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A Meta-Analysis Of Sleep-Promoting Interventions During Critical Illness

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Abstract

Background—Sleep quality and quantity are severely reduced in critically ill patients receiving mechanical ventilation with potential for adverse consequences. Our objective was to synthesize the randomized controlled trials (RCTs) that measured the efficacy of sleep-promoting interventions on sleep quality and quantity in critically ill patients.

Methods—We included RCTs that objectively measured sleep with electroencephalography or its derivatives and excluded observational studies and those that measured sleep by subjective reports. The research was performed according to PRISMA guidelines.

Results—Of 6,022 studies identified, 13 studies met eligibility criteria involving 296 critically-ill patients. Eight trials looked at different modes of mechanical ventilation as sleep interventions, and the remaining five involved pharmacological, non-pharmacological, or environmental interventions. Meta-analysis of the studies revealed that sleep-promoting interventions improved sleep quantity (pooled standardized mean of differences [SMD] 0.37, 95%CI: 0.05, 0.69; P=0.02) and sleep quality through reduction in sleep fragmentation (SMD −0.31; 95%CI −0.60, −0.01; P=0.04). Subgroup analysis revealed that timed-modes of ventilation improved sleep quantity when compared to spontaneous-modes of ventilation (SMD 0.45, 95%CI 0.10, 0.81; P=0.01). Non-mechanical ventilation interventions tended to improve sleep quantity (SMD 0.65; 95%CI; −0.03, 1.33; P=0.06) and tended to reduce sleep fragmentation (SMD −0.29; 95% CI −0.61, 0.03; P=0.07).

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Conflict of Interest: Drs. Chithra Poongkunran, Santosh G. John, Arun S. Kannan, Safal Shetty, MD and Christian Bime, MD do not have any conflicts of interest to disclose.

Authorship credit: Conceived and designed the experiments (CP, SGJ, ASK, SS, SP), Analyzed the data (CP, SGJ, ASK, SS, SP), Interpretation of data (CP, SGJ, ASK, SS, CB, SP), contributed reagents/materials/analysis tools (CP, SGJ, ASK, SS, CB, SP), drafted the article or revised it critically for important intellectual content (CP, SGJ, ASK, SS, CB, SP), final approval of the version to be published (CP, SGJ, ASK, SS, CB, SP). Sairam Parthasarathy, MD [Corresponding author] had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Conclusions—The synthesized evidence suggests that both mechanical ventilation and non-mechanical ventilation-based therapies improve sleep quantity and quality in critically ill patients but the clinical significance is unclear. In the future, adequately-powered multi-center RCTs involving pharmacological interventions to promote sleep in critically ill patients are warranted.

MeSH terms

sleep; critical illness; artificial respiration; Hypnotics and Sedatives; polysomnography; critical care; Positive-Pressure Respiration

Introduction

Sleep quality and quantity are severely reduced in critically ill patients with potential for adverse consequences[1–5]. In critically ill patients, lack of sleep may contribute to delirium and agitation and in healthy volunteers cause immune dysregulation and negative nitrogen balance[4,6–8]. In community-dwelling participants, lack of sleep has been associated with all-cause mortality[9–15]. Although abnormalities of sleep are extremely common in critically ill patients, the mechanisms are not well understood[4]. Intervention-based studies in critically ill patients can elucidate the mechanistic basis of sleep derangements and are direly needed. However, there is a paucity of such intervention-based mechanistic studies for sleep promotion in critically ill patients due to the arduous nature of conducting such intervention-based experiments; difficulties in surrogate consenting; and collecting electroencephalography signals in an artefact-ridden intensive care unit (ICU) environment[4]. Even the few randomized controlled trials (RCTs) of sleep in the ICU are limited by small sample size. Nevertheless, they were rigorous in study-design and conduct while exploring the effect of mechanical ventilation, pharmacological, environmental, and other non-pharmacological interventions on sleep in critically ill patients[16–19]. A meta-analysis, by combining such smaller RCTs could increase the overall power to estimate the efficacy of sleep promoting interventions during critical illness. Such an undertaking could help us better understand the mechanistic underpinnings of sleep derangements during critical illness, and ultimately inform future adequately-powered trials aimed at improving sleep and consequent patient-outcomes in critically ill patients.

Our primary objective was to synthesize the RCTs that measured the efficacy of sleep-promoting interventions on sleep quality and quantity in critically ill patients. Our secondary objective was to understand the treatment effects of sleep-promoting interventions that were categorized by mechanical ventilation versus other interventions.

Methods

Data source and searches

We conducted an electronic search of the literature in Medline, Cochrane central, Dynamed from 1966 to August 2014. We then updated the search in October 2014. We used a combination of MESH subheadings and keywords (sleep, sleep interventions, critical illness, mechanical ventilation, randomized controlled trials). We used “sleep AND critical illness” “sleep AND mechanical ventilation” “sleep interventions AND mechanical ventilation”

"sleep interventions AND critical illness" as well the above four combinations with "OR randomized controlled trials" with exploded search terms. We limited the entire list to studies published until October 2014 but there were no limits to age of the studies. We reviewed the bibliographies of the included studies and previous reviews to identify additional citations. The research was guided by an extraction protocol that followed PRISMA guidelines (Preferred Reporting Items for Systematic Reviews and Meta-Analyses)[20].

Definitions

Operational definitions of outcome variables were as follows: (a) Sleep quantity was defined as sleep efficiency which is time spent asleep expressed as a percentage of total recording time. (b) Sleep quality was defined as sleep fragmentation measured as arousals and awakenings per hour of sleep. (c) Information of proportion of time spent in various sleep stages were also extracted when available and proportioned into various non-rapid eye movement (stage N1, N2, slow wave sleep) and rapid eye movement (REM) sleep. Explanatory variables were interventions that were categorized into changes (or intervention) made to mechanical ventilation (mode of ventilation), pharmacological therapy (sedatives type or infusion method), environmental (noise reduction or music), non-pharmacological (such as massage) interventions.

Eligibility criteria

We included intervention-based studies if they were RCTs and objectively measured sleep in critically ill patients. We excluded observational studies and those that measured sleep without electroencephalography (EEG) or its derivatives. *A priori* we decided not to include articles that measured sleep through subjective reports, nursing assessments, or actigraphy due to known reservations about their test characteristics[21]. We included Bispectral index or fast fourier transformation of EEG signals because such automatically processed signals have good reproducibility characteristics and that there was a paucity of RCTs in this area of study identified through an iterative process[22]. The search was limited to RCTs that were published in English and studied human subjects.

Data extraction and quality assessment

One study team member (CP) reviewed all included papers (n=13) and abstracted all of the relevant data from them into formatted Windows Excel database. To validate the abstraction process, the other two study team members (SGJ, ASK) each reviewed a randomly selected sample so that at least two study members had abstracted each included paper. A third study member (SP) reviewed extracted data from all of the papers in order to identify differences in the abstraction between previous abstractions and resolve discrepancies by consensus. Data were extracted from each selected article using formatted Windows Excel database. Disagreement between the extracting investigators was resolved by consensus. We rated the study quality using United States Preventive Services Task Force (USPTF) criteria (Table 1)[23].

