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Non-pharmacological interventions for delirium in critically ill children: a scoping review

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ABSTRACT

Objectives Delirium is one of the most common forms of acute cerebral dysfunction in critically ill children, leading to increased morbidity and mortality. The aim was to identify studies describing or evaluating non-pharmacological interventions to prevent or treat paediatric delirium.

Design Scoping review.

Data sources Searches were performed in Medline, CINAHL, Cochrane Library, Ovid (Journals), EMBASE and Web of Science from January 2000 to April 2023. A hand search and update were conducted on 01 June 2024.

Eligibility criteria for selecting studies We included studies involving critically ill children (0–18 years) in intensive care settings that examined non-pharmacological interventions for the prevention or treatment of paediatric delirium. Only empirical studies and reviews with transparent methodology were considered.

Data extraction and synthesis Title and abstract screening and full-text review of articles were conducted by two reviewers based on prespecified inclusion criteria. Two reviewers extracted relevant information from the included studies in tabular form. Extracted variables included publication year, title, author(s), country, setting, population and age, design, sample size, intervention components, outcome(s) and findings.

Results Nine studies were included. In total, 16 different intervention components were identified. The most frequently reported components for preventing and treating paediatric delirium were promoting mobilisation, encouraging family presence and involvement, improving sleep, and standardised instruments or checklists for underlying aetiology. Most intervention studies were before-and-after studies; overall, seven different outcomes were used. Study results regarding the effects of delirium were inconsistent.

Conclusions Various non-pharmacological interventions are currently described to mitigate paediatric delirium, but the underlying evidence is limited. High-quality intervention research using relevant and comparable outcomes is needed to evaluate the effect of non-pharmacological interventions. Despite employing a comprehensive search strategy, we must consider the possibility that relevant articles were overlooked.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This scoping review was conducted according to the methodological guidance of the Joanna Briggs Institute.
⇒ Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews guidelines were followed with a preregistered study protocol.
⇒ A comprehensive search in six databases and citation tracking without language restrictions was performed.
⇒ No formal risk of bias was performed.

INTRODUCTION

Delirium is a neurocognitive disorder characterised by a sudden change in attention, cognition, and awareness caused by underlying medical conditions or treatments.[1–3] It is associated with negative treatment outcomes and poor prognosis. Delirium typically develops rapidly, within hours to days.[4] It can be classified into hypoactive, hyperactive or mixed forms. Symptoms may include restlessness, agitation, somnolence and psychomotor retardation, which can vary throughout the day.[1 5] Hypoactive and mixed delirium are the most common forms and typically last several days.[6–8] Paediatric delirium varies widely depending on the type and setting, ranging from 17% to 81%.[9–11] It is associated with increased mortality in children[1 11] and can have long-term consequences, affecting cognitive and functional development.[12] Delirium is a common challenge in paediatric and neonatal intensive care units (PICU/NICU).[13] Therefore, preventing delirium in critically ill children is essential.

Several studies have shown that the risk of developing delirium in critically ill children increases when certain conditions apply. These conditions can be disease-related factors (like mechanical ventilation, the use of benzodiazepines, and anticholinergics), patient-related factors (like developmental

delay, age below 2 years, etc.) or environmental factors (length of intensive care unit (ICU) stay).[14 15] Screening tools like the Cornell Assessment of Paediatric Delirium (CAPD) and assessment tools like the Paediatric Confusion Assessment Method-intensive care unit (pCAM-ICU) may help to identify delirium in children.[16]

In addition to pharmacological approaches (e.g., symptom severity control),[4 17] non-pharmacological interventions are recommended for preventing and treating delirium, as they mainly target the underlying precipitating risk factors.[18] Similar to adults,[19 20] combining several non-pharmacological interventions into a bundle may help to reduce the incidence of delirium in critically ill children in the PICU or NICU.[21–23] The interventions should be tailored to the child's stage of development and age.[24]

In recent years, the ABCDEF bundle (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) has emerged as a structured approach in intensive care settings to manage delirium. This framework, originally developed for adults, is now being adapted within paediatric and neonatal care settings.[25]

Intervention bundles for delirium prevention are considered complex interventions. This complexity is challenging in terms of investigating overall effectiveness and the specific impact of individual components.[26] Although reviews about paediatric delirium have been published, a systematic overview focussing on non-pharmacological interventions for critically ill children in PICU is lacking so far.[4 27 28] This is urgently needed to describe the current state of evidence by identifying relevant interventions, outcomes and study designs to identify possible evidence gaps and research needs. Therefore, this review aims to map the current evidence on non-pharmacological interventions for delirium prevention and treatment in paediatric patients. Specifically, the following review question was developed: which non-pharmacological interventions have been used to prevent and treat delirium in PICUs/NICUs, and what effects have been described?

