatment Assessment
16 Completed 6-Month Follow-up
16 Completed 6-Month Follow-up
15 Randomized
9 Assigned to Receive Cognitive Behavioral Therapy
6 Assigned to Receive Relaxation Training
9 Completed Posttreatment Assessment
6 Completed Posttreatment Assessment
8 Completed 6-Month Follow-up
6 Completed 6-Month Follow-up

Table 1. Demographic Characteristics and Therapist Assignment for the 3 Treatment Groups

Characteristic	Cognitive Behavioral Therapy (n = 25)	Relaxation Training (n = 25)	Placebo Therapy (n = 25)
Insomnia, mean (SD), y	13.0 (12.2)	13.2 (12.3)	14.8 (11.5)
Age, mean (SD), y	55.8 (12.1)	54.5 (10.2)	55.7 (9.5)
Sex			
Women	11	11	13
Men	14	14	12
Education, mean (SD), y	16.4 (3.6)	16.3 (3.3)	16.7 (2.7)
Marital status			
Married	18	19	17
Not married	7	6	8
Current hypnotic use			
None	21	16	21
<1 time/wk	0	2	3
1-4 times/wk	4	6	1
>4 times/wk	0	1	0
Therapist assignment			
Total for male therapist	12	13	13
Women	5	5	7
Men	7	8	6
Total <55 y	6	7	7
Women	3	3	3
Men	3	4	4
Total ≥55 y	6	6	6
Women	2	2	4
Men	4	4	2
Total for female therapist	13	12	12
Women	6	6	6
Men	7	6	6
Total <55 y	7	7	7
Women	3	3	3
Men	4	4	4
Total ≥55 y	6	5	5
Women	3	3	3
Men	3	2	2

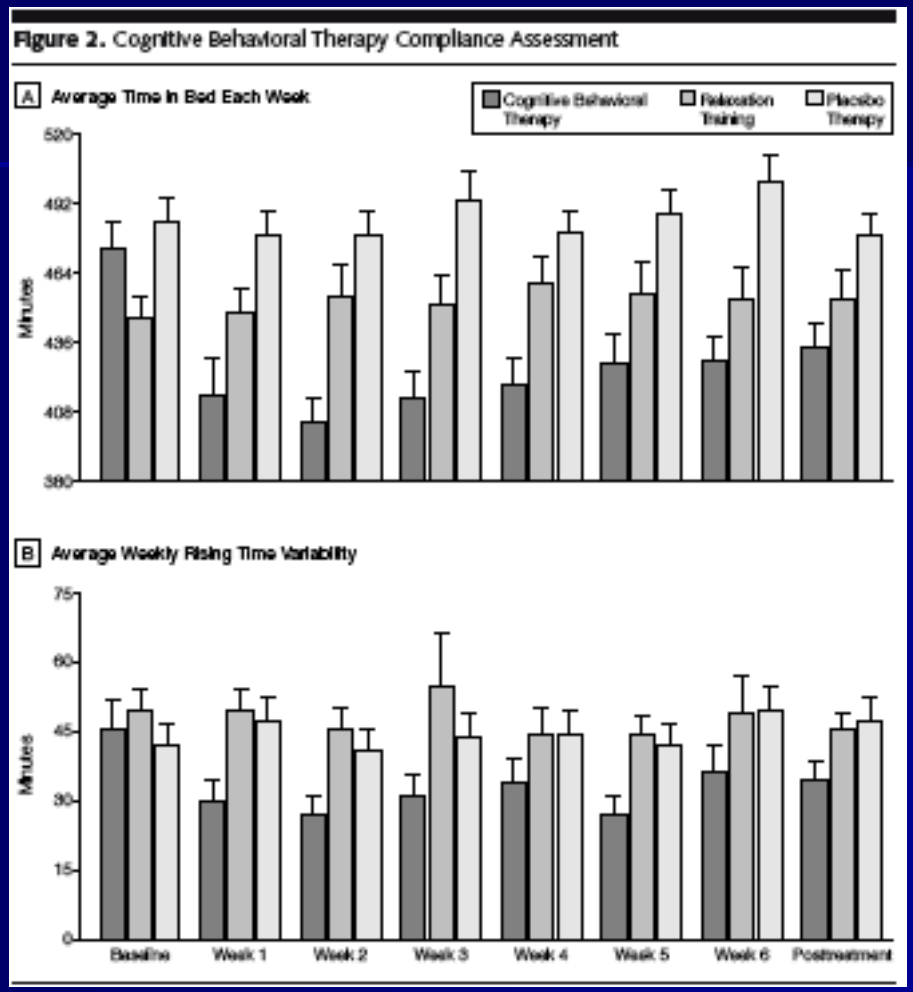
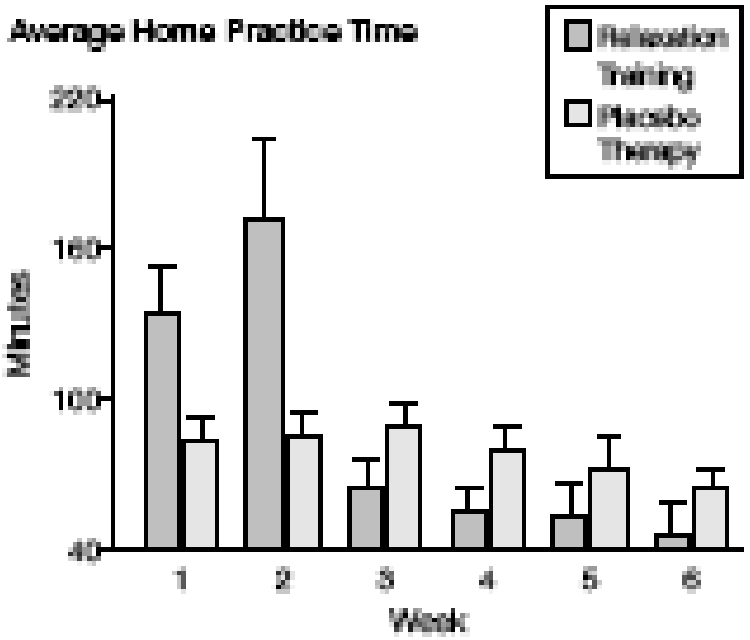


Figure 2. Cognitive Behavioral Therapy Compliance Assessment
A Average Time in Bed Each Week
Cognitive Behavioral Therapy
Relaxation Training
Placebo Therapy
520
492
464
436
408
380
Minutes
B Average Weekly Rising Time Variability
75
60
45
30
15
0
Minutes
Baseline
Week 1
Week 2
Week 3
Week 4
Week 5
Week 6
Posttreatment

Figure 3. Relaxation Training and Placebo Therapy Compliance Assessment



Data were obtained from the covert monitoring device used to monitor participants' home practice of assigned relaxation training and placebo therapy compliance exercises. Error bars represent SE values.

