



## Review paper

# Nonpharmacological interventions for agitation in the adult intensive care unit: A systematic review



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## ABSTRACT

**Background:** Person-centred nonpharmacological strategies should be used whenever possible to reduce agitation in the intensive care unit due to issues related to an overreliance on physical restraints and psychoactive drugs. However, the effect of nonpharmacological interventions to reduce agitation is unclear.

**Objectives:** The objectives of this study were to systematically review studies that evaluate the effectiveness of nonpharmacological interventions designed to prevent and minimise or manage patient agitation in the adult intensive care unit.

**Methods:** This systematic review was conducted following the Joanna Briggs Institute's Systematic Review of Effectiveness method and a priori PROSPERO protocol. Quantitative studies were identified from seven databases, including MEDLINE, EmCare, CINAHL, Web of Science, PsycINFO, Scopus, and Cochrane Library. In addition, grey literature from several repositories and trial registers was searched. The primary outcome of interest was the effect on prevention, minimisation, and management of agitation. The quality of the evidence was assessed using the Grading of Recommendations, Assessment, Development and Evaluation (GRADE).

**Results:** Eleven studies were included (n = 882). Meta-analyses of two studies demonstrated significantly lower levels of agitation (measured with the Richmond Agitation Sedation Scale) in the group receiving a multicomponent nonpharmacological intervention than in those receiving usual care. Individual studies showed a significant effect of nature-based sounds, music, foot reflexology, healing touch, and aromatherapy. The type of the endotracheal suction system did not affect levels of agitation. Overall, the certainty of the findings was rated very low. Harms and adverse effects were not reported in any studies.

**Conclusions:** Nonpharmacological interventions have the potential to reduce levels of agitation in the intensive care unit. However, inconsistencies in reporting, low quality of methodological designs, and small sample sizes impact the certainty of the results. Future trials must include larger sample sizes, use rigorous methods to improve knowledge in this field, and consider a range of other outcomes.

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## 1. Introduction

Patients in the intensive care unit (ICU) can exhibit many distressing neuropsychiatric symptoms such as anxiety, depression,

psychosis, agitation, and apathy. Agitation is particularly challenging<sup>1</sup> and is a major concern for clinicians internationally.<sup>2</sup> The behaviours are common,<sup>3–5</sup> often disrupting life-saving treatment, and are associated with a long list of adverse outcomes such as unplanned extubation,<sup>6,7</sup> line removal,<sup>8</sup> and increased length of stay.<sup>9</sup> Agitation can be disturbing for people experiencing it<sup>10–12</sup> as well as healthcare professionals<sup>2,13</sup> and family members.<sup>12,14,15</sup> Chevrolet et al. define agitation in ICU as “a psychomotor disturbance characterised by a marked increase in both motor and psychological activities, often accompanied by a loss of control of action

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and a disorganisation of thought".<sup>16</sup> Agitation has a behavioural component that can manifest on a continuum ranging from restlessness, tension, and irritability to hostility and aggressiveness. Clinicians tend to equate agitation with delirium,<sup>17</sup> but it is important to differentiate the two conditions. Patients can be agitated without being delirious,<sup>18</sup> as many other factors can contribute to agitation, including unmet needs or discomfort,<sup>19</sup> drug withdrawal,<sup>20</sup> poor gas exchange, metabolic disturbances,<sup>19</sup> and head trauma.<sup>21</sup> However, agitation is often seen in delirious ICU patients. Delirium has been described as a state of sudden severe confusion or altered level of consciousness<sup>22</sup> and manifests as hypoactive (43.5%), hyperactive (1.6%), or, most commonly, a mix of the two (54.9%).<sup>23</sup> Agitation is a symptom of delirious patients who are hyperactive, indicating major behavioural differences between hypoactive and hyperactive delirious states. Focusing on interventions for agitation may provide a more nuanced picture of how hyperactive delirious states can be managed, thus adding to the limited evidence of nonpharmacological interventions in this field<sup>24,25</sup> while also providing support for agitated patients who fall outside the delirium spectrum.

Traditionally, agitation in ICUs has been mitigated with pharmacological agents such as sedatives, antipsychotic drugs, and opioids. While these drugs still play an essential role in the ICU, particularly to facilitate weaning and extubation,<sup>26–28</sup> they should be used with caution due to significant adverse effects such as respiratory depression, haemodynamic instability, longer ICU stays, more days with mechanical ventilation, and, in some cases, worsening of agitation and delirium.<sup>26,29–31</sup> The 2013 International Guidelines for the Management of Pain, Agitation, and Delirium (PAD) advise clinicians to use nonpharmacological interventions when possible and before administering sedatives.<sup>22</sup> However, this guideline and the updated version from 2018<sup>26</sup> do not provide evidence-based recommendations on nonpharmacological interventions for agitation. Concerningly, research shows an overuse of sedation<sup>29–32</sup> and interventions that may not be patient-centred, such as physical restraints.<sup>32–34</sup> Patient-centred care is care based on each patient's unique needs, preferences, and values<sup>35,36</sup> and is essential to provide high-quality care and improve patient outcomes.<sup>37</sup> Clinicians feel uncertain about how to provide patient-centred care to agitated patients,<sup>2,38</sup> and decision-making is often based on personal views and experiences rather than on an evidence base.<sup>2,39</sup> Therefore, there is an urgent need to identify effective person-centred nonpharmacological approaches to reduce agitation.

