The Effects of Mind-Body Interventions on Sleep in Cancer Patients: A Meta-Analysis of Randomized Controlled Trials

Hsiao-Yean Chiu, PhD; Pei-Chuan Chiang, MSN; Nae-Fang Miao, PhD; En-Yuan Lin, MD; and Pei-Shan Tsai, PhD

ABSTRACT

Objective: To examine the effect of mind-body interventions (MBIs) on sleep quality among cancer patients, the moderating effects of the intervention components, subject characteristics, and methodological features of the relationship between MBIs and sleep.

Data Sources: Electronic databases, including PubMed, Cochrane Library, PsycINFO, and CINAHL, containing data with English-language restriction recorded up to September 15, 2013 were searched thoroughly using keywords related to various types of MBI and sleep.

Study Selection: Of the 114 identified citations, 99 were ineligible. Fifteen studies that followed 1,405 patients with cancer met the inclusion criteria and were analyzed.

Data Extraction: The primary outcome was change in the sleep parameter. Other variables related to components of MBIs, subject characteristics, and methodological features of the studies were also extracted.

Data Synthesis: The weighted mean effect size (ES) was −0.43 (95% confidence interval [CI], −0.24 to −0.62) and the long-term effect size (up to 3 months) was −0.29 (95% CI, −0.52 to −0.06). The sensitivity analysis revealed that MBIs had a significant effect on sleep ($g = -0.33$, $P < .001$). The moderating effects of components of the intervention, methodological features, subject characteristics, and quality of the studies on the relationship between MBIs and sleep were not found (all P values > .05).

Conclusions: This meta-analysis confirms that the MBIs yielded a medium effect size on sleep quality and the effect was maintained for up to 3 months. The findings support the implementation of MBIs into the multimodal approach to managing sleep quality in patients with cancer.

J Clin Psychiatry 2014;75(11):1215–1223

Submitted: *December 3, 2013; accepted February 21, 2014.*
Online ahead of print: *August 19, 2014 (doi:10.4088/JCP.13r08918).*
Corresponding author: *Pei-Shan Tsai, PhD, 250 Wu-Hsing St, Taipei, 110 Taiwan (ptsai@tmu.edu.tw).*

Disturbed sleep is one of the most common symptoms experienced by cancer patients before, during, and after cancer-related treatment,[1–5] with prevalence rates of 30%–70%.[6–8] Sleep disturbance is known to significantly correlate to psychological distress, reduced physical functioning, and impaired quality of life in cancer patients.[9–11] Despite their high prevalence and negative consequences, sleep problems experienced by cancer patients are often neglected and undertreated.[12]

Hypnotic pharmacotherapy is the most prescribed therapy for cancer patients with sleep disturbance.[13,14] However, because hypnotic pharmacotherapy produces side effects and possibly interacts with cancer treatments, many cancer patients use complementary and alternative medicine for managing sleep problems. Cognitive-behavioral therapy (CBT) is a safe and effective treatment for sleep disturbance[15]; nonetheless, the components of CBT are difficult to implement for cancer patients. Mind-body interventions (MBIs), which encompass numerous therapies such as hypnosis, meditation, yoga, biofeedback, qigong, tai chi, and music therapy, focus on the reciprocal relationship between the mind, body, and behavior.[16] Because of the low physical and emotional risks and the relatively low cost[17] associated with implementing MBIs, this type of treatment has been widely received by cancer patients.

Several reviews[18–20] and meta-analyses[21,22] have demonstrated the efficacy of MBIs for treating insomnia. The effect of MBIs on sleep has also been examined in cancer survivors. The authors of a recent meta-analysis of randomized controlled trials in which the effect of yoga on the quality of life and psychological functions of breast cancer patients was evaluated[23] tentatively concluded that yoga does not improve sleep quality. However, this conclusion was based on only 2 studies.[24,25] The authors of a systematic review determined that selected MBIs (ie, imagery, hypnosis, CBT, relaxation, and meditation) beneficially affect sleep in cancer patients.[26] Because the findings reported in relevant literature are conflicting, conducting a meta-analysis of randomized controlled trials to examine the effects of MBIs on sleep using a large sample size of cancer patients is required.

The purposes of this meta-analysis were to examine the overall efficacy of MBIs on sleep quality and to identify the treatment components that potentially influence the effect of MBIs on sleep quality. The moderating effects of methodological features and subject characteristics on the relationship between MBIs and sleep quality were also examined.

METHOD

This meta-analysis was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement, which provided detailed guidelines involving the preferred reporting items that should be used in conducting a systematic review and meta-analysis.[27] The type of participant (P), intervention (I), comparison (C), outcome (O), and study used in this investigation are described as follows:

Type of Participant

Participants aged 18 years or older who had been diagnosed with cancer were included.

Clinical Points

- Sleep disturbance is a pervasive symptom in cancer patients that impairs quality of life.
- A meta-analysis of mind-body interventions (yoga, mindfulness-based stress reduction, mind-body bridging, meditation, hypnosis, and qigong) among cancer patients yielded moderate improvement in sleep quality that persisted up to 3 months.
- Mind-body interventions should be considered as adjunctive or complementary therapies in the management of sleep problems experienced by cancer patients.

Type of Intervention

Studies in which MBIs have been used as interventions (ie, yoga, meditation, hypnosis, mindfulness, breathing training, qigong, tai chi, music therapy, and biofeedback) were included.

Type of Comparison

Studies that have included a control group that was either inactive (ie, waiting list, no treatment, or usual care) or active (sleep education or alternative active treatment) were included.

Type of Outcome Measure

Studies that have reported on the sleep parameter and presented the data at baseline and after intervention were included.

Type of Study

The studies included in this investigation were prospective randomized clinical trials (RCTs) in which MBIs have been used for improving sleep, studies with a total number of randomization subjects greater than 10 ($n \geq 10$), studies that have been reported in the English language, and those that have been published or accepted for publication in a peer-reviewed journal.