Table 2. Baseline Comparisons of Treatment Groups Across All Outcome Measures*

Measure	Adjusted Mean (SE)			$F_{2,72}$	*P* Value
	Cognitive Behavioral Therapy	Relaxation Training	Placebo Therapy		
Total sleep time, min					
Sleep logs	348.1 (61.7)	315.1 (56.6)	347.1 (68.0)	2.28	.11
Polysomnography	361.6 (81.8)	342.2 (59.5)	352.5 (77.1)	0.44	.65
Middle wake time after sleep onset, min					
Sleep logs	55.0 (25.3)	52.8 (32.3)	60.6 (32.7)	0.44	.64
Polysomnography	44.1 (38.6)	45.1 (44.6)	63.0 (50.6)	1.40	.25
Terminal wake time after sleep onset, min					
Sleep logs	43.0 (33.6)	49.5 (45.6)	50.6 (36.5)	0.28	.76
Polysomnography	9.6 (12.4)	16.5 (26.1)	16.2 (28.6)	0.69	.51
Sleep efficiency, %					
Sleep logs	73.7 (11.4)	70.1 (12.9)	71.6 (11.6)	0.39	.68
Polysomnography	80.3 (10.5)	78.3 (10.4)	74.8 (13.4)	1.47	.24
Sleep quality (logs)	2.87 (0.52)	2.83 (0.41)	2.83 (0.52)	0.06	.94
Questionnaires					
Insomnia Symptom Questionnaire	54.4 (12.4)	58.5 (11.2)	51.7 (14.0)	1.85	.16
Self Efficacy Scale	43.5 (14.0)	43.0 (16.4)	51.0 (14.0)	2.28	.11
Beck Depression Inventory	4.9 (2.7)	6.6 (4.5)	4.9 (3.8)	1.79	.17

*Sleep quality ratings vary between 1 (poor) and 5 (excellent); Insomnia Symptom Questionnaire and Self Efficacy Scale scores may range from 0 to 100. High scores on the Insomnia Symptom Questionnaire and low scores on the Self Efficacy Scale are pathological. Beck Depression Inventory scores range from 0 (no depression) to 63 (severe depression).

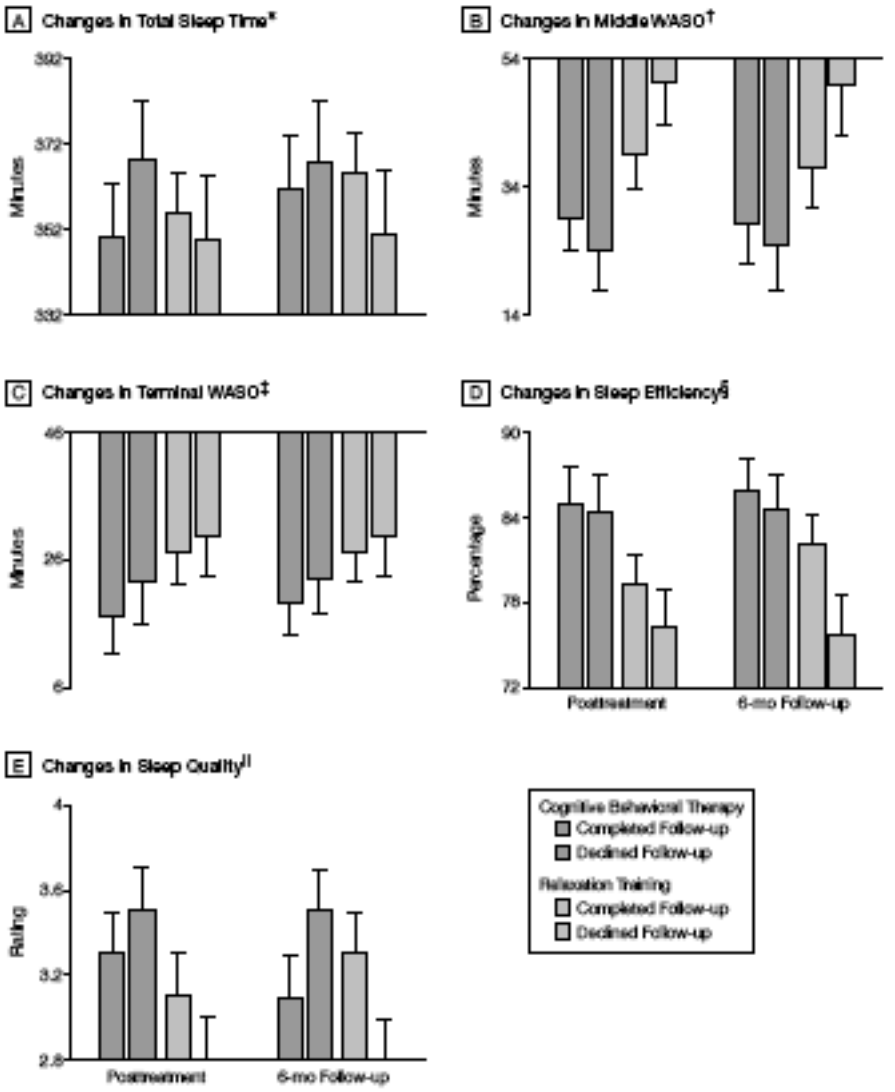
Table 3. Adjusted Results for Posttreatment Comparisons*

Measure	Adjusted Baseline Mean*	Adjusted Mean (SE)†			$F_{2,71}$	*P* Value	Post-hoc Tests‡
		Cognitive Behavioral Therapy (CBT)	Relaxation Training (RT)	Placebo Therapy (PT)			
Total sleep time, min							
Sleep logs	336.8	360.0 (8.4)	362.0 (8.6)	361.0 (8.4)	0.01	.99	NA
Polysomnography	352.1	372.4 (10.6)	337.9 (10.6)	334.0 (10.6)	3.96	.02	CBT > PT
Middle wake time after sleep onset, min							
Sleep logs	56.2	28.1 (4.2)	44.4 (4.2)	47.1 (4.2)	6.06	.004	CBT < RT and PT
Polysomnography	50.8	30.1 (8.9)	50.6 (8.9)	66.4 (9.0)	4.12	.02	CBT < PT
Terminal wake time after sleep onset, min							
Sleep logs	47.7	21.1 (6.4)	36.2 (6.3)	47.0 (6.3)	4.19	.02	CBT < PT
Polysomnography	14.1	4.2 (2.0)	10.2 (2.0)	12.4 (2.0)	4.39	.02	CBT < PT
Sleep efficiency, %							
Sleep logs	72.0	84.3 (1.7)	78.1 (1.6)	76.2 (1.6)	6.64	.002	CBT > RT and PT
Polysomnography	77.8	85.5 (1.9)	78.1 (1.9)	75.7 (2.0)	6.80	.002	CBT > RT and PT
Sleep quality (logs)	2.8	3.4 (0.1)	2.9 (0.1)	3.1 (0.1)	4.00	.02	CBT > RT
Questionnaires							
Insomnia Symptom Questionnaire	54.9	41.9 (2.5)	47.6 (2.6)	52.9 (2.6)	4.73	.01	CBT < PT
Self Efficacy Scale	45.8	62.8 (2.8)	60.6 (2.8)	52.9 (2.6)	3.35	.04	CBT > PT
Beck Depression Inventory	5.5	4.0 (0.5)	2.9 (0.5)	4.8 (0.5)	3.66	.03	RT < PT

*NA indicates no post-hoc tests were performed.
†Analysis of covariance was used.
‡Significant differences found in Bonferroni-corrected paired comparisons.