Data synthesis and analysis

We conducted a meta-analysis assuming random effects on sleep quantity and quality that provided enough detail to calculate standardized mean differences (SMD; n= 13) (RevMan, Version 5.3.5 Copenhagen, Denmark). Two studies had three study arms each and therefore the comparisons of the experimental groups versus the control or usual group were used and identified as such. Sensitivity analysis by both including and excluding the duplicate representation of the control (or usual care) arms of these two studies were performed. Considering that some of the studies reported medians and inter-quartile range, we calculated standard deviation from the inter-quartile range and used the median as the mean[24].

Risk for bias in individual studies was assessed by gauging selection bias (random sequence generation and allocation concealment), performance bias (blinding of participants), detection bias (outcome assessors), attrition bias (incomplete outcome data), and selective reporting or other bias. Risk for bias across studies (publication bias) was performed by making funnel plots and using the Begg and Mazumdar test[25] (SPSS version 22, IBM SPSS, Armonk, NY). We also performed meta-analysis of subgroups involving studies that employed mechanical ventilation versus non-mechanical ventilation interventions, timed versus spontaneous mode of ventilation, and performed sensitivity analysis by including and excluding studies with large effect size that may be unduly influencing the meta-analysis.

Results

Of the 6,022 studies that were screened and assessed for eligibility, 29 studies were included in the qualitative analysis that eventually yielded 13 RCTs (with 296 patients) which were then included in the meta-analysis (Figure 1; PRISMA compliant flow-diagram). All of the 13 studies qualified as level I according to USPTF hierarchy of study design[23]. Eight trials looked at different modes of mechanical ventilations as sleep-promoting interventions, and the remaining five involved pharmacological, non-pharmacological, or environmental interventions[16,19,26–37]. For each of the 13 RCTs, patient characteristics, intervention, comparators, outcomes, and study design are provided in Table 1. The risk of bias within each study is provided in Table 2.

Sleep-promoting interventions, that was mediated by changes to mechanical ventilation or other sleep promotion therapies (environmental, pharmacological, or non-pharmacological), increased sleep quantity as measured by sleep efficiency (figure 2). There was high heterogeneity among these studies (I^2 = 62%; P=0.0007). Sensitivity analysis performed by removal of study by Oto 2011[19] removed the heterogeneity (I^2=26%; P=0.17) but did not materially change the results (SMD 0.26, 95% CI 0.03, 0.49; P=0.02). Sleep-promoting interventions improved sleep quality by reducing sleep fragmentation (figure 3). There was moderate heterogeneity among these studies (I^2 =49%; P=0.02). Sensitivity analysis performed by removal of study by Parthasarathy 2002[32] significantly reduced heterogeneity (I^2=0%; P=0.98), but did not materially change the results (SMD −0.19, 95% CI −0.39, 0.02; P=0.08).

Subgroup and sensitivity analysis

Change to mechanical ventilation modes in eight RCTs tended to improve sleep quantity by increasing sleep efficiency (figure 4). There was no heterogeneity among these studies (P=0.11). Change in mechanical ventilation modes tended to improve sleep quality by decreasing sleep fragmentation (figure 5). There was significant heterogeneity among these studies (I^2=68%). Sensitivity analysis performed by removal of study by Parthasarathy 2002 significantly reduced heterogeneity (I^2=0%; P=0.98) but made the results for improvement in sleep quality non-significant (P=0.43).

Subgroup comparison of four RCTs that compared timed versus spontaneous modes of ventilation was undertaken (figure 6 and 7). Timed-mode of mechanical ventilation improved sleep quantity when compared to spontaneous mode of ventilation (figure 6). There was no heterogeneity among these studies (I^2=12%; P=0.3). Timed-mode of mechanical ventilation did not influence sleep quality measured as sleep fragmentation (figure 7). There was significant heterogeneity among these studies (I^2 = 87%; P<0.0001). Sensitivity analysis performed by removal of one study Parthasarathy 2002[32] did not change the results materially.

Subgroup comparison of five RCTs that compared environmental, pharmacological or non-pharmacological methods to promote sleep was undertaken (figure 8 and 9; Table 1). Non-mechanical ventilation-based interventions improved sleep quantity. There was significant heterogeneity among these studies (figure 8). Removal of one study Oto 2011[19] removed the heterogeneity (I^2=10%; P=0.35), but did not change the results significantly (SMD 0.32, −0.01, 0.65; P=0.06). Non-mechanical ventilation-based interventions tended to improve sleep quality (figure 9). There was significant heterogeneity among these studies.

There were two studies (Cabello 2008 and Richards 1998) that had three arms in the RCT[16,33]. In the presented comparisons, for each study, the control arms were included twice. Sensitivity analysis was performed by removing these studies from the meta-analysis. Such sensitivity analysis did not materially change the results. Furthermore, stratification of results by proportion of time spent in various sleep stages (stage N1, N2, slow wave sleep, REM) revealed small effects on slow wave sleep (web-only supplementary material [eTable 1]).

Assessment of bias

By *a priori* design, we only chose RCTs for this meta-analysis. Therefore the within study bias was minimal (Table 2). Bias across studies was assessed by funnel plots (figure 10). There was no evidence for publication bias assessed by Begg and Mazumdar's test[25] (Kendall's tau b=0.12; P=0.52).

Discussion

To our knowledge this is the first meta-analysis that assessed the efficacy of sleep-promotion in critically ill patients. Several general observations of the main findings can be made. First, sleep-promoting interventions improved both sleep quantity and quality in critically ill patients, but the effect size was small with heterogeneity across studies. Second,

both mechanical ventilation-based as well as non-mechanical ventilation-based interventions improved sleep quantity and quality in critically ill patients, but the effect size of non-mechanical ventilation appeared to be larger than that of mechanical ventilation-based interventions. Third, timed-mode of mechanical ventilation improved sleep quantity when compared to spontaneous mode of ventilation. Fourth, the sleep-promoting interventions were heterogeneous in nature requiring us to collapse the interventions by mechanistic approach (such as mechanical ventilation, environmental, pharmacological and non-pharmacological interventions). Fifth, although the studies were of good quality with low risk for bias within such studies (table 2), these studies were limited by small sample size and generalization was limited due to lack of any multi-center studies. Sixth, although sleep quality and quantity are important outcomes, these RCTs did not uniformly focus on the effect of sleep on other important patient outcomes – such as delirium, duration of hospitalization, or mortality – despite the existence of sound rationale for such a potential impact[9–14,18,38–40]. Lastly, there was no evidence for publication bias across studies (figure 10).