Data Source and Searches

Electronic databases, including PubMed, PsycINFO, the Cochrane Central Register of Controlled Trials, and the CINAHL (through September 15, 2013) were examined. The keywords used to search for the studies were *(mind-body intervention* OR *mindfulness-based stress reduction* OR *meditation* OR *yoga* OR *hypnosis* OR *breathing training* OR *exercise* OR *qigong* OR *tai chi* OR *music therapy* OR *biofeedback)* AND *(sleep* OR *sleep disturbance* OR *sleep quality* OR *insomnia)* AND *(cancer)*.

Study Selection

Two authors of this meta-analysis (H-Y.C., P-S.T.) independently screened the titles and abstracts of potentially eligible articles using the aforementioned search strategy. Initially, duplicates were removed from the total number of potentially eligible articles. The full-text articles of the remaining studies were then retrieved and reviewed. Finally, the studies that fulfilled the inclusion criteria were selected for meta-analytic evaluation.

Data Collection

Two authors of this meta-analysis (H-Y.C., P-C.C.) developed a data extraction sheet and extracted the data from each study, which included the study characteristics (eg, author's name and year of publication), subject characteristics (type of cancer, age, number of participants in each group, and percentage of women), intervention details (type of intervention, frequency, duration, dosage, provider, delivery setting, and home practice), and outcome details (instrument, time of follow up, whether sleep was the primary outcome, and whether the presence of sleep problems was required for eligibility) (Table 1). Disagreements were resolved by discussion, and a consensus was reached.

Methodological Quality Assessment

To confirm the internal validity of each included study, 2 authors of this study (H-Y.C., P-C.C.) individually evaluated potential sources of bias using criteria recommended in the *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.1.0.[28] Six domains related to risk of bias were assessed: (1) random sequence generation, (2) allocation concealment, (3) the blinding of participants and personnel, (4) the blinding of outcome assessment, (5) incomplete outcome data addressed, and (6) selective reporting. Discrepancies were rechecked by the corresponding author and consensus reached by discussion.

Data Analysis

Quantitative data were entered into Comprehensive Meta-Analysis software, Version 2.0 (Biostat, Englewood, New Jersey) and the *P* values were 2-sided. The standardized mean differences (SMD) were calculated using the means and standard deviation (SD) or change scores for each intervention. All of the analyses were performed using the inverse variance random-effect model because this model is more conservative than the fixed-effect model.[29]

Heterogeneity. The between-study heterogeneity was appraised using the Cochran Q and I^2 statistics.[30] Q statistics were used to calculate the probability value for the heterogeneity of the studies (significant heterogeneity was indicated by $P < .05$). The I^2 was used to estimate the amount of variance in a pooled effect size that can be attributed to the heterogeneity of the sample of studies. An I^2 value of approximately 50% or greater represented substantial heterogeneity, whereas an I^2 value of 40% or less indicated no problem in heterogeneity. Visual examinations of a forest plot were also used to evaluate heterogeneity. When substantial heterogeneity was observed, we determined the potential reasons for this phenomenon by removing the study with the largest effect on overall SMD to examine the magnitude of the effect produced by that study.

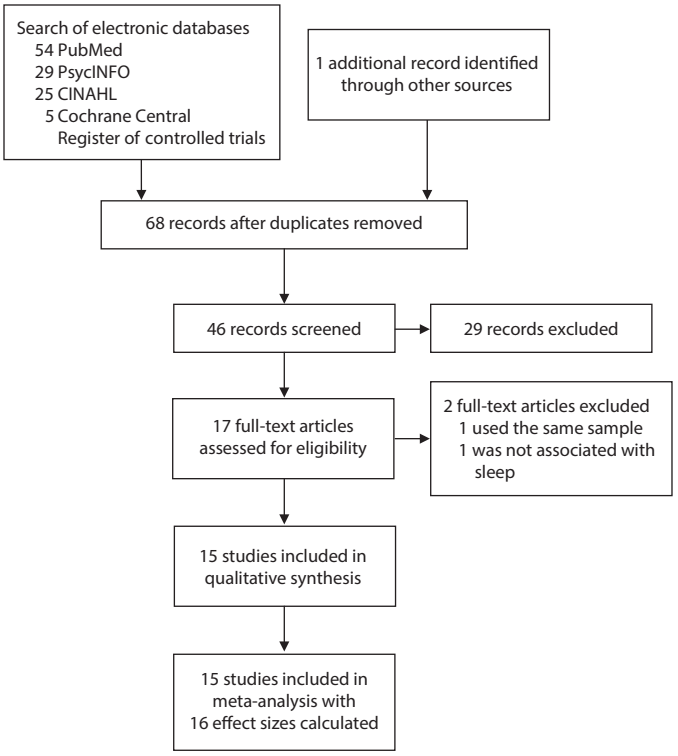
Publication bias. Potential publication bias was examined using the fail-safe N, which provides an estimate for the number of unpublished studies with a nonsignificant