METHODS

A scoping review (ScR) was conducted according to the methodological guidance of the Joanna Briggs Institute.[29] ScRs are useful to map the breadth and nature of existing evidence without evaluating the quality of evidence. The manuscript is structured according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews checklist.[30]

Patient and public involvement

Patients and/or the public were not involved in this research's design, conduct, reporting or dissemination plans.

Protocol and registration

A protocol was published a priori, and no changes were made.[31]

Eligibility criteria

The following inclusion criteria were applied: (i) child or adolescent populations, 0–18 years with critical illness; (ii) any non-pharmacological interventions to prevent or treat paediatric delirium; (iii) PICUs and NICUs and (iv) studies providing empirical data or reviews having clear review questions, using transparent methods and reporting. No language restrictions were applied. Sources of unpublished studies, grey, and other types of literature were excluded.[31] Studies were excluded if they focused primarily on adult populations or if data for paediatric patients could not be clearly disaggregated. In cases where studies included mixed-age populations (eg, adults and children), only those that provided separate analyses or clearly reported findings for the paediatric subgroup were included. Similarly, studies covering both neonates and older children were included if the population fell within the age range and the results were reported in an age-differentiated manner or applicable to the full paediatric spectrum. If no clear separation of age-specific data was possible, such studies were excluded to maintain population specificity.

Interventions were defined as any non-pharmacological activity being used to prevent or manage delirium in critically ill children in NICU and PICU settings. This includes a wide range of strategies, such as educational programmes, behavioural and environmental modifications, as well as organisational changes and specific protocols aimed at minimising the risk of delirium or mitigating its effects. This includes individual-related interventions (e.g., reorientation, mobilisation) and environment-related (ward-wide) interventions (e.g., daily structure, environmental adaptation).

Information sources

In April 2023, the databases Medline via PubMed, CINAHL via EBSCOHost, Cochrane Library, Journals@Ovid, EMBASE via Ovid and Web of Science Core Collection were searched. The search period was between January 2000 and April 2023. Additionally, backward citation searching was conducted via Web of Science by reviewing the reference lists of included full-text articles to identify any additional relevant literature. Furthermore, forward citation tracking was conducted in January 2024 to identify any pertinent additional publications by tracking articles that cited any of the full texts included up to that date. In June 2024, a focused search update was conducted by MZ in Medline via PubMed, as all previously included studies were indexed in this database. This targeted approach was considered sufficient to identify newly published literature relevant to the review.

Search

The search strategy for this ScR was developed by experienced researchers with expertise in conducting systematic reviews, creating search strategies and based on previous studies. The search strategies for the individual databases are shown in online supplemental Appendix 1. The search terms were translated for each database supported by Systematic Review—Accelerator.[32]

Selection of the source of evidence

MZ performed the searches across all databases. Two reviewers (MZ and ND) independently screened titles, abstracts, and full texts. All retrieved resources were imported into EndNote V.20.2.1/30 November 2021, for Windows (Clarivate Analytics, PA, USA), and duplicates or retracted references were removed. The screening process was facilitated by using RAYYAN.[33] Any disagreements between MZ and ND during each stage of the selection process were resolved through discussion or with a third reviewer of the author team.

Data charting process and data items

Two reviewers (ND/MZ) extracted the data. Data extraction included general information, such as aim, design, population, sample size, a description of the interventions, and details about the outcomes and results.[31]

Critical appraisal of individual sources of evidence

Critical appraisal was not conducted.

Synthesis of results

The extracted data are presented in tabular and narrative form. A detailed results mapping was conducted, including a tabular representation of the study characteristics, outcomes, and interventions. To ensure systematic descriptions, the intervention components were categorised according to the ABCDEF bundle,[25] a comprehensive set of evidence-based practices aimed at improving outcomes for critically ill paediatric patients. Additionally, the components were aligned with the three domains proposed for non-pharmacological delirium management bundles in PICU patients, as proposed by Stenkjer *et al*.[24] We also distinguished between individual-related and environment-related interventions.