A Danish/Australian advisory group consisting of patients, family members, clinicians, and topic experts provided advice on critical areas of a proposed guideline. The guideline scope was determined from this advice, and an *a priori* protocol<sup>40</sup> for this systematic review was formed. Advisory group members believed recommendations for nonpharmacological interventions for agitation in the ICU were needed due to existing inconsistent practices, a need to protect the most vulnerable ICU patients, overuse of sedation and restraints, and poor staff well-being due to injuries and feelings of powerlessness. Synthesising the evidence for nonpharmacological interventions to reduce agitation is a critically important topic. Therefore, this systematic review aimed to evaluate the effectiveness of nonpharmacological interventions designed to prevent, minimise, or manage patient agitation in the adult ICU.

## 2. Methods

This systematic review followed a *a priori* PROSPERO protocol (CRD42021254918),<sup>40</sup> the Joanna Briggs Institute's (JBIs) method for Systematic reviews of effectiveness,<sup>41</sup> and was reported as per

the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.<sup>42</sup> Published and unpublished studies in English describing nonpharmacological interventions for agitation in the adult ICU were considered for inclusion. Studies that mixed nonpharmacological and pharmacological components were excluded to enable a more precise indication of the effect of nonpharmacological interventions. Based on advice from the advisory group, the primary outcome measure was the effect on prevention, minimisation, and management of agitation, which had to be measured using a validated tool. Parameters such as heart rate, stress hormones, and antipsychotic or sedative drugs were not considered exclusively related to agitation as these could be related to other factors in the ICU. Intermediate outcomes considered were the use of pharmacology and physical restraints to reduce agitation and staff and family confidence in managing agitated behaviours. Secondary outcomes included adverse events such as unplanned extubations, nosocomial infections and device removal, length of ICU stay, quality of life, risk of patient post-traumatic stress, patient satisfaction, family satisfaction, and workforce injuries. This review considered studies that used comparative designs such as randomised controlled trials (RCTs), quasi-experimental studies, and before-and-after studies with comparators such as usual care (i.e., usual nursing care). Systematic reviews on nonpharmacological interventions for agitation have been criticised for only including RCTs as this experimental design is often inappropriate or unfeasible for nonpharmacological interventions.<sup>43</sup> Cohen-Mansfield et al.<sup>44</sup> argue that due to the lack of effective nonpharmacological interventions, any evidence of effect is a step in the right direction. When reviews include only RCTs, there is a risk that meaningful studies are excluded and clinicians are left with insufficient or untimely treatment options.<sup>44</sup> Due to these arguments, this review also considered analytical and descriptive observational studies if there were no higher levels of evidence. No date limitations were applied as the effect of interventions was unlikely to have changed over time.

### 2.1. Search strategy

This review aimed to identify both published and unpublished studies. An initial limited search in MEDLINE was undertaken to identify relevant topic keywords and Medical Subject Headings. A search strategy was developed from the keywords and Medical Subject Headings and checked by an experienced librarian before being adapted for each database. An overview of all search strategies can be found in [Supplementary material 1](#). Databases included MEDLINE (OVID, 1946–June 2021), EmCare (OVID 1995–June 2021), Cumulative Index to Nursing and Allied Health Literature (CINAHL, 1982–June 2021), Web of Science (1956–June 2021), PsycINFO (1806–June 2021), and Scopus (1788–June 2021). In addition, the following repositories and registers were searched: Cochrane Central Register of Controlled Trials, Australian New Zealand Clinical Trials Register (ANZCTR), EU Clinical Trials Register (<https://www.clinicaltrialsregister.eu/ctr-search/search>), the World Health Organization International Clinical Trial Registry Platform ([www.who.int/ictrp/search/en](http://www.who.int/ictrp/search/en)), US National Library of Medicine Trials Register ([www.clinicaltrials.gov](http://www.clinicaltrials.gov)), ProQuest Dissertations & Thesis Global, and OpenGrey. Reference lists of all relevant studies were also screened.

### 2.2. Study selection

Records identified in the searches were exported into Covidence software,<sup>45</sup> where all duplicates were removed. AA and TC independently screened a random selection of record titles and

abstracts to determine if they appeared to meet the inclusion criteria. After reaching an agreement on these articles, AA screened the remaining articles. Relevant articles were retrieved in full text and assessed in detail against the inclusion criteria by two independent reviewers (AA/DC/TC). A third reviewer was invited to provide their view when disagreements occurred between the two independent reviewers. Reasons for excluding full-text articles are provided in [Supplementary material 2](#).

### 2.3. Assessment of methodological quality

All studies meeting the inclusion criteria were assessed for external and internal validity by two independent reviewers using the JBI's standardised appraisal tools for RCTs and quasi-experimental studies ([Supplementary material 3](#)).<sup>41</sup> Disagreements were resolved by discussion, and where consensus could not be reached, a third reviewer was involved. When the studies lacked essential information, primary authors were contacted. The questions in the appraisal tool were rated 'Yes', 'No', 'Unclear', or 'Not applicable'. 'Not applicable' was, for example, used when the reviewers believed blinding methods were not possible. The overall methodological quality of each study was then calculated by adding all 'Yes' ratings and dividing them with the number of applicable questions to get a percentage. Studies were rated 'low methodological quality' if rated less than 50%, adequate if rated between 50 and 69%, moderate if rated between 70 and 85%, and strong if rated between 86 and 100%. Since studies of low quality may compromise the quality of systematic review practice recommendations,<sup>46,47</sup> it was decided to exclude all studies with 'low methodological quality'.

### 2.4. Data extraction

Two independent reviewers extracted data using a purposefully designed data extraction template ([Supplementary material 4](#)). Data included details about the populations, study methods, interventions, and outcomes of significance to the review objective.