Table 1. Characteristics of Included Randomized Controlled Trial Studies

First Authors, y	Population	MBI/ Control	Age (y)[a]	Women (%)	Sample Size (MBI/ Control)	Frequency	Duration (wk)	Dose of Intervention (min)	Instrument	Home Practice	Intervention Provider	Sleep as Primary Outcome	Only Individuals With Sleep Disturbance	Follow-Up (mo)
Andersen et al, 2013[37]	Breast cancer	MBSR/ Usual care	54.3	100	168/168	Weekly 2-hour class + 5-hour silent retreat at wk 7	8	1260	MOS-SS	Yes	Psychologist	Yes	No	6 and 12
Bower et al, 2012[38]	Breast cancer	Yoga/ Health education	53.9	100	16/15	Two 90-min classes per wk	12	2160	PSQI	No	Yoga instructor	No	No	3
Carson et al, 2009[39]	Breast cancer	Yoga/ Wait list	54.0	100	17/20	Weekly 120-min class	8	960	Daily diary	Yes	Yoga instructor	No	No	3
Chandwani et al, 2010[25]	Breast cancer	Yoga/ Wait list	51.4	100	30/31	Two 60-min classes per wk	6	720	PSQI	Yes	Yoga instructor	No	No	1 and 3
Chen et al, 2013[40]	Breast cancer	Qigong/ Wait list	45.0	100	49/47	Weekly 40-min class	5 or 6	200	PSQI	Yes	Qigong master	No	No	1 and 3
Cohen et al, 2004[41]	Lymphoma	Yoga/ Wait list	51.0	31	19/19	Weekly 1.5-hour class	7	630	PSQI	Yes	Yoga instructor	Yes	No	No
Danhauer et al, 2009[24]	Breast cancer	Yoga/ Wait list	55.8	100	13/14	Weekly 75-min class	10	750	PSQI	No	Yoga instructor	No	No	No
Dhruva et al, 2012[42]	Cancer[b]	Yoga/ Wait list	54.0	88	8/8	Weekly 60-min class	24	1440	GSDS	Yes	Yoga instructor	No	No	No
Elkins et al, 2008[36]	Breast cancer	Hypnosis/ No treatment	56.5	100	27/24	Weekly 50-min class	5	250	MOS-SS	Yes	Psychologist	No	No	No
Farrell-Carnahan et al, 2010[47]	Cancer[c]	IBSH/ Wait list	56.7	85.7	14/14	180-min session in the first wk and 180-min classes in the remaining 3 wks	4	360	ISI	No	Internet program	Yes	Yes	No
Lengacher et al, 2012[43]	Breast cancer	MBSR/ Wait list	58.0	100	40/42	Two-hour sessions per wk	6	720	MDASI	Yes	Psychologist	No	No	No
Milbury et al, 2013[44]	Breast cancer	Meditation/ Wait list	53.6	100	18/24	Two 60-min classes per wk	6	720	PSQI	Yes	Meditation instructor	No	No	1
Mustian et al, 2013[45]	Cancer[d]	Yoga/ Usual care	54.1	96	206/204	Two 75-min classes per wk	4	600	PSQI	Yes	Yoga instructor	Yes	Yes	No
Nakamura et al, 2013[46]	Cancer[e]	Meditation/ Sleep hygiene	51.2	78.9	20/18	Two-hour classes per wk	3	360	MOS-SS	Yes	Social workers	Yes	Yes	2
Nakamura et al, 2013[46]	Cancer[e]	MBB/ Sleep hygiene	53.5	73.0	19/18	Two-hour classes per wk	3	360	MOS-SS	Yes	Social workers	Yes	Yes	2
Vadiraja et al, 2009[48]	Breast cancer	Yoga/ Usual care	30 to 70	100	42/33	Three 60-min classes per wk	6	1080	QOL-C30	Yes	Yoga instructor	No	No	No

[a]Age presented as a mean.
[b]Gastrointestinal, gynecologic, lymphoproliferative disease, and lung cancer.
[c]Did not mention.
[d]Hematologic, gynecologic, alimentary, and other cancer.
[e]Ovarian, endometrial, testicular, prostate, lung, melanoma, ependymona, leukemia, kidney, lymphomas (non-Hodgkin, CNS), skin carcinoma, brain, thyroid, and peritoneal cancer.
Abbreviations: GSDS = General Sleep Disturbance Scale, IBSH = Internet-based self-hypnosis, ISI = Insomnia Severity Index, MBB = mind-body bridging, MBI = mind-body intervention, MBSR = mindfulness-based stress reduction, MDASI = MD Anderson Symptom Inventory, MOS-SS = Medical Outcomes Study Sleep Scale, PSQI = Pittsburgh Sleep Quality Index, QoL-C30 = The European Organization for Research and Treatment of Cancer Quality of Life Questionnaire.

Figure 1. PRISMA Flow Diagram[a]



[a]Flow diagram based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (www.prisma-statement.org).
Abbreviation: CINAHL = Cumulative Index to Nursing and Allied Health Literature.

intervention effect required to reduce the overall estimation of effect size to a nonsignificant level ($P > .05$).[31] Begg rank correlation test[32] and Egger intercept test[33] were also used, and the significant level was set as .05. A funnel plot was used to examine the publication bias, and the trim and fill method[34] was used to test and adjust for possible bias in the overall effect size by considering the effect sizes from the estimated number of missing studies.

Moderator analysis. To explore the possible reasons for the observed heterogeneity (ie, Q statistics < 0.05 and I^2 value > 50%), moderator analyses were performed. In this study, the moderator analyses were limited to instances in which groups were represented by at least 3 studies to ensure that sufficient data could be obtained for analysis. For categorical moderators, the mixed-effect model was used to compare the difference in effect sizes in each comparison.[35] Meta-regression was used for analyzing continuous moderators.[35] In the current study, analyses of moderators were divided into 4 categories: analysis of the components of MBIs, subject characteristics, methodological features, and quality of studies.

RESULTS

Search Results

The flow of the review is illustrated in Figure 1. The electronic searches identified 114 studies. Among these, 68 duplicates were excluded by using Endnote software. Twenty-eight articles were excluded after initial screening because they were not RCTs or subjects and interventions were not related to the PICO. Eighteen articles were maintained for further screening. Of these, 3 were excluded for the following reasons: one used the same sample, one was not associated with sleep outcome, and one did not provide sufficient data to compute an effect size. Finally, 15 studies were included in the analysis.[24,25,36–48] Because 1 study used 2 relevant intervention conditions,[46] 16 effect sizes were used for analysis.

Study Characteristics

Table 1 summarizes the characteristics of the 15 included studies in which MBIs used for improving sleep quality in cancer patients were investigated (one study[46] used 2 interventions). The trial sample sizes ranged from 16 to 410 with a total of 1,405 randomized subjects. The majority of the studies (10 studies) were conducted on patients with breast cancer. Five studies were conducted on patients with other types of cancer (Table 1), and 1 involved patients with lymphoma. Among the 16 reviewed RCTs, yoga was used in 8 trials, mindfulness-based stress reduction was used in 2 trials, meditation was used in 2 trials, hypnosis was used in 2 trials, mind-body bridging was used in 1 trial, and qigong was used in 1 trial. Two types of control conditions were used for comparison: inactive groups (waiting list, usual care, and no treatment) and active groups (health education and sleep hygiene). The mean dose of intervention was 785.63 minutes, ranging from 200 minutes to 2,160 minutes. Thirteen studies required or encouraged participants to practice MBIs at home during and/or after treatment. The most frequently used sleep measures were the Pittsburgh Sleep Quality Index, which was used in 7 studies, and the Medical Outcomes Study Sleep Scale, which was used in 3 studies.