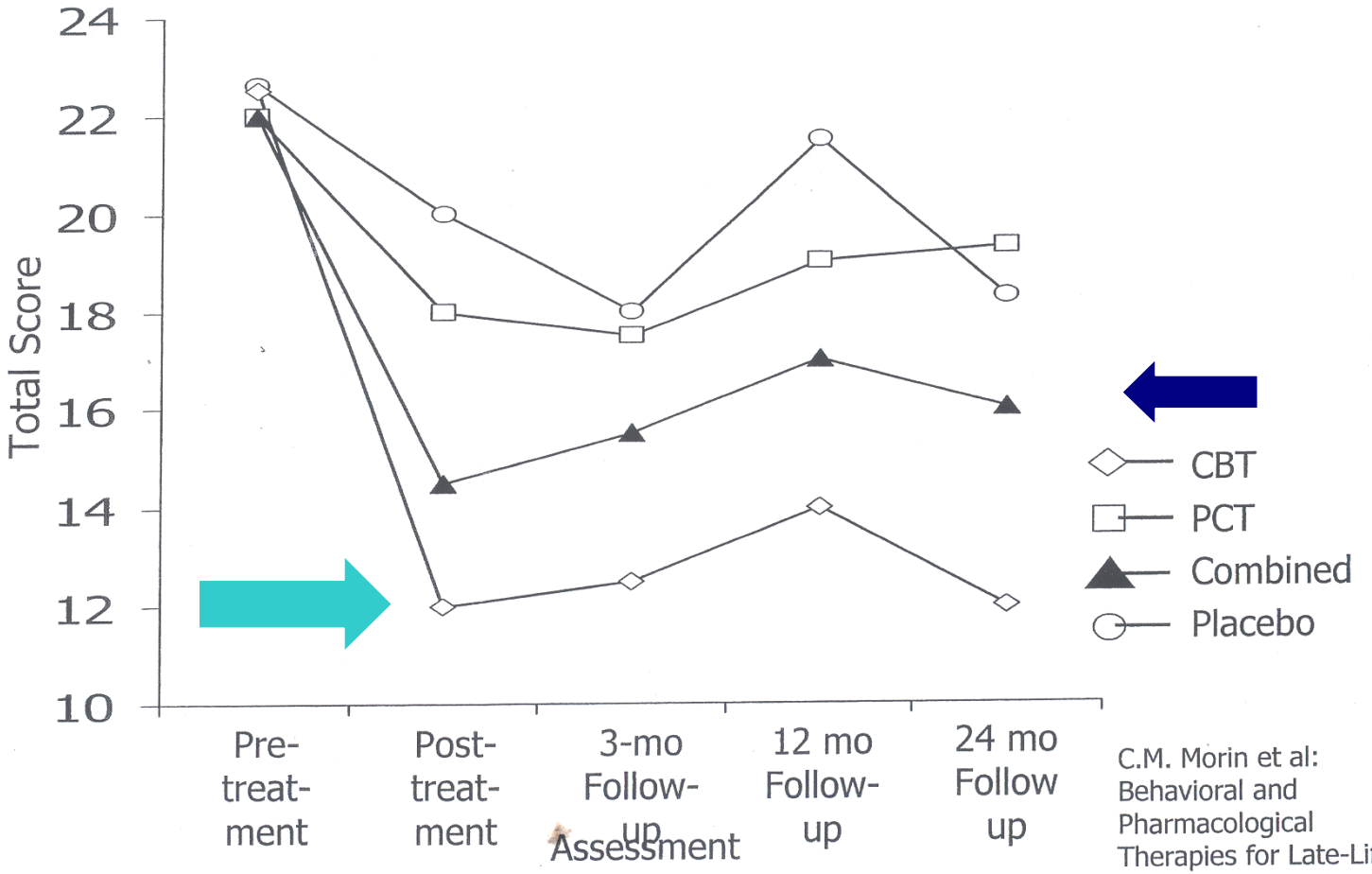
We assessed the clinical significance of our results by computing the proportion of each group achieving at least a 50% reduction in pretreatment WASO (MWASO and TWASO) by the end of treatment. Sleep logs showed 64% (16/25) met this criterion for CBT, 12% (3/25) for RT, and 8% (2/25) for PT ($\chi^2 = 24.2$; $P = .001$). Cognitive behavorial therapy was significantly superior to RT ($P = .001$) and PT ($P = .001$). Using polysomnogram data, 40% (10/25) of the CBT group, 28% (7/25) of the RT group, and 12% (3/25) of the PT group met this criterion ($\chi^2 = 5.0$; $P = .08$). Additionally, we computed the proportions in each group having post-treatment ISQ scores of 41 or less, a cut point score with 92% sensitivity and 64% specificity for normal sleepers. Eliminating those below this cut-off at study entry, we found 59.1% (13/22) for CBT, 29.2% (7/24) for RT, and 4.8% (1/21) for PT went below this normative ISQ score on study completion ($\chi^2 = 14.8$; $P = .001$). The CBT group differed ($P = .001$) from PT by this criterion whereas the RT group did not ($P > .05$).

Figure 4. Cognitive Behavioral Therapy vs Relaxation Training After Treatment and at Follow-up: Sleep Log Data



Analysis of covariance was used for adjusted means (SEs). The x-axis in each part represents the adjusted baseline mean. Asterisk indicates a treatment effect of $F_{1,48}=.02$, $P=.90$. Dagger indicates a treatment effect of $F_{1,48}=8.77$; $P=.005$. WASO indicates wake time after sleep onset. Double dagger indicates a treatment effect of $F_{1,48}=4.24$; $P=.05$. Section symbol indicates a treatment effect of $F_{1,48}=9.10$; $P=.004$; the subgroup treatment effect (interaction of treatment multiplied by subgroups, such as completed vs declined follow-up) was $F_{1,48}=5.93$; $P=.02$. Data plotted are from the 29 (14 cognitive behavorial therapy and 15 relaxation training) who completed and the 21 (11 cognitive behavorial therapy and 10 relaxation training) who did not complete sleep logs at follow-up.

Changes in Total Scores for the Sleep Impairment Index



C.M. Morin et al: Behavioral and Pharmacological Therapies for Late-Life-Insomnia. JAMA, 1999, 281, 11: 991-999

Reviews and Overviews

Comparative Meta-Analysis of Pharmacotherapy and Behavior Therapy for Persistent Insomnia

Michael T. Smith, Ph.D.
Michael L. Perlis, Ph.D.
Amy Park, B.S.
Michelle S. Smith, Ph.D.
JaeMi Pennington, B.S.
Donna E. Giles, Ph.D.
Daniel J. Buysse, M.D.

