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Review paper

Effectiveness of nonpharmacological interventions to prevent adverse events in the intensive care unit: A review of systematic reviews

Stefanie Suclupe, RN, MSc [a, b, *], Percy Efrain Pantoja Bustillos, MD, MPH [b], Javier Bracchiglione, MD, MSc [a, b, c], Carolina Requeijo, MD, MPH [d], Karla Salas-Gama, MD, MPH [a, e], Ivan Solà, MSc [b, d, f], Angela Merchán-Galvis, MD, MSc [b, g], Jaume Uya Muntaña, RN, MSc [h], Gemma Robleda, RN, PhD [b, i], Maria Jose Martinez-Zapata, PhD, MD [a, b, f]

[a] Universitat Autònoma de Barcelona, Spain; [b] Iberoamerican Cochrane Centre, Biomedical Research Institute Sant Pau (IIB Sant Pau), Spain; [c] Interdisciplinary Centre for Health Studies (CIESAL), Universidad de Valparaíso, Chile; [d] Epidemiology and Public Health Department, Hospital de La Santa Creu I Sant Pau, Institut de Recerca IIB Sant Pau, Barcelona, Spain; [e] Vall D'Hebron University Hospital, Barcelona, Spain; [f] CIBER of Epidemiology and Public Health (CIBERESP), Spain; [g] Department of Social Medicine and Family Health, Universidad Del Cauca, Colombia; [h] Hospital Universitario de Bellvitge, Instituto Català de Salut, Nursing Research Group, Bellvitge Institute for Biomedical Research, Spain; [i] Nursing School of Barcelona, Campus Docent Sant Joan de Déu-Private Foundation, University of Barcelona, Spain

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Background: Different types of interventions have been assessed for the prevention of adverse events. However, determining which patient-safety practice is most effective can be challenging when there is no systematised evidence synthesis. An overview following the best methodological standards can provide the best reliable integrative evidence.

Objectives: The objective of this study was to provide an overview of effectiveness nonpharmacological interventions aimed at preventing adverse events in the intensive care unit.

Methods: A review of systematic reviews (SRs) was conducted according to the Cochrane Handbook and PRISMA recommendations. PubMed, CINAHL, and Cochrane Library were searched for SRs published until March 2022. Two reviewers independently assessed the study's quality, using AMSTAR-2, and extracted data on intervention characteristics and effect on prevention of adverse events.

Results: Thirty-seven SRs were included, and 27 nonpharmacological interventions were identified to prevent 11 adverse events. Most of the reviews had critically low methodological quality. Among all the identified interventions, subglottic secretion drainage, semirecumbent position, and kinetic bed therapy were effective in preventing ventilator-associated pneumonia; the use of earplugs, early mobilisation, family participation, and music in reducing delirium; physical rehabilitation in improving muscle strength; use of respiratory support in preventing reintubation; the use of a computerised physician order entry system in reducing risk of medication errors; and the use of heated water humidifier was effective in reducing artificial airway occlusion.

Conclusions: Some nonpharmacological interventions reduced adverse events in the intensive care setting. These findings should be interpreted carefully due to the low methodological quality. SRs on preventing adverse events in the intensive care unit should adhere to quality assessment tools so that best evidence can be used in decision-making.

1. Introduction

Adverse events (AEs) are undesirable or unintended patient outcomes associated with healthcare management resulting in prolonged hospitalisation, disability at the time of hospital discharge, or death.[1] The occurrence of AEs due to unsafe care is approximately one in every 10 patients, and half of them are judged

* Corresponding author. Iberoamerican Cochrane Centre, Hospital de la Santa Creu i Sant Pau (IIB Sant Pau), C/ Sant Antoni Maria Claret, 167, Pabellón 18, planta 0, 08025, Barcelona, Spain. Tel.: +34 657023927.

E-mail addresses: stefanie.suclupe@autonoma.cat, stefanie.suclupe@gmail.com (S. Suclupe).

@Stef_Chriss (S. Suclupe)

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to be preventable. Most of these incidents are related to invasive clinical procedures and therapeutic management.[2] In addition, 12% of preventable patient harm causes permanent disability or death.[3]

Developing preventive interventions to reduce patient harm has become an international policy priority.[4] Moreover, the recognition that many AEs are not preventable has increased awareness to focus on preventable AEs.[5,6] Strengthening the focus of investigations on preventable AEs interventions can lead to greater clinical benefits and improved translation of patient-safety interventions into clinical practice.[6,7]

Patients in intensive care units (ICUs) are at a greater risk for AEs not only due to their inherent clinical conditions that lead to multiple treatments but also because they are in a highly complex environment.[8–12]

SRs are considered at the highest level in the hierarchy of evidence, reflecting the current scientific knowledge and therefore guiding evidence-informed decision-making. However, their conclusions are limited due to the methodological quality and the certainty of the evidence based on included primary studies.[13–16]

Due to the increasing number of SRs and the multiple preventive interventions being published, it is important to evaluate the current status and provide a summary of effective interventions to prevent them.[3,10,17–19] In this way, a review of SRs (overview) can provide the best reliable integrative evidence.[13] Hence, the objective of this article is to provide an overview of SRs assessing non-pharmacological interventions (NPIs) to prevent AEs in the ICU.

2. Method

2.1. Design

We conducted a review of SRs following a protocol registered in PROSPERO (CRD42019147956). Amendments to information provided in the protocol are described in Supplementary material 1.

Reviews of SRs use explicit and systematic methods to collate and appraise the methodological quality and to summarise and analyse their results across our research question identifying specific areas of available or limited evidence. A comprehensive overview can provide an accurate description of the current state of research and thus guide future research.[20–22] The overview was performed according to the Cochrane Handbook on methods for overviews,[13] and we followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) checklist[23] (Supplementary material 2).

2.2. Search methods

We developed a systematic search strategy for MEDLINE, CINAHL, and the Cochrane Library to identify studies published from inception until March 2022. English and Spanish language studies were included. The reference list of included SRs was screened to identify potentially relevant studies.

The keywords were selected according to the main components of our clinical question, after a discussion between the research team and tested by an experienced systematic search reviewer before publishing the final version of the protocol. The full search strategy is available in Supplementary material 3.

A pair of trained reviewers independently assessed the inclusion eligibility of the SRs. The first screening was based on the SR title and abstract. We identified papers of peer-reviewed SRs. A full-text assessment was conducted to determine the definitive inclusion of the selected SR. Disagreements in the selection of reviews were resolved by a third reviewer.