The methodological quality of the included studies according to the *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.1.0 is reported in Table 2. Most of the studies achieved the quality of random sequence generation (13 low risk), incomplete outcome data addressed (14 low risk), and selective reporting (15 low risk). Forty percent of the studies involved concealed allocation, and 20% of the studies included blinded assessors. None of studies blinded participants and personnel.

Quantitative Data Synthesis

Overall effect. The effect sizes for all of the studies included in the meta-analysis are shown in Figure 2. The weighted average effect size among the 16 trials was −0.42 ($P < .001$). No outliner was determined because all of the effect sizes fell within 2 SDs of the mean. By calculating the statistics I^2 and Cochran Q, heterogeneity was identified ($Q = 37.057$, $df = 15$, $P = .001$; $I^2 = 59.522$). Therefore, moderator analyses were performed according to the components of intervention, subject characteristics, methodological features, and the

Table 2. Risk of Methodological Bias Score of the Studies

First Authors	Random Sequence Generation	Allocation Concealment	Blinding of Participants and Personnel	Blinding of Outcome Assessment	Incomplete Outcome Data Addressed	Selective Reporting
Andersen et al[37]	+	–	–	–	+	+
Bower et al[38]	+	+	–	+	+	+
Carson et al[39]	+	+	–	+	+	+
Chandwani et al[25]	+	–	–	–	+	+
Chen et al[40]	+	–	–	–	+	+
Cohen et al[41]	+	+	–	–	?	+
Danhauer et al[24]	?	–	–	–	+	+
Dhruva et al[42]	+	+	–	–	+	+
Farrell-Carnahan et al[47]	+	–	–	–	+	+
Elkins et al[36]	+	–	–	–	+	+
Lengacher et al[43]	?	–	–	+	+	+
Milbury et al[44]	+	–	–	–	+	+
Mustian et al[45]	+	+	–	–	+	+
Nakamura et al[46]	+	–	–	–	+	+
Vadiraja et al[48]	+	+	–	–	+	+

Symbols: + = low risk, – = high risk, ? = unclear risk of bias.

quality of the studies. In addition, sensitivity analysis was performed by removing the study in which the greatest effect was produced.[36] As shown in Figure 2, the effects of MBIs on sleep quality improvement remained statistically significant ($g = -0.33$, $P < .001$).

The long-term effects that occurred in the intervention groups were calculated by examining only the changes that occurred between the pretest and follow-up. Six studies have measured effects up to 3 months posttest. As shown in Figure 2, the result indicated a small and significant effect ($g = -0.29$, $P = .02$).

Moderator analysis. Yoga interventions* yielded comparable effect size compared with that of other interventions[36,37,40,43–47] ($g = -0.40$ and $g = -0.49$, $P = .71$). Studies in which participants were required or encouraged to practice interventions at home[25,36–42,44–46,48] yielded a greater effect ($g = -0.48$) than did studies in which participants were not required or encouraged to practice at home[24,43,47] ($g = -0.16$), but the difference was not statistically significant ($P = .23$). Effect size was not significantly associated with the number of treatment dosages, sessions, or the duration of treatment in weeks ($P = .34$, .39, and .20, respectively).

Studies on breast cancer participants[24,25,36–40,43,44,48] and those of participants with other types of cancer[41,42,45–47] have reported comparable effects ($g = -0.43$ and $g = -0.45$, $P = .92$). Effect size was not significantly associated with age ($P = .34$) or the percentage of female participants ($P = .76$).

Studies with sample size > 31[25,36–41,43–46,48] reported larger effects compared with those of studies with sample size ≤ 30[24,42,47] ($g = -0.45$ and $g = -0.25$), but the difference was not statistically significant ($P = .51$). The pooled effect size of the studies in which an active control[38,46] (ie, health education and sleep hygiene education) was used and those in which an inactive control[24,25,36,37,39–45,47,48] was used was not significantly different ($P = .63$). Defining individuals with sleep problems as an inclusion criterion before enrollment did not influence outcomes ($P = .82$). Studies in which sleep problems have been the primary outcome[37,41,45–47] have reported a lower effect size than that of studies in which sleep has been a secondary outcome,[24,25,36,38–40,42–44,48] but the difference was not statistically significant ($g = -0.38$ and $g = -0.46$, $P = .71$).

To assess the influence of study quality on sleep, we individually examined the criteria of allocation concealment and the blinding of outcome assessment as potential moderators of intervention effects (Table 3). No statistically significant difference in the criteria of allocation concealment and blinding of outcome assessment was observed between high-risk and low-risk studies ($P = .70$ and $P = .68$, respectively).

Publication bias. The fail-safe N was 169, indicating that publication bias was not a problem. According to Egger test, the intercept of the effect size was −1.34 and $t = 1.75$ (2-tailed $P = .11$). According to Begg test, Kendall tau with continuity correction was −0.27 and $Z = 1.44$ ($P = .15$). The results of both of these tests were not indicative of publication bias. However, the funnel plot indicated a slight selection bias. Therefore, the mean effect size was calculated again while imputing missing studies using the trim and fill procedure. The adjusted effect size was −0.32 (95% CI, −0.54 to −0.09).

DISCUSSION

In this meta-analysis, we investigated the effect of MBIs on the improvement of sleep quality among cancer patients. The results indicated that MBIs had a medium-size effect ($g = -0.42$) on the improvement of sleep quality and this effect persisted up to 3 months after treatment ($g = -0.29$). In comparison with previous systematic reviews and meta-analyses,[23,26] we applied more specific inclusion criteria, rigorously assessed the quality of the included studies using 2 independent raters, and systematically tested for moderators that were clinically relevant in this meta-analysis. Thus, the overall results of this meta-analysis can be considered credible.

