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Review paper

Effects of nonpharmacological interventions on sleep improvement and delirium prevention in critically ill patients: A systematic review and meta-analysis

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ABSTRACT

Objective: Sleep disturbance and delirium are common problems experienced by critically ill patients in the intensive care unit (ICU). These interrelated issues increase the length of stay in the ICU but might also negatively affect long-term health outcomes. The objective of this study was to identify the nonpharmacological interventions provided to improve sleep or prevent delirium in ICU patients or both and integrate their effect sizes.

Review methods: This study was a registered systematic review and meta-analysis. We searched MEDLINE, CINAHL, EMBASE, Web of Science, and Cochrane Library from their inception until December 2021. We included randomised controlled trials and nonrandomised controlled trials-(RCT) that provided nonpharmacological interventions and reported sleep or delirium as outcome variables. Studies not published in English or whose full text was not available were excluded. The quality of the evidence was assessed with version 2 of the Cochrane risk-of-bias tool for RCTs and the Risk Of Bias In Non-randomised Studies of Interventions (ROBINS-I).

Results: The systematic review included 118 studies, and the meta-analysis included 100 studies. Overall nonpharmacological interventions had significant effects on subjective sleep quality (standardised mean difference = 0.30, 95% confidence interval [CI] = 0.05 to 0.56), delirium incidence (odds ratio = 0.62, 95% CI = 0.53 to 0.73), and delirium duration (standardised mean difference = −0.68, 95% CI = −0.93 to −0.43). In individual interventions, aromatherapy, music, and massage effectively improved sleep. Exercise, family participation, information giving, cognitive stimulation, bright light therapy, architectural intervention, and bundles/protocols effectively reduced delirium. Light/noise blocking was the only intervention that ensured both sleep improvement and delirium prevention.

Conclusions: Our results suggest nonpharmacological interventions improve sleep and prevent delirium in ICU patients. We recommend that ICU nurses use nonpharmacological interventions that promote person–environment compatibility in their clinical practice. The results of our review can guide nurses in adopting interventions related to sleep and delirium.

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1. Introduction

As the goal of critical care extends beyond survival to the patient's physical and psychological comfort, the importance of managing sleep disruption and delirium in the intensive care unit (ICU) is emphasised. Among ICU patients, 59%–80% experience

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sleep disruption such as sleep latency, fragmentation, and circadian rhythm disturbance.[1–3] Delirium is an acute brain dysfunction that causes changes in the level of consciousness and behaviour over hours or days, occurring in 20%–80% of ICU patients.[4–6] Sleep disruption and delirium can have negative physical and psychological effects on critically ill patients.[4,7,8] These conditions persist beyond ICU discharge, with 50%–67% of patients experiencing various sleep disorders 1 month after discharge and 28% even after 1 year.[9] Delirium is a major risk factor for cognitive impairment after ICU discharge.[10] Therefore, sleep disruption and delirium are important issues to be addressed to improve patients' ICU experience and long-term outcomes.

Although most studies report sleep and delirium as separate outcome variables, the relationship between the two is worth exploring. Studies on the sleep patterns of patients with delirium reported long daytime sleep, short rapid eye movement (REM) sleep, and low-quality sleep.[11–14] In addition, there was a negative correlation between sleep quality and delirium incidence,[15,16] and interventions for sleep were effective in reducing delirium incidence and duration.[15–18] Flannery et al.[19] reported the results of a systematic review that sleep interventions appear to improve delirium-related outcomes. However, they could not perform quantitative synthesis due to the small number of studies reporting both variables together and heterogeneity and bias issues. Based on these facts, a relationship between sleep and delirium can be inferred, but its nature remains ambiguous.

The 2018 Clinical Practice Guidelines for the Prevention and Management of Pain, Agitation/Sedation, Delirium, Immobility, and Sleep Disruption (PADIS) recommended the use of nonpharmacological multicomponent interventions to promote sleep and prevent delirium in critically ill patients.[20] Nonpharmacological interventions reported to be effective for the prevention of ICU delirium included multicomponent, physical environment, daily interruption of sedation, exercise, patient education, automatic warning system, family participation, and sedation reducing protocols.[21] Among the nonpharmacological interventions for ICU sleep promotion, ventilator mode or type, earplugs or eye masks or both, massage, relaxation interventions, foot baths, music interventions, nursing interventions, valerian acupressure, aromatherapy, and sound masking were reported to be the most effective.[22]

A recent network meta-analytic study[23] also suggested multicomponent strategies as the most appropriate nonpharmacological intervention to prevent delirium. However, multicomponent interventions include different types of interventions, possibly limiting ICU nurses' clinical application and making it difficult to decide which individual interventions are effective. Additionally, the PADIS guidelines and relevant studies analysed sleep and delirium interventions separately, so it is necessary to review and analyse the interventions for these two together.[19–22] To facilitate the clinical application of nonpharmacological interventions for sleep improvement and delirium prevention, it is necessary to systematically classify various interventions and integrate their effect sizes.

Although the cause of delirium has not been clearly understood, relevant literature suggests that stressful environments in the ICU, such as high levels of background noise, absence of natural light, and nocturnal care activities, may increase the risk of delirium by affecting the patient's circadian biomarkers cortisol and melatonin secretion and causing chronodisruption.[24–26] Most nonpharmacological interventions aim to control the symptoms and stress experienced by patients in the unique environment and therapeutic context of the ICU.[19] According to the environmental stress model (ESM), enhancement of person–environment compatibility (EP-EC) may reduce stress-induced problems, such as sleep disruption and delirium in the ICU.[27] EP-EC refers to the relationship between the ICU environment (stressor) and patient response (stress). The three EP-EC measures include 'interdisciplinary planning and abatement of hazards', 'ongoing reduction of remaining hazards', and 'instruction of environmental occupants in control/coping with remaining hazards'.[27] We used the EP-EC as a framework for the classification of nonpharmacological interventions. Therefore, a comprehensive review of nonpharmacological interventions for sleep improvement and delirium prevention and the classification of interventions based on EP-EC will help establish the direction of sleep and delirium management in the ICU.

