fluid. Several recent consensus statements and guidelines, as well as the Centers for Medicare and Medicaid Services (management bundle NQF 0500), called for individualized fluid titration, based on the assessment of fluid responsiveness, to ensure patients receive the right amount of fluid at the right time (13, 14). Several methods are now available to easily and quickly predict fluid responsiveness at the bedside: the assessment of PPV (or surrogate parameters) and the assessment of changes in stroke volume or of changes in PPV during PLR or a fluid challenge (Fig. 1). These methods have limitations (6, 7) but are complementary. They offer clinicians the opportunity to raise standards for fluid management, improve quality of care, and decrease healthcare costs at the same time (15).

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Earplugs, Sleep Improvement, and Delirium: A Noisy Relationship*

John W. Devlin, PharmD, FCCM
Division of Pulmonary, Critical Care and Sleep Medicine
Tufts Medical Center, School of Pharmacy
Northeastern University
Boston, MA

Gerald L. Weinhouse, MD
Division of Pulmonary and Critical Care Medicine
Brigham and Women's Hospital
Boston, MA

Delirium occurs frequently during critical illness and is associated with negative outcomes both during the ICU admission and after ICU discharge; prevention efforts during the period of critical illness are therefore essential (1). The occurrence of delirium is dependent on a complex interplay between predisposing and precipitating risk factors (2). Efforts to reduce the burden of delirium should be focused on risk factor reduction and proven nonpharmacologic interventions such as early mobilization (3).

Sleep disruption is common in the ICU and has been hypothesized to be a risk factor for delirium (4). Cognitive dysfunction, alterations of cerebral perfusion and cortical metabolism, and circadian rhythm disturbances are common to both delirium and sleep deprivation (4, 5). Critically ill patients frequently report poor sleep as one of their worst memories and an important source of stress and anxiety (6). Thus, sleep promotion has been identified as a potential strategy for reducing the prevalence of ICU delirium and improving patients' ICU quality of life (7).

One such strategy for sleep promotion has been noise reduction. Noise levels in modern ICUs far exceed World Health Organization requirements and may be associated with sleep disturbances (8). In this issue of *Critical Care Medicine*, Litton et al (9) report the result of a systematic review of studies that evaluated the efficacy of nocturnal ear plug placement as a strategy to reduce delirium in the ICU. Across five studies

*See also p. 992.

Key Words: delirium; ear protective devices; intensive care; noise; prevention; sleep

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(n = 832 participants), earplug placement was associated with a significant reduction in delirium prevalence (relative risk, 0.59 [95% CI, 0.44–0.78]). This difference was similar between randomized and nonrandomized trials and between studies that evaluated earplugs alone versus those that evaluated earplugs as part of a multifaceted sleep protocol. Although the risk of bias was high for all five studies, heterogeneity between the studies for this outcome was low. Overall compliance with ear plug use was high, and no safety concerns were detected.

One interesting finding from this meta-analysis, and other systematic reviews that have evaluated sleep-promoting interventions in the ICU, is that although delirium is consistently reduced, improvements in sleep quality are not (9–11). It may be that we are simply unable to detect small differences in sleep quality and quantity, whether clinically relevant, with our current diagnostic armamentarium—especially those assessment tools based on patient self-reporting (12). So it is still possible that these patients will sleep better with the use of earplugs and other similar interventions; we just have not been able to prove it yet.

Even if earplugs truly do not improve the sleep of the critically ill, they may still have a valuable role in reducing anxiety and minimizing sedative use. The addition of music to noise cancelling strategies like earplugs, for example, may be even more beneficial than noise cancelling strategies alone. In one large multicenter randomized study, music therapy administered via noise-cancelling headphones reduced patient anxiety and sedative use more than noise-cancelling headphones without music (13). Unfortunately, neither sleep quality nor delirium was reported in this investigation.

Should earplugs be applied to all ICU patients? Some ICU patients may not like having earplugs placed. And without reminders, nurses might forget to take them out leading to prolonged periods where a patient would be more disconnected from their environment and thus more susceptible to delirium. Patients enrolled in earplug or noise-cancelling head phone studies have generally been relatively awake and able to self-report pain and anxiety; little evidence exists to support earplug use in patients who are sicker or who require deeper levels of sedation (14).