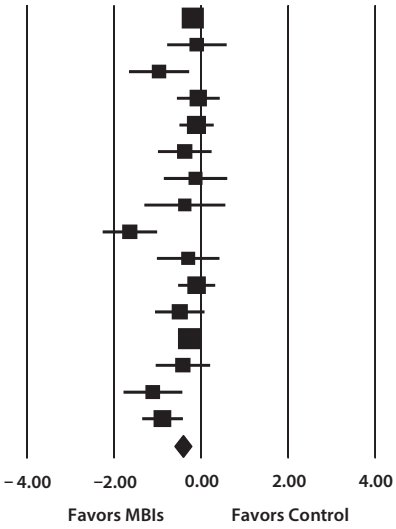
One possible mechanism underlying the effect of MBIs on sleep quality improvement in cancer patients is the attenuation

*References 24, 25, 38, 39, 41, 42, 45, 48.

Figure 2. Forest Plots of Mean Effect Size (A), Sensitivity Analysis (B), and Long-Term Effect Size (C) for Studies Measuring Sleep

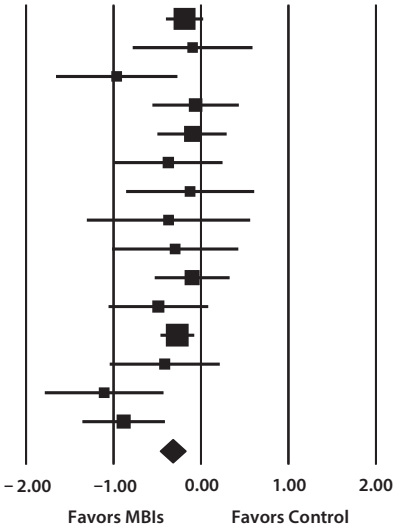
A. Mean Effect Size

Study	Hedges *g*	Standard error	Variance	Upper limit	Lower limit	*Z* Value	*P* Value
Anderson et al, 2013[37]	−0.187	0.109	0.012	0.027	−0.401	−1.716	.086
Bower et al, 2012[38]	−0.095	0.350	0.123	0.591	−0.782	−0.272	.785
Carson et al, 2009[39]	−0.963	0.355	0.126	−0.268	−1.659	−2.716	.007
Chandwani et al, 2010[25]	−0.061	0.253	0.064	0.435	−0.556	−0.240	.810
Chen et al, 2013[40]	−0.102	0.203	0.041	0.295	−0.499	−0.504	.615
Cohen et al, 2004[41]	−0.372	0.317	0.100	0.248	−0.993	−1.176	.240
Danhauer et al, 2009[24]	−0.124	0.374	0.140	0.609	−0.857	−0.332	.740
Dhruva et al, 2012[42]	−0.371	0.477	0.228	0.565	−1.306	−0.777	.437
Elkins et al, 2008[36]	−1.635	0.320	0.103	−1.007	−2.262	−5.107	.000
Farrell-Carnahan et al, 2010[47]	−0.295	0.369	0.136	0.428	−1.019	−0.800	.424
Lengacher et al, 2012[43]	−0.100	0.219	0.048	0.329	−0.530	−0.458	.647
Milbury et al, 2013[44]	−0.487	0.291	0.085	0.084	−1.058	−1.672	.095
Mustian et al, 2013[45]	−0.270	0.099	0.010	−0.076	−0.465	−2.731	.006
Nakamura et al, 2013	−0.415	0.322	0.103	0.216	−1.045	−1.289	.197
Nakamura et al, 2013[46]	−1.107	0.347	0.120	−0.427	−1.786	−3.193	.001
Vadiraja et al, 2009[48]	−0.884	0.241	0.058	−0.411	−1.357	−3.663	.000
	−0.425	0.097	0.009	−0.235	−0.615	−4.375	.000



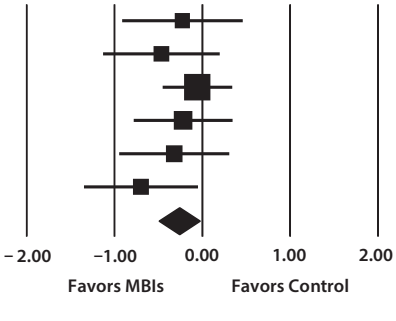
B. Sensitivity Analysis

Study	Hedges *g*	Standard error	Variance	Upper limit	Lower limit	*Z* Value	*P* Value
Anderson et al, 2013[37]	−0.187	0.109	0.012	0.027	−0.401	−1.716	.086
Bower et al, 2012[38]	−0.095	0.350	0.123	0.591	−0.782	−0.272	.785
Carson et al, 2009[39]	−0.963	0.355	0.126	−0.268	−1.659	−2.716	.007
Chandwani et al, 2010[25]	−0.061	0.253	0.064	0.435	−0.556	−0.240	.810
Chen et al, 2013[40]	−0.102	0.203	0.041	0.295	−0.499	−0.504	.615
Cohen et al, 2004[41]	−0.372	0.317	0.100	0.248	−0.993	−1.176	.240
Danhauer et al, 2009[24]	−0.124	0.374	0.140	0.609	−0.857	−0.332	.740
Dhruva et al, 2012[42]	−0.371	0.477	0.228	0.565	−1.306	−0.777	.437
Farrell-Carnahan et al, 2010[47]	−0.295	0.369	0.136	0.428	−1.019	−0.800	.424
Lengacher et al, 2012[43]	−0.100	0.219	0.048	0.329	−0.530	−0.458	.647
Milbury et al, 2013[44]	−0.487	0.291	0.085	0.084	−1.058	−1.672	.095
Mustian et al, 2013[45]	−0.270	0.099	0.010	−0.076	−0.465	−2.731	.006
Nakamura et al, 2013[46]	−0.415	0.322	0.103	0.216	−1.045	−1.289	.197
Nakamura et al, 2013[46]	−1.107	0.347	0.120	−0.427	−1.786	−3.193	.001
Vadiraja et al, 2009[48]	−0.884	0.241	0.058	−0.411	−1.357	−3.663	.000
	−0.329	0.074	0.005	−0.184	−0.474	−4.445	.000