The purpose of this study was to systematically review nonpharmacological interventions to improve sleep and prevent delirium based on ESM and to identify the effects of these interventions on sleep and delirium in ICU patients. This review was an update on the studies published after the 2018 PADIS guidelines,[20] which separately suggested interventions for sleep and delirium and provided insight into the relationship between sleep and delirium and the status of relevant studies.

2. Methods

2.1. Study design

This systematic review and meta-analytic study classified nonpharmacological interventions for sleep improvement, delirium prevention, or both in ICU patients and integrated their effect sizes. The review protocol was registered with the International Prospective Register of Systematic Reviews (reference number: CRD42021230815). We conducted and reported the study according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses.[28]

2.2. Key question and inclusion criteria

The key question of this study was, 'Do non-pharmacological interventions improve sleep or reduce delirium in ICU patients?' The population included adult patients (P) admitted to the ICU, and the interventions (I) were nonpharmacological interventions. Comparator (C) was usual care; outcomes (O) were sleep, delirium, or both; and the study design (SD) was a randomised controlled trial (RCT) or non-RCT (follow-up studies, uncontrolled before-after studies, controlled before-after studies).

Inclusion criteria were (i) quantitative studies including RCTs and non-RCTs, (ii) studies published in a journal by December 2021, (iii) studies with adult patients admitted to the ICU, (iv) studies that provided nonpharmacological interventions, and (v) studies that reported one or more outcome variables, such as subjective sleep quality, sleep time, sleep efficiency, delirium incidence, and delirium duration. In addition, we excluded studies that were not published in English or whose full text was not available.

2.3. Literature search and selection

We searched the literature in five databases—MEDLINE (PubMed), Cochrane Library, CINAHL, EMBASE, and Web of Science—and performed a hand search. The primary search terms were ((intensive OR critical* OR ICU OR SICU OR MICU OR CCU) AND (intervention OR nurs* OR manage* OR protocol OR program OR bundle OR prevention)) AND ((sleep* OR REM OR insomn* OR hyposomn* OR hypersomn* OR dyssomn* OR parasomn* OR narcolep* OR somnolen*) OR (deliriu* OR confus* OR intensive care psychosis OR metabolic encephalopathy OR toxic encephalopathy OR acute psycho organic OR cloud* OR exogenous psycho* OR toxic psycho*)). Two authors (J.K. and M.L.), who have completed the

Cochrane workshop and have multiple research experiences conducting meta-analyses, designed specific search strategies for each database, presented in Supplementary Table 1. Two authors (Y.S.C. and M.L.) independently performed a literature search and selection. A third author (J.H.) was consulted to achieve consensus if any discrepancy or difficulty arose in the literature searches.

2.4. Coding and classification

Two authors (S.Y. and Y.J.J.) independently extracted the data from the selected studies, including author, publication year, country, study design, participants, interventions, controls, outcome variables, statistical values, and measurement tools. Other authors (J.H., S.K., and Y-.H.W.) reviewed inconsistencies in the coded data and reached a consensus.

We classified nonpharmacological interventions reported in individual studies by EP-EC type of ESM. Type A, interdisciplinary planning, and abatement of hazard included interventions that required the collaboration of various healthcare professionals, for example, the quiet time protocol or the awakening and breathing coordination, delirium monitoring/management, early exercise/mobility, and family engagement/empowerment (ABCDEF) bundle, and delirium detection or prevention protocol. These multicomponent interventions were provided as unit-based rather than to individual patients. Type B, ongoing reduction of remaining hazards, comprised interventions related to light/noise blocking and architectural interventions. Light/noise blocking involved eye masks or earplugs, while architectural interventions were related to the structure of the ICU room. Type C, instruction of environmental occupants in control/coping with remaining hazards, consisted of interventions provided for individual patients. It included aromatherapy, massage, bright light, music, cognitive stimulation, information giving, family participation, exercise, and mindfulness.

2.5. Assessment of study quality

We assessed the quality of studies using Cochrane's risk-of-bias tool for randomised trials (RoB 2) and the Risk Of Bias in Non-randomised Studies of Interventions (ROBINS-I).[29,30] The RoB2 consists of five domains: randomisation process, intended interventions, missing outcome data, outcome measurement, and reported result. The ROBINS-I consists of seven domains: confounding, participant selection, intervention classification, deviations from intended interventions, missing data, outcome measurement, and selection of reported results. The risk of bias was assessed as low risk, some concerns, or high risk in the RoB 2 and as low, moderate, serious, or critical in the ROBINS-I based on responses to signal questions in each domain. Two authors (Y.S.C. and M.L.) independently assessed the study quality and arrived at a consensus through discussion in case of disagreement.