Sleep quality and quantity are severely reduced in critically ill patients with potential for adverse consequences[1–5]. In community-dwelling participants, poor sleep quantity and quality due to chronic insomnia has been independently associated with all-cause and cardiopulmonary mortality[9–14]. Some of the mechanistic basis for such an association may be mediated by systemic inflammation[14]. Such a mechanistic pathway is supported by controlled experiments in healthy volunteers that revealed elevation in pro-inflammatory cytokines following sleep loss[41]. Although, there is rich evolving body of work on the effect of sleep quality and quantity on well-being in ambulatory patients and population-based studies, there is a paucity of sleep research in critically ill patients. Conceivably, critically ill patients may be even more susceptible to the harmful effects of poor sleep than ambulatory patients and community-dwelling participants. In our meta-analysis, we were able to find only 13 small RCTs conducted prior to October 2014 that undertook rigorous sleep measurement methodology without any time restrictions to the age of these studies. A paucity of such intervention-based mechanistic studies for sleep promotion in critically ill patients may be due to the arduous nature of conducting such intervention-based studies in critically ill patients[4]. Even these RCTs of sleep in the ICU were limited by small sample size in individual studies with a maximum of 24 patients per study arm. Nevertheless, they were rigorous in study-design and measurement methodology while they explored the effect of mechanical ventilation, pharmacological, environmental, and other non-pharmacological interventions on sleep in critically ill patients[16–19]. Our meta-analysis, by combining 13 such smaller RCTs increased the overall power to estimate the efficacy of sleep-promoting interventions during critical illness with a cumulative sample size of 296 critically ill patients. Such an undertaking was quite revealing and we discuss the findings here along with caveats and other limitations.

Sleep-promoting interventions improved both sleep quantity and quality in critically ill patients, but the effect size was small and heterogeneous. We performed sensitivity analysis to reduce the heterogeneity and found that sleep quantity and to some extent sleep quality is indeed modifiable in critically ill patients. We noticed that the effect size although small, was relatively larger for non-mechanical ventilation-based interventions than mechanical

ventilation-based approaches for promoting sleep, with pharmacological interventions manifesting the *greatest* effect size. We were limited by the heterogeneous nature of the sleep-promoting interventions but handled this problem by performing subgroup analysis by mechanistic approach of the sleep interventions. This is a limitation of our study, but again highlights the need for a uniform intervention in a larger adequately powered study. An additional observation was the lack of sufficient head-to-head studies of sedative agents in improving sleep quantity and quality. Additionally, the critically ill patient sub-populations were heterogeneous and variably involved patients with exacerbations of chronic obstructive pulmonary disease, heart failure, Acute Respiratory Distress Syndrome, or pneumonia. Considering the greater effect of non-mechanical ventilation-based interventions, the lack of head-to-head studies of pharmacological agents, and inhomogeneous patient population and interventions, there is clearly an identifiable knowledge gap for performing RCTs with pharmacological interventions (with active control group) to promote sleep quality and quantity in a homogenous group of critically ill patients.

In subgroup analysis, timed mode of ventilation was better than spontaneous mode of ventilation in improving sleep quantity and quality in critically ill patients (figures 6 and 7). This is in line with findings in ambulatory patients with sleep-disordered breathing who manifested better sleep quality with a back-up respiratory rate due to reduction in respiratory events and improvement in pattern of breathing[29]. Despite the small number of studies in this sub-group analysis, the findings were homogeneous. Future studies that test other non-mechanical ventilation based interventions need to control for such a potential confounder.

In conclusion, sleep promoting-interventions, both timed mode of mechanical ventilation and non-mechanical ventilation-based therapies, can improve sleep quantity and quality in critically ill patients but the effect size was small and heterogeneous with unclear clinical significance. We believe that these findings provide rationale for performing larger, multi-center, adequately-powered trials for promoting sleep in critically ill patients. Specifically, there is identifiable knowledge gap for performing a pharmacological intervention (with active control group) to promote sleep quality and quantity in a homogenous group of critically ill patients. Such studies should be adequately powered to measure important patient-outcomes that are mechanistically downstream to sleep – such as delirium, systemic inflammation, duration of hospitalization, or even mortality – while carefully measuring the mediating effects of sleep.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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patent UA 14-018 U.S.S.N. 61/884,654; PTAS 502570970 (Home breathing device) pending. The above-mentioned conflicts including the patent are unrelated to the topic of this paper.

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Clinical Significance

Sleep-promoting interventions improved sleep quantity in critically ill patients.

Timed-modes improved sleep quantity when compared to spontaneous-modes of ventilation

Effect size of sleep promotion interventions was small and heterogeneous in the critically ill.

Effect size of non-mechanical ventilation was larger than mechanical ventilation-based interventions.

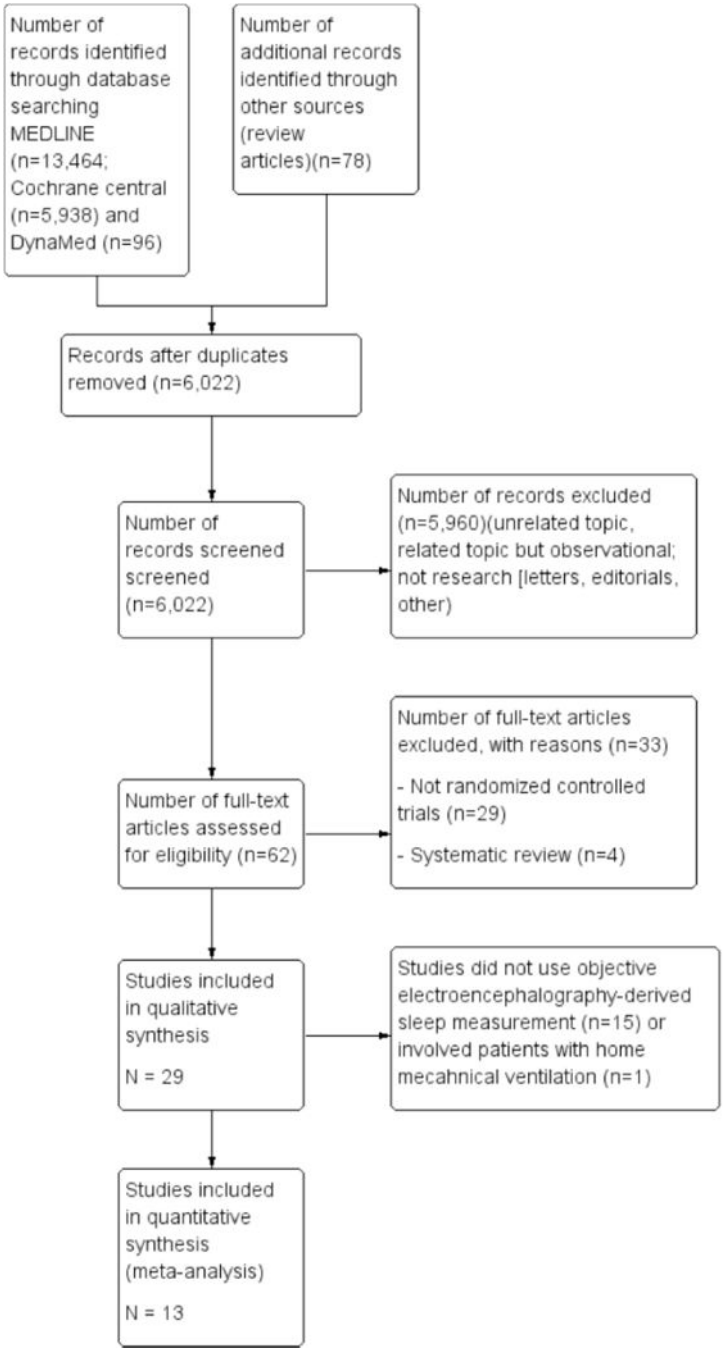


Figure 1.