Earplugs may have a role in sleep promotion for select ICU patients who self-report delayed sleep onset and in whom an opportunity to improve "the opportunity for sleep" is identified by bedside clinicians. But with our current technology, it will take large randomized controlled trials that control for confounders, manage patients with an ABCDEF bundle approach (i.e., Assess, prevent, and manage pain; Both spontaneous awakening trials and spontaneous breathing trials; Choice of analgesia and sedation; Delirium assess, prevent, and manage; Early-mobility and exercise; and Family engagement and empowerment), and are large enough to evaluate delirium-related outcomes to clearly define the role of earplugs in the ICU (1, 3, 15).

What seems most important in all this, however, is that there is a growing movement away from the reflex to give mind-altering substances to fix a mind-altering problem (sometimes due to the mind-altering substances in the first place) in favor of a more holistic approach to healing characterized by more judicious use of medications, early mobilization, and environmental control. If this movement continues, we could have a substantial impact on our patients' ICU course and potentially their post-ICU recovery. If that occurs, we should all be able to sleep better.

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The Efficacy of Earplugs as a Sleep Hygiene Strategy for Reducing Delirium in the ICU: A Systematic Review and Meta-Analysis*

Edward Litton, MBChB, FCICM, MSc[1,2]; Vanessa Carnegie, MBBS[3]; Rosalind Elliott, RN, PhD[4]; Steve A. R. Webb, MBBS, FRACP, FCICM, MPH, PhD[5,6]

Objective: A systematic review and meta-analysis to assess the efficacy of earplugs as an ICU strategy for reducing delirium.

Data Sources: MEDLINE, EMBASE, and the Cochrane Central Register of controlled trials were searched using the terms "intensive care," "critical care," "earplugs," "sleep," "sleep disorders," and "delirium."

Study Selection: Intervention studies (randomized or nonrandomized) assessing the efficacy of earplugs as a sleep hygiene strategy in patients admitted to a critical care environment were included. Studies were excluded if they included only healthy volunteers, did not report any outcomes of interest, did not contain an intervention group of interest, were crossover studies, or were only published in abstract form.

Data Extraction: Nine studies published between 2009 and 2015, including 1,455 participants, fulfilled the eligibility criteria and were included in the systematic review. Studies included earplugs as an isolated intervention ($n = 3$), or as part of a bundle with eye shades ($n = 2$), or earplugs, eye shades, and additional sleep noise abatement strategies ($n = 4$). The risk of bias was high for all studies.

Data Synthesis: Five studies comprising 832 participants reported incident delirium. Earplug placement was associated with a relative risk of delirium of 0.59 (95% CI, 0.44–0.78) and no significant heterogeneity between the studies (I^2, 39%; $p = 0.16$). Hospital mortality was reported in four studies ($n = 481$) and was associated with a relative risk of 0.77 (95% CI, 0.54–1.11; I^2, 0%; $p < 0.001$). Compliance with the placement of earplugs was reported in six studies ($n = 681$). The mean per-patient noncompliance was 13.1% (95% CI, 7.8–25.4) of those assigned to receive earplugs.

Conclusions: Placement of earplugs in patients admitted to the ICU, either in isolation or as part of a bundle of sleep hygiene improvement, is associated with a significant reduction in risk of delirium. The potential effect of cointerventions and the optimal strategy for improving sleep hygiene and associated effect on patient-centered outcomes remains uncertain. (*Crit Care Med* 2016; 44:992–999)

Key Words: delirium; ear-protective devices; ICUs; noise; sleep

*See also p. 1022.

[1]Department of Intensive Care Medicine, St John of God Hospital Subiaco, Subiaco, WA, Australia.

[2]School of Medicine and Pharmacology, University of Western Australia, Crawley, WA, Australia.

[3]Department of Intensive Care Medicine, Fiona Stanley Hospital, Murdoch, Perth, WA, Australia.

[4]Department of Intensive Care Medicine, Faculty of Health, University of Technology Sydney, Sydney, NSW, Australia.

[5]Department of Intensive Care Medicine, Royal Perth Hospital, Perth, WA, Australia.

[6]School of Medicine and Pharmacology, University of Western Australia, Crawley, WA, Australia.

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For information regarding this article, E-mail: ed.litton@health.wa.gov.au; ed_litton@hotmail.com

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Sleep disruption impairs physical, immunologic, and neurocognitive function (1–4). As a consequence of both acute illness and the environment, sleep disruption is common in critically ill patients admitted to ICU and is associated with the development of delirium and poor psychologic recovery (5–7). Even in normal healthy volunteers, sustained sleep disruption results in impaired cognition (4, 8). Imaging studies in sleep disruption demonstrate changes in cerebral perfusion and metabolism of the prefrontal cortex, thalamus, and posterior parietal cortex that are similar to those seen in delirium (9, 10).