RESULTS

Selection of sources of evidence

After deduplication, removal of retracted references or other reasons, 4896 records were screened. After screening of titles and abstracts, 4822 references were excluded, and 68 were read in full text. Three additional references were identified from citation searching. Finally, nine primary research articles[21–23 25 34–38] were included. The flowchart of the search and screening process is shown in Figure 1. The update has not produced any further results.

Characteristics of sources of evidence

Detailed descriptions of the included studies are provided in online supplemental Appendix 2-4. The

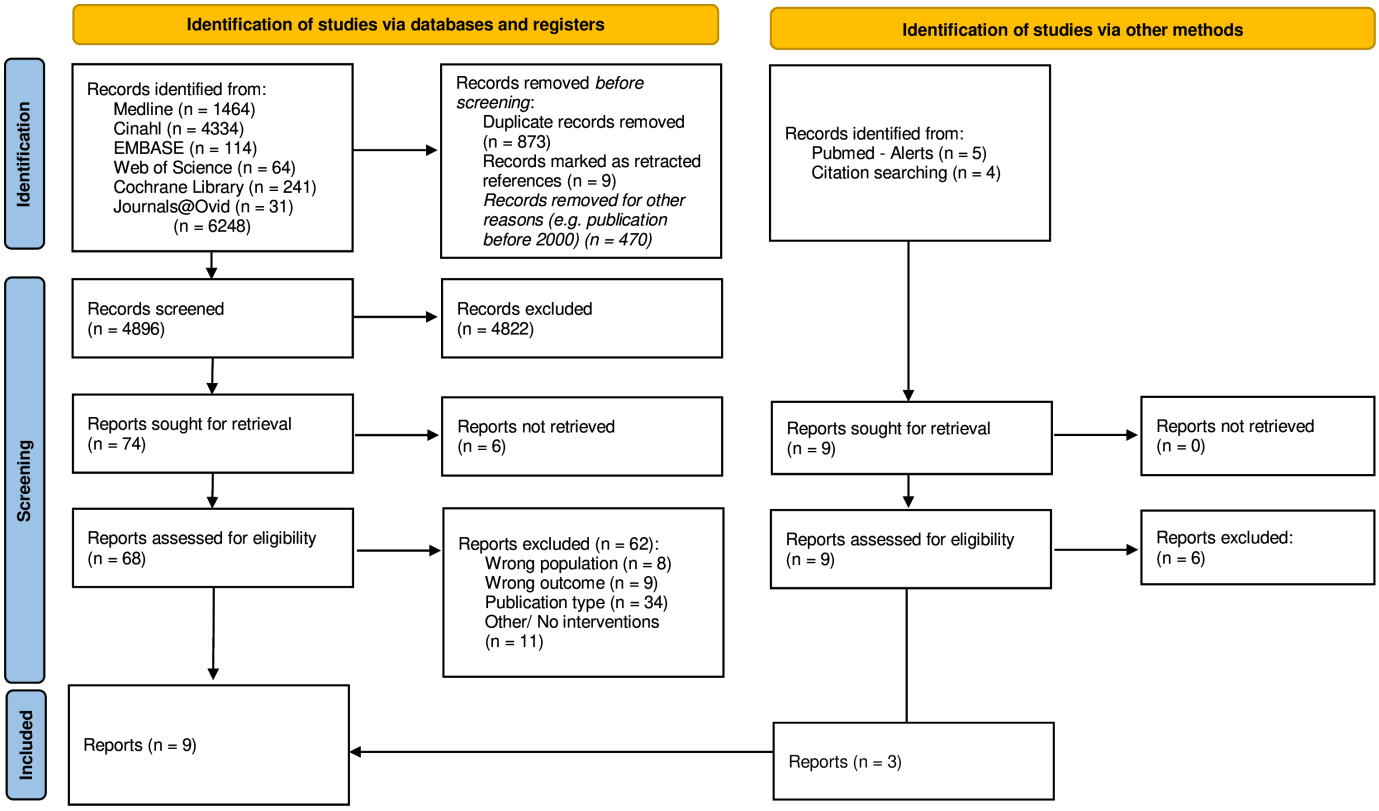

Figure 1 Preferred Reporting Items for Systematic Reviews and Meta-Analyses flowchart.

main characteristics of the included studies is described in Table 1.