C. Long-Term Effect Size

Study	Hedges *g*	Standard error	Variance	Upper limit	Lower limit	*Z* Value	*P* Value
Bower et al, 2012[38]	−0.227	0.351	0.123	−0.915	0.462	−0.645	.519
Carson et al, 2009[39]	−0.466	0.340	0.115	−1.131	0.200	−1.371	.170
Chen et al, 2013[40]	−0.057	0.203	0.041	−0.454	0.340	−0.279	.780
Milbury et al, 2013[44]	−0.218	0.288	0.083	−0.783	0.346	−0.759	.448
Nakamura et al, 2013[46]	−0.320	0.320	0.103	−0.947	0.308	−0.998	.318
Nakamura et al, 2013[46]	−0.699	0.332	0.110	−1.349	−0.048	−2.105	.035
	−0.269	0.118	0.014	−0.499	−0.038	−2.280	.023



Abbreviation: MBIs = mind-body interventions.

Table 3. Moderator Analyses in Determining Various Moderator Effects

Parameter	k	Effect Size (*g*)	95% CI	*P*
Components of intervention				
Type of intervention				
Yoga	8	−0.40	−0.70 to −0.09	.71
Others[a]	8	−0.49	−0.77 to −0.19	
Requiring or encouraging home practice				
No	3	−0.16	−0.65 to 0.32	.23
Yes	13	−0.48	−0.70 to −0.27	
No. of treatment sessions	16	*B* = 0.003		.29
No. of treatment weeks	16	*B* = 0.05		.20
No. of treatment dose	16	*B* = 0.0002		.33
Subject characteristics				
Cancer type				
Breast cancer	10	−0.43	−0.68 to −0.17	.92
Others[b]	6	−0.45	−0.80 to −0.09	
Age	15	*B* = −0.03		.34
Percentage of women participants	16	*B* = 0.002		.76
Methodological considerations				
Sample size				
> 31	13	−0.45	−0.66 to −0.24	.51
≤ 30	3	−0.25	−0.81 to 0.30	
Type of control group				
Active	3	−0.55	−1.03 to −0.04	.63
Inactive	13	−0.41	−0.19 to −0.02	
Only individuals with sleep disturbance				
No	12	−0.42	−0.66 to −0.18	.82
Yes	4	−0.47	−0.89 to −0.06	
Sleep as the primary study outcome				
Yes	6	−0.38	−0.68 to −0.02	.71
No	10	−0.46	−0.71 to −0.20	
Quality of studies				
Allocation concealment				
High risk	10	−0.40	−0.14 to −0.66	.70
Low risk	6	−0.49	−0.14 to −0.83	
Blinding of outcome assessment				
High risk	13	−0.45	−0.23 to −0.66	.68
Low risk	3	−0.34	−0.13 to −0.80	

[a]Meditation, yoga, mindfulness-based stress reduction, mind-body bridging, and qigong.
[b]Gastrointestinal, gynecologic, lymphoproliferative disease, hematologic, endometrial, testicular, prostate, lung, melanoma, ependymoma, leukemia, kidney, skin carcinoma, brain, thyroid, and peritoneal cancer.
Abbreviation: CI = confidence interval.

of sympathetic activity.[49] A recent study revealed that the salivary α-amylase levels of cancer patients decline after they receive MBIs.[49] This finding provides partial evidence that MBIs may improve sleep by mitigating the stress response and eliciting the relaxation response. However, further investigation of this underlying mechanism is warranted.

The finding of moderator analysis on types of intervention revealed that both yoga and other types of intervention (ie, meditation, hypnosis, mindfulness-based stress reduction, and qigong) yield comparable effects on sleep among cancer patients. This finding contradicts the results derived from a previous meta-analysis in which no significant effect of yoga on sleep was observed in breast cancer patients,[23] but is consistent with a recent systematic review.[50] The conflicting findings could be because a relatively small number of trials were included in the previous meta-analysis.[23] The current meta-analysis included more RCTs and a larger sample size than the previous systematic review and meta-analysis did; thus, the finding in the present study provides further evidence to support the beneficial effects of MBIs on sleep in cancer patients.

The results also revealed that studies emphasizing home practice have achieved more substantial improvement in sleep quality than did those that have not emphasized home practice ($g = -0.48$ and $g = -0.16$, respectively). As behavioral change takes time to occur, additional practice sessions at home may help sustain and maintain behavioral change. In addition, models of behavioral change[51,52] should be considered as the basis of home practice. On the basis of this standpoint, future studies should consider behavioral changes and identify the determinants of behavioral changes (home practice) in cancer survivors, which could help clinicians and health care providers design specific intervention strategies for this population.

The results of this study support the notion that MBIs exert specific treatment effects on sleep because we discovered that the studies in which an active control (eg, sleep hygiene) was used achieved an effect size of −0.55, which is even larger than that of studies in which an inactive control was used ($g = -0.41$).

The present meta-analysis is subject to several limitations. Although we conducted a comprehensive review of the literature, the selection criteria necessarily limited the studies included for review, and the various methods used for conducting search strategies may have influenced the set of articles obtained. Moreover, publication bias was determined in the RCTs of MBIs used for improving sleep quality. Consequently, studies with minor or negative results could have been missed. Despite this limitation, the result of the trim and fill process indicated that MBIs yield moderate effects on the improvement of sleep quality.

This meta-analysis also contains several strengths. First, this meta-analysis included a large sample size. Second, the inclusion of only randomized controlled trials contributed to high internal validity.