Delirium is common in ICU and is associated with prolonged mechanical ventilation, prolonged ICU and hospital length of stay, impaired cognitive outcomes, and increased mortality and costs (11–14). Noise is a potentially modifiable risk factor that may contribute to sleep disruption and the occurrence of delirium. As a consequence, excessive noise may have an adverse

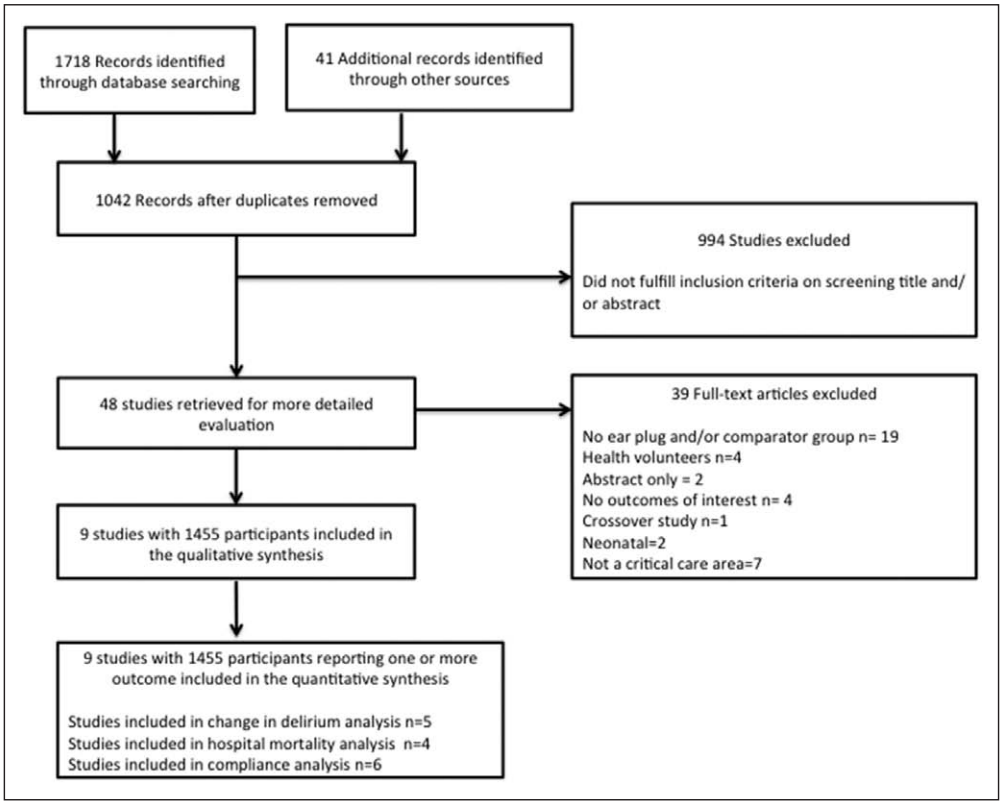

Figure 1. Derivation of studies.

impact on patient-centered outcomes. Patients frequently cite noise as a main contributor to sleep disruption, and noise levels in hospital are high and may be increasing over time (15, 16).

Whether noise abatement with earplugs reduces sleep disruption, delirium, and other adverse consequences in patients admitted to ICU is uncertain. We undertook a systematic review and meta-analysis, the primary aim of which was to assess the efficacy of earplugs as an ICU strategy for reducing delirium. The secondary aims were to assess the compliance with a policy of earplugs use and to assess the effect of earplugs on ICU and hospital length of stay, ICU and hospital mortality, sleep quality, earplug safety, and costs.

METHODS

The study was undertaken according to a prespecified analysis plan and Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (17). A complete PRISMA 2009 checklist is provided in **Supplementary Appendix 1** (Supplemental Digital Content 1, http://links.lww.com/CCM/B576).