### 2.5. Data synthesis

Due to the variability of study characteristics (design, intervention, population) and lack of reported data, meta-analysis was not possible for all included studies. A narrative summary is presented for studies not included in a meta-analysis. Two RCTs describing multicomponent nonpharmacological interventions were pooled using the JBI System for the Unified Management, Assessment, and Review of Information (SUMARI) tool.<sup>48</sup> The effect sizes were expressed as standardised mean difference for continuous data. Their 95% confidence intervals (CIs) were calculated for analysis. Statistical heterogeneity was assessed using the standard chi-squared and I-squared tests. Statistical analyses were performed using the fixed-effects model based on guidance by Tufanaru et al.<sup>49</sup> Publication bias could not be assessed due to the low number of included studies.

### 2.6. Assessing certainty in the findings

Clinicians need to know how trustworthy a body of evidence is before making clinical decisions.<sup>50</sup> The certainty of the evidence was rated using the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach.<sup>51</sup> Two researchers did the ratings and developed a Summary of Findings table ([Table 3](#)) using GRADEpro GDT.<sup>52</sup>

## 3. Results

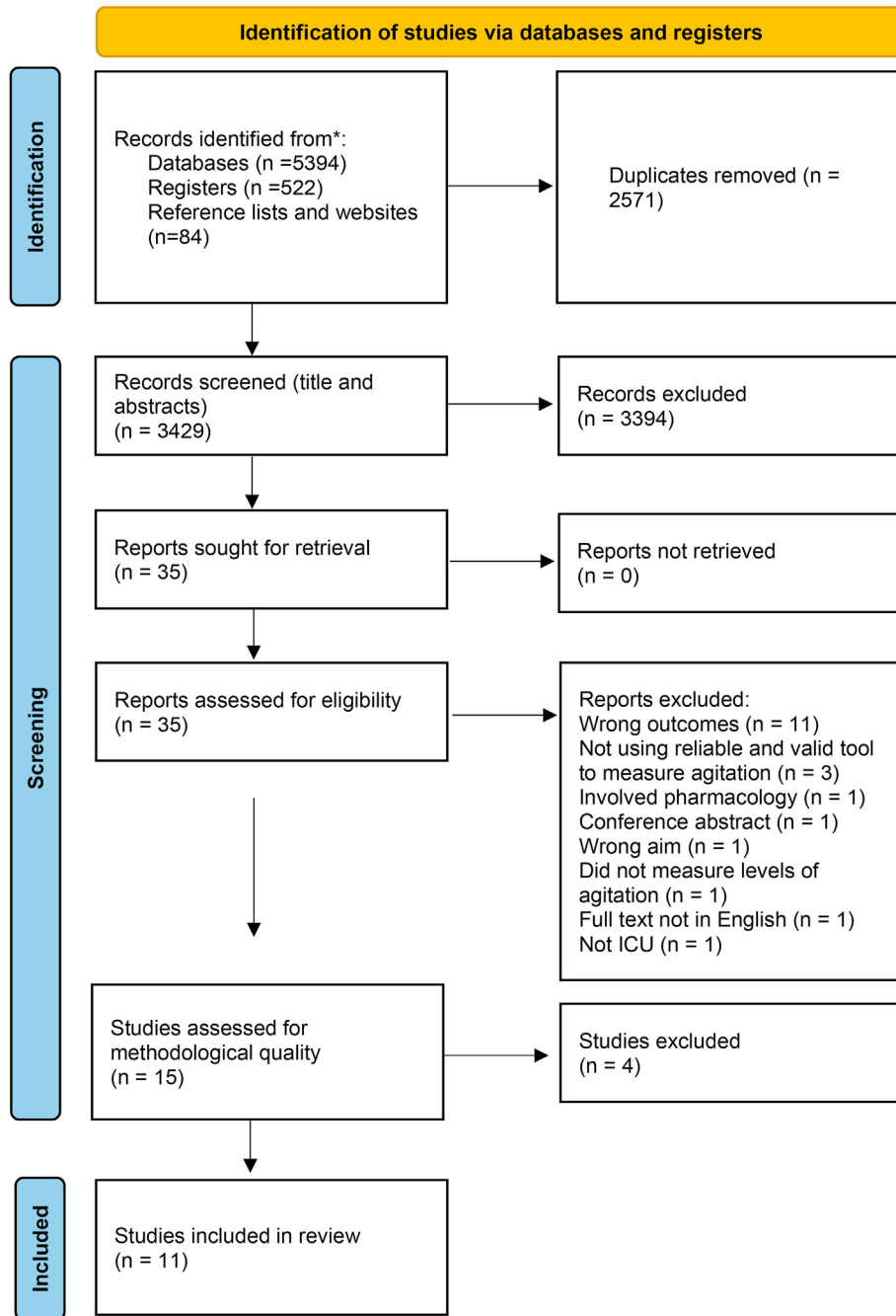
The results from the search process are presented in [Fig. 1](#) (See [Supplementary material 5](#) for a full list of results). A total of 6000 potentially relevant articles were identified; 2571 duplicates were removed. Titles and abstracts were screened of the remaining 3429 articles, excluding 3394 records. Overall, 35 studies went through a full-text analysis, leaving 15 articles for quality appraisal. Four studies were of low methodological quality and were excluded, leaving eight RCTs and three quasi-experimental studies for inclusion.