Objective: Although four meta-analytic reviews support the efficacy of pharmacotherapy and behavior therapy for the treatment of insomnia, no meta-analysis has evaluated whether these treatment modalities yield comparable outcomes during acute treatment. The authors conducted a quantitative review of the literature on the outcome of the two treatments to compare the short-term efficacy of pharmacotherapy and behavioral therapy in primary insomnia.

Method: They identified studies from 1966 through 2000 using MEDLINE, psycINFO, and bibliographies. Investigations were limited to studies using prospective measures and within-subject designs to assess the efficacy of benzodiazepines or benzodiazepine receptor agonists or behavioral treatments for primary insomnia. Benzodiazepine receptor agonists included zolpidem, zopiclone, and zaleplon. Behavioral treatments included stimulus control and sleep restriction therapies. Twenty-one studies summarizing outcomes for 470 subjects met inclusion criteria.

Results: Weighted effect sizes for subjective measures of sleep latency, number of awakenings, wake time after sleep onset, total sleep time, and sleep quality before and after treatment were moderate to large. There were no differences in magnitude between pharmacological and behavioral treatments in any measures except latency to sleep onset. Behavior therapy resulted in a greater reduction in sleep latency than pharmacotherapy.

Conclusions: Overall, behavior therapy and pharmacotherapy produce similar short-term treatment outcomes in primary insomnia.

(Am J Psychiatry 2002; 159:5–11)

TABLE 1. Characteristics of 21 Studies of Pharmacotherapy and Behavioral Treatment for Persistent Insomnia

Type of Study and Source	Year	Treatment Type	Number of Subjects	Mean Age (years)	Female Sex (%)	Duration of Treatment (weeks)	Diagnosis[a]
Pharmacological treatment studies (220 subjects)							
Kripke et al. (53)	1990	Flurazepam, 15 mg/day (N=24) and 30 mg/day (N=24); midazolam, 15 mg/day (N=24)	72	37.9	61	3	Mixed insomnia
Lahmeyer et al. (51)	1997	Zolpidem, 10 mg/day (N=37) and 15 mg/day (N=37)	74	45.0	33	1	Mixed insomnia
Mamelak et al. (48)	1983	Zopiclone, 7.5 mg/day	6	45.0	33	1	Mixed insomnia
Mamelak et al. (50)	1984	Quazepam, 30 mg/day (N=6); triazolam, 5 mg/day (N=6)	12	45.0	33	1	Mixed insomnia
McClure et al. (52)	1988	Lorazepam, 2 mg/day (N=8); flurazepam, 30 mg/day (N=8)	16	46.1	88	1	Mixed insomnia
Milby et al. (54)	1993	Triazolam, 25 mg/day	7	35.0	53	3	Initial insomnia
Morin et al. (34)	1999	Temazepam, 7.5 mg/day or more	17	65.0	64	8[b]	Mixed insomnia
Roth et al. (49)	1979	Quazepam, 25 mg/day	16	18–65	0	<1	Mixed insomnia
Behavioral treatment studies (250 subjects)							
Alperson anad Biglan (56)	1979	Stimulus control therapy	14	<55.0 (N=7) and ≥55.0 (N=7)	50	4	Initial insomnia
Bliwise et al. (47)	1995	Sleep restriction therapy	16	68.7	69	5	Mixed insomnia
Edinger et al. (43)	1992	Stimulus control therapy/sleep restriction therapy	7	61.9	57	6	Sleep maintenance insomnia
Espie et al. (44)	1989	Stimulus control therapy	43	45.5	68	8	Initial insomnia
Guilleminault et al. (41)	1995	Stimulus control therapy	30	44.0	60	4	Mixed insomnia
Jacobs et al. (35)	1993	Stimulus control therapy/sleep restriction therapy	12	37.8	58	10	Initial insomnia
Lacks et al. (55)	1983	Stimulus control therapy	7	43.0	60	4	Mixed insomnia
Lacks et al. (58)	1983	Stimulus control therapy	15	40.6	60	4	Initial insomnia
Morin et al. (57)	1993	Stimulus control therapy/sleep restriction therapy	24	67.1	71	8	Sleep maintenance insomnia
Morin et al. (34)	1999	Stimulus control therapy/sleep restriction therapy	18	64.4	64	8	Mixed insomnia
Puder et al. (45)	1983	Stimulus control therapy	16	67.0	81	4	Initial insomnia
Riedel et al. (40)	1995	Sleep restriction therapy	25	≥60.0	—[c]	4	Mixed insomnia
Stanton (42)	1989	Stimulus control therapy	15	40.0	58	4	Initial insomnia
Zwart and Lisman (46)	1979	Stimulus control therapy	8	21.0	47	3	Initial insomnia

[a] Mixed insomnia is both initial insomnia and sleep maintenance insomnia.
[b] Intermittent dosing schedule.
[c] Not reported.

TABLE 2. Efficacy of Pharmacotherapy Compared With Behavioral Therapy in 21 Studies of Persistent Insomnia

Subjective Sleep Outcome Measure (Based on Sleep Diary)	Pretreatment Value		Posttreatment Value		Difference Between Pretreatment and Posttreatment Means		Number of Studies	Number of Subjects	Weighted Effect Size[a]		95% CI for Difference Between Effect Sizes
	Mean	SD	Mean	SD	Value	%			Mean	SD	
Sleep latency (minutes)											0.17 to 1.04
Pharmacotherapy	48.85	29.73	34.36	26.26	–14.49	29.7	6	129	0.45	0.28	
Behavioral therapy	54.24	28.52	30.93	16.03	–23.31	43.0	12	225	1.05[b]	0.76	
Number of awakenings											–1.24 to 1.5
Pharmacotherapy	3.00	1.99	1.83	1.37	–1.17	39.0	4	108	0.97	1.00	
Behavioral therapy	2.44	1.84	1.67	1.59	–0.77	31.6	4	58	0.83	1.30	
Wake time after sleep onset (minutes)											—[c]
Pharmacotherapy	55.09	37.80	29.49	19.50	–25.60	46.5	1	17	0.89	0.29	
Behavioral therapy	68.60	40.27	30.22	23.98	–38.38	55.9	5	81	1.03	0.19	
Total sleep time (minutes)											–0.25 to 1.01
Pharmacotherapy	332.08	55.32	372.59	48.97	40.51	12.2	6	130	0.84	0.76	
Behavioral therapy	333.28	63.66	352.89	44.22	19.61	5.9	8	146	0.46	0.62	
Sleep quality rating[d]											–1.70 to 1.22
Pharmacotherapy	3.10	0.64	3.73	0.93	0.63	20.3	4	109	1.20	1.30	
Behavioral therapy	3.38	0.66	4.34	1.30	0.96	28.4	5	82	1.44	1.20	

[a] Overall weighted effect size calculated by the formula (Σ[di*N]/Σ[N]), where *di* is the effect size of the individual study.
[b] Behavioral therapy showed greater reductions in sleep latency than pharmacotherapy (t=2.88, df=20.62, p=0.01, unequal variance).
[c] Confidence interval was not calculated because there was only one pharmacological study that included wake time after sleep onset.
[d] Sleep quality ratings were standardized across studies so that higher scores reflect better sleep quality.