2.6. Statistical analysis

The characteristics of the studies selected for review were presented using descriptive statistics. We performed a meta-analysis using Comprehensive Meta-Analysis software, version 3.0 (Biostat Englewood, NJ). We calculated the effect size of subjective sleep quality, sleep time, sleep efficacy, delirium duration as standardised mean difference (SMD), and delirium incidence as odds ratio (OR). The random-effect model was used if Cochrane's Q test results were heterogeneous with $I^2 \geq 50\%$ or $p < .10$, and homogeneous cases were analysed using the fixed-effect model. For SMD calculation of subjective sleep quality, sleep scores of individual studies were recoded in the same direction so that the higher the score, the higher the quality of sleep. When calculating the OR, the inverse variance method was applied for the fixed-effect model, and the DerSimonian and Laird inverse variance method was applied for the random-effect model.[31] To minimise the violation of the independence assumption and information loss during the analysis process, 'shifting unit of analysis' was applied.[32]

As a subgroup analysis, effect sizes for outcome variables were calculated for individual interventions. As an additional analysis, meta-analysis of variance was used to analyse the difference in effect size between statistically significant individual interventions. A sensitivity analysis was performed to evaluate the effect of study quality and design on effect size integration. We analysed publication bias with a funnel plot, and it was determined that there was no bias since it was visually symmetrical. In the case of asymmetry, if the effect size corrected using the trim-and-fill method differed by more than 10%, it would be considered that there was a publication bias issue.[33]

We interpreted the effect size based on the criteria of Cohen:[34] SMD = 0.20, OR = 0.69 (1.44) = small; SMD = 0.5, OR = 0.40 (2.48) = moderate; SMD = 0.8, OR = 0.23 (4.27) = large.

3. Results

3.1. Study selection

Fig. 1 shows the results of the search and selection process. We identified a total of 6282 articles through the electronic databases. After removing 727 duplicates, we screened the title and abstract for the remaining articles, and 5301 were excluded because they did not meet the inclusion criteria. We further examined the remaining 254 full-text articles, and 155 articles that did not meet the criteria were excluded (Supplementary Table 2). We additionally identified 19 relevant studies from the reference list of the included studies, leaving a total of 118 articles for systematic review (Supplementary Table 3). Finally, we performed a meta-analysis on 100 of these studies, which provided statistical values to enable effect size integration (subjective sleep quality, sleep time, sleep efficacy, and delirium duration as SMD and delirium incidence as OR).

3.2. Characteristics of studies

Table 1 shows the characteristics of the 118 studies selected for systematic review. A total of 36,356 participants were included; 33.0% of the studies comprised 51–100 participants. Regarding study design, 50.0% were RCTs, and the rest were non-RCTs, including controlled before-after studies and interrupted time-series studies. As outcome variables, 33.1% reported sleep, 57.6% reported delirium, and 9.3% reported both sleep and delirium. Among studies reporting sleep, delirium, and both, the proportion of RCTs were 51.3%, 50.0%, and 54.5%, respectively. For measurement of outcome variables, most studies that reported subjective sleep quality used the Richards–Campbell Sleep Questionnaire or the Verran and Snyder-Halpern Sleep Scale. Sleep time and efficiency were measured using polysomnography and accelerometry. The most common delirium measurement tool was the Confusion Assessment Method-ICU (CAM-ICU), used in 72.2% of the studies. Other studies used the Richmond Agitation Sedation Scale (RASS) (24.1%), Intensive Care Delirium Screening Checklist (12.7%), and Neelon and Champagne Confusion Scale (6.3%).

3.3. Nonpharmacological interventions to improve sleep and prevent delirium

Table 2 shows the 119 interventions classified by the EP-EC type of ESM and the outcome variables of the final 118 studies. Type A interventions comprised the ABCDEF multi-intervention approach,