### 3.1. The methodological quality of included studies

An overview of the critical appraisal is provided in [Tables 1 and 2](#). Four studies were excluded due to low methodological qualities<sup>53–56</sup> (See [Supplementary material 6](#) for detailed explanations). Of the included studies, four were of adequate quality,<sup>57–60</sup> six of moderate quality,<sup>61–66</sup> and one of strong quality.<sup>67</sup> Some studies reported using random allocation techniques but did not describe how true randomisation was achieved;<sup>61,64</sup> others did not describe appropriate concealment methods.<sup>60,65</sup> In some studies, participants were not similar at baseline; this was related to levels of agitation<sup>60,61,64</sup> and the proportion of males and females.<sup>57,61,66</sup> Due to the nature of the interventions, blinding participants and assessors was sometimes impossible or would have little effect on the outcome. For example, knowing if a suction system was open or closed was unlikely to affect levels of agitation.<sup>60</sup> Creative methods or placebos were used for blinding in some studies. For example, Aghaie et al.<sup>62</sup> did not inform participants about the group they were assigned to, the purpose of wearing headphones, and the outcome measures until after the experiment. In terms of measurements of outcomes, one study was unclear about when measurements were done,<sup>58</sup> and many studies did not describe how inter-rater reliability was ensured.<sup>57–61,66</sup> In two studies, the exact differences between the interventions and usual care were unclear.<sup>58,65</sup> The statistical methods used were often unclear, insufficient, or results inadequately reported.<sup>57,63,64,66,67</sup>

### 3.2. Characteristics of the studies

The characteristics of the 11 included studies are provided in [Table 4](#). Data of publication ranged from 2012 to 2021. Six studies were undertaken in Iran,<sup>57,58,60,62,64,66</sup> one in Korea,<sup>67</sup> one in China,<sup>65</sup> one in India,<sup>63</sup> one in the USA,<sup>59</sup> and one in Canada.<sup>61</sup> The sample sizes varied from 6 to 160. A total of 882 participants were involved, with the youngest mean age of a group being 41.23 ± 15.31 years<sup>66</sup> and the oldest 73.7 ± 5.2 years.<sup>65</sup> Although this review included all types of quantitative studies, only RCTs<sup>58,60–66</sup> and quasi-experimental studies<sup>57,59,67</sup> were identified. The inclusion criteria varied. Most studies excluded patients with a mental illness,<sup>60,62–67</sup> with drug or alcohol addiction<sup>57,62–66</sup> and neurological disorder.<sup>60,63–67</sup> Some studies only included conscious participants<sup>60,62</sup> or had a Glasgow Coma Scale score of at least 7<sup>57</sup> or 9.<sup>63,66</sup> Some only included patients who were able to communicate.<sup>66,67</sup> Most studies did not define criteria for levels of consciousness.<sup>58,59,61,64,65</sup> One study<sup>57</sup> included patients who were agitated, while another<sup>59</sup> excluded patients who were very agitated or combative. Three studies excluded patients receiving sedatives during the intervention,<sup>57,61,67</sup> one if they received high doses of sedatives,<sup>60</sup> and one if participants needed an emergency stat dose of sedatives.<sup>63</sup> Most studies did not describe or control for the use of sedation, antipsychotic drugs or analgesia before, during, and after the interventions.<sup>58,59,62–66</sup> All studies used the Richmond Agitation Sedation Scale (RASS) to measure levels of agitation,



**Fig. 1.** PRISMA Flowchart. Under this can be the explanation of ICU: intensive care unit, \*Report of records identified from each database or register searched. See [Supplementary material 5](#).

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* 2021; 372:n71. doi: 10.1136/bmj.n71.

except one study<sup>61</sup> using the Ramsay Sedation Scale. Apart from two studies measuring the ICU length stay,<sup>58,63</sup> none of the included studies measured any of the secondary or intermediate outcomes considered for this review.

### 3.3. Effect of interventions

The interventions in this review fell under five categories: multicomponent interventions, nature-based sounds, music therapy, sensory interventions, and suction methods. Due to the heterogeneity of the included studies and lack of data, pooling for

meta-analysis was only possible for two studies. The overall strength of the evidence is summarised in [Table 3](#). The GRADE ratings show our confidence that the observed effect of the interventions reflects a true effect of the intervention. Although seven individual interventions<sup>57,59,62–64,66,67</sup> and a meta-analysis of two studies<sup>58,65</sup> demonstrated a statistically significant effect on agitation and one study showed some effect,<sup>61</sup> the overall certainty of this evidence was very low. Two studies examined the effect on length of ICU stay: one found a significant effect,<sup>58</sup> and another did not find any differences between the intervention and control groups.<sup>63</sup> The certainty of the evidence for this outcome was also

**Table 1**  
Quality assessment of methodological quality using JBLs' checklist of randomised controlled trials.

Study	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12	Q13	Total (%)	Methodological quality
Abbasinia et al. <sup>58</sup>	Y	Y	Y	Y	NA	N	U	Y	Y	U	U	Y	Y	67	Adequate
Aghaie et al. <sup>64</sup>	U	Y	N	Y	NA	Y	Y	Y	Y	Y	Y	N	Y	75	Moderate
Allahbakhhsian et al. <sup>62</sup>	Y	Y	Y	NA	NA	N	Y	Y	Y	Y	Y	U	Y	82	Moderate
Dastdadeh et al. <sup>60</sup>	Y	U	H	NA	NA	NA	Y	Y	Y	Y	U	U	Y	60	Adequate
Guo et al. <sup>65</sup>	Y	U	Y	N	NA	Y	U	Y	Y	Y	Y	Y	Y	75	Moderate
Rajora et al. <sup>63</sup>	Y	Y	Y	NA	NA	U	Y	Y	Y	Y	U	N	Y	73	Moderate
Saadatmand et al. <sup>66</sup>	Y	Y	N	Y	NA	Y	Y	Y	Y	Y	U	U	Y	75	Moderate
To et al. <sup>61</sup>	U	Y	N	Y	Y	Y	Y	Y	Y	Y	U	Y	Y	77	Moderate

N, no; N/A, not applicable; U, unclear; Y, yes.