Circadian rhythm disorders

- Some circadian rhythm disorders such as advanced or delayed sleep phase syndromes overlap with insomnia in their clinical presentation.
- Bright light exposure (BLE) has been used to treat sleep maintenance insomniacs. Core body temperature was advanced by one hour and sleep efficiency was increased from 78% to 90%.
- Another study used BLE from 8 pm to midnight. The sleep phase was delayed by an hour TST increased.

Clinical significance of treatment outcome

- Investigator typically measure tx efficacy by examining changes in SOL, time awake after sleep onset and TST, but no consensus exists as to what are clinically meaningful changes.
- Markers for clinical significance include proportion of patients who improve more than 50%, have awake time of less than 30 min, have sleep efficiency of more than 80%, or discontinue or reduce hypnotic usage.

Clinical significance of treatment outcome - cont.

- Half to two-thirds of patients who receive treatment meet these standards of clinical significance.
- Clinically significant changes in clinical patients are more modest as reported in one study with 39% achieving reliable change and 23% becoming good sleepers. Further improvements were obtained at 1-year follow-up.

Methods and targets of outcome assessment

- Treatment efficacy has been primarily documented with prospective, daily sleep diaries.
- Some studies have used PSG and wrist-actigraphy.
- The magnitude of change recorded on the objective measures is usually smaller than sleep diaries the finding reported have been parallel.
- These finding indicate that CBT not only alters sleep perceptions on diaries, but produces objective changes on EEG measures.

Methods and targets of outcome assessment - cont.

- Most studies have neglected to address improvements in daytime functioning such as alertness, mood, psychological well being and quality of life.
- Important measures to consider include multiple measures of sleep, daytime functioning (attention, memory, concentration), fatigue, psychological symptoms, functional impairments, satisfaction with treatment anf quality of life.

Cost effectiveness

- Insomnia entails significant cost to both individuals and society.
- $1.7 billion and $11.96 are spent on sleep promoting substances and health care services, respectively for insomnia.
- Direct and indirect cost (loss of productivity, accidents) have been estimated at $30 to $35 billion annually

Cost effectiveness - cont.

- The direct costs of CBT for insomnia may seem higher than prescribing a hypnotic because CBT is more time consuming.
- However, preliminary findings suggest that insomniacs treated with CBT use health care services less after tx than those treated with hypnotic medication.

Feasibility - Treatment implementation models

- Despite extensive evidence supporting the efficacy of non-pharmacological interventions for insomnia they are under-utilized .
- Several barriers (time, cost, access) compromise large scale use.
- Alternative models of treatment have been tested recently, such as brief consultations, group therapy, and self help interventions.

Feasibility - Treatment implementation models - cont.

- Results of investigations using 1) cognitive-behavioral bibliotherapy where subjects received CBT in a written format and 2) a 'sleep service line' where callers received advice on sleep hygiene and behavioral practices for insomnia have been promising.
- A comparison study of CBT implemented either individually, in a group or by phone found similar improvements among the treatment conditions.

Feasibility - Treatment implementation models - cont.

- These results provide evidence that insomnia treatment may be implemented at minimal cost.
- Research on effective methods to disseminate these minimal treatment models is now required.

Effect of cognitive behavioural therapy for insomnia on sleep architecture and sleep EEG power spectra in psychophysiological insomnia

KATERINA CERVENA[1,3], YVES DAUVILLIERS[1,2], FABRICE ESPA[1,2], JACQUES TOUCHON[1,2], MILOS MATOUSEK[3], MICHEL BILLIARD[1] and ALAIN BESSET[1,2]

[1]Sleep and Wake Disorder Unit, Gui de Chauliac Hospital, Montpellier, [2]La Colombiere Hospital, Montpellier, France and [3]EEG-Sleep Laboratory, Prague Psychiatric Center, Bohnice, Czech Republic

Table 4 Polysomnographic data and Wilcoxon test comparisons in insomniac subjects before and after cognitive behavioural therapy for insomnia (CBT-I)

Sleep parameters	*Before CBT-I*	*After CBT-I*	*Z*	*P*	*ES*
Sleep continuity					
Sleep latency (min)	28.17 (13.94)	6.39 (4.08)	−2.67	0.008	−2.02
WASO (min)	113.17 (26.17)	49.00 (39.60)	−2.67	0.008	−1.82
Awakenings index	8.98 (4.90)	6.89 (4.71)	−2.67	0.008	−0.46
μ Arousals index	14.29 (7.78)	13.05 (6.36)	−0.77	0.441	−0.17
Sleep efficiency (%)	67.41 (7.82)	86.52 (8.61)	−2.67	0.008	−2.21
Sleep architecture					
Total sleep time (min)	323.67 (37.32)	415.39 (41.35)	−2.67	0.008	−2.22
Stage 1 (min)	37.50 (15.96)	39.50 (12.68)	−0.77	0.441	−0.13
Stage 1 (%)	11.67 (4.92)	9.59 (3.15)	−1.95	0.051	0.48
Stage 2 (min)	168.39 (33.35)	206.06 (46.60)	−2.67	0.008	−0.89
Stage 2 (%)	52.37 (11.26)	49.36 (8.99)	−2.67	0.008	0.28
Slow wave sleep (min)	62.56 (33.30)	86.50 (23.77)	−2.55	0.01	−0.79
Slow wave sleep (%)	19.09 (9.21)	21.21 (7.13)	−1.24	0.214	−0.24
REM sleep (min)	55.22 (20.33)	83.33 (23.63)	−2.24	0.025*	−1.21
REM sleep (%)	16.87 (5.11)	19.85 (4.97)	−1.60	0.110	−0.56

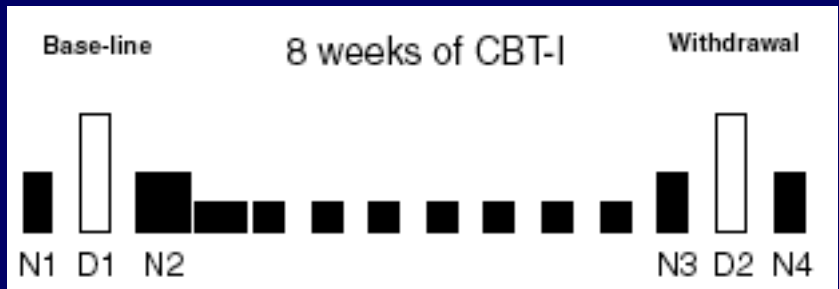


Figure 1. Design of the study: black rectangles represent polygraphic nights. N1 and N3 are adaptation and screening nights, N3 and N4, PSA nights. White rectangle represent 16 daytime hours of controlled wakefulness. Hatched rectangles represents weeks of cognitive behavioural therapy for Insomnia.