Eligibility Criteria

We searched for interventional studies (randomized or nonrandomized), assessing the efficacy of earplugs as a sleep hygiene strategy in patients admitted to a critical care environment. Studies were excluded if they included only healthy volunteers, did not report any outcomes of interest, did not contain an intervention group of interest, were crossover studies, or were only published in abstract form. The primary outcome of interest was delirium. The secondary outcomes of interest were ICU and hospital length of stay, ICU and hospital mortality, validated sleep survey questionnaire responses, total sleep time (TST) and efficiency measured by polysomnography or actigraphy, compliance with a policy of earplug placement, and cost-effectiveness.

Search Strategy

The primary search was conducted using MEDLINE, EMBASE, and the Cochrane Central Register of controlled trials using the terms "intensive care," "critical care," "earplugs," "sleep," "sleep disorders," and "delirium." The initial search included the time period between 1966 and May 2015 and was conducted without language restrictions. The search was updated in July 2015 but did not identify any additional studies for inclusion. We searched the reference lists of all the included studies as well as relevant review articles. Where relevant, study authors were contacted for clarification or further data. The search was conducted separately by two authors (E.L., V.C.). A copy of the entire MEDLINE search terms is provided in **Supplementary Appendix 2** (Supplemental Digital Content 2, http://links.lww.com/CCM/B577).

Study Selection

The titles for all articles from the search were reviewed, and full-text articles from potentially relevant abstracts were retrieved for assessment of eligibility. Data from all included studies were transcribed independently by two authors (E.L., V.C.) into a prespecified proforma, with disagreement resolved by consensus.

Data Analysis

The primary outcome of interest was the efficacy of earplugs in reducing the relative risk (RR) of incident delirium. Prespecified outcomes with at least three studies with relevant endpoints were pooled for meta-analysis using a random-effects model. RR and standardized mean difference for categorical and continuous variables were used. The 95% CIs were calculated for the point estimate of all pooled outcome variables with a p value of less than 0.05 taken as significant. Heterogeneity was assessed using the I^2 statistic, and an I^2 greater than 40% was considered as significant heterogeneity. The risk of bias for the included studies was assessed using established validity assessment tools for randomized controlled trials and nonrandomized intervention studies (18, 19). Where sufficient study numbers contributed to the pooled analysis, sensitivity

TABLE 1. Description of Characteristics and Outcomes of Studies Included in the Systematic Review

Name	Year	*n*	Study Type	Setting	Intervention	Cointervention
Chlan et al (20)	2013	373	RCT	Mixed ICU	Three-arm study including patient-directed music therapy arm, noise-cancelling headphone arm, and control arm	No cointervention used in the two arms included (noise-cancelling headphones and control)
Foreman et al (21)	2015	12	RCT	Neurosurgical ICU	Passive noise-cancelling headphones (noise reduction rating 30 dB) or soft foam earplugs	Fabric eye covers and melatonin
Hu et al (22)	2015	50	RCT	Cardiothoracic ICU	Earplugs from 3 d prior to scheduled cardiac surgery (9 PM till next morning)	Eye masks from 3 d prior to scheduled surgery, relaxing music twice daily for 30 min
Jones and Dawson (23)	2012	100	Before/after	Single-center mixed ICU	Earplugs	Eye mask
Kamdar et al (24)	2013	300	Before/after	Medical ICU	Earplugs	Eye mask, soothing music, environmental intervention
Le Guen et al (25)	2013	46	RCT	Surgical postanesthesia care unit	Earplugs	Eye mask
Patel et al (26)	2014	338	Before/after	Mixed ICU	Earplugs	Eye mask, environmental stimulus reduction
Scotto et al (27)	2009	100	RCT	Two mixed ICUs	Earplugs	No cointervention
Van Rompaey et al (28)	2012	136	RCT	Mixed ICU	Earplugs	No cointervention

LOS = length of stay, RCT = randomized controlled trial, RCSQ = Richards-Campbell Sleep Questionnaire.

analyses were planned examining the efficacy of the intervention in studies with a low reported risk of bias and studies examining earplugs as a stand-alone intervention. Publication bias was assessed by funnel plot and the statistical analysis conducted using STATA (SE version 13; StataCorp, College Station, TX).

RESULTS

The primary electronic search returned 1,718 citations. After screening titles and abstracts, 48 were retrieved for full-text examination. A total of nine studies, published between 2009 and 2015, and including 1,455 adult participants, fulfilled the eligibility criteria and were included in the systematic review (20–28). All nine studies provided outcome data suitable for inclusion in one or more aggregate analysis. We received no additional data from contacted authors. The flow chart of study inclusion is presented in **Figure 1**.