2.3. Inclusion and exclusion criteria

2.3.1. Type of studies

SRs of primary studies, including randomised controlled trials (RCTs), quasi-RCTs and controlled observational studies, investigating the effect of NPIs on AEs were included. We considered as an SR any evidence synthesis with a clear systematic methodological approach, a detailed search strategy using at least two database sources, eligible criteria relevant to our research objective, and a narrative synthesis and/or meta-analysis.

2.3.2. Type of patients

Adult ICU patients aged 18 years and above in medical and surgical ICUs were included.

2.3.3. Type of interventions

Any NPIs to prevent AEs focused on patient safety was included, described as new strategies, practices, behaviour, actions, procedures, or environment.

We considered control interventions to be usual care or standard ICU care defined as not providing any therapy specifically aimed at preventing AEs.

2.3.4. Types of outcome measures

Primary outcomes were incidence and ICU mortality related to AEs such as infections (mechanical ventilation–associated pneumonia, bloodstream infection (BSI), central catheter infection, peripheral catheter infection), delirium, reintubation, airway occlusion, pressure ulcers, physical function deterioration, and medication errors. *Secondary outcomes* were hospital mortality, length of mechanical ventilation, and stay in the ICU or in hospital. Outcomes that reported consequences of AEs in terms of extra treatment(s) or readmission were not the focus of this overview.

2.4. Data extraction

Data from studies such as trial design, the number of included studies, type of intervention, type of AEs, comparator, and outcomes were extracted by one reviewer and checked for accuracy by a second reviewer. Disagreement was resolved through discussion, and a third reviewer was consulted if needed.

2.5. Quality appraisal

Methodological quality of the reviews was assessed using AMSTAR-2,[24] which provides overall ratings (high, moderate, low, critically low) based on weaknesses in critical domains. A pair of reviewers independently assessed the quality of each study. Disagreements were resolved by a third reviewer. Moreover, we described the confidence in the evidence using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach for the primary outcomes when the SRs reported them.

2.6. Data analysis and synthesis

The study characteristics and patient outcomes for all the SRs that met our inclusion criteria were grouped by types of AEs in a tabular form. To assess the overlap of primary studies among included SRs, we created a matrix of evidence as a grid, placing all the included SRs in the columns and their respective primary studies in the rows. We calculated the corrected covered area (CCA) for the whole matrix and for each pair of SRs,[25] according to previously defined methods.[26] We considered overlap to be low if the CCA was below 5%, moderate if the CCA was between 5% and 10%, high if the CCA was between 10% and 15%, and very high if the CCA was above 15%. We repeated this process for each outcome, creating custom matrices including only the SRs and primary studies providing data for each specific comparison. We reported overlap for this custom matrix using the same thresholds mentioned above.

We compiled the pooled effect sizes of meta-analyses reported in the SRs and analysed the intervention components. Most of the effect sizes were expressed in odds ratio (OR); however, when risk ratio (RR) was reported, these were converted to OR if the number of events per group was provided.

Statistical analyses were performed using Review Manager V5.3 (The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, 2014). Analysis of forest plots was descriptive, and metanalysis was not performed due to the clinical diversity of intervention by outcomes and overlap among primary studies included in the SRs.

3. Results

3.1. Search results

The initial search of all databases yielded 3812 articles (Fig. 1). After the removal of duplicates, 3225 articles remained and were screened via review of their titles and abstracts. The screening resulted in 261 articles that underwent full-text review. A total of 224 articles were excluded because they did not meet our selection criteria. Fifty-six articles were excluded because the intervention was pharmacological, bundles, or educational interventions. A list of excluded studies with the reason for exclusion can be found in Supplementary material 4. Finally, 37 systematic reviews were included in this review.

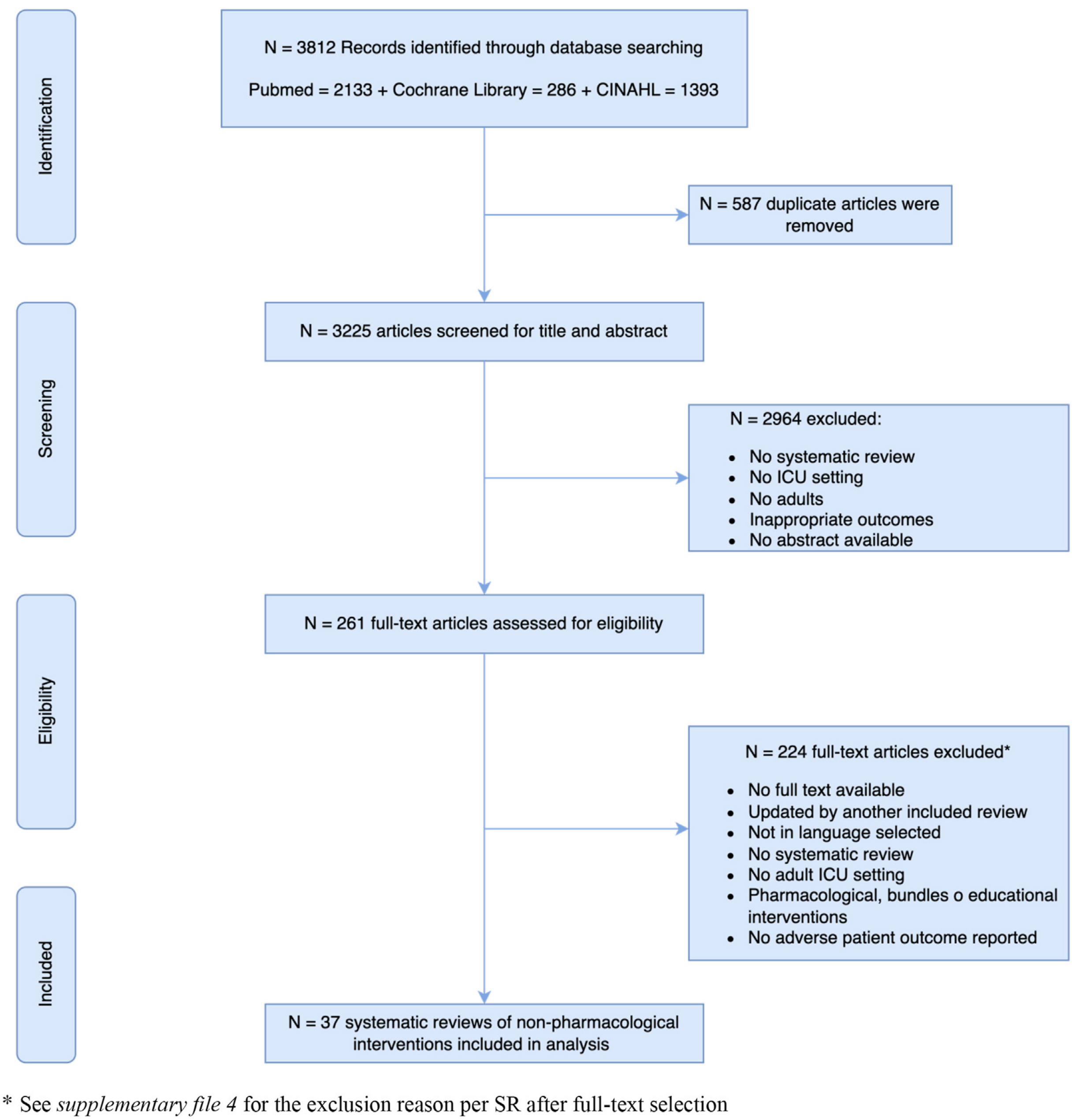


Fig. 1. Summary of search and selection – PRISMA 2020. ICU, intensive care unit; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