PRISMA compliant flow chart summarizing the number of abstracts and papers reviewed and the reasons for excluding them from the meta-analysis.

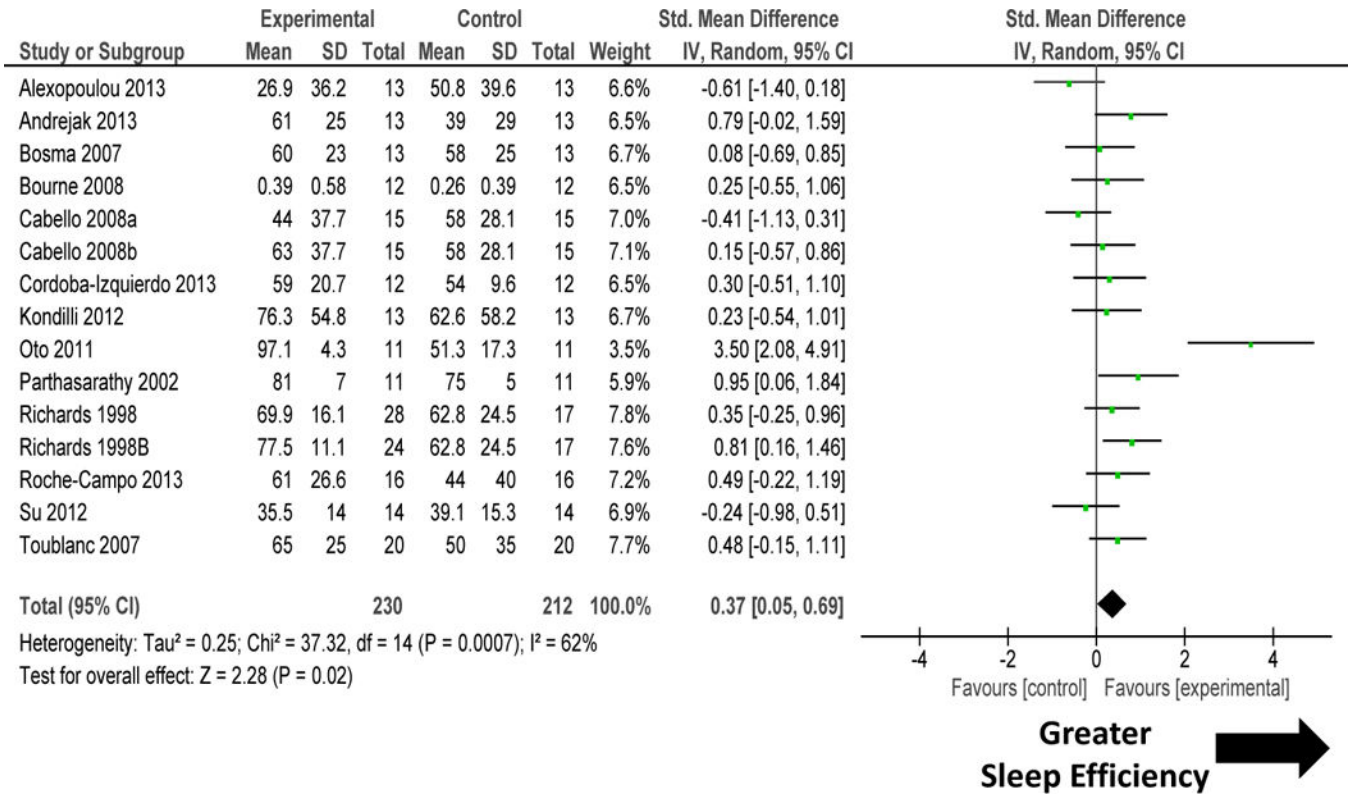


Figure 2.

Forest plot for sleep efficiency during sleep-promoting intervention (mechanical ventilation and non-mechanical ventilation). The size of the box reflects the study's relative weight based on the standard error. The diamond indicates the 95 percent confidence interval of the summary estimate. Sleep promotion interventions improved sleep efficiency in the 13 randomized controlled trials. There was high heterogeneity among these studies (I^2 =62%). Sensitivity analysis performed by removal of study by Oto 2011[19] did not materially change the results (SMD 0.26, 95% CI 0.03, 0.49; P=0.02) but significantly reduced heterogeneity (I^2=26%).

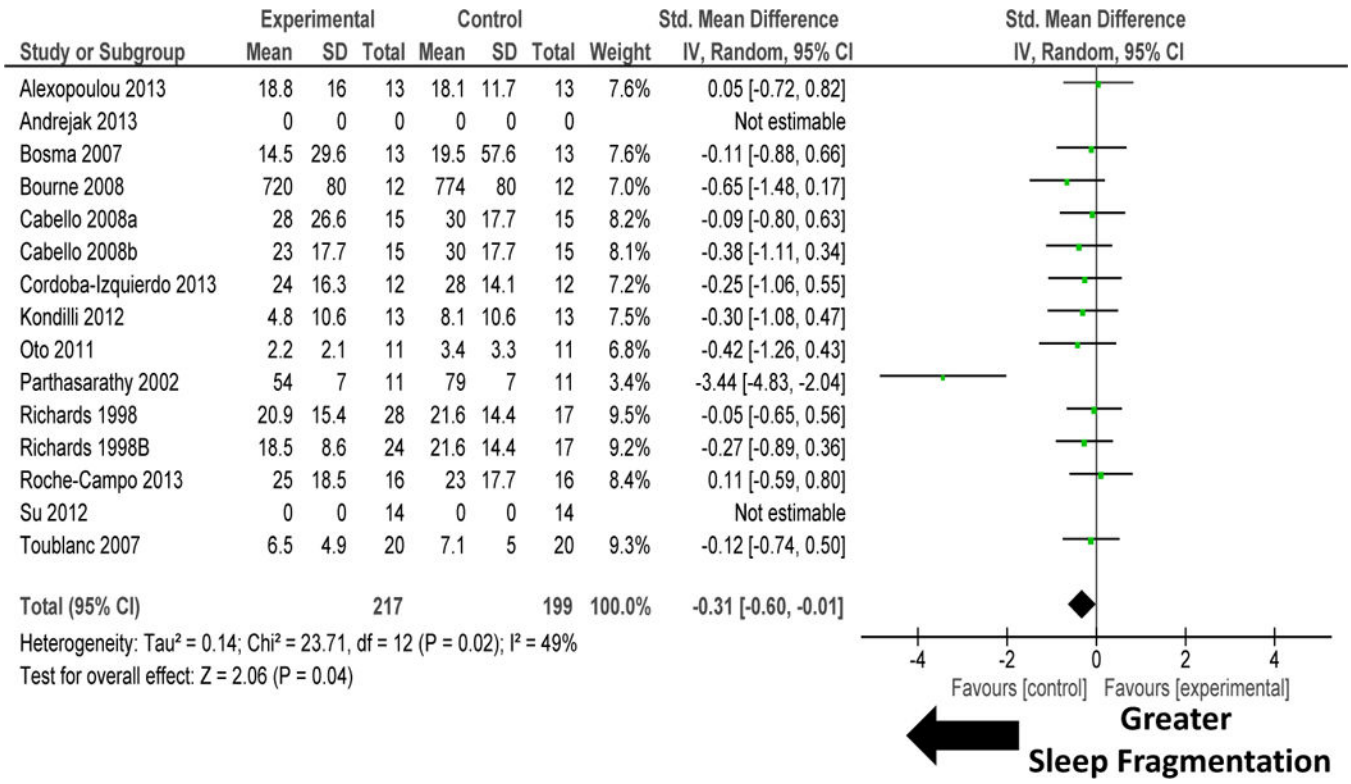


Figure 3.