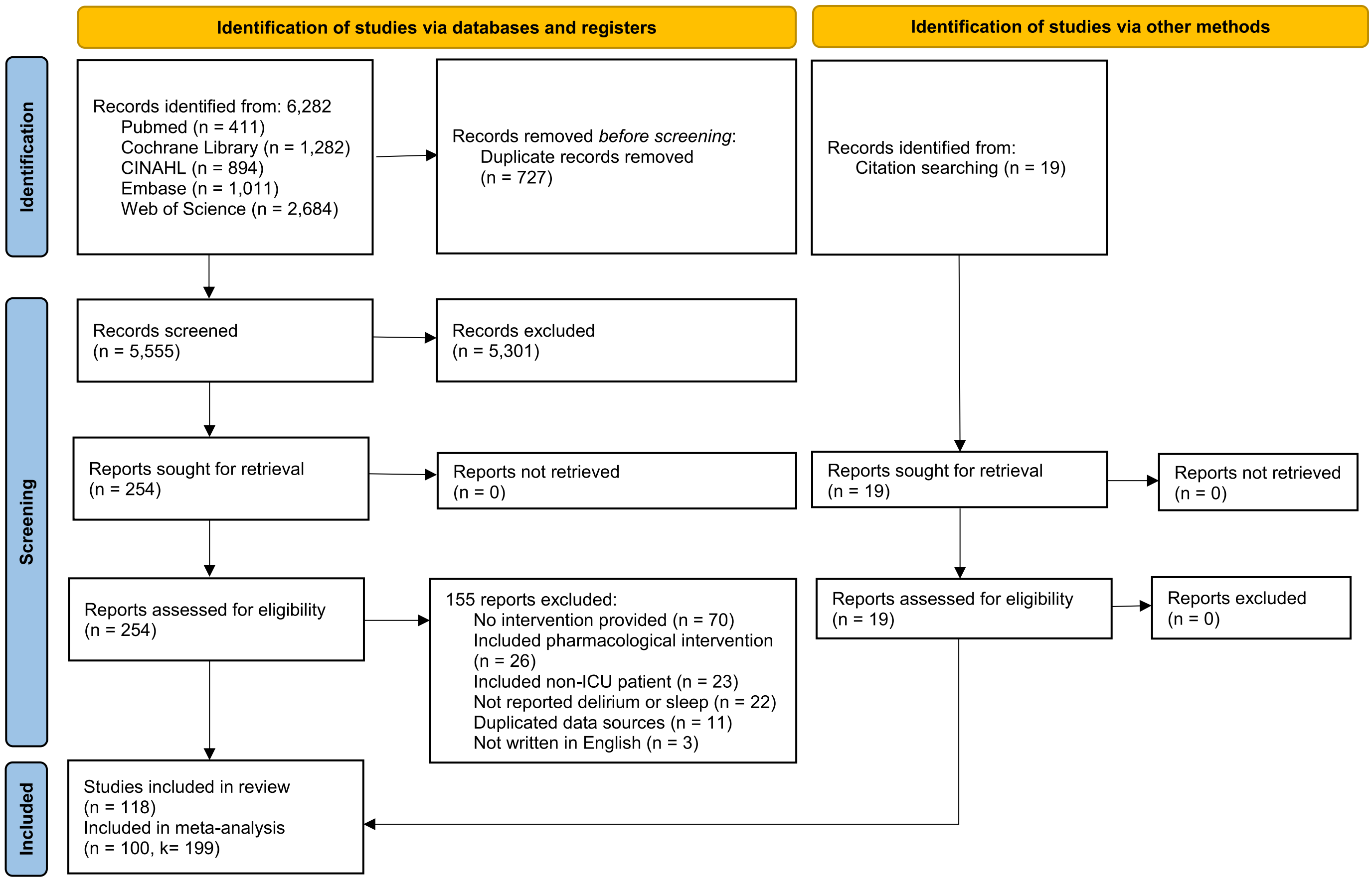

Fig.1. Flow diagram of study selections process.[28]

delirium early detection protocol, delirium prevention protocol, and quiet time protocol; the first three targeted delirium, and the last focused on sleep or both sleep and delirium. Type B included architectural interventions and light/noise blocking, and four out of 18 light/noise blocking interventions targeted both sleep and delirium. Type C included 10 interventions, such as aromatherapy, music, information giving, mindfulness, combined interventions, and bright light interventions. Among these, massage and bright light targeted both sleep and delirium.

3.4. Study quality

We assessed the quality of the 100 studies that provided statistical values for meta-analysis. There were 56 RCTs evaluated using RoB 2; and the domain with the lowest risk of bias was 'selection of reported results', and that with the highest risk of bias was 'deviations from intended interventions'. As for the overall risk of bias, 14 studies were ranked low, eight were of some concern, and 34 were ranked high (Fig. 2, Supplementary figure 1). In addition, there were 44 non-RCTs evaluated using the ROBINS-I; the domain with the lowest risk of bias was 'missing data'; that with the highest risk was 'confounding'. As for the overall risk of bias, 15 studies were ranked low, 11 were of moderate concern, and 18 were serious (Fig. 3, Supplementary figure 2).

4. Meta-analysis

4.1. Pooled analysis

Subsequent to integrating 199 effect sizes reported in 100 studies involving 32,085 ICU patients, nonpharmacological interventions were found to have significant effects on subjective sleep quality (SMD = 0.30, 95% confidence interval [CI] = 0.05 to 0.56), delirium incidence (OR = 0.62, 95% CI = 0.53 to 0.73), and delirium duration (SMD = −0.68, 95% CI = −0.93 to −0.43). However, the effects on sleep time (SMD = 0.51, 95% CI = −0.10 to 1.13) and sleep efficiency (SMD = 0.06, 95% CI = −0.40 to 0.52) were not significant (Supplementary figure 3).

4.2. Subgroup analysis

The subgroup analyses for individual interventions showed that aromatherapy significantly improved subjective sleep quality (SMD = 1.90, 95% CI = 0.52 to 3.29), while massage had significant effects on subjective sleep quality (SMD = 0.54, 95% CI = 0.04 to 1.03) and sleep time (SMD = 3.08, 95% CI = 1.53 to 4.63). Light/noise blocking had significant effects on subjective sleep quality (SMD = 0.40, 95% CI = 0.04 to 0.76), sleep time (SMD = 0.49, 95% CI = 0.29 to 0.69), and delirium incidence (OR = 0.42, 95% CI = 0.22 to 0.80). Exercise interventions were effective in reducing delirium incidence (OR = 0.23, 95% CI = 0.09 to 0.64) and delirium duration (SMD = −0.98, 95% CI = −1.88 to −0.09). Family participation had significant effects on reducing delirium incidence (OR = 0.31, 95% CI = 0.21 to 0.46), while information giving had significant effects on delirium incidence (OR = 0.38, 95% CI = 0.25 to 0.59). The ABCDEF multi-intervention approach had significant effects on reducing delirium duration (SMD = −0.80, 95% CI = −1.22 to −0.38). Delirium early detection and prevention protocols had significant effects on reducing delirium incidence ([OR = 0.61 95% CI = 0.47 to 0.80] and [OR = 0.51, 95% CI = 0.37 to 0.72], respectively). Combined intervention had significant effects on reducing delirium incidence (OR = 0.37, 95% CI = 0.14 to 0.98) (Fig. 4).

Table 1
Characteristics of the studies ($N = 118$).