Study Characteristics and Validity Assessment

Of the nine studies included in the systematic review, five were RCTs with between 12 and 373 participants and four were nonrandomized, interventional studies with between 100 and 338 participants. Earplugs were studied as an isolated intervention in three studies and were part of a bundle with eye shades alone (two studies) or earplugs, eye shades, and additional sleep noise abatement strategies (four studies). A summary of the included studies is provided in **Table 1**. The risk of bias was high for all studies. The results of the validity assessment are shown in **Table 2**.

Quantitative Data Synthesis

Efficacy of Earplugs in Reducing Delirium. A total of five studies comprising 832 participants reported incident delirium. Earplug placement was associated with a RR of 0.59 (95% CI, 0.44–0.78) (**Fig. 2**). Heterogeneity between the studies was measured using I^2 (39%; $p = 0.16$), and the results were not substantially different comparing randomized and nonrandomized trials (Fig. 2). On sensitivity analysis, the results were also not substantially different when comparing earplugs alone (28) to earplugs as part of a bundle of sleep hygiene (21, 24–26) (RR, 0.58; 95% CI, 0.40–0.85; and RR, 0.56; 95% CI, 0.35–0.90, respectively). Equally, the results were similar when the association between earplug use and delirium was assessed using a fixed-effects model (RR, 0.59; 95% CI, 0.50–0.70). The funnel plot assessing the risk of publication bias for the five included studies is provided in **Supplementary Appendix Figure 1** (Supplemental Digital Content 3, http://links.lww.com/CCM/B578).

Efficacy of Earplugs in Reducing Hospital Mortality. Hospital mortality was reported in four studies ($n = 481$). Overall, earplug placement was associated with an RR of 0.77 (95% CI, 0.54–1.11), with no significant heterogeneity between studies (I^2, 0%; $p < 0.001$) (**Fig. 3**).

Outcomes Measures							
Delirium	Survey	Polysomnography or Actigraphy	ICU LOS	Hospital LOS	ICU Mortality	Hospital Mortality	Compliance	Other
Yes						Yes (30-d mortality)	Yes	Anxiety, sedation intensity, and sedation frequency
Yes		Yes				Yes		
	Yes (RCSQ)		Yes	Yes		Yes	Yes	Nocturnal melatonin and cortisol
			Yes				Yes	
Yes	Yes (RCSQ)				Yes	Yes		
Yes	Yes (Medical Outcomes Study Sleep scale)	Yes					Yes	Pain control
Yes	Yes (RCSQ)		Yes					Noise and light levels
	Yes (Verran-Snyder-Halpern Sleep Scale)						Yes	
Yes								

Compliance With Earplugs Placement. Compliance with the placement of earplugs was reported in six studies ($n = 681$). The mean, per-patient, noncompliance was 13.1% (95% CI, 7.8–25.4) of those assigned to receive earplugs. Reasons for noncompliance were variably and incompletely cited and included intolerance of earplugs, earplugs falling out, or the intervention being abandoned due to clinical need.

Outcomes With Insufficient Data for Quantitative Synthesis. Only two studies, by Kamdar et al (24) and Patel et al (26), evaluated the impact of earplugs on delirium burden. Both studies found a significant improvement associated with earplugs in delirium-/coma-free days (272 [43%] before vs 339 [48%] after; $p = 0.04$) and time spent in delirium (3.4 d [SD, 1.4 d] before vs 1.2 d (SD, 0.9 d) after; $p = 0.02$), respectively.

A variety of different validated and unvalidated sleep surveys were used in the included studies. The most common validated survey was the Richardson Campbell Sleep Questionnaire, which was used in three studies (22, 24, 26). Hu et al and Patel et al found earplugs to be associated with substantial improvement in self-reported sleep as measured by the Richards-Campbell Sleep Questionnaire, whereas Kamdar et al found self-reported sleep to be similar between the two groups. Heterogeneity was high (I^2 99%; $p < 0.01$); therefore, the pooled results have not been reported.

Only two studies attempted to objectively measure TST (21, 25). Le Guen et al (25) measured TST using actigraphy and found a TST over the first postoperative night of 319 minutes (SD, 147) in those receiving earplugs compared with 253 minutes (SD, 129) in those randomized to care without earplugs. Foreman et al (21) attempted to measure TST using polysomnography, however, found that only 2 of 12 patient recordings could not be scored according to accepted criteria. No studies reported any safety issues with the placement of earplugs.