Forest plot for sleep fragmentation (arousals and awakenings) during sleep-promoting intervention (mechanical ventilation and non-mechanical ventilation). Sleep promotion interventions improved sleep quality through reduction in sleep fragmentation in the 13 randomized controlled trials. There was moderate heterogeneity among these studies (I^2 = 49%). Sensitivity analysis performed by removal of study by Parthasarathy 2002[32] did not materially change the results (SMD −0.19, 95% CI −0.39, 0.02; P=0.08) but significantly reduced heterogeneity (I^2=0%). Explanation of symbols is provided in legend of figure 2.

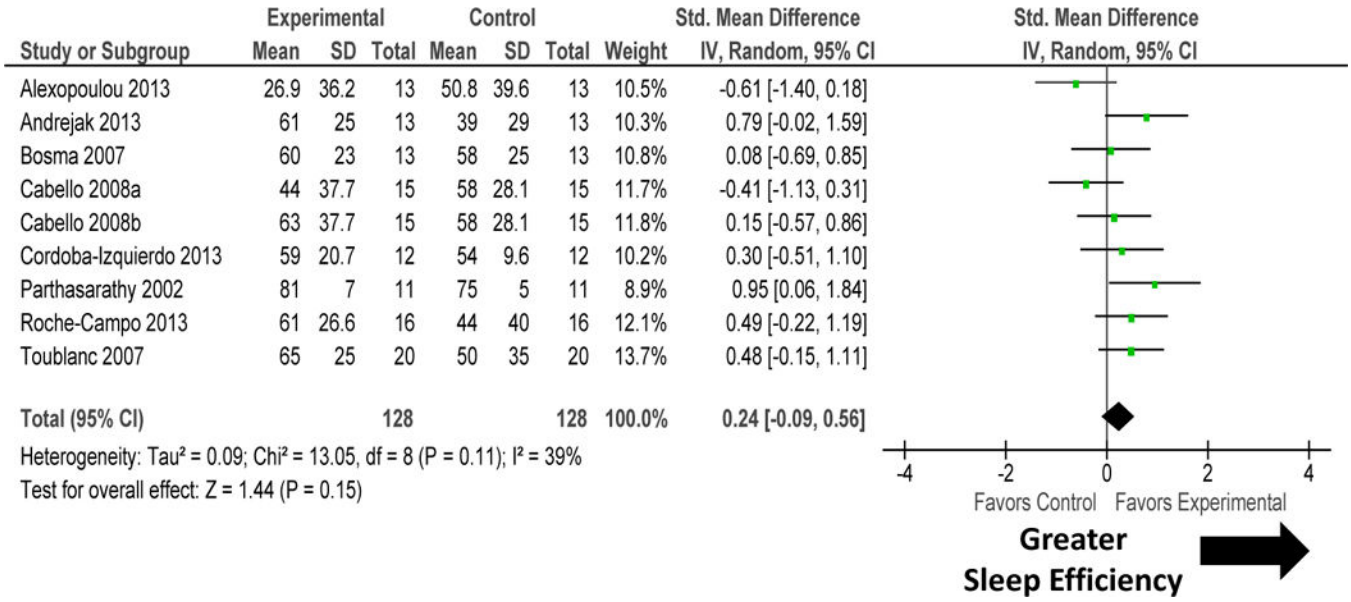


Figure 4.

Forest plot for sleep efficiency during intervention accomplished by adjusting mechanical ventilation modality. Change in mechanical ventilation modes tended to improve sleep quantity by increasing sleep efficiency. There was no heterogeneity among these studies. Explanation of symbols is provided in legend of figure 2.

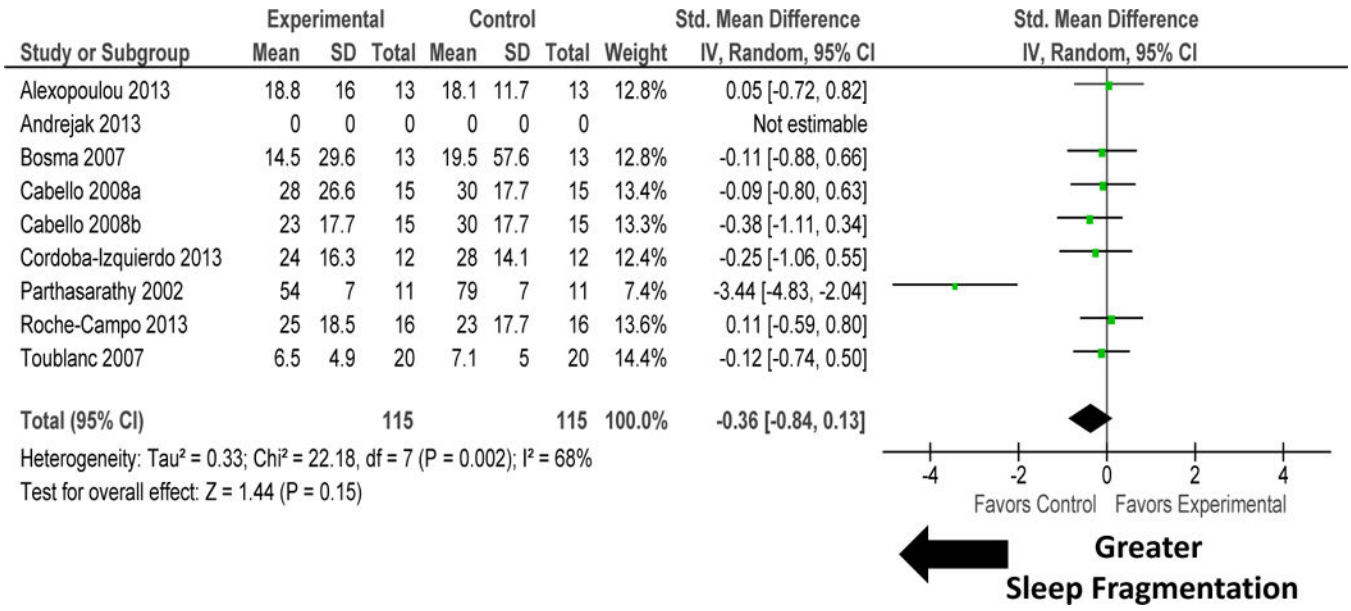


Figure 5.