Variable	Category	n	%
Year	2003−2015	45	38.1
	2016−2021	73	61.0
Continents	Asia	42	35.6
	North America	40	33.9
	Europe	28	23.7
	Others	8	6.8
Design	Randomised controlled trials	59	50.0
	Nonrandomised controlled trials	59	50.0
	Follow-up studies	26	22.0
	Controlled before-after studies	20	16.9
	Uncontrolled before-after studies	13	11.0
Sample size	≤50	23	19.5
	51−100	40	33.0
	101−300	32	27.1
	>300	22	18.6
	Unknown	1	0.8
Outcomes	Sleep	39	33.1
	Delirium	68	57.6
	Both	11	9.3
Measurement	Sleep		
	Subjective sleep quality		
	RCSQ	22	44.0
	VSH	9	18.0
	ICT-p	6	12.0
	PSQI	4	8.0
	SMHSQ	4	8.0
	SICUQ	2	4.0
	Others	5	10.0
	Nurse observation	4	8.0
	Objective measurement		
	Polysomnography	6	12.0
	Accelerometer	5	10.0
	Delirium		
	CAM-ICU	57	72.2
	RASS	19	24.1
	ICDSC	10	12.7
	NEECHAM	5	6.3
	DSM-IV	2	2.5
	Others	6	7.6

CAM-ICU = Confusion Assessment Method-Intensive Care Unit; DSM-IV = Diagnostic and Statistical Manual of Mental Disorder Criteria-IV; ICDSC = Intensive Care Delirium Screening Checklist; ICT-p = investigator created tool-patient; NEECHAM = Neelon and Champagne Confusion Scale; PSQI = Pittsburgh Sleep Quality Index; RASS = Richmond Agitation Sedation Scale; RCSQ = Richards−Campbell Sleep Questionnaire; SICUQ = Sleep in the Intensive Care Unit Questionnaire; SMHSQ = St. Mary's Hospital Sleep Questionnaire; VSH = Verran and Snyder-Halpern Sleep Scale.

4.3. Additional analysis

As for the results of meta-analysis of variance with individual interventions as moderators, there were no significant differences among aromatherapy, massage, and light/noise blocking in improving subjective sleep quality ($p = .120$). There was a significant difference between massage and light/noise blocking in increasing sleep time ($p = .001$). However, there were no significant differences among exercise intervention, family participation, information giving, light/noise blocking, delirium early detection protocol, delirium prevention protocol, and combined intervention in reducing delirium incidence ($p = .270$). In addition, there was no significant difference between exercise intervention and ABCDEF multi-intervention approach in reducing delirium duration ($p = .711$).

4.4. Sensitivity analysis

We performed a sensitivity analysis to evaluate the effect of study quality and design on effect size integration. Specifically, the effects of nonpharmacological interventions on sleep or delirium were reanalysed in 36 studies, excluding 64 studies in which the risk of bias was high or serious. Nonpharmacological interventions were found to be effective for delirium incidence (OR = 0.64, 95% CI = 0.51 to 0.81) and delirium duration (SMD = −0.28, 95% CI = −0.55 to −0.01), but no statistical significance was found for subjective sleep quality (SMD = 0.46, 95% CI = −0.02 to 0.94), sleep time (SMD = 0.21, 95% CI = −0.29 to 0.70), and sleep efficiency (SMD = 0.08, 95% CI = −0.68 to 0.84), similar to the results of the overall analysis except in the case of subjective sleep quality.

As a result of analysing only 56 RCT studies, nonpharmacological interventions were found to be effective for subjective sleep quality (SMD = 0.45, 95% CI = 0.13 to 0.77), delirium duration (SMD = −0.83, 95% CI = −1.39 to −0.26), and delirium incidence (OR = 0.54, 95% CI = 0.43 to 0.68), and but not sleep time (SMD = 0.71, 95% CI = −0.21 to 1.62) or sleep efficiency (SMD = 0.28, 95% CI = −0.07 to 0.63), similar to the results of the overall analysis.

4.5. Publication bias

Funnel plots for the effect sizes of subjective sleep quality, sleep time, sleep efficiency, delirium incidence, and delirium duration are presented in supplementary figure 4. All funnel plots for sleep outcomes were symmetric, and the effect size changes using the trim-and-fill method were also less than 10%, indicating minimal publication bias. Funnel plots for delirium occurrence and duration were asymmetric. The change in the effect size of delirium incidence was less than 10%, but the duration of delirium was more than 10%.

5. Discussion

According to the ESM, we reviewed and classified nonpharmacological interventions for sleep and delirium in critically ill patients and integrated their effect sizes. A meta-analysis of 100 studies with 32,085 patients showed that nonpharmacological interventions effectively improve sleep or reduce delirium. Specifically, the individual interventions that were effective in improving sleep were aromatherapy and massage. In addition, exercise, family participation, information giving, and protocols (ABCDEF multi-intervention approach, delirium early detection protocol, and delirium prevention protocol) effectively reduced delirium. The only intervention that was effective for both sleep and delirium was light/noise blocking. The 2018 PADIS guidelines recommended noise/light reduction strategies and multicomponent protocols to improve sleep and multicomponent interventions to prevent delirium.[20] Similarities and differences between our results and the PADIS guidelines are discussed in the following for each intervention.

Unlike previous meta-analyses that included only RCTs,[35,36] about half of the studies mentioned in this review adopted a non-RCT design, and most had more than one risk of bias domain in terms of study quality. It could be because it is difficult to measure preintervention sleep and delirium in the ICU, and many interventions are provided to all the patients in the ICU rather than individuals. Specifically, among the intervention types based on the EP-EC framework in this study, type A interventions were guidelines or protocols provided by multidisciplinary healthcare professionals. Interventions provided to the entire ICU, such as guidelines and protocols, have a strong possibility of confounding variables, and it is not easy to apply the RCT design. Therefore, we extended the inclusion criteria in this review to non-RCT studies. These limitations of the study design need to be supplemented through a cluster randomised approach in which ICUs are randomly assigned to a specific group.[19]

Table 2
Interventions classified by EP-EC type of ESM and outcome variables ($N = 119$).