Six of the nine studies are intervention studies designed as before-and-after or quality improvement projects, which evaluated the effect of implementing non-pharmacologic interventions on the occurrence of paediatric delirium.[21–23 34 35 38] Three were observational studies.[25 36 37] Most studies were monocentric,[21–23 34–38] and one study was multicentric.[25] One study focused on improving early mobilisation and its effect on delirium.[35] One study focused on the feasibility and safety of a PICU bundle,[34] and the other[36] determined the frequency and risk factors of paediatric delirium. One observational study assessed the occurrence of delirium following the PICU Liberation ABCDEF bundle utilisation.[25]

The included studies reported different clinical and implementation outcomes. A variety of outcomes were measured across the included studies, with delirium occurrence (n=9) being the most commonly reported. Other frequently assessed outcomes included delirium duration (n=3), time to delirium onset (n=2), and adherence to delirium screening (n=3). Less commonly reported were delirium type, recurrent delirium and delirium severity scores, each measured in only one study. The measured outcome variables of paediatric delirium are provided in online supplemental Appendix 5. All included studies used standardised outcome measurement instruments, particularly CAPD.[39] Michel *et al*[22] and Adel *et al*[35] used the Sophia Observation Withdrawal Symptoms Scale for Paediatric Delirium.[40] Lin *et al*[25] decided to leave the choice of outcome measurement instruments to the discretion of each centre, for example, the CAPD[39] or pCAM-ICU.[16]

Results of individual sources of evidence

Delirium prevention included various interventions involving multiple components administered in bundles, encompassing delirium screening, prevention, and treatment. In total, nine individual multicomponent intervention bundles were identified. The review identified a broad range of non-pharmacological intervention components used across studies, with considerable variability in their composition and implementation. The most frequently reported strategies included the use of standardised instruments or checklists for underlying aetiology (n=9), mobilisation (n=7), involvement of relatives (n=7), sleep enhancement (n=7), and (re) orientation and day structuring (each n=6). Additional commonly applied components involved staff education, environmental adaptations, and analgesia/sedation protocols. A detailed description of the individual interventions and components is shown in online supplemental Appendix 4. A basic distinction was made between individual-related (eg, reorientation or mobilisation) and environment-related (eg, daily structure, environmental adaptation) interventions. Then, the structured frameworks (ABCDEF bundle,[25] and Stenkjaer et[24] al. domains) were applied. The categorisation of components for a systematic description is shown in table 2.

Mobilisation, involvement of relatives, sleep enhancement and the use of standardised instruments or checklists for underlying aetiology were activities that were most often part of the multicomponent interventions. Michel *et al* developed and tested the most extensive multicomponent intervention.[22] The effects of the included studies were heterogeneous and depended on the outcomes and how they were defined (see online supplemental appendices). Only one of the included studies presented a decreased delirium occurrence and a significant decline in delirium cases.[21] The other studies did not demonstrate a significant effect or association with delirium occurrence.[22 25 35 37 38] However, in a subgroup of patients with cardiovascular problems, patients with surgical treatment and those of a young age, positive effects regarding the occurrence or duration of delirium were reported.[22 38] Yontem *et al* described that a psychosocial intervention was associated with a lower likelihood of delirium development, and the number of days in the PICU was associated with increasing odds of delirium.[36] Franken *et al*[23] and Di Nardo *et al*[34] did not report any information on delirium occurrence in their studies.

Synthesis of results

The study designs, samples, and reported effects of the included studies were heterogeneous. Seven different non-comparable outcomes (eg, delirium occurrence, duration, and adherence to screening) were measured. Nine non-pharmacological intervention bundles with varying components (eg, mobilisation, involvement of relatives, sleep enhancement, etc) were used in different combinations. Individual intervention descriptions are not comparable. For example, the intervention sleep enhancement includes activities such as decreasing light at night or reducing noise, or it can also include a specific sleep protocol. Study results regarding delirium prevention effects (eg, delirium occurrence) were inconsistent, and the subgroup analysis provides an initial indication of a possible positive impact.