Forest plot for sleep fragmentation during intervention accomplished by adjusting mechanical ventilation modality. Change in mechanical ventilation modes tended to improve sleep quality by decreasing sleep fragmentation. There was significant heterogeneity among these studies. Sensitivity analysis performed by removal of study by Parthasarathy 2002[32] made the results non-significant (P=0.43) and significantly reduced heterogeneity (I^2=0%; P=0.98). Explanation of symbols is provided in legend of figure 2.

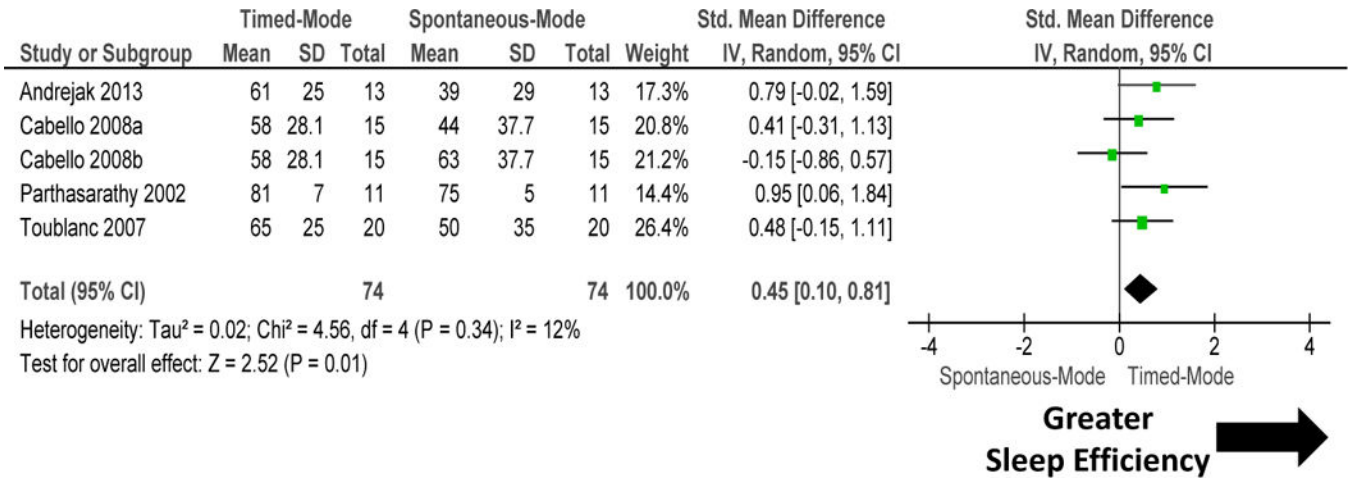


Figure 6.

Forest plot for sleep efficiency during intervention accomplished by timed versus spontaneous modes of mechanical ventilation. Timed-mode of mechanical ventilation improved sleep quantity when compared to spontaneous mode of ventilation. There was no heterogeneity among these studies (I^2 =12%). Explanation of symbols is provided in legend of figure 2.

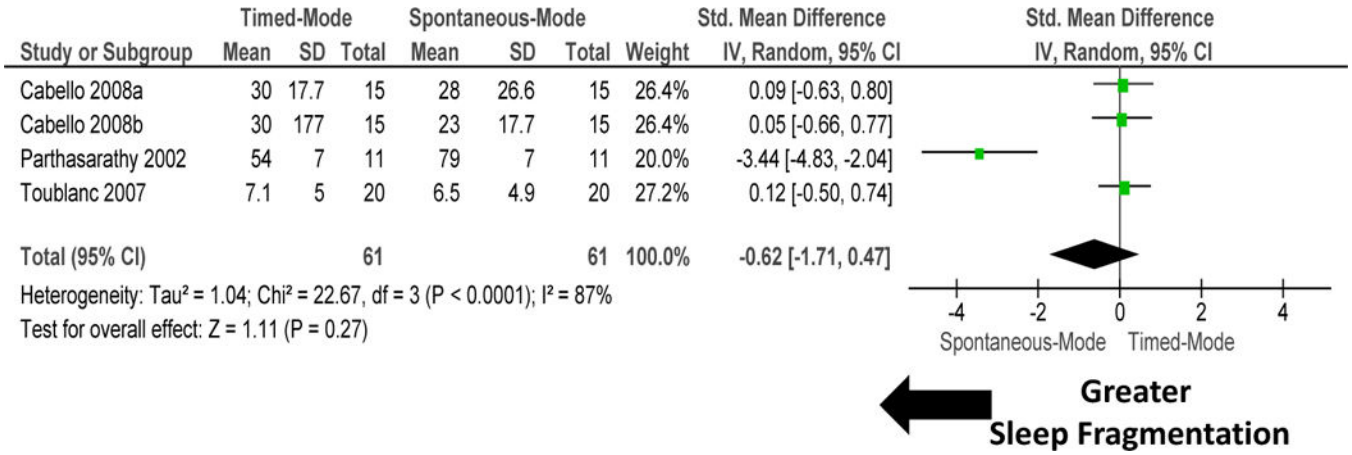


Figure 7.

Forest plot for sleep fragmentation during intervention accomplished by timed versus spontaneous modes of mechanical ventilation. Timed-mode of mechanical ventilation did not improve sleep quality measured as sleep fragmentation. There was significant heterogeneity among these studies (I^2 =87%). Sensitivity analysis performed by removal of one study by Parthasarathy 2002[32] did not change the results materially. Explanation of symbols is provided in legend of figure 2.

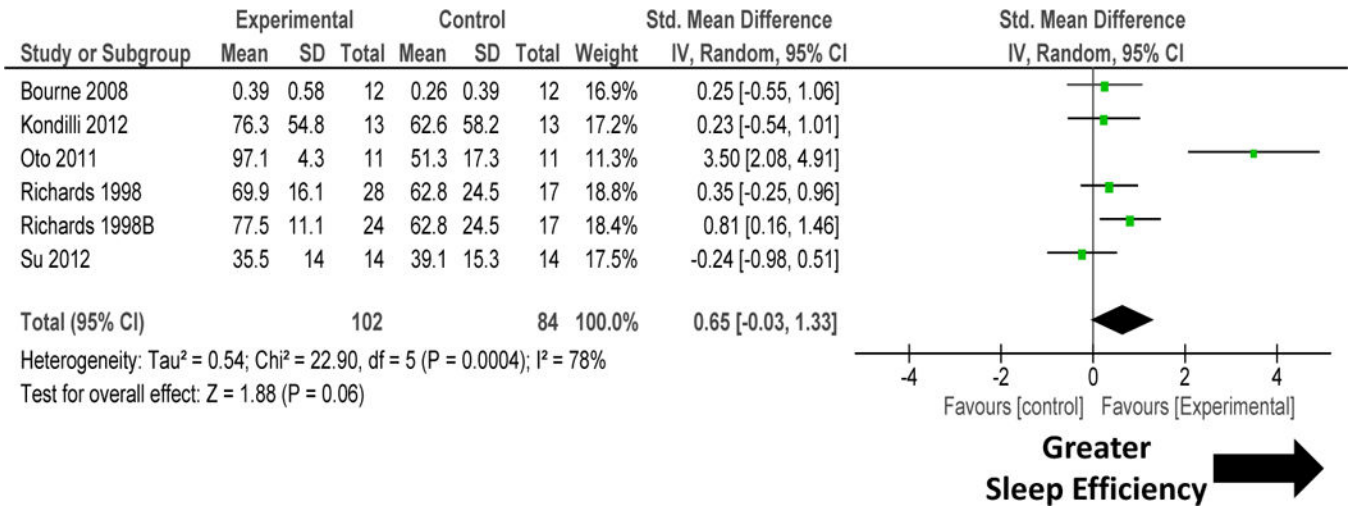


Figure 8.