3.2. Characteristics of the included systematic reviews

The characteristics of the included NPI SRs are summarised in Table 1. More than half (n = 21) of the included SRs were published after 2016. These reviews incorporated a range of study designs; however, most of them (n = 30) included only randomised controlled trials (RCTs). Thirty-two SRs performed a meta-analysis (86.4%).

The total number of eligible primary studies in the SRs ranged from 2[27–30] to 24[31] studies. The number of patients in the eligible studies ranged from 454[32] to 3369[33] and was not reported or unknown in nine (24.3%) reviews.

The included reviews covered 11 different AEs: ventilator-associated pneumonia (VAP) (11 SRs),[33–43] delirium (six SRs),[29,44–48] physical function deterioration (five SRs),[32,49–52] reintubation (four SRs),[53–56] medication error (three SRs),[31,57,58] artificial airway occlusion or hospital-acquired pneumonia (two SRs),[59,60] healthcare-associated infections (HAIs; two SRs),[61,62] pressure injury (two SRs),[30,63] and tube displacement or tube occlusion (two SRs).[27,28,54] The total number of interventions evaluated was 27, and VAP was the most frequent AE studied with seven NPIs. Usual care, defined as the standard care received by patients and determined by the treating centre during ICU admission, standard medical, and nursing care, was the most common control group.

3.3. Methodological quality of SRs

The AMSTAR-2 quality scores of the included reviews are described in Table 2. Twenty-eight (75.6%) SRs scored critically low on methodological quality, six (16.2%) SRs scored low, three (8.1%) scored moderate, and only one (2.7%) scored high. The main deficiencies noted in critical domains were failure to report a prior registered protocol, adequacy of the literature search, and justification for excluding studies, while in noncritical domains, the main deficiencies were reasons for study design selection and describing the included studies in adequate detail. None of the included SRs fulfilled all the AMSTAR-2 criteria. Regarding the certainty of the evidence, only six (16.2%) SRs reported the certainty of evidence for the primary outcomes.

3.4. Methodological quality of the primary studies included in the SRs

The Cochrane Risk of Bias tool (RoB) was the most-used tool to determine methodological quality of the primary studies (62.2%), while 10 (24.3%) SRs only provided a narrative discussion of quality, and five (13.5%) SRs did not assess RoB. Most review authors noted that results should be interpreted with caution due to methodological study limitations.

3.5. Overlap assessment

The 37 included SRs comprised a total of 246 individual primary studies. The overall CCA, considering all SRs and all primary studies included in the reviews, was 1.0% (slight overlap). Supplementary material 5 provides a detailed assessment of the overall overlap among SRs.

Six of 17 comparisons regarding VAP outcomes included at least two SRs. Considering only SRs and primary studies providing data for each specific comparison, the overall CCA and detailed CCA by pair of reviews were very high for all the comparisons. For example, comparison 1.1.1 includes four SRs, comprising a total of 17 individual primary studies. Of these, seven were included in all SRs. This is reflected in the detailed overlap assessment, which shows that all SRs have a CCA of at least 47.1% (very high overlap).

One comparison regarding the incidence of delirium included four SRs and the overlap assessment was high (10.3%). Two comparisons regarding reintubation outcomes included at least two SRs, and the overlap assessment was high for the comparison of high flow nasal cannula (HFNC) versus conventional oxygen therapy (COT) and very high for the comparison noninvasive ventilation (NIV) versus conventional oxygen therapy (Supplementary material 6).

For other AEs studied, comparisons included only one SR; therefore, no overlap assessment was possible.

3.6. Effects of patient-safety interventions

3.6.1. Ventilator-associated pneumonia

3.6.1.1. Incidence of VAP. VAP definition varied among the studies depending on the diagnosis criteria used. Eight SRs considered VAP according to clinical, laboratory, and imaging findings, and three SRs did not provide this information.

Eleven SRs[33–43] assessed seven different NPIs for preventing VAP. Subglottic secretion drainage (SSD) compared with no drainage was assessed in four SRs, with a total of 44 RCTs and 10,193 patients. Results showed a statistically significant effect ranging from an OR of 0.48 (95% confidence interval [CI]: 0.38, 0.60) to an OR of 0.55 (95% CI: 0.46, 0.66).

Semirecumbent position compared with supine position was evaluated in two SRs[34,40] with 11 RCTs and 1096 patients. Results showed a statistically significant effect ranging from an OR of 0.42 (95% CI: 0.29, 0.59) to an OR of 0.47 (95% CI: 0.27, 0.82). Only one of them[40] assessed the certainty of the evidence, and it was graded as moderate.

Use of kinetic bed compared with usual bed was analysed in a single SR[35] and showed a statistically significant reduction in the incidence of VAP: (OR: 0.38; 95% CI: 0.28, 0.52). This effect was based on a total of 10 RCTs and 967 patients. The other comparison showed no differences between the experimental and control group for this outcome (Fig. 2a).

3.6.1.2. ICU mortality related to VAP. Five different NPIs for preventing ICU mortality related to VAP were assessed in six SRs.[35,37–40,43]

Respiratory physiotherapy compared with usual care was analysed in a single SR[38] and showed a statistically significant reduction in the ICU mortality related to VAP (OR: 0.67; 95% CI: 0.47, 0.96). This effect was based on five RCTs and 603 patients. The other comparison showed no differences between the experimental and control group for this outcome (Fig. 2b).

3.6.1.3. Hospital mortality related to VAP. Five experimental interventions for preventing hospital mortality related to VAP were assessed in eight SRs;[33,34,36,37,40–43] however, none of them showed significant results.

The comparison that drew most SRs (four)[33,37,41,43] was SSD compared with no drainage, with a total of 35 RCTs and 8520 patients. Measures of effect ranged from an OR of 0.91 (95% CI: 0.73, 1.13) to an OR of 1.03 (95% CI: 0.80, 1.32) (Fig. 2c).