DISCUSSION

In this study, implementation of a sleep hygiene intervention including placement of earplugs in patients admitted to the ICU was associated with a significant reduction in risk of delirium. Compliance with earplug placement was high, and no studies reported any safety concern associated with the intervention. Several previous reviews have reported on the effect of sleep improvement strategies in the critical care setting (29, 30). Our study expands on the existing reviews, providing a quantified, pooled estimate of treatment effect on clinically important endpoints including delirium and mortality.

Sleep disruption is nearly universal in critically ill patients. However, earplugs are not included in any set of guidelines for patient care in the ICU. As a safe and simple intervention, our findings suggest that earplugs may have a broad role in

TABLE 2. Risk of Bias for Studies Included in the Systematic Review

Name	Random Sequence Generation	Allocation Concealment	Blinding of Participants and Personnel	Blinding of Outcome Assessment	Incomplete Outcome Data	Selective Reporting	Other Bias
Chlan et al (20)	Low; computer generated	Low; computer generated	High; research nurses not blinded to intervention	Unclear	High; only 241 of 373 included in the anxiety analysis	Unclear	Low
Foreman et al (21)	Low	Unclear	High	High	High; unable to measure total sleep time in nearly half of enrolled patients; only aggregate data reported	Low	Low
Hu et al (22)	Unclear	Unclear	High	Unclear	High	High	Low
Jones and Dawson (23)	High; prestudy and poststudy	High; prestudy and poststudy	High	High	Unclear	High; convenience sample used	Unclear; unvalidated data collection tool
Kamdar et al (24)	High	High	High	High	High	High	High
Le Guen et al (25)	Unclear; randomization was performed on admission	Low; sealed envelopes	High	High	High	Unclear	Low
Patel et al (26)	High; prestudy and poststudy	High; prestudy and poststudy	High	High	High; 59 of 338 completed questionnaire	Low	Low
Scotto et al (27)	Unclear	Unclear	High	High	High; 100 patients randomized, but only 88 included in analysis	High	Unclear, results only presented as *t* tests, absolute numbers of respondents unclear
Van Rompaey et al (28)	Low; computer program	Unclear; assignment by an independent nurse researcher	Unclear	Unclear	High; variable follow-up beyond first night	Unclear	Unclear; calibration and discrimination of Neecham scale compared with other delirium measures uncertain

improving sleep hygiene through noise abatement in critically ill patients. Earplugs use in the ICU represents a potentially ubiquitous therapy and, as such, is perhaps best tested and applied as a policy implemented at the unit level, with integration of sleep hygiene as part of the general care of critically ill patients (31).

Our study did not find a significant difference in hospital mortality associated with earplug use. However, the number of patients with fatal outcomes included in the meta-analysis was relatively small, and the confidence limit around the point estimate was wide. An improvement in mortality is plausible and cannot be excluded on the basis of this analysis but would require a trial with sufficient size to detect small but clinically significant differences in mortality.

The primary aim of the study was to assess the efficacy of earplugs in the ICU setting. In a number of the included