In conclusion, by conducting the largest meta-analysis of RCTs to date, we confirmed that MBIs have a medium-size effect on the improvement of sleep quality among cancer patients and that a small-size effect can be maintained for up to 3 months. Therefore, we suggest that MBIs should be considered for inclusion as adjunctive or complementary therapies in the management of sleep problems experienced by cancer patients. In terms of moderator analyses, we did not find any significant moderator that could explain the heterogeneity among studies. To further investigate the moderating effect, more high quality RCTs are required. Because moderator variables that might help explain gradients in treatment effects in meta-analysis cannot be assumed to be statistically independent,[53,54] conclusions drawn from the present meta-analysis regarding what

characteristics would or would not affect treatment outcomes and what methodological characteristics would or would not bias study findings about those outcomes must be interpreted with caution.

Author affiliations: Graduate Institute of Nursing, College of Nursing, Taipei Medical University, Taipei (Drs Chiu, Miao, and Tsai and Ms Chiang); Sleep Science Center, Taipei Medical University Hospital, Taipei, and Department of Nursing, Wan Fang Hospital, Taipei Medical University, Taipei (Dr Tsai); and Department of Neurosurgery, Taipei Medical University Hospital, Taipei, Taiwan (Dr Lin).
Potential conflicts of interest: None reported.
Funding/support: This investigation was supported by a grant awarded to Dr Tsai by the National Science Council, Taiwan (NSC 102-2628-B-038-004-MY3) and the postdoctoral fellowship funding given to Dr Chiu by the National Science Council, Taiwan (NSC 102-2811-B-038-028).
Role of the sponsor: The sponsor had no role in the development of the study design, collection and management of the data, data analysis and interpretation, or manuscript approval.