DISCUSSION

Summary of evidence

The review results indicate that many different intervention components are used as part of delirium prevention bundles in the ICU setting. Overall, the reported intervention components address precipitating delirium risk factors, which are similar to those in adults.[19 20] Noteworthy is that the interventions should be tailored to the child's stage of development and age,[24] which is different to adult delirium and will make it difficult to develop standardised protocols for delirium care. Overall, findings suggest that preventive interventions in adult care may be used to guide paediatric delirium prevention in the ICU.[19 20] This is also supported by the aetiology of

Table 1 Description of included studies

Authors/ publication year	Chaiyakulsil and Thadahirunchot[38]	Gilbert *et al*[37]	Lin *et al*[25]	Adel *et al*[35]	Michel *et al*[22]	Yontem *et al*[36]	Di Nardo *et al*[34]	Franken *et al*[23]	Simone *et al*[21]
Country of origin	Thailand	USA	USA	Netherlands	Germany	Turkey	Italy	USA	USA
Setting	Tertiary Care Hospital	Children's Hospital	Eight academic PICUs	Tertiary Care Paediatric Hospital	Tertiary Care University Hospital	Tertiary Care University Hospital	Tertiary Care Paediatric Hospital	Paediatric Hospital	Tertiary Care Paediatric University Hospital
Population	Critically ill children	Critically ill children admitted to the PICU with a daily documented CAPD and RASS	All critically ill children admitted to the PICU with expected PICU stay longer than 2 days and need for mechanical ventilation	Critically ill children with expected stay ≥3 days	Critically ill children	Critically ill children with a Paediatric Cerebral Performance Category scale score of <5 for more than 48 hours	Critically ill children aged who required PICU admission for more than 72 hours	Critically ill children aged with expected stay ≥48 hours	All consecutive admitted critically ill children
Age	1 months to 15 years	n.r.	Higher than 2 months	3 months to 18 years	0–18 years	n.r.	1 day and 18 years	2–18 years	n.r.
Study design	Interventional	Observational	Observational	Interventional	Interventional	Observational	Interventional	Interventional	Interventional
Sample size	n=120	n=192	n=622	n=113	n=792	n=142	n=225	n=321	n=1875
	(n=58 before/ n=62 after)	(n=104 before/ n=88 after)		(n=55 before/ n=58 after)	(n=415 before/ n=377 after)		(n=137 before/ n=88 after)	(n=108 before/ n=213 after)	

CAPD, Cornell Assessment of Paediatric Delirium; n.r., not reported; PICU, paediatric intensive care unit; RASS, Richmond Agitation Sedation Scale.

Table 2 Assignment of the intervention components according to the ABCDEF bundle and the domains described by Stenkjaer *et al*

Components of intervention bundles	Lin *et al*[25]	Stenkjaer *et al*[24]
Standardised instruments/checklist for underlying aetiology	Analgesia/comfort and consciousness assessment	/
Mobilisation	Early mobilisation	Physical activity
Involvement of relatives	Family engagement	Cognition
Sleep enhancement	Comfort and consciousness assessment	Sleep
(Re)orientation	Delirium	Cognition
Day structuring	Delirium	Sleep
Staff education	Delirium	/
Environmental adaptations—personal Items	Delirium	Cognition
Analgesia and/or sedation protocol	Analgesia/comfort and consciousness assessment	Sleep
Provision of aids	Delirium	Physical activity
Environmental adaptations—general	Delirium	Cognition
Environmental adaptations—watch television	Delirium	Cognition
Activities and/or cognition	Delirium	Cognition
Environmental adaptations—decorate room with familiar pictures	Family engagement	Cognition
Environmental adaptations—digital devices	Delirium	Cognition
Medical team surveillance of lines, catheters and restraints	Delirium	/

ABCDEF, 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.

delirium in children, which is similar to that of adult patients.[41]

Another key finding is that the interventions described and tested in the included studies are often poorly defined. Their composition, delivery, and intensity varied considerably, and the descriptions often lacked sufficient detail to allow replication or comparison. This lack of standardisation hampers not only the synthesis of evidence but also the practical implementation of these interventions in clinical settings. To address this, we recommend categorising individual intervention components using established methodological frameworks (see online supplemental Appendix 4).[24 25] During data extraction, defining the interventions proved to be challenging due to inconsistent or incomplete reporting. A more rigorous and transparent use of reporting guidelines, such as the Template for Intervention Description and Replication (TIDieR) checklist,[42] is essential to improve the clarity, reproducibility and transferability of future interventions. Without well-defined descriptions, it remains unclear which elements drive the observed effects, limiting the development of targeted and effective strategies for paediatric delirium prevention. In addition, future studies may consider aligning their intervention descriptions with emerging frameworks such as the one proposed by Stenkjaer *et al*, which encompasses three domains: cognition, sleep, and physical activity.[24]