0–49%: low methodological quality; 50–69%: adequate methodological quality; 70–85: moderate methodological quality; 86–100: strong methodological quality.

Q1. Was true randomization used for assignment of participants to treatment groups?

Q2. Was allocation to treatment groups concealed?

Q3. Were treatment groups similar at baseline?

Q4. Were participants blind to treatment assignment?

Q5. Were those delivering treatment blind to treatment assignment?

Q6. Were outcomes assessors blind to treatment assignment?

Q7. Were treatment groups treated identically other than the intervention of interest?

Q8. Was follow-up complete and, if not, were differences between groups in terms of their follow-up adequately described and analysed?

Q9. Were participants analysed in the groups to which they were randomized?

Q10. Were outcomes measured in the same way for treatment groups?

Q11. Were outcomes measured in a reliable way?

Q12. Was appropriate statistical analysis used?

Q13. Was the trial design appropriate, and any deviations from the standard RCT design (individual randomization, parallel groups) accounted for in the conduct and analysis of the trial?

very low. The studies were grouped into five categories, as described in the following section.

**3.3.1. Multicomponent nonpharmacological interventions**

Two RCTs<sup>58,65</sup> investigated the effectiveness of multicomponent nonpharmacological interventions to reduce agitation. The studies included patients undergoing oral tumour resection<sup>65</sup> and coronary artery bypass graft<sup>58</sup> and provided a preoperative video<sup>58</sup> or a visit to the ICU.<sup>65</sup> Both studies were built on the Hospital Elder Life Program (HELP) for the prevention of delirium. They involved reorientation, therapeutic activities, promotion of sleep, adequate hydration and nutrition, provision of vision and hearing aids, and staff training. Abbasinia et al.<sup>58</sup> also included reduction of psychoactive drugs and early mobilisation, while the study by Guo et al.<sup>65</sup> added music therapy. Both interventions lasted for approximately 3 days. Abbasinia et al.<sup>58</sup> only measured the RASS once a day, and it is unclear when this was done. Levels of agitation may vary depending on the time of the day and procedures carried out around the patient; therefore, not stating when agitation was measured and whether it was measured consistently poses a threat to internal validity. Both studies lacked

information on how the interventions differed from usual care and if patients received psychoactive drugs before or after the interventions.

The study by Abbasinia et al.<sup>58</sup> saw lower levels of agitation in the intervention group (0.06 ± 0.25) than in the control group (0.36 ± 0.80) on the last day; however, these differences were not statistically significant (P = 0.057). Guo et al.<sup>65</sup> saw a significantly lower level of agitation in the intervention group (0.2 ± 0.3) than in the control group (0.5 ± 0.4) on the last day (P = < 0.001). The two studies were pooled in a meta-analysis, including 220 participants. The pooled analysis showed that multicomponent nonpharmacological interventions significantly reduce levels of agitation (see Fig. 2).

**3.3.2. Nature-based sounds**

Three RCTs<sup>63,64,66</sup> investigated the effect of nature-based sounds versus placebo. In all three studies, the nature-based sounds consisted of birds' songs, soothing rain sounds, river streams, and waterfall sounds. The sounds were played once in the intervention groups using a media player and headphones for between 60 min<sup>63</sup> and 90 min.<sup>66</sup> In the study by Aghaie et al.,<sup>64</sup> the duration of the

**Table 2**  
Quality assessment of methodological quality using JBLs' checklist of quasi-experimental studies.

Study	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Total (%)	Methodological quality
Davies <sup>59</sup>	Y	Y	NA	N	Y	U	Y	U	U	50	Adequate
Jong Yoen Park <sup>67</sup>	Y	Y	Y	Y	Y	Y	Y	Y	U	89	Strong
Mashouf <sup>67</sup>	Y	N	NA	N	Y	Y	Y	U	N	50	Adequate

N, no; N/A, not applicable; U, unclear; Y, yes.

0–49%: low methodological quality; 50–69%: adequate methodological quality; 70–85: moderate methodological quality; 86–100: strong methodological quality.

Q1 = Is it clear in the study what is the 'cause' and what is the 'effect' (i.e., there is no confusion about which variable comes first)?

Q2 = Were the participants included in any comparisons similar?

Q3 = Were the participants included in any comparisons receiving similar treatment/care, other than the exposure or intervention of interest?

Q4 = Was there a control group?

Q5 = Were there multiple measurements of the outcome both pre and post the intervention/exposure?

Q6 = Was follow-up complete and if not, were differences between groups in terms of their follow-up adequately described and analysed?

Q7 = Were the outcomes of participants included in any comparisons measured in the same way?

Q8 = Were outcomes measured in a reliable way?

Q9 = Was appropriate statistical analysis used?