Table 2 Sleep diary data and Wilcoxon test comparisons in insomniac subjects before and after cognitive behavioural therapy for insomnia (CBT-I)

Sleep parameters	*Before CBT-I*	*After CBT-I*	*Z*	*P*	*ES*
Total sleep time (min)	281,22 (40.53)	402.66 (37.96)	−2.666	0.008	2.95
Sleep latency (min)	41.63 (40.39)	15.11 (13.51)	−2.521	0.012	−0.84
WASO (min)	125.68 (23.14)	38.01 (15.84)	−2.666	0.008	−4.21
Sleep efficiency (%)	63.14 (10.88)	88.28 (6.40)	−2.666	0.008	2.82

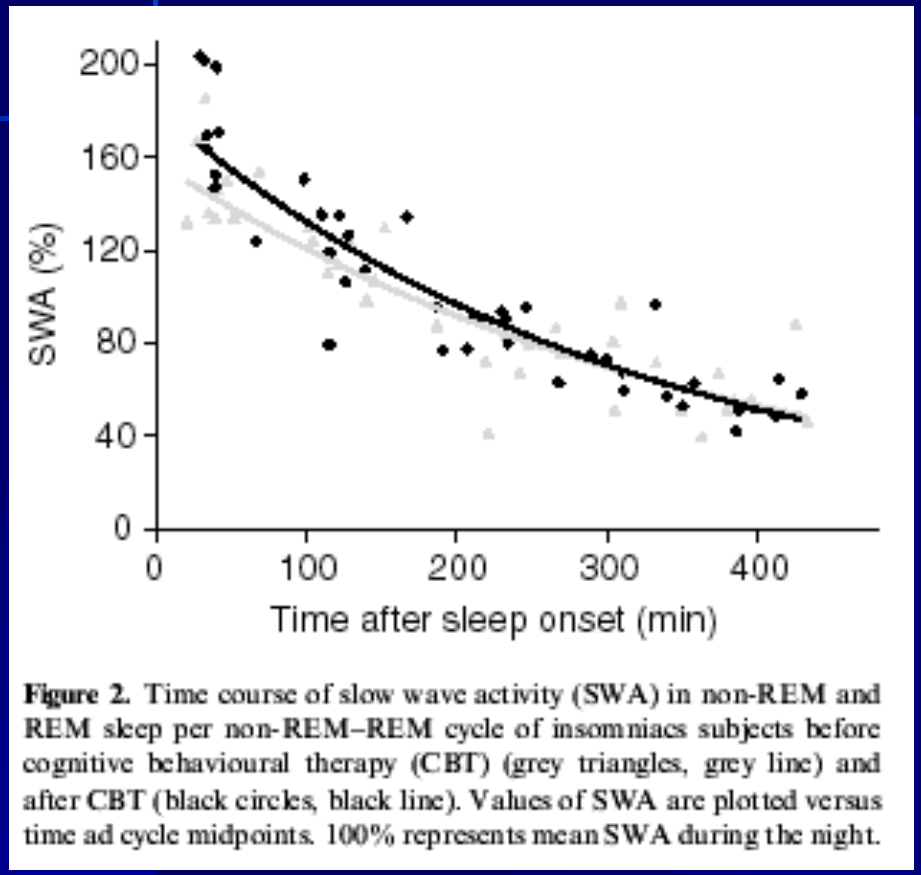


Figure 2. Time course of slow wave activity (SWA) in non-REM and REM sleep per non-REM–REM cycle of insomniacs subjects before cognitive behavioural therapy (CBT) (grey triangles, grey line) and after CBT (black circles, black line). Values of SWA are plotted versus time ad cycle midpoints. 100% represents mean SWA during the night.

Table 6 The PSA measures of EEG frequency bands in NREM sleep and REM sleep and Wilcoxon test comparisons in insomniac subjects before and after cognitive behavioural therapy for insomnia (CBT-I)

Frequency bands	*Before CBT-I*	*After CBT-I*	*Z*	*P*	*ES*
NREM					
SWA†	2.82 (0.25)	2.92 (0.21)	−3.75	0.0001	−0.41
SWA‡	71.90 (8.42)	76.96 (6.89)	−3.88	0.0001	−0.66
Theta†	2.09 (0.19)	2.12 (0.16)	−2.24	0.02*	−0.16
Theta‡	13.56 (2.87)	11.34 (2.81)	−3.88	0.0001	0.86
Alpha†	1.81 (0.17)	1.85 (0.17)	−2.80	0.005	−0.22
Alpha‡	7.58 (2.90)	6.58 (3.19)	−2.69	0.007	0.33
Sigma†	1.62 (0.25)	1.62 (0.23)	−0.97	0.33	0.00
Sigma‡	5.47 (3.65)	3.88 (2.11)	−3.07	0.002	0.53
Beta†	1.06 (0.18)	1.13 (0.26)	−0.90	0.37	−0.30
Beta‡	1.50 (0.96)	1.23 (0.72)	−2.26	0.02*	−0.32
REM					
SWA†	2.32 (0.26)	2.37 (0.17)	−1.85	0.064	−0.22
SWA‡	57.03 (11.28)	58.66 (9.02)	−1.04	0.29	−0.16
Theta†	1.89 (0.26)	1.93 (0.18)	−2.09	0.037	−0.17
Theta‡	21.36 (4.59)	21.46 (2.47)	−0.36	0.787	−0.03
Alpha†	1.59 (0.26)1	1.59 (0.23)	−1.33	0.184	0.00
Alpha‡	11.41 (5.98)	10.39 (3.92)	−1.24	0.214	0.20
Sigma†	1.21 (0.27)	1.21 (0.23)	−1.35	0.18	0.00
Sigma‡	5.47 (3.73)	4.62 (2.51)	−1.57	0.12	0.27
Beta†	1.13 (0.27)	1.22 (0.29)	−2.15	0.03*	−0.31
Beta‡	4.72 (3.85)	4.84 (2.60)	−0.38	0.72	−0.04