3.6.2. Delirium

3.6.2.1. Incidence of delirium. Six SRs[29,44–48] assessed interventions to prevent delirium. Some authors compared environmental intervention (changes in light or sound/hearing) vs usual care in 26 RCTs. Results were not significant, ranging from an OR of 0.83 (95% CI: 0.49, 1,41) to an OR of 1.22 (95% CI: 0.92, 1.62). Only one of

Table 1
Characteristics of the included studies.

Adverse event	Author	Year	N studies included	Intervention(s)	Comparison(s)	Outcome(s)	ROB assessment	Meta-analysis
Ventilator-associated pneumonia (VAP)	Alexiou	2009	7 RCT	Semirecumbent position; prone position	Supine position	Incidence of VAP; hospital mortality; duration of mechanical ventilation; ICU length of stay	Yes	Yes
	Caroff	2016	17 RCT	SSD	Usual care (standard endotracheal tubes)	Incidence of VAP; ICU mortality; hospital mortality; duration of mechanical ventilation; ICU length of stay	Yes[a]	Yes
	Delaney	2006	15 RCT	Kinetic or rotating bed therapy	Usual care (kinetic or rotating bed therapy)	Incidence of VAP; ICU mortality; duration of mechanical ventilation; ICU length of stay	Yes[a]	Yes
	Faradita	2018	5 RCT	Closed endotracheal suctioning system	Open endotracheal suctioning system	Incidence of VAP; hospital mortality	Yes	Yes
	Frost	2013	9 RCT	SSD	Usual care (no drainage)	Incidence of VAP; ICU mortality; hospital mortality	No	Yes
	Muscedere	2011	13 RCT	SSD	Usual care (standard endotracheal tubes)	Incidence of VAP; ICU mortality; hospital mortality; ICU length of stay; duration of mechanical ventilation	No	Yes
	Pozuelo	2018	5 RCT	Respiratory physiotherapy interventions	Usual care, not receiving physiotherapy, any co-interventions	Incidence of VAP; ICU mortality; ICU length of stay	Yes[a]	Yes
	Siempos	2008	9 RCT	Closed endotracheal suctioning system	Open endotracheal suctioning system	Incidence of VAP; ICU mortality; duration of mechanical ventilation	Yes	Yes
	Wang, Li	2016	10 RCT	Semirecumbent position	Supine position	Incidence of VAP; ICU mortality; hospital mortality; ICU length of stay; duration of mechanical ventilation	Yes[a]	Yes
	Wang	2012	10 RCT	SSD	Usual care (no drainage)	Incidence of VAP; hospital mortality; ICU length of stay; duration of mechanical ventilation	Yes	Yes
	Wen	2017	8 RCT	Continuous subglottic secretion drainage	Intermittent subglottic secretion drainage	Incidence of VAP; hospital mortality; duration of mechanical ventilation	Yes[a]	Yes
Delirium	Burry	2021	12 RCT	Enviromental intervention	Usual care*	Incidence of delirium, hospital mortality; duration of mechanical ventilation; ICU length of stay	Yes[a]	Yes
	Deng Lu-Xi	2020	9 RCT	Enviromental intervention	Usual care*	Incidence of delirium, duration of ICU delirium	Yes	Yes
	Herling	2018	12 RCT	Enviromental intervention	Usual care*	Incidence of delirium	Yes[a]	Yes
	Kang	2018	15 RCT	NPhIs	Usual care*	Incidence of delirium; ICU	Yes[a]	Yes

Table 1 (*continued*)

Adverse event	Author	Year	N studies included	Intervention(s)	Comparison(s)	Outcome(s)	ROB assessment	Meta-analysis
						mortality; duration of ICU delirium; ICU length of stay		
	Litton	2016	5 RCT; 2 NRCT	Use of earplugs as a sleep hygiene strategy (physical environment)	Usual care*, other interventions	Incidence of delirium; hospital mortality	Yes[a]	Yes
	Liang Surui	2021	15 RCT	Early mobilisation, family participation, music, patient education, physical environment	Usual care*	Incidence of delirium	Yes[a]	Yes
Physical function deterioration	Adler	2012	7 NRCT; 3 RCT	Early mobilisation and physical therapy	Usual care*	Muscle strength; physical function: mobility	No	No
	Doiron	2018	4 RCT	Early mobilisation	Usual care (no mobilisation/active exercise, or mobilisation/active exercise given later than the intervention group)	Muscle strength; physical function: mobility	Yes[a]	No
	Menges	2021	4 RCT	Systematic early mobilisation standard	Early mobilisation (mobilisation initiated within 7 days but less systematically)	Muscle strength; physical function: mobility	Yes[a]	No
	Tipping	2016	14 RCT	Active mobilisation and rehabilitation	Usual care (standard physical therapy)	Muscle strength, ICU mortality; hospital mortality	Yes[a]	Yes
	Waldauf	2020	18 RCT	Physical rehabilitation	Usual Care*	Hospital mortality	Yes	Yes
Reintubation	Granton	2020	6 RCT	HFNC	Usual care (COT; NIV)	Incidence of reintubation; hospital mortality	Yes[a]	Yes
	Hua-Wei	2018	7 RCT	HFNC	Usual care (COT; NIV)	Incidence of reintubation	Yes[a]	Yes
	Liang Sujuan	2021	12 RCT	HFNC	Usual care (COT; NIV)	Incidence of reintubation; ICU mortality; hospital mortality	Yes[a]	Yes
	Xiaoyang Zhou	2020	15 RCT	HFNC; NIV	Usual care (COT; NIV)	Incidence of reintubation	Yes[a]	Yes
Medication error	Manias	2012	2 RCT and 22 QES	CPOE systems	Paper-based ordering	Rate of medication error	No	No
	Prgomet	2017	16 RCT and NRCT	CPOE systems	Paper-based ordering	Incidence of medication error; ICU mortality; ICU length of stay	Yes	Yes
	Wang	2015	8 NRCT	Pharmaceutical intervention (deliver pharmaceutical care in the ICU and not those solely involved in drug dispensing)	Usual service	Risk of general MEs	Yes[a]	Yes
Hospital-acquired pneumonia or artificial airway occlusion	Vargas	2017	18 RCT	HME	HWH	Incidence of artificial airway occlusion; incidence of hospital-acquired pneumonia; hospital mortality	Yes[a]	Yes
	Maertens	2018	6 RCT	Use of endotracheal tapered cuffs	Use of endotracheal nontapered cuffs (standard cuffed ET)	Incidence of hospital-acquired pneumonia; ICU mortality	Yes[a]	Yes
Healthcare-associated infections (VAP excluded)	Frampton	2014	5 RCT	Implementation of checklists	Usual care*	Hospital mortality related to catheter BSI	Yes[a]	No
	Chang	2019	4 RCT and BA	Universal gloving	Nongloving	Incidence of healthcare-	Yes	Yes