**Table 3**  
Summary of findings.

Nonpharmacological interventions for reducing agitation in the adult ICU			
Outcomes	Effect	No of participants (studies)	Certainty of the evidence
<b>Multicomponent nonpharmacological care interventions compared to usual care</b>			
<b>Agitation</b> Follow-up: day 3 of the intervention.	Meta-analysis showed SMD difference 0.75 lower (95% CI: -1.02 to 0.47), indicating a large effect size.	220 (2 RCTs)	⊕○○○ Very low <sup>a,b,c</sup>
<b>Length of ICU stay</b>	Meta-analysis was not possible. Significantly lower in I (3.53 ± 0.57 days) compared with C (4.06 ± 1.28 days), P = 0.042	60 (1 RCT)	⊕○○○ Very low <sup>a,b,c</sup>
<b>Nature-based sounds compared to placebo</b>			
<b>Agitation</b> Follow-up: immediately after the intervention.	Meta-analysis was not possible. Studies found a significant reduction of agitation in the intervention group.	300 (3 RCTs)	⊕○○○ Very low <sup>b,c,d,e</sup>
<b>Length of ICU stay</b>	No significant differences of length of stay between the groups	120 (RCT)	⊕⊕○○ Low <sup>b,c</sup>
<b>Music therapy</b>			
<b>Agitation</b> Follow-up: immediately after the intervention.	Meta-analysis was not possible. One RCT with 25 patients showed a trend toward lower levels of agitation. A pilot study with 6 participants showed a significant decrease of agitation.	56 (one RCT and one quasi-experimental study)	⊕○○○ Very low <sup>c,f,g,h</sup>
<b>Sensory interventions</b>			
<b>Agitation</b> Follow-up: immediately after the intervention.	Meta-analysis was not possible. One RCT and three quasi-experimental studies showed a significant effect.	327 (one RCT and three quasi-experimental studies)	⊕○○○ Very low <sup>b,c,f,i</sup>
<b>Suction methods – closed compared to open suction systems</b>			
<b>Agitation</b> Follow-up: immediately after the intervention.	Meta-analysis was not possible. The type of suction system used had no effect on the level of patient agitation.	60 (one RCT)	⊕○○○ Very low <sup>b,c,j</sup>

CI, confidence interval; MD, mean difference; RCT, randomised controlled trial; SMD, standardised mean difference.

**GRADE Working Group grades of evidence:**

High certainty: We are very confident that the true effect lies close to that of the estimate of the effect.

Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect.

Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect.

<sup>a</sup> Serious risk of bias (differences between intervention and usual care unclear).

<sup>b</sup> Serious indirectness (psychoactive drugs received before/during the intervention is unclear).

<sup>c</sup> Serious imprecision (related to small sample size/short intervention/short-term follow-up).

<sup>d</sup> Serious risk of bias (lack of inter-rater reliability).

<sup>e</sup> Serious risk of bias: data analysis and reporting unclear.

<sup>f</sup> Serious indirectness (different intervention components between studies).

<sup>g</sup> Serious risk of bias (unclear if true randomisation was used).

<sup>h</sup> Serious risk of bias (control and intervention groups not similar at baseline).

<sup>i</sup> Serious indirectness (mostly men included).

<sup>j</sup> Serious risk of bias (three patients were deeply sedated throughout the study).

intervention was unclear. The placebo groups wore headphones without sound. Meta-analysis was not possible due to inadequate data reporting. The study by Saadatmand et al.<sup>66</sup> found that the intervention group had significantly lower levels of agitation ( $P \leq 0.01$ ). Aghaie et al.<sup>64</sup> replicated the study by Saadatmand et al. except that their intervention was carried out during weaning from mechanical ventilation. Nevertheless, the authors found similar results to Aghaie et al. A more recent study by Rajora et al.<sup>63</sup> on 120 patients from the respiratory ICU found a significant reduction of agitation from baseline among the intervention group. This study also found no significant differences in ICU length of stay between the groups.

### 3.3.3. Music therapy

Two pilot studies, one RCT<sup>61</sup> and one crossover quasi-experimental study,<sup>67</sup> investigated the effect of music therapy. The designs, content, and frequency of interventions varied across the two studies, and therefore, pooled effect sizes could not be calculated. The RCT by To et al.<sup>61</sup> took place in the general ICU during a 4-h sedation vacation (interrupting sedation infusions). Twenty-five patients (intervention group) listened to Mozart piano sonatas via headphones, and 25 patients (placebo group) used headphones without music. If patients became restless and agitated at any time, sedation infusion was commenced, and the 'sedation vacation' was seen as unsuccessful. While patients in the

**Table 4**  
Characteristics of included studies.

Study details	Design	Sample (I/C/P) and characteristics	Setting	Intervention	Comparison	Duration and frequency	Scale and measurement points	Study results	Limitations
<b>Multicomponent nonpharmacological care interventions</b>									
Abbasinia 2021 <sup>58</sup> Iran	RCT	I: n = 30, mean age 56.46 ± 9.89 C: n = 30, mean age 58.93 ± 10.57 Mechanical ventilation unclear. Patients recovering from CABG	Cardiac ICU	Multicomponent nonpharmacological intervention (preoperative video and HELP including reorientation, therapeutic activities, reduced use of psychoactive drugs, promotion of sleep, early mobilisation, adequate hydration/nutrition and provision of vision and hearing adaptations).	Usual care	Until ICU discharge ≈ day 4.	RASS Once daily on day 2 and 3	<b>Agitation:</b> no significant differences in levels of agitation between I (0.06 ± 0.25) and C (0.36 ± 0.80), P = 0.057. <b>Length of ICU stay:</b> significantly lower in I (3.53 ± 0.57 days) than in C (4.06 ± 1.28 days), P = 0.042.	Staff training required. Part of intervention outside ICU Short-term follow-up. Assessments only done once daily - unclear when. Unclear if/how inter-rater reliability was ensured. Participants and assessors not blinded Differences between intervention and usual care unclear. Unclear if patients received psychoactive drugs during the intervention and if they were mechanically ventilated.
Guo, 2016 <sup>65</sup> China	RCT	I: n = 81, mean age 73.3 ± 6.1 C: n = 79, mean age 73.7 ± 5.2 Mechanical ventilation unclear. Patients recovering from oral cancer resection surgery.	Surgical ICU	Multicomponent nonpharmacological intervention (preoperative visit to ICU, modified HELP including reorientation, therapeutic activities, promotion of sleep, adequate hydration/nutrition, music, etc.).	Usual care	Until ICU discharge ≈ day 4.	RASS Twice a day, between 7 and 8 morning and between 19 and 20 evening for 3 days post-surgery.	<b>Agitation:</b> levels of agitation were lower in I than in C all 3 days after surgery, P < 0.05. Levels of agitation in the last day were 0.5 ± 0.04 in C compared 0.2 ± 0.3, in I, P = <0.001.	Staff training required. Part of interventions outside ICU Allocation concealment unclear Participants not blinded. No arguments for sample size. Long-term effect not investigated. Differences between intervention and usual care unclear. Unclear if patients received psychoactive drugs during the intervention
<b>Nature-based sounds</b>									
Rajora, 2019 <sup>63</sup> India	RCT	I: n = 60, mean age 47.07 ± 10.66 C: n = 60, mean age 46.90 ± 10.95 All mechanically ventilated.	Respiratory ICU	Nature-based sounds via headphones.	Placebo: headphones without nature-based sounds	60 min × 1	RASS Before, then 15, 30, 45, and 60 min after commencing the intervention, and 30 min after the intervention.	<b>Agitation:</b> significant reduction of agitation in I compared to C at all time points. (P = 0.003 at 15 min, P = 0.001 at 30 min, P = 0.001 at 45 min, P = 0.001 at 60 min and P = 0.001 after 30 min) <b>Length of stay</b> No significant	Brief intervention period with short-term follow-up. Unclear if assessor was blinded. Unclear how inter-rater reliability was ensured. Lack of appropriate statistical analysis. Unclear if patients received psychoactive