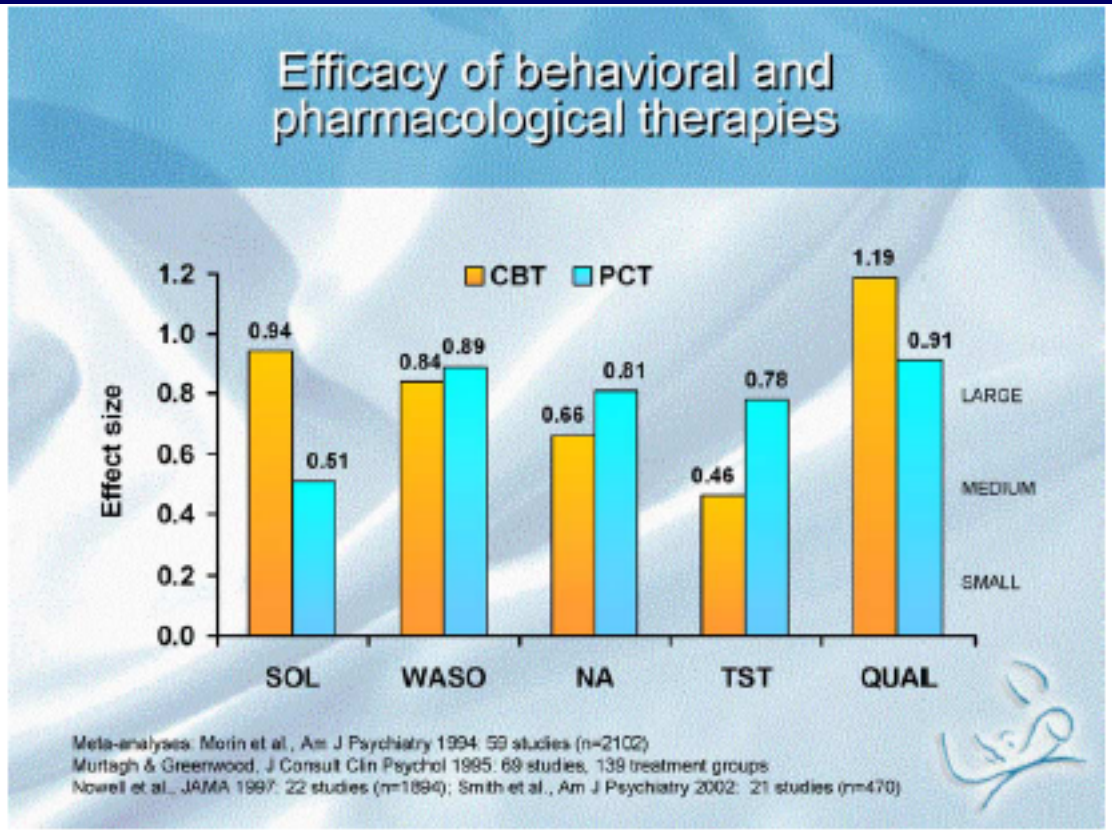


Fig. 1. Comparative efficacy of behavioral and pharmacological therapies on sleep parameters, as assessed in a number of meta-analyses [9,12–14]. SOL, sleep onset latency; WASO, wake after sleep onset; NA, night-time awakening; TST, total sleep time; QUAL, quality of life; CBT, cognitive behavioral therapy; PCT, pharmacotherapy.

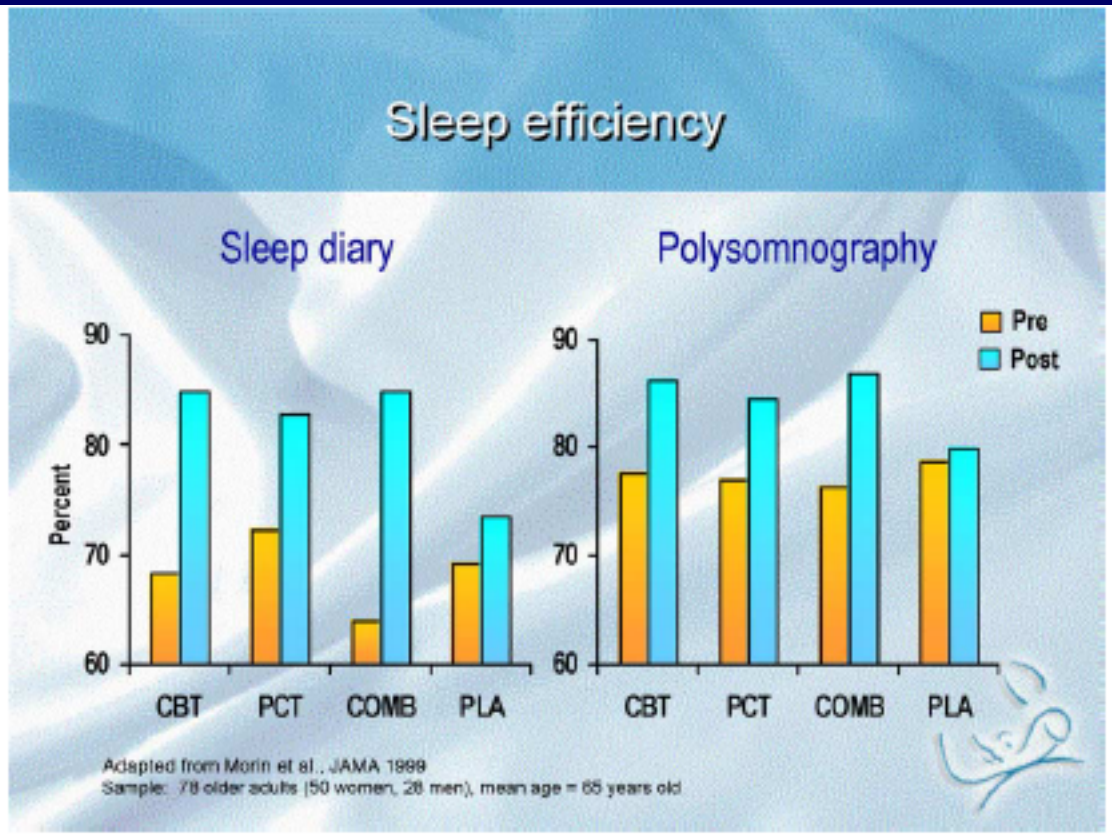


Fig. 2. Sleep efficiency before and after treatment in patients receiving CBT, temazepam, combination therapy or placebo [10]. CBT, cognitive behavioral therapy; PCT, pharmacotherapy; COMB, combination therapy; PLA, placebo.