Category	Intervention	Study outcomes		
		Sleep (n)	Delirium (n)	Sleep and delirium (n)
Type A	Delirium prevention protocol	0	16	0
	Delirium early detection protocol	0	9	0
	ABCDEF multi-intervention approach	0	8	0
	Quiet time protocol	10	0	5
Type B	Light/noise blocking	14	0	4
	Architectural intervention	0	6	0
Type C	Exercise intervention	0	11	0
	Family participation	0	5	0
	Information giving	1	4	0
	Bright light therapy	0	3	1
	Cognitive stimulation	0	2	0
	Music	2	1	0
	Massage	4	1	1
	Aromatherapy	4	0	0
	Mindfulness	1	1	0
	Combined	3	2	0
	Total	39	69	11

Type A = Interdisciplinary planning (n = 48); Type B = Reduction of remain hazard (n = 24); Type C = Control/coping with remaining hazard (n = 47).
ABCDEF = awakening and breathing coordination, delirium monitoring/management, early exercise/mobility, and family engagement/empowerment; EP-EC = enhancement of person–environment compatibility; ESM = environmental stress model.

In terms of outcome variables, most sleep studies in this review reported subjective sleep quality, and only 11 studies measured objective sleep, such as sleep time or efficacy. ICU patients may have difficulty communicating due to the disease itself or various medical devices and equipment and the influence of sedatives; therefore, the accuracy and reliability of self-report sleep assessment may be low.[37] Objective sleep measures such as polysomnography, accelerometry, and bispectral index monitoring also have limitations in device availability, workforce, analysis, and interpretation. In addition, wearable accelerometers have low measurement accuracy for critically ill patients with little body movement.[38,39] Measuring sleep in ICU patients using a valid and reliable method is vital to understanding the relationship between delirium and sleep-related outcomes. In addition to the patient's self-report, the physiologic assessment of sleep quality and the biomarker of circadian rhythmicity must be measured simultaneously.[19] In the case of delirium measurement, CAM-ICU or RASS were used in most studies, thus suggesting that these two are currently the main tools to measure ICU delirium. Reflecting this situation, recently, there has been a trend to enable nurses to detect delirium early by embedding the CAM-ICU or RASS in the ICU electronic health record system.[40]

The effect sizes of type A and B interventions were small to moderate, whereas type C had large effect sizes on sleep quality, sleep time, and delirium. Type A interventions were group interventions to control the environmental hazards of the ICU, whereas type C included individual interventions to increase patients' ability to cope with harmful environmental stimuli.[27] It is possible that the intensity of type C interventions was perceived as high by individual patients and, accordingly, the effect size was also large. Our findings that type A interventions were effective were consistent with the 2018 PADIS guidelines recommending multicomponent interventions for delirium prevention.[20] However, it is worth noting that the effect sizes of type A interventions were relatively small compared to type C, which were individual interventions. Systematic refining of type A protocols or bundles for diverse critical care environments can be one of the ways to increase the effect size of interventions.[41] This step will allow interdisciplinary team members to incorporate type A interventions into their clinical practice more easily.

In our meta-analysis, the interventions that were effective in improving sleep in ICU patients were massage, aromatherapy and light/noise blocking. The 2018 PADIS guidelines did not recommend aromatherapy and acupressure due to the low quality of evidence, and in the case of light/noise blocking, although the quality of evidence was low, it was suggested as a conditional recommendation.[20] In contrast, in our meta-analysis, the effect sizes of both massage and aromatherapy were larger than that of light/noise blocking. The 2018 PADIS guidelines[20] were based on studies published from 1990 to 2015. The effect size may have increased because more recent studies have reported positive results of aromatherapy and massage than studies published during that period. Aromatherapy and massage are known to improve sleep by inducing sedation, muscle relaxation, pain reduction, and enhancement of comfort.[42,43] These interventions do not require special equipment or space and are relatively easy to apply;

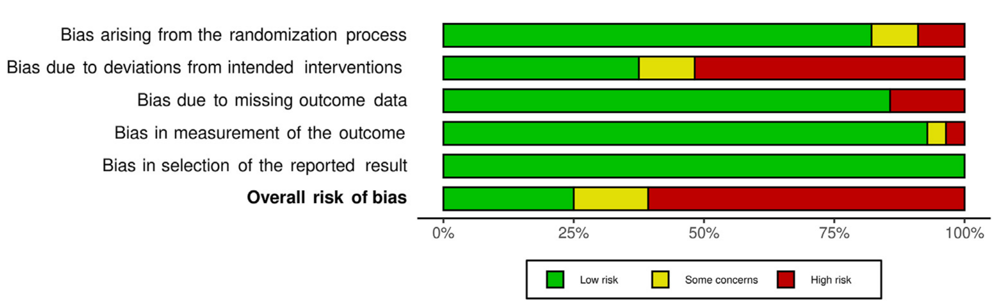

Fig.2. Risk of bias summary for randomised controlled trial studies.