(*continued on next page*)

Table 1 (*continued*)

Adverse event	Author	Year	N studies included	Intervention(s)	Comparison(s)	Outcome(s)	ROB assessment	Meta-analysis
						associated infections		
Pressure injury	Lovegrove	2022	2 RCT	Reactive bed surface	Standard mattress	Incidence of pressure injury	Yes[a]	No
	Nieto-García	2021	5 RCT	Pre-early mobility programme	Post-early mobility programme	Incidence of pressure injury	Yes[a]	No
Tube displacement or tube occlusion	Gardner	2005	1RCT; 6 NRCT	ETT stabilisation (twill or cotton tape, adhesive tape, gauze, or a manufactured device)	Other ETT stabilisation	Incidence of endotracheal tube displacement	No	Yes
	Bench	2003	2 RCT	HME	HWH	Incidence of tracheal tube occlusion; incidence of VAP	Yes	No

BA = before-and-after study; COT = conventional oxygen therapy; CPOE = computerised physician order entry; ETT = endotracheal tube; HFNC = high-flow nasal cannula; HME = heat moisture exchange; HWH = heated water humidifier; ICU = intensive care unit; NIV = noninvasive ventilation; NPhI = nonpharmacological intervention; NRCT = nonrandomised controlled trial; QES = quasi-experimental study; RCT = randomised controlled trial; SSD = subglottic secretion drainage.
Usual Care*: Receiving standard care as determined by the treating centre during the ICU admission and standard medical and nursing care.
[a] Assessment using Cochrane risk-of-bias tool (RoB: Risk of Bias).

them[48] assessed the certainty of the evidence, and it was graded as low (Fig. 3).

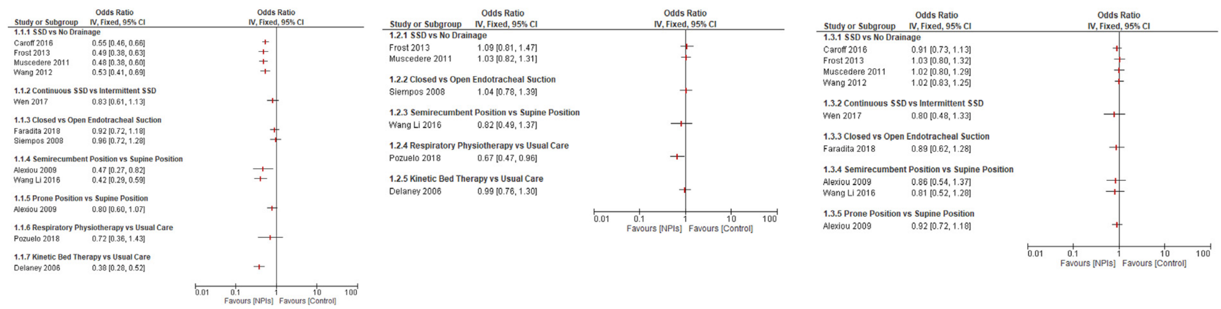
Litton et al.[45] found that earplug use was associated with a lower incidence of delirium than usual care: an OR of 0.59 (95% CI: 0.44, 0.79). This effect was based on five RCTs and 832 patients.

Kang et al.[44] grouped different NPIs and found these were effective in reducing incidence of delirium with an OR of 0.66 (95%

Table 2
AMSTAR-2 assessment.

Reference	AMSTAR-2 domains																
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	Overall quality
Adler 2012	Yes	No	No	PY	No	No	No	PY	No	No	NMA	NMA	No	No	NMA	No	Critically low
Alexiou 2009	Yes	No	No	PY	Yes	Yes	No	PY	PY	No	Yes	No	No	Yes	No	No	Critically low
Bench 2003	Yes	No	No	PY	No	No	Yes	Yes	PY	No	NMA	NMA	No	No	NMA	No	Critically low
Burry 2021	Yes	Yes	No	PY	Yes	Yes	No	PY	Yes	Yes	Yes	No	Yes	No	No	Yes	Critically low
Caroff 2016	Yes	No	Yes	PY	No	Yes	No	PY	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Critically low
Chang 2019	Yes	No	No	PY	Yes	Yes	No	Yes	PY	Yes	No	No	Yes	Yes	Yes	Yes	Critically low
Delaney 2006	Yes	PY	No	Yes	Yes	Yes	No	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Low
Deng Lu-Xi 2020	Yes	PY	No	PY	Yes	Yes	No	PY	PY	No	Yes	No	No	Yes	Yes	Yes	Critically low
Doiron 2018	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	NMA	NMA	Yes	Yes	NMA	Yes	High
Faradita 2018	Yes	No	Yes	No	Yes	Yes	No	No	Yes	No	No	No	No	No	No	No	Critically low
Frampton 2014	Yes	PY	No	PY	Yes	Yes	Yes	Yes	Yes	Yes	NMA	NMA	Yes	Yes	NMA	Yes	Moderate
Frost 2013	Yes	No	No	PY	No	No	No	No	No	No	Yes	No	No	Yes	Yes	No	Critically low
Gardner 2005	Yes	No	No	PY	Yes	No	No	PY	No	No	Yes	No	Yes	Yes	No	No	Critically low
Granton 2020	Yes	Yes	No	No	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Critically low
Herling 2018	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Low
Hua-Wei Huang 2018	Yes	PY	No	PY	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Moderate
Kang Lee 2018	Yes	No	No	PY	Yes	Yes	No	PY	PY	Yes	No	Yes	Yes	No	Yes	Yes	Critically low
Lian Sujuan 2021	Yes	No	No	No	No	Yes	No	PY	Yes	No	Yes	No	No	Yes	Yes	Yes	Critically low
Liang Surui 2021	Yes	Yes	No	No	Yes	Yes	No	PY	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Critically low
Litton 2016	Yes	No	No	PY	Yes	Yes	No	PY	PY	No	No	No	Yes	Yes	Yes	Yes	Critically low
Lovegrove 2022	Yes	Yes	No	No	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No	Yes	No	Yes	Critically low
Maertens 2018	Yes	No	Yes	Yes	No	No	Yes	PY	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Low
Manias 2012	Yes	No	No	No	Yes	Yes	No	PY	PY	Yes	NMA	NMA	No	No	NMA	Yes	Critically low
Menges 2021	Yes	Yes	Yes	PY	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Low
Muscedere 2011	Yes	No	Yes	PY	Yes	Yes	No	PY	No	No	Yes	No	No	Yes	No	Yes	Critically low
Nieto Garcia 2020	Yes	No	No	No	Yes	Yes	No	PY	Yes	No	Yes	No	No	No	No	No	Critically low
Pozuelo 2018	Yes	No	Yes	PY	Yes	Yes	No	PY	Yes	No	Yes	Yes	Yes	Yes	No	Yes	Critically low
Prgomet 2017	Yes	PY	No	PY	Yes	No	No	PY	Yes	No	No	No	No	No	No	Yes	Critically low
Siempos 2008	Yes	No	Yes	No	Yes	Yes	No	PY	PY	Yes	No	No	No	Yes	Yes	No	Critically low
Tipping 2017	Yes	PY	Yes	Yes	Yes	Yes	No	PY	PY	No	No	Yes	Yes	Yes	No	Yes	Critically low
Vargas 2017	Yes	No	Yes	PY	Yes	Yes	No	PY	Yes	No	Yes	Yes	Yes	No	Yes	Yes	Critically low
Waldauf 2020	Yes	Yes	No	PY	Yes	Yes	No	PY	PY	Yes	Yes	No	No	No	Yes	Yes	Critically low
Wang F. 2012	Yes	No	Yes	PY	No	Yes	No	No	Yes	No	Yes	Yes	No	No	Yes	Yes	Critically low
Wang L. 2016	Yes	Yes	Yes	PY	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Moderate
Wang T. 2015	Yes	No	Yes	PY	Yes	No	No	PY	PY	No	No	No	Yes	No	No	No	Critically low
Wen 2017	Yes	No	Yes	PY	Yes	Yes	No	PY	Yes	No	No	No	No	No	No	No	Critically low
Zhou Xiaoyang 2020	Yes	Yes	No	PY	Yes	Yes	Yes	PY	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Low