Forest plot for sleep quantity during non-mechanical ventilation-based interventions that included pharmacological, non-pharmacological, or environmental interventions. Non-mechanical ventilation-based interventions improved sleep quantity. There was significant heterogeneity among these studies. Explanation of symbols is provided in legend of figure 2.

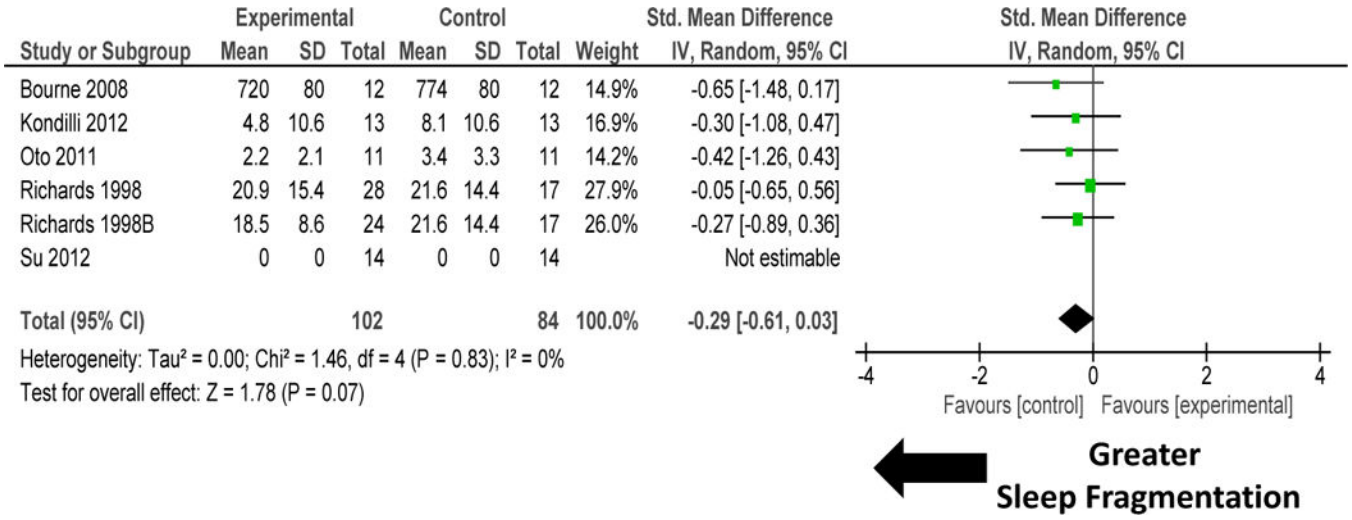


Figure 9.

Forest plot for sleep fragmentation during non-mechanical ventilation-based interventions that included pharmacological, non-pharmacological, or environmental interventions. Non-mechanical ventilation-based interventions improved sleep quality by reducing sleep fragmentation. There was no heterogeneity among these studies ($I^2 = 0\%$). Explanation of symbols is provided in legend of figure 2.

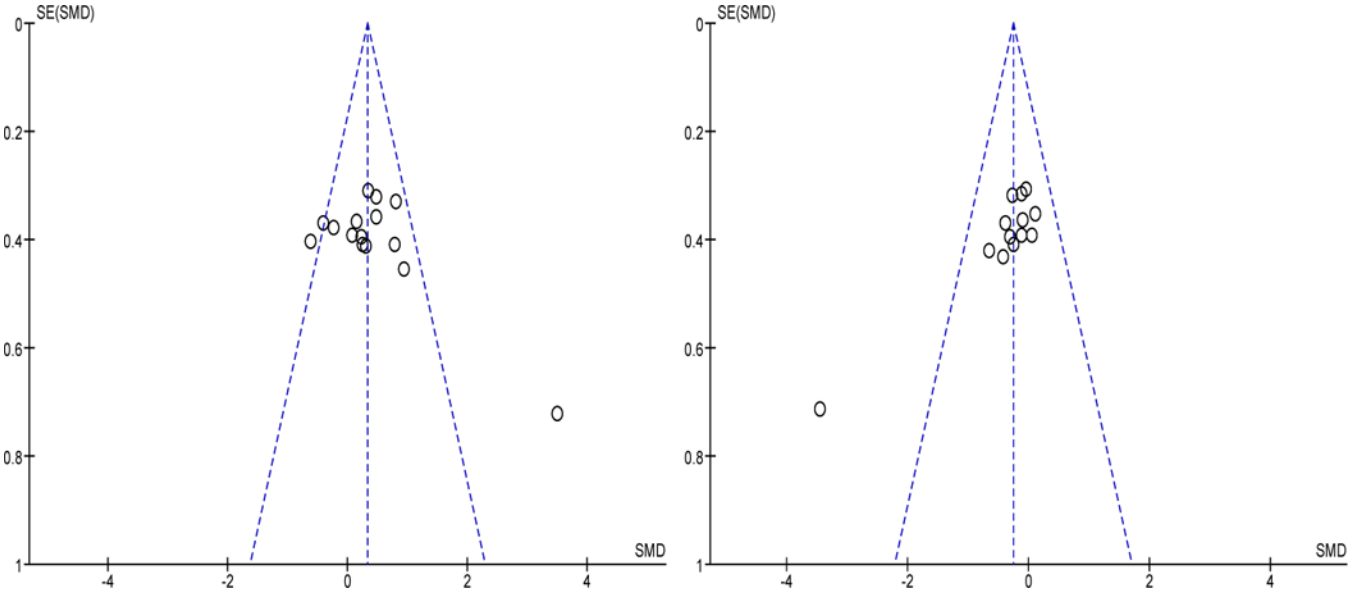


Figure 10.

Funnel plots for sleep efficiency (left panel) and sleep fragmentation (right panel) during sleep-promoting interventions. There was no evidence for publication bias.