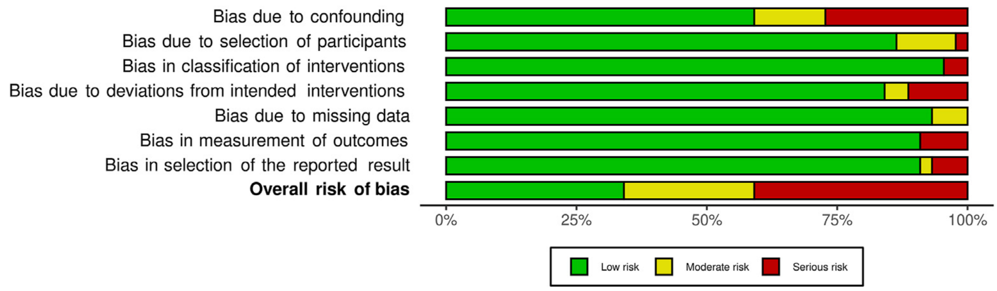

Fig.3. Risk of bias summary for nonrandomised controlled trial studies.

therefore, it is recommended that ICU nurses implement them to improve patients' sleep.

The nonpharmacological intervention with the largest effect size for delirium was exercise, which effectively reduced delirium incidence and duration. Compared with the 2018 PADIS guidelines recommending exercise as part of the ABCDEF multi-intervention approach,[20] the results of our study report that the effectiveness of exercise as an individual intervention is significant. In addition, a recent network meta-analysis study recommended exercise as a feasible and cost-effective intervention to prevent ICU delirium.[23] Exercise interventions adopted in individual studies were early ambulation, range of motion exercises, and functional electrical stimulation cycling.[44–46] It seems that exercise could prevent delirium by improving venous and cerebral blood flow, increasing tissue oxygen, and maintaining a normal circadian rhythm by enhancing daytime activity.[47,48] However, an exercise intervention

Outcome	Intervention (category)[a]	k	Heterogeneity		Model	Effect size			
						SMD/OR	95% CI		*p*
			I^2	*p*			Lower	Upper	
Subjective sleep quality									
	Aromatherapy (C)	5	96.0	<.001	R	1.90	0.52	3.29	0.007
	Massage (C)	8	82.7	<.001	R	0.54	0.04	1.03	0.034
	Light/ noise blocking (B)	24	91.4	<.001	R	0.40	0.04	0.76	0.030
	Quiet time protocol (A)	7	67.6	0.005	R	0.18	-0.46	0.82	0.582
	Combined (C)	2	91.4	0.001	R	-0.11	-1.87	1.65	0.901
	Music therapy (C)	16	91.3	<.001	R	0.10	-0.23	0.43	0.771
Sleep time									
	Massage (C)	3	91.1	<.001	R	3.08	1.53	4.63	<.001
	Light/ noise blocking (B)	6	0.0	0.697	F	0.49	0.29	0.69	<.001
Sleep efficacy									
	Music therapy (C)	2	0.0	0.966	F	0.20	-0.32	0.73	0.446
	Light/ noise blocking (B)	3	36.7	0.206	F	0.18	-0.19	0.54	0.336
Delirium duration									
	Delirium prevention protocol (A)	2	98.4	<.001	R	-1.52	-3.49	0.45	0.130
	Exercise intervention (C)	5	96.2	<.001	R	-0.98	-1.88	-0.09	0.031
	ABCDEF multi-intervention approach (A)	5	93.7	<.001	R	-0.80	-1.22	-0.38	<.001
	Family participation (C)	4	0.0	0.537	F	-0.15	-0.59	0.29	0.508
Delirium incidence									
	Exercise intervention (C)	7	78.1	<.001	R	0.23	0.09	0.64	0.004
	Family participation (C)	6	51.9	0.070	F	0.31	0.21	0.46	<.001
	Combined (C)	3	47.4	0.150	F	0.37	0.14	0.98	0.045
	Information giving (C)	4	0.0	0.525	F	0.38	0.25	0.59	<.001
	Light/noise blocking (B)	3	0.0	0.496	F	0.42	0.22	0.80	0.008
	Delirium prevention protocol (A)	23	84.3	<.001	R	0.51	0.37	0.72	<.001
	Quiet time protocol (A)	2	85.7	<.001	R	0.54	0.21	1.35	0.188
	Delirium early detection protocol (A)	21	65.8	<.001	R	0.61	0.47	0.80	<.001
	Bright light therapy (C)	4	64.7	0.037	R	0.89	0.57	1.40	0.620
	Architectural intervention (A)	7	67.1	0.006	R	0.90	0.65	1.24	0.515
	Massage (C)	4	0.0	0.750	F	0.90	0.45	1.81	0.770
	ABCDEF multi-intervention approach (A)	7	78	<.001	R	0.93	0.65	1.33	0.675
	Cognitive stimulation (C)	2	0.0	0.600	F	0.99	0.59	1.67	0.980