NMA = no meta-analysis; PY = partial yes.



(a) Incidence of VAP (b) ICU mortality related to VAP (c) Hospital mortality related to VAP

Fig. 2. Forest plot of the influence of non-pharmacological interventions to reduce ventilator-associated pneumonia (VAP). (a) Incidence of VAP. (b) ICU mortality related to VAP. (c) Hospital mortality related to VAP. CI = confidence interval; ICU, intensive care unit; SSD = subglottic secretion drainage.

CI: 0.50, 0.87). This effect was based on 14 studies (cohort and RCTs) and 3372 patients.

Liang Surui et al.[48] found that early mobilisation (moderate-certainty evidence), family participation (moderate-certainty evidence), and music (low-certainty evidence) have a statistically significant effect on decreasing delirium incidence.

3.6.2.2. Mortality related to delirium. Only Kang et al.[44] assessed *ICU mortality*, including three studies (cohort and RCTs), and results were not statistically significant (OR: 0.81; 95% CI: 0.61, 1.07).

Concerning the outcome *hospital mortality related to delirium*, this was reported in two SRs,[45,46] and results were not statistically significant ranging from an OR of 0.77 (95% CI: 0.54, 1.10) to an OR of 0.91 (95% CI: 0.63, 1.31).

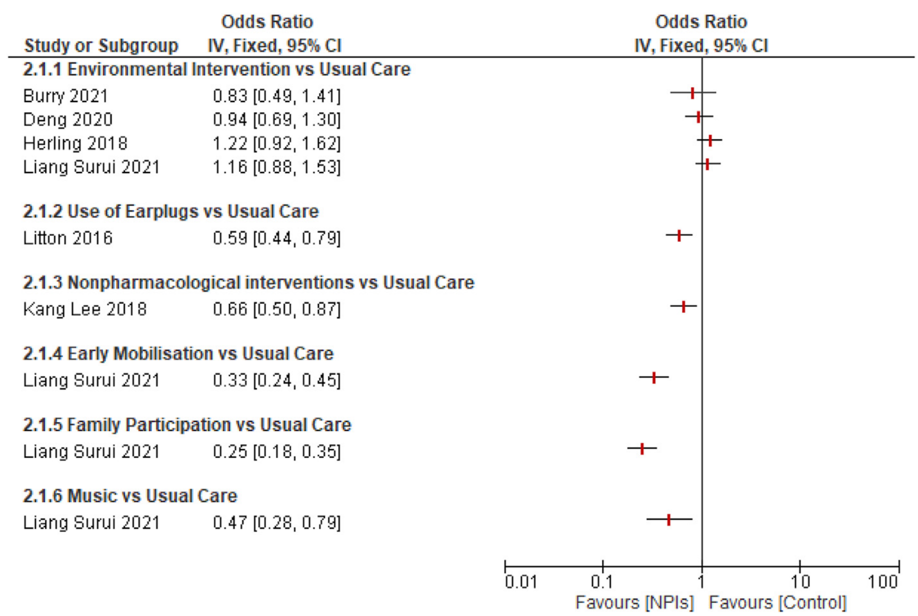
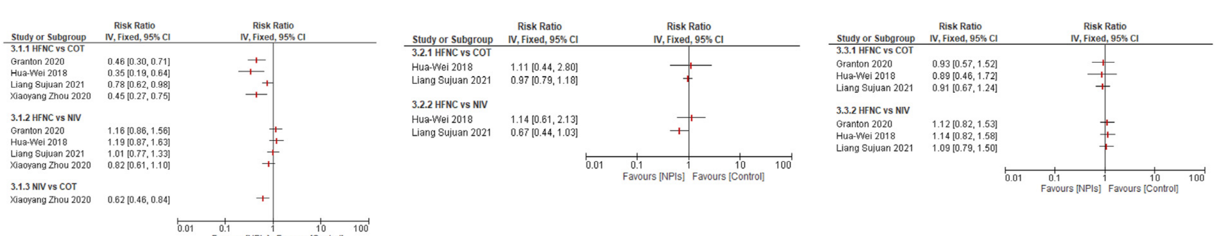


Fig. 3. Forest plot of the influence of nonpharmacological interventions to reduce incidence of delirium. CI = confidence interval.



(a) Rate of reintubation (b) ICU mortality related to reintubation (c) Hospital mortality related to reintubation

Fig. 4. Forest plot of the influence of non-pharmacological interventions to reduce reintubation. (a) Rate of reintubation. (b) ICU mortality related to reintubation. (c) Hospital mortality related to reintubation. CI = confidence interval; COT = conventional oxygen therapy; HFNC = high flow nasal cannula; ICU = intensive care unit; NIV = noninvasive ventilation; NPI = nonpharmacological interventions; SSD = subglottic secretion drainage.