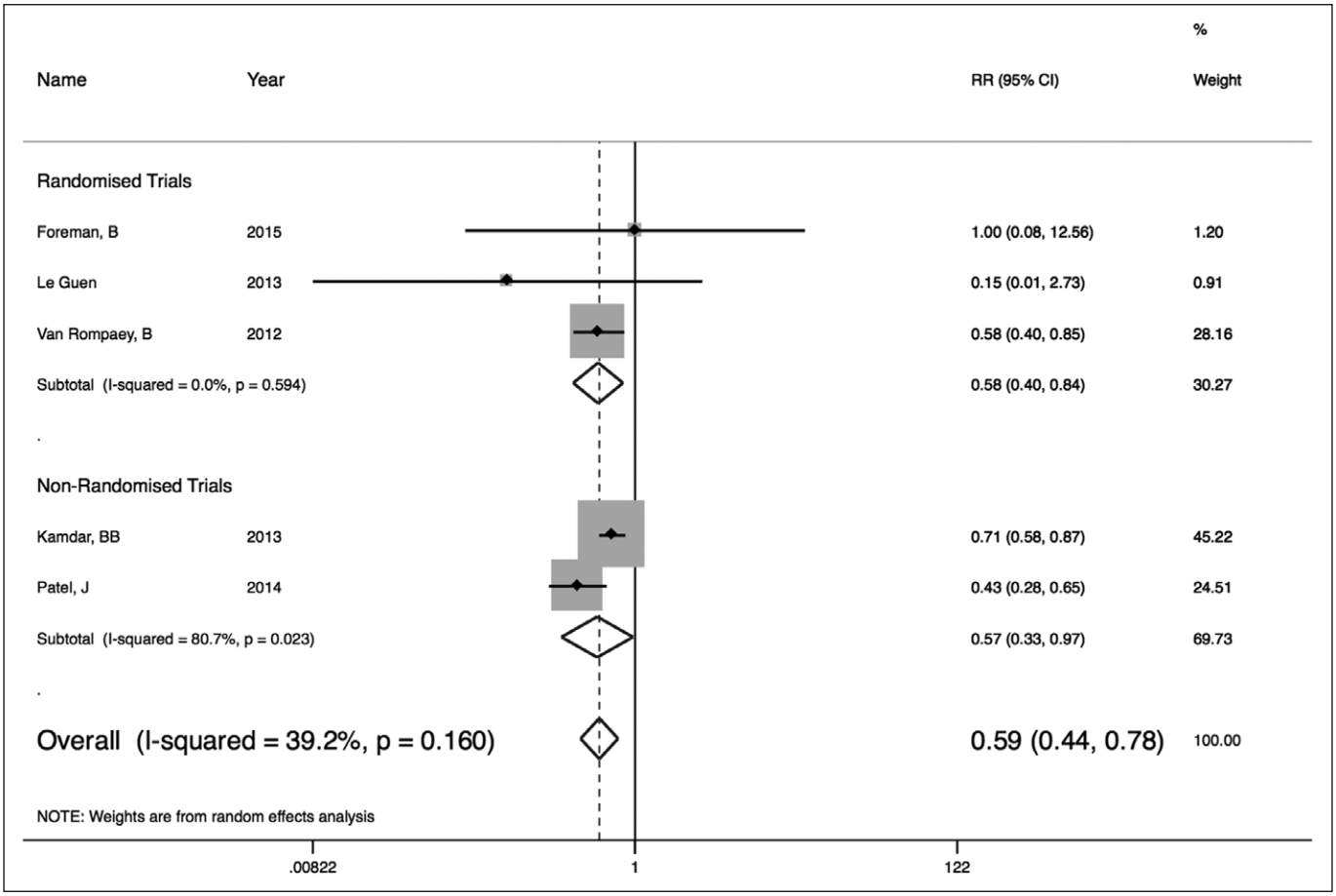

Figure 2. Forrest plot relative risk (RR) of delirium with earplugs.

studies, however, the intervention included earplugs as part of a bundle of sleep hygiene initiatives (Table 1). The use of cointerventions may confound the estimate of independent treatment effect associated with earplugs. The RR of delirium was similar between the largest study of earplugs alone, which accounted for only 28% of the meta-analysis weighting, and the overall point estimate. This suggests that either earplugs are the primary driver of improvement in sleep hygiene within the context of the tested interventions or that the introduction of earplugs alone results in a number of other unmeasured changes in unit behavior as moderators for the effect of earplugs on delirium. Contamination may introduce bias in the point estimate of this meta-analysis and also requires careful consideration in future interventional studies of sleep hygiene strategies in ICU.

Our review found an association between earplug use and incident delirium, but only two of the included studies measured TST using polysomnography. There were insufficient data to undertake a network analysis investigating the relationship between earplugs, sleep, and delirium. Measuring sleep in ICU is made more difficult by the disruption to typical diagnostic electroencephalographic patterns of sleep that frequently occur with critical illness. For example, Foreman et al (21) found that 65% of patient recordings could not be scored according to standardized criteria. Further studies are required to explore the effect of earplugs on measures of sleep and the causal pathway between sleep hygiene initiatives and patient-centered outcomes.

Although we found that a sleep hygiene intervention including earplugs reduced incident delirium, the included studies were generally small, single-center studies with a high risk of bias, and such studies may overestimate the treatment effect. Furthermore, we were not able to demonstrate that the reduction in risk of delirium was associated with a significant improvement in patient-centered outcomes. Although delirium is associated with increased morbidity and mortality, whether this relationship is causal remains uncertain. Nevertheless, the use of a cheap, simple, and noninvasive strategy that improves sleep quality and reduces the incidence and/or severity of delirium in patients admitted to the ICU may be of value through a reduction in ICU length of stay and costs alone.