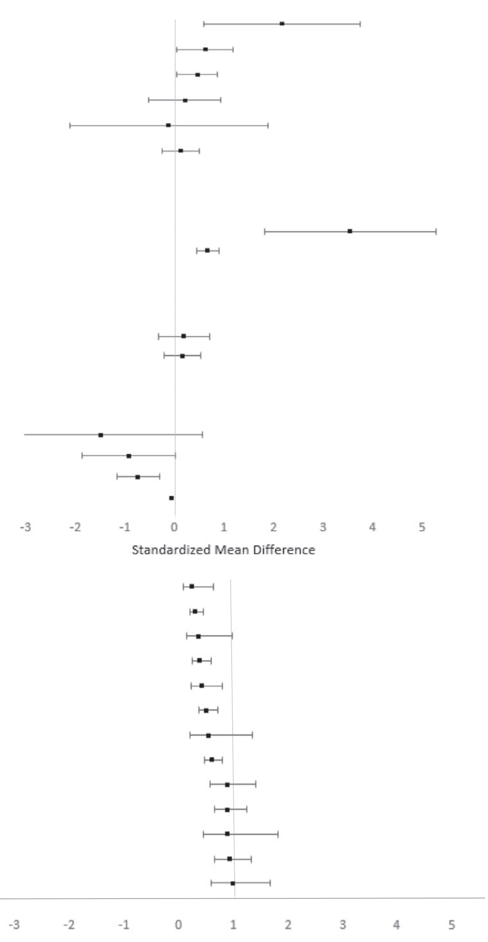

Fig.4. Effect size of individual intervention. ABCDEF = awakening and breathing coordination, delirium monitoring/management, and early exercise/mobility, family engagement/empowerment; CI = confidence interval; F = fixed-effect model; OR = odds ratio; R = random-effect model; SMD = standardised mean difference. [a]The category of intervention: A = Interdisciplinary planning; B = Reduction of remain hazard; C = Control/coping with remaining hazard.

in the ICU is difficult to implement due to the high disease severity, various kinds of life support equipment, and the workload of the medical staff.[49] To implement an exercise intervention in the ICU, it will be necessary to enhance the staff's awareness, reinforce the workforce, and implement structured strategies, such as establishing a protocol containing the steps and procedures of the exercise.[50] None of the studies we reviewed measured sleep as an outcome variable after exercise intervention. Therefore, clinical trials that can investigate the effects of an exercise intervention on the sleep of ICU patients are needed. In addition, they could provide clues about the link between sleep and delirium and the effects of exercise.

In our study, light/noise blocking had a significant effect on both sleep improvement and delirium reduction. The 2018 PADIS guidelines recommended this intervention to improve sleep, and their multicomponent interventions for the prevention of delirium included optimising sleep interventions.[20] Light/noise blocking, a relatively simple intervention implemented using an eye mask or earplugs, seems to have prevented delirium by improving sleep.[51] Light and noise are major environmental hazards that interfere with sleep in ICU patients and are associated with shorter REM sleep and changes in the sleep–wake cycle.[20,52] The sleep stage and sleep–wake cycle are considered important links between sleep and delirium. Potharajaroen et al.[53] reported that bright light therapy effectively promoted sleep and reduced delirium. Bright light therapy is an intervention that aims to restore circadian rhythm by illuminating 1000–5000 Lx of bright light during the daytime.[54] Sleep disturbance and disruption of circadian rhythms in critically ill patients were reported as significant risk factors for delirium in a recent prospective case–control study comparing sleep, melatonin, and cortisol levels between delirious and nondelirious patients.[24] Considering these aspects, the recovery of the sleep–wake cycle in the ICU is likely to be a key point in preventing delirium. However, out of the 100 studies in our meta-analysis, only eight reported both sleep and delirium, and only three interventions, including light/noise blocking, quiet time protocol, and bright light therapy, were adopted in those studies. Due to the limited number of interventions and studies targeting both sleep and delirium outcomes, we could not establish a relationship between these two variables.

This study is significant because it suggests an improvement in effect size for clinical applicability of multicomponent interventions through the classification of interventions based on ESM. Second, our results showed that light/noise blocking was effective for both sleep and delirium; individual interventions, such as aromatherapy, massage, and exercise, had a large effect size but measured only for a single outcome variable, can guide the clinical practice of ICU nurses, and provide a direction for future research.

Nonetheless, this study has several limitations. First, we may not have included all relevant studies in the literature search and selection process. Second, the quality of the studies included in the meta-analysis was generally low. We supplemented this issue by presenting the sensitivity analysis according to the overall risk of bias and study design. It is worth noting that the new criteria of Cochrane collaboration are quite strict, suggesting that if the risk of bias in any one domain is high, the overall risk of bias should be rated as high. A third limitation was the heterogeneity of the studies. To compensate for the heterogeneity of studies, we applied a random-effect model when pooling the overall effect size. We also conducted subgroup and sensitivity analyses to understand the meta-analysis results reflecting heterogeneity. Fourth, there was a risk of publication bias in studies of the delirium duration, and this should be considered in the interpretation of the relevant results. Fifth, we could not statistically analyse the relationship between sleep and delirium due to the lack of studies that measured these two variables together. Further studies are needed to measure the outcomes of aromatherapy, massage, and exercise interventions for both sleep and delirium.

6. Conclusions

Following the systematic review and meta-analysis of 100 studies with 32,085 ICU patients, nonpharmacological interventions were found to be effective in improving subjective sleep quality and reducing delirium incidence and duration. Specifically, aromatherapy and massage were effective in improving sleep. Exercise, family participation, information giving, architectural intervention, and bundles/protocols reduced delirium. An intervention that was effective for both sleep and delirium was light/noise blocking. We recommend that ICU nurses use these nonpharmacological interventions in their clinical practice to improve sleep and reduce delirium in critically ill patients. In addition, it is necessary to analyse the relationship between sleep and delirium by conducting studies that measure these variables together.

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CRediT authorship contribution statement

J.K. supervision, conceptualisation, writing - original draft, and funding acquisition. Y.S.C. data curation, formal analysis, visualisation, and writing – review & editing. M.L. formal analysis and writing. J.K., Y.S.C., M.L., S.Y., Y.J.J., and Y-.H.W. investigation. All authors read and approved the final manuscript.

Conflict of interest

The authors declare that they have no conflict of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.aucc.2022.04.006.

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