3.6.3. Physical function deterioration

Five SRs reported results on physical function deterioration. Three of them[32,49,51] assessed muscle strength at ICU discharge using the Medical Research Council scale and physical function using the Barthel Index or Short Form (SF-36) questionnaire to measure mobility–disability. We could not pool results from those SRs because the interventions assessed were different.

Tipping et al.[50] assessed physical functional status and muscle strength using the WHO International Classification of Functioning, Disability and Health. Physical rehabilitation in the ICU was assessed in comparison to usual care, and the experimental group demonstrated an improvement in muscle strength (mean difference (MD): 8.62; 95% CI: 1.39, 15.86).

For early or systematic mobilisation compared with late or standard care, authors[32,49,51] found no statistically significant benefit on muscle strength. Tipping et al.[50] and Waldauf et al.[52] showed that active mobilisation and physical rehabilitation compared with usual care did not impact mortality related to physical deterioration.

3.6.4. Reintubation

3.6.4.1. Rate of reintubation. Four SRs[53–56] assessed two different NPIs for preventing reintubation. HFNC compared with conventional oxygen therapy was assessed in six RCTs and 1558 patients. Results showed a statistically significant effect ranging from an OR of 0.35 (95% CI: 0.19, 0.64) to an OR of 0.78 (95% CI: 0.62, 0.98). The certainty of the evidence was moderate for two reviews[53,56] and low for one of them.[54]

HFNC-compared NIVs included seven RCTs and 1839 patients. Results did not demonstrate statistically significant effects on decreasing intubation rate, ranging from an OR of 0.82 (95% CI: 0.61, 1.10) to an OR of 1.19 (95% CI: 0.87, 1.63). NIV compared with conventional oxygen therapy was assessed in nine trials, and results did not show a statistically significant effect (OR: 0.62; 95% CI: 0.46, 0.84, moderate-certainty evidence) (Fig. 4a).

3.6.4.2. Mortality related to reintubation. Two SRs[54,55] compared HFNC with conventional oxygen therapy (OR: 0.97; 95% CI: 0.79, 1.18 to OR: 1.11; 95% CI: 0.44, 2.80; 6RCTs, 1749 participants) and HFNC with NIV (OR: 0.67; 95% CI: 0.44, 1.03 to OR: 1.14; 95% CI: 0.61, 2.13; 5RCTs, 1434 participants). Results had no statistically significant effects on the ICU mortality outcome (Fig. 4b).

Concerning the outcome of hospital mortality related to reintubation, this was reported in three SRs[53–55] that compared HFNC with conventional oxygen therapy (OR: 0.89; 95% CI: 0.46, 1.72 to OR: 0.93; 95% CI: 0.57, 1.52; 6RCTs, 1321 participants) and HFNC with NIV (OR: 1.09; 95% CI: 0.79, 1.50 to OR: 1.14; 95% CI: 0.82, 1.58; 5 RCTs, 1284 participants). Results had no statistically significant effects. Only one SR, for each comparison, reported certainty evidence, and it was graded as moderate (Fig. 4c).

3.6.5. Medication error

All SRs examining medication error (ME) included RCTs and NRCTs. We found that pharmaceutical intervention vs usual care did not show significant effects.[58] However, computerised physician order entry system vs paper-based ordering was associated with a significant reduction in MEs, with an RR of 0.71 (95% CI: 0.68–0.75).[57] This result was based on 16 studies.

3.6.6. Artificial airway occlusion or hospital acquired pneumonia (non-VAP)

Heat moisture exchangers compared with headted water humidifier for preventing artificial airway occlusion were assessed in one SR,[60] including 14 RCTs and 2125 patients. Results were statistically significant, favouring headted water humidifier with an OR of 2.51 (95% CI: 1.27, 4.95), but there were no differences in the prevention of hospital-acquired pneumonia.

Endotracheal tapered cuffs vs endotracheal nontapered cuffs were also assessed in one SR,[59] which included six RCTs and 1324 patients, for prevention of ICU mortality related to hospital-acquired pneumonia, but results were not statistically significant.

3.6.7. HAIs: catheter BSI

Two SRs assessed the implementation of checklists[61] and universal gloving[62] compared with usual care for preventing HAI: catheter BSI. One SR[61] affirmed that there were insufficient data to draw conclusions, and the other SR[62] found that results were not statistically significant when only RCTs were pooled.

3.6.8. Pressure injury

Two SRs were included; one of them compared reactive bed surface with a standard mattress, and the other compared pre-early with post-early mobility programs to reduce pressure injury incidence. No one showed statistically significant results, and findings were inconclusive due to the differences in clinical characteristics and length of stay of patients.

There were other interventions to prevent AEs (tube displacement and tube occlusion), but we found few SRs included for each one. The individual results of them are summarised in Supplementary material 7.

4. Discussion

To the best of our knowledge, this is the first overview to systematically summarise and assess the quality of SRs and overlap of primary studies on NPIs for preventing AEs in ICU patients. We included 37 SRs of NPIs that evaluated 27 patient-safety interventions to reduce 11 different AEs.

We found the overall confidence of results based on the AMSTAR-2 was critically low because 73.7% of the SRs included had important methodological quality limitations. The main failures in critical domain assessment were reporting without a registered protocol, inadequacy of the literature search, and lack of justification for excluding studies, remaining the unawareness of the reason for their exclusion.[13,24]

Despite a slight overall overlap for the overview as a whole, our overlap assessment at the outcome level showed a high and very high overlap for 12 comparisons. This overlapping raises awareness of redundant SRs publications in this area.[64,65]

There were several interventions to prevent VAP, which remains among the most frequent infections in the ICU setting.[64] Most current guidelines focus on therapy and diagnosis recommendations of VAP, not prevention.[65,66] However, from seven types of NPIs, only three showed significant effects in reducing the incidence of VAP: subglottic secretion, elevating the head of the patient, and kinetic bed therapy. A literature review also found other pharmacological interventions but concluded that these implemented practices should be reviewed due to the low level of evidence.[67]

Many included SRs showed a reduction in the incidence of delirium. Early mobilisation showed a significant effect on preventing delirium; this finding is consistent with a previous clinical practice guideline that recommend performing early mobilisation of adult ICU patients whenever feasible to reduce the incidence of delirium.[68] A recent review found that multicomponent (pharmacological and nonpharmacological) interventions were optimal for preventing delirium,[47] and family participation resulted in better outcomes for reducing the incidence of delirium.[47,48] In fact, our findings are supportive of international guidelines, suggesting the use of NPIs as part of a multimodal approach, especially in the management of delirium.[69,70]

We have not included guidelines or health technology assessments in our search; therefore, possible SRs have not been identified. We have found two guidelines, Devlin et al. (update of the Barr et al. guideline) and DAS-TASK 2015[68,69,71] that performed SRs to answer questions and made recommendations. The guideline of Devlin et al. addresses the management of pain, agitation/sedation, delirium, immobility, and sleep disruption, whereas the guideline of DAS-TASK 2015 tackles the management of delirium, analgesia, and sedation. Our overview agrees with these two guidelines in evaluating the nonpharmacological preventive measures to avoid delirium and the effects of immobility. We agree on the inclusion of most primary studies, except for the benefits of rehabilitation and mobilisation, of which Devlin included 16 RCTs, whereas we included 12 RCTs. However, the evidence was very similar.