REFERENCES

1. Berger AM, Farr LA, Kuhn BR, et al. Values of sleep/wake, activity/rest, circadian rhythms, and fatigue prior to adjuvant breast cancer chemotherapy. *J Pain Symptom Manage*. 2007;33(4):398–409.
2. Berger AM, Grem JL, Visovsky C, et al. Fatigue and other variables during adjuvant chemotherapy for colon and rectal cancer. *Oncol Nurs Forum*. 2010;37(6):E359–E369.
3. Palesh OG, Roscoe JA, Mustian KM, et al. Prevalence, demographics, and psychological associations of sleep disruption in patients with cancer: University of Rochester Cancer Center-Community Clinical Oncology Program. *J Clin Oncol*. 2010;28(2):292–298.
4. Savard J, Simard S, Blanchet J, et al. Prevalence, clinical characteristics, and risk factors for insomnia in the context of breast cancer. *Sleep*. 2001;24(5):583–590.
5. Savard J, Ivers H, Villa J, et al. Natural course of insomnia comorbid with cancer: an 18-month longitudinal study. *J Clin Oncol*. 2011;29(26):3580–3586.
6. Davidson JR, MacLean AW, Brundage MD, et al. Sleep disturbance in cancer patients. *Soc Sci Med*. 2002;54(9):1309–1321.
7. Mercadante S, Girelli D, Casuccio A. Sleep disorders in advanced cancer patients: prevalence and factors associated. *Support Care Cancer*. 2004;12(5):355–359.
8. Sela RA, Watanabe S, Nekolaichuk CL. Sleep disturbances in palliative cancer patients attending a pain and symptom control clinic. *Palliat Support Care*. 2005;3(1):23–31.
9. Romito F, Cormio C, De Padova S, et al. Patients attitudes towards sleep disturbances during chemotherapy [published online ahead of print August 16, 2013]. *Eur J Cancer Care (Engl)*.
10. Le Guen Y, Gagnadoux F, Hureaux J, et al. Sleep disturbances and impaired daytime functioning in outpatients with newly diagnosed lung cancer. *Lung Cancer*. 2007;58(1):139–143.
11. Koopman C, Nouriani B, Erickson V, et al. Sleep disturbances in women with metastatic breast cancer. *Breast J*. 2002;8(6):362–370.
12. Savard J, Morin CM. Insomnia in the context of cancer: a review of a neglected problem. *J Clin Oncol*. 2001;19(3):895–908.
13. Derogatis LR, Feldstein M, Morrow G, et al. A survey of psychotropic drug prescriptions in an oncology population. *Cancer*. 1979;44(5):1919–1929.
14. Savard J, Simard S, Ivers H, et al. Randomized study on the efficacy of cognitive-behavioral therapy for insomnia secondary to breast cancer, part 1: sleep and psychological effects. *J Clin Oncol*. 2005;23(25):6083–6096.
15. Espie CA, Fleming L, Cassidy J, et al. Randomized controlled clinical effectiveness trial of cognitive behavior therapy compared with treatment as usual for persistent insomnia in patients with cancer. *J Clin Oncol*. 2008;26(28):4651–4658.
16. Complementary, alternative, or integrative health: what's in a name? National Center for Complementary and Alternative Medicine. 2013. http://nccam.nih.gov/health/whatiscam. Updated May 2013. Accessed October 2, 2013.
17. Caudill M, Schnable R, Zuttermeister P, et al. Decreased clinic use by chronic pain patients: response to behavioral medicine intervention. *Clin J Pain*. 1991;7(4):305–310.
18. Morin CM, Hauri PJ, Espie CA, et al. Nonpharmacologic treatment of chronic insomnia: an American Academy of Sleep Medicine review. *Sleep*. 1999;22(8):1134–1156.
19. Lichstein KL, Riedel BW. Behavioral assessment and treatment of insomnia: a review with an emphasis on clinical application. *Behav Ther*. 1994;25(4):659–688.
20. Kozasa EH, Hachul H, Monson C, et al. Mind-body interventions for the treatment of insomnia: a review. *Rev Bras Psiquiatr*. 2010;32(4):437–443.
21. Morin CM, Culbert JP, Schwartz SM. Nonpharmacological interventions for insomnia: a meta-analysis of treatment efficacy. *Am J Psychiatry*. 1994;151(8):1172–1180.
22. Murtagh DR, Greenwood KM. Identifying effective psychological treatments for insomnia: a meta-analysis. *J Consult Clin Psychol*. 1995;63(1):79–89.
23. Zhang J, Yang KH, Tian JH, et al. Effects of yoga on psychologic function and quality of life in women with breast cancer: a meta-analysis of randomized controlled trials. *J Altern Complement Med*. 2012;18(11):994–1002.
24. Danhauer SC, Mihalko SL, Russell GB, et al. Restorative yoga for women with breast cancer: findings from a randomized pilot study. *Psychooncology*. 2009;18(4):360–368.
25. Chandwani KD, Thornton B, Perkins GH, et al. Yoga improves quality of life and benefit finding in women undergoing radiotherapy for breast cancer. *J Soc Integr Oncol*. 2010;8(2):43–55.
26. Kwekkeboom KL, Cherwin CH, Lee JW, et al. Mind-body treatments for the pain-fatigue-sleep disturbance symptom cluster in persons with cancer. *J Pain Symptom Manage*. 2010;39(1):126–138.
27. Moher D, Liberati A, Tetzlaff J, et al; PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Ann Intern Med*. 2009;151(4):264–269, W64.
28. Higgins J, Green S. *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.1.0. The Cochrane Collaboration, 2011. http://handbook.cochrane.org/. Updated March 2011. Accessed September 1, 2013.
29. DerSimonian R, Laird N. Meta-analysis in clinical trials. *Control Clin Trials*. 1986;7(3):177–188.
30. Higgins JP, Thompson SG, Deeks JJ, et al. Measuring inconsistency in meta-analyses. *BMJ*. 2003;327(7414):557–560.
31. Orwin RG. A fail-safe N for effect size in meta-analysis. *J Educ Stat*. 1983;8(2):157–159.
32. Begg CB, Mazumdar M. Operating characteristics of a rank correlation test for publication bias. *Biometrics*. 1994;50(4):1088–1101.
33. Egger M, Davey Smith G, Schneider M, et al. Bias in meta-analysis detected by a simple, graphical test. *BMJ*. 1997;315(7109):629–634.
34. Duval S, Tweedie R. Trim and fill: a simple funnel-plot-based method of testing and adjusting for publication bias in meta-analysis. *Biometrics*. 2000;56(2):455–463.
35. Lipsey M, Wilson D, eds. *Practical Meta Analysis*. Thousand Oaks, CA: Sage; 2001.
36. Elkins G, Marcus J, Stearns V, et al. Randomized trial of a hypnosis intervention for treatment of hot flashes among breast cancer survivors. *J Clin Oncol*. 2008;26(31):5022–5026.
37. Andersen SR, Würtzen H, Steding-Jessen M, et al. Effect of mindfulness-based stress reduction on sleep quality: results of a randomized trial among Danish breast cancer patients. *Acta Oncol*. 2013;52(2):336–344.
38. Bower JE, Garet D, Sternlieb B, et al. Yoga for persistent fatigue in breast cancer survivors: a randomized controlled trial. *Cancer*. 2012;118(15):3766–3775.
39. Carson JW, Carson KM, Porter LS, et al. Yoga of Awareness program for menopausal symptoms in breast cancer survivors: results from a randomized trial. *Support Care Cancer*. 2009;17(10):1301–1309.
40. Chen Z, Meng Z, Milbury K, et al. Qigong improves quality of life in women undergoing radiotherapy for breast cancer: results of a randomized controlled trial. *Cancer*. 2013;119(9):1690–1698.
41. Cohen L, Warneke C, Fouladi RT, et al. Psychological adjustment and sleep quality in a randomized trial of the effects of a Tibetan yoga intervention in patients with lymphoma. *Cancer*. 2004;100(10):2253–2260.
42. Dhruva A, Miaskowski C, Abrams D, et al. Yoga breathing for cancer chemotherapy-associated symptoms and quality of life: results of a pilot randomized controlled trial. *J Altern Complement Med*. 2012;18(5):473–479.
43. Lengacher CA, Reich RR, Post-White J, et al. Mindfulness based stress reduction in post-treatment breast cancer patients: an examination of symptoms and symptom clusters. *J Behav Med*. 2012;35(1):86–94.
44. Milbury K, Chaoul A, Biegler K, et al. Tibetan sound meditation for cognitive dysfunction: results of a randomized controlled pilot trial [published online ahead of print May 9, 2013]. *Psychooncology*.
45. Mustian KM, Sprod LK, Janelsins M, et al. Multicenter, randomized controlled trial of yoga for sleep quality among cancer survivors. *J Clin Oncol*. 2013;31(26):3233–3241.
46. Nakamura Y, Lipschitz DL, Kuhn R, et al. Investigating efficacy of two brief mind-body intervention programs for managing sleep disturbance in cancer survivors: a pilot randomized controlled trial. *J Cancer Surviv*. 2013;7(2):165–182.
47. Farrell-Carnahan L, Ritterband LM, Bailey ET, et al. Feasibility and preliminary efficacy of a self-hypnosis intervention available on the web for

cancer survivors with insomnia. *Electronic J Appl Psychol*. 2010;6(2):10–23.
48. Vadiraja SH, Rao MR, Nagendra RH, et al. Effects of yoga on symptom management in breast cancer patients: a randomized controlled trial. *Int J Yoga*. 2009;2(2):73–79.
49. Lipschitz DL, Kuhn R, Kinney AY, et al. Reduction in salivary α-amylase levels following a mind-body intervention in cancer survivors—an exploratory study. *Psychoneuroendocrinology*. 2013;38(9):1521–1531.
50. Mustian KM. Yoga as treatment for insomnia among cancer patients and survivors: a systematic review. *EMJ Oncol*. 2013;1:106–115.
51. Prochaska JO, Velicer WF, Rossi JS, et al. Stages of change and decisional balance for 12 problem behaviors. *Health Psychol*. 1994;13(1):39–46.
52. Ryan P. Integrated theory of health behavior change: background and intervention development. *Clin Nurse Spec*. 2009;23(3):161–170; quiz 171-162.
53. Thompson SG, Higgins JP. How should meta-regression analyses be undertaken and interpreted? *Stat Med*. 2002;21(11):1559–1573.
54. Lipsey MW. Those confounded moderators in meta-analysis: good, bad, and ugly. *Ann Am Acad Pol Soc Sci*. 2003;587(1):69–81.