Currently, there is limited focus on preventing and treating delirium in the PICU.[21–23] We were unable to identify any empirical evidence in the NICU setting. The literature mainly consists of case reports[43–45] and is limited in general.[41] In addition, critical research questions remain unanswered, such as what distinguishes the research on paediatric/neonatal delirium from delirium in adults or what interventions are most effective. No randomised controlled trials have been conducted, unlike delirium trials in adults.[4 41] The studies have an interventional character, but the frequently chosen before-and-after approach harbours the potential for bias. The objectives and designs of future studies must be improved. However, because of the complex nature of delirium in critically ill children, the question can be discussed: to what extent are randomised controlled trials possible or needed, and should we focus on hybrid implementation studies instead?[46] Given the complex nature of delirium in critically ill children, the question arises as to whether randomised controlled trials, as the preferred study design, are truly sufficient or whether complementary approaches, such as hybrid implementation studies,[46–48] qualitative research or mixed-methods designs should receive greater consideration. While randomised controlled trials continue to be regarded as the gold standard for evaluating the effectiveness of interventions,[49] they often face significant challenges

in the context of paediatric intensive care and complex interventions. Complex research questions, such as those associated with delirium interventions, require a deeper understanding of practical implementation, contextual factors, and mechanisms of action, insights that can be particularly well captured through mixed-methods designs.[49 50] Against this backdrop, hybrid study designs that evaluate clinical effectiveness and implementation simultaneously may represent an alternative. Furthermore, unlike delirium in adults, there is no harmonised set of outcomes for interventional studies; thus, outcome comparability is limited.[51] This is reflected in the included studies, in which the definitions and understanding of the outcomes were very heterogenous. In addition to effectiveness outcomes, process outcomes were also addressed (eg, adherence to delirium screening), and it is well known that a relationship between processes and outcomes cannot always be assumed.[52] It is also unclear whether the Diagnostic and Statistical Manual of Mental Disorders—V criteria are applicable to paediatric and neonatal delirium based on how the included studies defined paediatric delirium.[41] The CAPD is not validated for infants younger than 37 weeks corrected gestational age, and the pCAM-ICU is validated for patients aged 6 months to 5 years. We did not limit our review based on the validation status of these tools. Consequently, we have included all reported data to provide a comprehensive overview of the existing literature.

Given the severe consequences of delirium and the current limitations in population-specific insights, there is a critical need for well planned, conducted, and reported trials. Future research should employ standardised intervention bundles that consider population-specific characteristics and focus on relevant high-priority outcomes to demonstrate their effectiveness. The findings from Stenkjaer *et al*,[24] along with the insights from this review, could be used to develop an effective intervention bundle that aligns with the recommendations of the MRC framework for complex interventions.[26]

Limitations

Despite employing a comprehensive search strategy, there is the possibility that relevant articles were overlooked. No formal risk of bias was performed. The update was made only in Medline. This might have introduced bias, because other studies meeting the eligibility criteria might have been missed. The quality of evidence was not assessed.

CONCLUSIONS

Various non-pharmacological intervention bundles are used to prevent or treat paediatric delirium. Due to the limited number of clinical trials available, along with high heterogeneity and inconsistency in outcomes, measurement instruments and description of the bundles, it seems to be impossible to identify effective interventions. The adoption and adaptation of delirium prevention interventions from adult settings might be a starting point for developing evidence-based strategies in critically ill children. However, it is crucial to adapt these interventions with consideration of the child's age and individual developmental stage. Due to the high occurrence of delirium in the PICU/NICU[8–11 53] and the negative consequences,[1 11 12] as well as the current neglect of interventions to prevent or reduce delirium, there is a need to identify and subsequently develop non-pharmacological interventions and provide evidence of their effects. As we focused explicitly on the ICU settings, our findings only reflect the current evidence within this specific context. Therefore, the generalisability of our findings to other paediatric care settings, for example, the emergence of delirium, is limited.[27]

Contributors MZ conceptualised and designed the study and carried out the analysis. He conducted the preliminary search, used the results to refine search criteria and wrote the first draft. MZ is responsible for the overall content as guarantor. ND conceptualised and designed the study, carried out the analysis and reviewed and revised the manuscript. JK and AT supervised the review planning and conduct, as well as data analysis, and reviewed and revised the manuscript. All authors critically reviewed and revised the manuscript, approved the final manuscript as submitted, agreed to be accountable for all aspects of the work and met the criteria recommended by the ICMJE.

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