Table 1

Studies Assessing Sleep-promoting Interventions in Critically ill Patients

Study	Quality scores*	Study design	Participants	Intervention	Control	Outcome measure	Comment
Alexopoulou 2013[26]	I	RCT, cross-over	Intubated, COPD, n=13	PAV	PSV	PSG-derived Sleep efficiency Sleep fragmentation index	PAV failed to improve sleep in mechanically ventilated patients
Andrejak 2013[37]	I	RCT, cross-over	Intubated; n=35 (n=9 discarded)	PCV	PSV	PSG-derived Sleep efficiency Sleep fragmentation index	Sleep quantity and quality were significantly improved with PCV compared to low-PSV
Bosma 2007[27]	I	RCT, cross-over	Intubated; n=16 (n=3 discarded)	PAV	PSV	PSG-derived Sleep efficiency Sleep fragmentation index	PAV resulted in fewer patient-ventilator asynchronies and better sleep quality.
Bourne 2008[28]	I	RCT	Tracheostomized patients undergoing weaning (n=24)	Melatonin (10 mg)	Placebo	Bispectral index (time spent <80; sleep efficiency); area under curve (sleep quality)	Melatonin use was associated with increased nocturnal sleep efficiency over 4 nights
Cabello 2008[16]	I	RCT, cross over, 3 arms	Intubated and tracheostomized patients (n=15)	Clinically adjusted PSV (Cabello 2008a) or automatically adjusted PSV (Cabello 2008b)	ACV	PSG-derived Sleep efficiency Sleep fragmentation index	The ventilatory mode did not influence sleep pattern, arousals and awakenings.
Cordoba-Izquierdo 2013[30]	I	RCT	Non-invasive ventilation; n=25 (n=1 discarded)	Dedicated ICU ventilator	Conventional noninvasive ventilator	PSG-derived (Sleep efficiency and Sleep fragmentation index)	There were no observed differences in sleep quality corresponding to the type of ventilator used despite slight

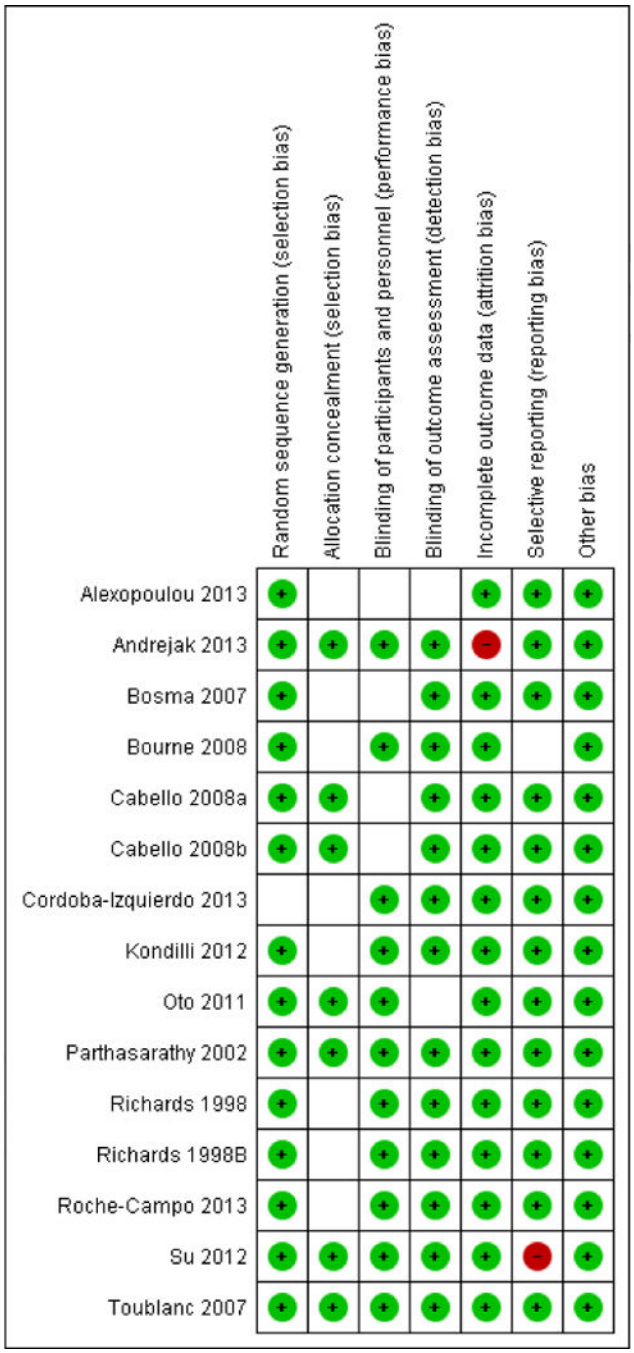
Study	Quality scores*	Study design	Participants	Intervention	Control	Outcome measure	Comment
							differences in patient–ventilator as differences in patient–ventilator as differences in patient–ventilator as differences in patient–ventilator as
Kondilli 2012[31]	I	RCT, cross-over	Invasive ventilation; n=13 (n=1 discarded)	Propofol	No propofol	PSG-derived (Sleep efficiency and Sleep fragmentation index)	In critically ill patients ventilated on assisted modes, propofol administration to achieve the recommended level of sedation suppresses the REM sleep stage and further worsens the poor sleep quality of these patients.
Oto 2011[19]	I	RCT	Invasive ventilation; n=22	Continuous infusion	Daily interruption of sedation	PSG-derived (Sleep efficiency and Sleep fragmentation index)	In the continuous infusion group, sleep efficiency was greater and sleep fragmentation was lower when compared to group with daily sedation interruption.
Parthasarathy 2002[32]	I	RCT, cross-over	Intubated patients, n=11	ACV	PSV	PSG-derived (Sleep efficiency and Sleep fragmentation index)	PSV was associated with sleep fragmentation when compared to ACV
Richards 1998[33]	I	RCT, cross-over, 3 arms	Critically ill men admitted to ICU (n=71); 2 subjects were excluded	Two of 3 arms back massage (n=24)	Usual care (n=17)(Richa rds 1998) or music & relaxation (n=28)(Richa rds 2008b)	PSG-derived (Sleep efficiency and Sleep fragmentation index)	Back massage was useful in promoting sleep in critically ill older men

Study	Quality scores*	Study design	Participants	Intervention	Control	Outcome measure	Comment
Roche-Campo 2013[34]	I	RCT, cross-over	Tracheostomized patients undergoing weaning from mechanical ventilation (n=16)	PSV	Spontaneous ventilation (control)	PSG-derived (Sleep efficiency and Sleep fragmentation index)	Sleep quality was similar with or without the ventilator. Sleep quantity was higher during mechanical ventilation.
Su 2012[35]	I	RCT	28 patients in a medical ICU	Music therapy	Usual care	PSG-derived sleep efficiency (sleep fragmentation was not measured)	Greater amount of slow wave sleep in the music group
Toublanc 2007[36]	I	RCT, cross-over	Intubated patients (n=22) (2 patients were discarded)	ACV	PSV	PSG-derived (Sleep efficiency and Sleep fragmentation index)	ACV was significantly associated with a better sleep quality than those recorded during PSV

PAV = proportional assist ventilation; PSV = pressure support ventilation; COPD = chronic obstructive pulmonary disease; RCT = randomized controlled trial; PSG = polysomnography; ICU = Intensive care unit. USPTF Hierarchy of research design with range of I, II-1, II-2, II-3, and III (with I being best and defined as, “Evidence obtained from at least one properly randomized controlled trial”).

Table 2

Risk of Bias Summary



Green symbols signify low risk for bias, blank spaces signify unclear risk for bias, and red symbols signify high risk for bias. Last name of first author and year of publication are provided. See table 1 for PICOS information and reference number for the publications.