CONCLUSIONS

Placement of earplugs in patients admitted to the ICU, either isolation or as part of a bundle of sleep hygiene improvement, is associated with a significant reduction in risk of delirium. The potential effect of cointerventions and the optimal strategy for improving sleep hygiene remains uncertain.

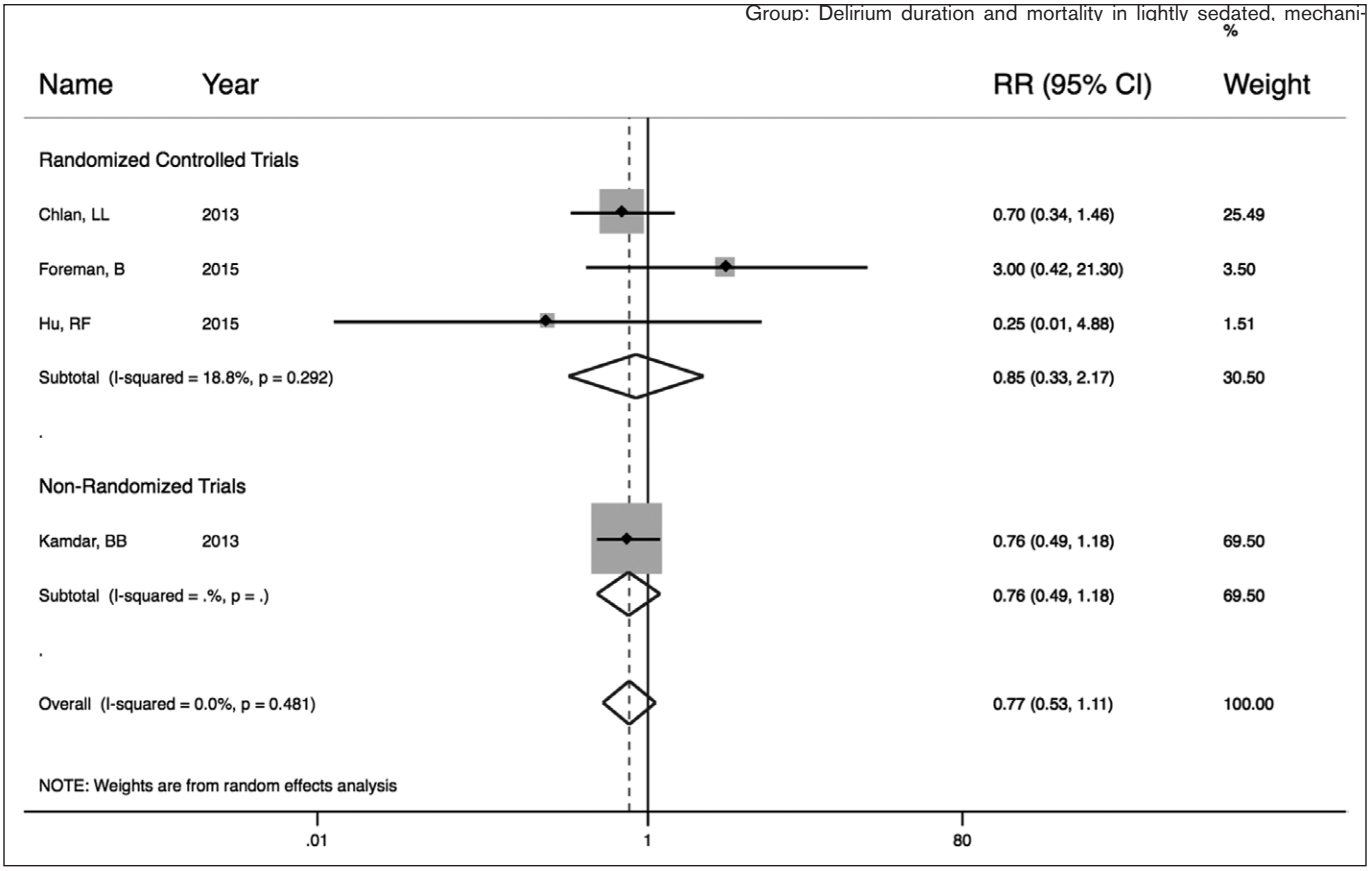

Figure 3. Forrest plot relative risk (RR) of mortality with earplugs.

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