(continued on next page)

Table 4 (continued)

Study details	Design	Sample (I/C/P) and characteristics	Setting	Intervention	Comparison	Duration and frequency	Scale and measurement points	Study results	Limitations
Aghaie et al. 2014 <sup>64</sup> Iran	RCT	I: n = 60, mean age 58.10 ± 6.05 C: n = 60, mean age 56.66 ± 5.84 All mechanically ventilated. Patients recovering from CABG surgery.	Cardiac ICU	Nature-based sounds via headphone.	Placebo: headphones without nature-based sounds	During weaning from mechanical ventilation, unclear for how long.	RASS Agitation recorded at baseline, and after the first trigger (unclear what this means) and at 20 min intervals throughout the procedure, immediately after the procedure, and 20 and 30 min after extubation.	differences between the groups. <b>Agitation:</b> authors report that I had significant lower levels of agitation than C.	drugs during the intervention Unclear if true randomisation was used. Data analysis and reporting very unclear. Only included patients between 45 and 65 years of age (different levels of agitation at baseline) Brief intervention period with short-term follow-up. Unclear if patients received psychoactive drugs during the intervention
Saadatmand <sup>66</sup> Iran	RCT	I: n = 30, mean age 41.23 ± 15.31 C: n = 30, mean age 46.60 ± 16.76 All mechanically ventilated.	General ICU	Nature-based sounds via headphones.	Placebo: headphones without nature-based sounds.	90 min	RASS Before and at the 30th, 60th, 90th minutes and 30 min after intervention.	<b>Agitation:</b> a significant difference was found between the agitation scores in the two groups (P < 0.001). The odds of having higher scores of agitation in C was ≈ 11.24 times of the same odds in the I.	Control group included 20 males and 10 females. Unclear how inter-rater reliability was ensured. Brief intervention period with short-term follow-up. Unclear if patients received psychoactive drugs during the intervention
<b>Music therapy</b> Jong Yoen Park, 2019 <sup>67</sup> Korea	QE crossover	I: n = 3, C: n = 3, overall mean age 45.33 ± 16.49 All mechanically ventilated.	Surgical ICU	Music therapy (preferred music first, classical relaxation music last).	Music therapy (Classical relaxation music first, preferred music last).	30 min with classical or preferred music, 60 min washout period, 30 min with classical or preferred music.	RASS Before and after each music session.	<b>Agitation:</b> significantly lower levels after both the preferred music intervention (Z = -2.24, P = 0.025) and classical relaxation music intervention (Z = -2, P = 0.046) than before. There was no significant difference in the decrease in the median RASS score between the two music interventions (U = 15, P = 0.523)	Pilot study (inadequately powered). Participants their own controls Short “wash out” period Assessors not blinded. Brief intervention period with short-term follow-up.
To <sup>61</sup> Canada	RCT	I: n = 25, mean age 50.25 + 19.25 C: n = 25, mean age 50.52 + 17.45 All mechanically ventilated.	General ICU	Mozart Piano Sonatas via headphones.	Placebo: headphones without music.	4 h	RAMSEY sedation scale Measurements were obtained at baseline, at every 30 min during the	<b>Agitation:</b> there was a trend for more successful sedation vacations (meaning no agitation) in the	Pilot study (inadequately powered). Unclear if true randomisation was used.