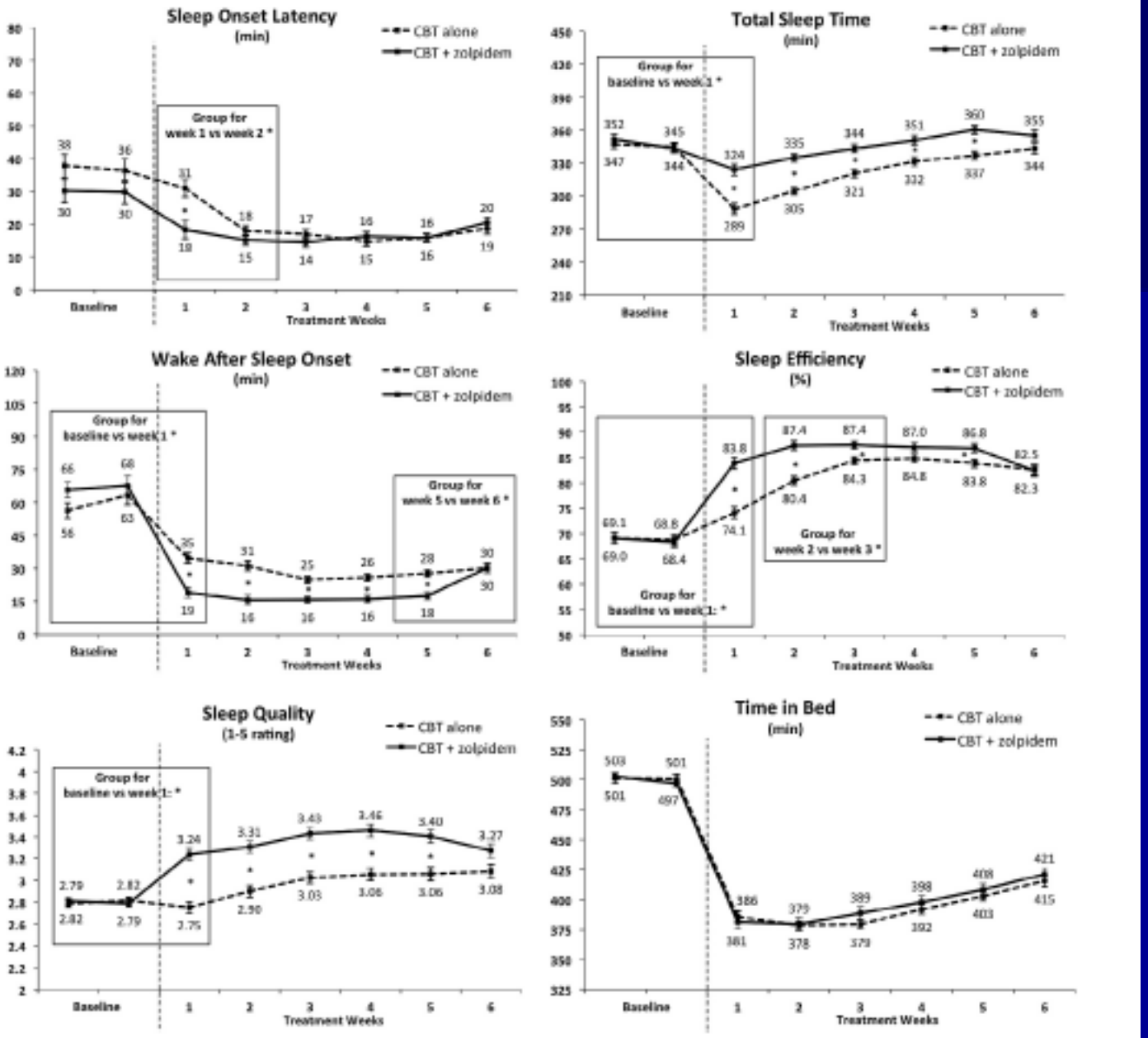
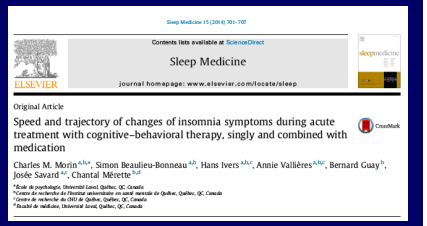


Fig. 1. Weekly sleep diary data (adjusted means and standard errors) over two-week baseline and six-week acute treatment periods for sleep onset latency, wake time after sleep onset, total sleep time, sleep efficiency, sleep quality, and time in bed for cognitive–behavioral therapy (CBT) alone and CBT plus zolpidem conditions. Contrasts (i.e. group effect for treatment weeks 1–6, and for change score from baseline to week 1, and from each treatment week to the following week) are flagged for statistical significance.



Sleep Medicine 15 (2014) 701–707

Contents lists available at ScienceDirect

Sleep Medicine

journal homepage: www.elsevier.com/locate/sleep

Original Article

Speed and trajectory of changes of insomnia symptoms during acute treatment with cognitive–behavioral therapy, singly and combined with medication

Charles M. Morin[a,b,*], Simon Beaulieu-Bonneau[a,b], Hans Ivers[a,b,c], Annie Vallières[a,b,c], Bernard Guay[b], Josée Savard[d,e], Chantal Mérette[b,d]

[a] École de psychologie, Université Laval, Québec, QC, Canada
[b] Centre de recherche du l'Institut universitaire en santé mentale de Québec, Québec, QC, Canada
[c] Centre de recherche du CHU de Québec, Québec, QC, Canada
[d] Faculté de médecine, Université Laval, Québec, QC, Canada

Trattamenti combinatI:
- maggiore rapidità
-- effetti finali non diversi da sola CBT

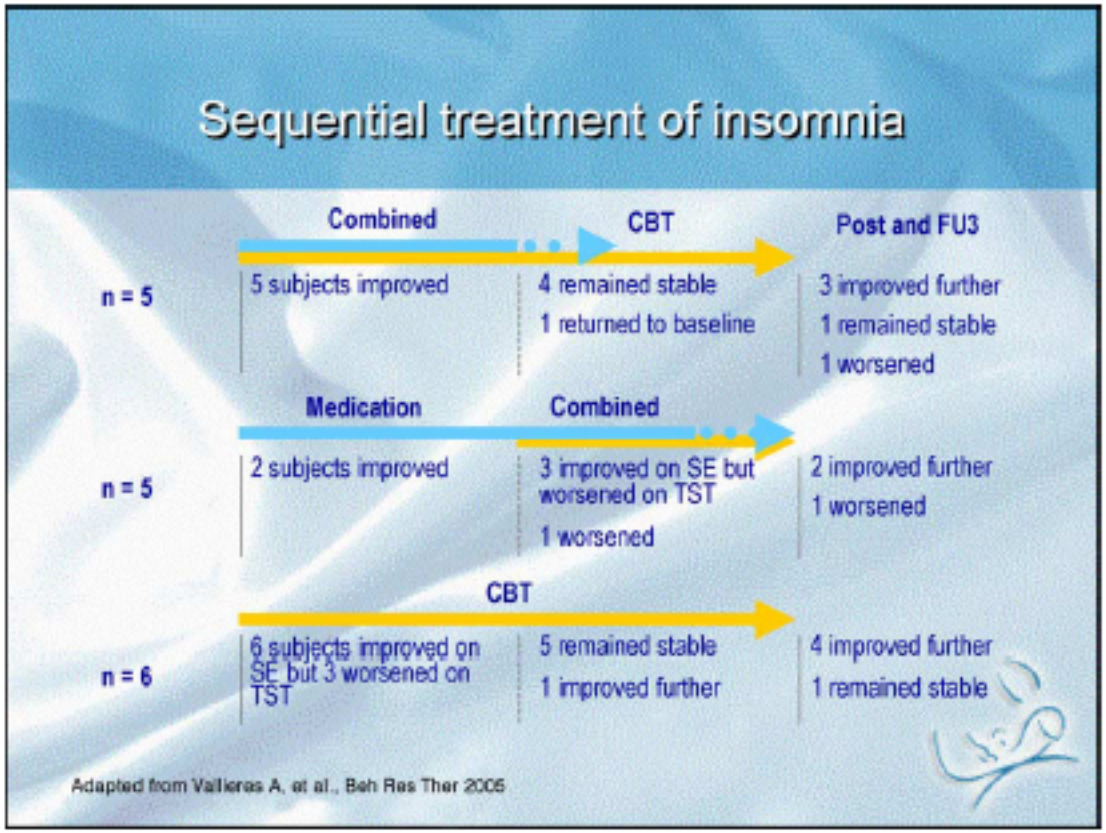


Fig. 3. Results from a pilot study of three sequences of combination therapy involving CBT with or without zopiclone [19]. CBT, cognitive behavior therapy; SE, sleep efficiency; TST, total sleep time; TWT, total wake time.