Patients' physical rehabilitation and active mobilisation on their own combined with therapy prevents physical deterioration. However, some authors suggest that best outcomes in physical function are associated with good pain management, awakening, and breathing coordination, delirium management, and early exercise/mobility.[69,72]

HFNC or NIV compared to conventional oxygen therapy reduced the rate of reintubation, but there were no significant effects on ICU or hospital mortality. The certainty evidence varied among reviews from low to high. These findings are consistent with European Respiratory guidelines regarding the NIV in patients at high risk of reintubation as a conditional recommendation, given the low certainty of evidence.[73] Furthermore, the European Society of Intensive Care Medicine made a conditional recommendation for HFNC following extubation (moderate certainty) in reducing rates of reintubation.[74]

We found that in the ICU setting, the use of a computerised physician order entry system reduces the risk of general medication errors compared with paper-based ordering. However, computerised physician order entry systems are implemented in only about one-third of hospitals. Further research is needed to better characterise links to patient harm.[75,76]

We only found one SR that indicated that headted water humidifier significantly reduced the incidence of artificial airway occlusion. However, due to the small number of studies included and the low quality of this evidence, it is difficult to be confident about this finding.[77]

Similarl to our findings, other authors have affirmed that there is little evidence on the effects of interventions to prevent HAIs such as infection control programs.[78] For a better understanding, a more detailed analysis of the infection type and where and how this AE occurs is required.[79]

Even our findings on using reactive bed surfaces or implementing a pre-early mobility programme did not show benefits in reducing pressure injuries; the European guideline for prevention and treatment of pressure ulcers remarks that those can be a preventive measure. However, the strength of the recommendation is weak. Moreover, early mobilisation in critical patients is based on good practice statements that are not supported by evidence to be significant for clinical practice.[80] While it is true that preventing AEs should be considered a patient safety goal, comfort is the principal consideration in supportive care, especially in critical patients.[81]

4.1. Limitations

We did not search for potential SRs included in the guidelines published; thus, information on other nonpharmacological preventive interventions may have been omitted. Furthermore, our overview is limited by the methodological quality of the SRs and its included primary studies. Results are presented descriptively using findings from SRs, but we did not conduct a meta-analysis grouping data. Participants among SRs included were heterogeneous. Even when patients were in the adult ICU, they had a wide variety of diseases, patient characteristics, reasons for ICU admission, and variation in standard intensive care practices. Furthermore, not all comparisons reported certainty of evidence, which limited drawing conclusions about NPIs.

The main strength is that the overview was carried out rigorously following the Cochrane methodology, with an updated comprehensive literature search, prespecified criteria for searching and analysis, and the selection and quality assessment of included studies evaluated independently by two authors.

Studies should be better conducted and reported to provide adequate information on preventive interventions focused on patient safety and outcomes. Future SRs should be properly designed and conducted using the AMSTAR-2 checklist, principally by providing a research protocol, performing study selection and data extraction in duplicate, providing a list of both included and excluded studies, and assessing the risk of bias in the primary studies. Moreover, we need to synthesise other types of interventions to prevent AEs, including pharmacological intervention, educational programs, and multicomponent interventions, as well as focus the intervention on patient outcomes. Some AEs studied in this overview are not yet included in standard documents or considered quality indicators to optimise patient care. Therefore, our findings could be considered in developing or updating clinical practice guidelines to prevent AEs.

One major limitation to this project is that the search strategy did not include professional guidelines that were constructed using the process of systematic review where the term 'systematic review' was not in the title. Readers are cautioned to search for guidelines and review those in addition to this summary prior to making practice changes. Future authors are cautioned to filter the search strategy by 'systematic review' instead of searching for the words 'systematic review' in the title as it is now standard practice for professional guidelines to be written using the process of systematic review.

5. Conclusions

We found some nonpharmacological interventions reduced AEs in an intensive care setting. A significant effect was found for SSD, semirecumbent position, and kinetic bed therapy in reducing the incidence of VAP; for the use of earplugs, early mobilisation, family participation, and music in reducing delirium; for physical rehabilitation in improving muscle strength; for the use of respiratory support in preventing reintubation; for use of a computerised physician order entry system in reducing ICU mortality related to medication errors; and for the use of headted water humidifier in reducing artificial airway occlusion. However, the findings are questionable due to the variety of patient characteristics, lack of certainty of evidence reported, the very high overlap for some comparisons, and the critically low quality of SRs included, making it difficult to be confident about them. In situations where strength of the evidence to support the evidence is low, clinical leaders are advised to deploy an evidence-based practice model when translating these interventions into practice to monitor quality outcomes. SRs about preventing AEs in the ICU should adhere to quality assessment tools so that best evidence can be used with greater confidence in decision-making.

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Credit authorship contribution statement

Stefanie Suclupe: Conceptualisation, Writing - original draft, Formal analysis, Data curation, Writing - review & editing

Percy Efrain Pantoja Bustillos: Formal analysis, Data curation, Writing - review & editing

Javier Bracchiglione: Formal analysis, Data curation, Writing - review & editing

Carolina Requeijo: Data curation, Writing - review & editing

Karla Salas-Gama: Data curation, Writing - review & editing

Ivan Solà: Data curation, Writing - review & editing

Angela Merchán-Galvis: Data curation, Writing - review & editing

Jaume Uya Muntaña: Data curation

Gemma Robleda: Conceptualisation, Review & editing

Maria Jose Martinez–Zapata: Conceptualisation, Supervision, Writing - original draft, Formal analysis, Data curation, Writing - review & editing.

All authors approved the final version of the study.

Conflict of interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Ethical statement

Ethical statement not applicable the authors undertook a systematic review, no ethical statements to declare.

Registration of reviews

The protocol was registered in PROSPERO (International Prospective Register of Systematic Reviews); number CRD42019147956; https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42019147956

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.aucc.2022.11.003.

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