		Patients undergoing 4-h sedation vacation					intervention and ended at 4 h.	music group (64%) compared to the control group (52%).	Higher levels of agitation in music group at baseline 10 females in control group compared to 3 in intervention group. Brief intervention period with short-term follow-up.
<b>Sensory interventions</b>									
Allahbakhhsian 2020 <sup>62</sup>	RCT	I: n = 40, mean age 55.90 ± 8.31 C: n = 40, mean age 56.30 ± 7.11p : n = 40, mean age 57.32 ± 8.62 Not mechanically ventilated. Recovering from CABG	Cardiac ICU	Foot reflexology	Control: usual care Placebo: superficial heel touch.	15 min × 1	RASS Before (T1), after (T2), and 10 min after (T3) the intervention.	<b>Agitation:</b> agitation was reduced in all groups from T1 to T3 (P < 0.05). I showed a significantly higher reduction at T2 (P < 0.001) and T3 (P < 0.001). In I, agitation levels reduced by 1.844 scores (95% CI: -2,768, 0.921), while the reduction was only 0.822 scores (95% CI: -1.792, 0.147) for the placebo group.	Researcher trained by a professional reflexologist for 1 year Assessor not blinded. Serious indirectness as only men included Brief intervention period with short-term follow-up. Unclear if patients received psychoactive drugs during the intervention
Davies 2020 <sup>59</sup>	QE	n = 87, mean age = 63.38 ± 16.09 Mechanical ventilation unclear.	5 general ICUs	Healing touch (HT)	No comparison	7–15 min once daily in 1–2 days.	RASS Before, after, and 5 min after.	<b>Agitation:</b> significant decreases in agitation scores following HT Pre (-0.59 ± 1.25) to post (-0.86 ± 1.16) first session, P < 0.01. Pre (-1.03 ± 1.61) to post (-1.52 ± 1.48) second session, P < 0.002.	Staff training required. Feasibility study (inadequately powered). Mean RASS scores were all below 0. No comparisons. Unclear how inter-rater reliability was ensured. Brief intervention period with short-term follow-up. Unclear if patients received psychoactive drugs during the intervention
Mashouf, 2017. <sup>57</sup>	QE	n = 40, mean age 49.36 Gender (m/f): 26/14 All mechanically ventilated.	General ICUs	Aromatherapy by lavender oil	No control	60 min × 1	RASS Before, every 15 min during the intervention, then every 30 min until 2 h after the intervention.	<b>Agitation:</b> levels before and after aromatherapy was significant (P < 0.001). The greatest reduction of agitation was seen 180 min after the intervention.	No comparison group No arguments for sample size. 65% males. Unclear how inter-rater reliability was ensured. Brief intervention period with short-term follow-up. <i>(continued on next page)</i>

Table 4 (continued)

Study details	Design	Sample (I/C/P) and characteristics	Setting	Intervention	Comparison	Duration and frequency	Scale and measurement points	Study results	Limitations
<b>Suction methods</b> Dastdadeh, <sup>60</sup> Iran	RCT	I: n = 30, mean age 65 ± 18 C: n = 30, mean age 66 (±20) All mechanically ventilated.	General ICU	Open endotracheal suction	Closed endotracheal suction	One suctioning	Before, during, and immediately after, 5 min after and 15 min after the suctioning	<b>Agitation:</b> the type of suctioning system used had no effect on the level agitation (P < 0.126).	Allocation concealment unclear. Three participants in the "open suction" group were deeply sedated throughout the intervention. Brief intervention period with short-term follow-up. Unclear if patients received psychoactive drugs during the intervention

C, control group; CABG, coronary artery bypass graft; HELP, Hospital Elder Life Program; I, intervention group; ICU, intensive care unit; P, placebo; QE, quasi-experimental; RASS, Richmond Agitation Sedation Scale; RCT, randomised controlled trial.

music group were more likely to remain off sedation infusions than the control group (64% vs 52% success), a major limitation is that the control group had higher levels of agitation at baseline (Ramsay 4 vs 3 in the music group). Statistical significance is not reported. In the crossover quasi-experimental study by Jong Yoen et al.,<sup>67</sup> six mechanically ventilated patients listened to either preferred music or classical relaxation music for 30 min, and after a 60-min break, they would swap to the other music option (either preferred or classical relaxation music). This study found no significant difference in agitation between the two music interventions, but a significant decrease in agitation after both preferred music (P = 0.025) and classical music (P = 0.046), suggesting that both classical music and preferred music were effective in reducing levels of agitation. A significant limitation of this study was the inclusion of only six participants.

### 3.3.4. Sensory interventions

One RCT<sup>62</sup> and two quasi-experimental studies<sup>57,59</sup> evaluated the effect of sensory interventions. The RCT focused on foot reflexology,<sup>62</sup> and the others on healing touch<sup>59</sup> and aromatherapy.<sup>62</sup> Due to these studies' different designs and interventions, the results could not be statistically pooled.

A three-armed RCT examined the effect of foot reflexology on male patients in the cardiac ICU.<sup>62</sup> This study included an intervention group (n = 40) receiving 15 min of foot reflexology, a control group (n = 40) receiving usual care, and a placebo group (n = 40) group receiving 15 min of superficial heel touch. The intervention was carried out by the researcher, who had received training for 1 year by a professional reflexologist. The study found that agitation reduced significantly in all three groups. However, the intervention group showed a significantly higher reduction immediately after (P < 0.01) and 10 min after the intervention (P < 0.001).

In a quasi-experimental feasibility study, Davies et al.<sup>59</sup> aimed to identify the effect of healing touch on 87 patients from five general ICUs. A caring relationship between the nurse and the critically ill patient provided a foundation of this healing touch intervention. All nurses involved had received at least one of four healing touch courses. The study found a significant reduction of agitation after both the first healing touch session (before  $-0.59 \pm 1.25$ , after  $-0.86 \pm 1.16$ , P < 0.01) and the second healing touch session (before  $-1.03 \pm 1.61$ , after  $-1.52 \pm 1.48$ , P < 0.02). A major limitation of this study was the low RASS scores, making it challenging to interpret the findings.

A quasi-experimental study with 40 participants examined the effect of lavender oil aromatherapy.<sup>57</sup> According to the authors, aromatherapy with lavender oil has proven effective on a range of conditions such as inflammation, pain, stress, depression, and muscle spasm. This study found a significant reduction of agitation after aromatherapy with lavender (P < 0.001) and that the greatest reduction of agitation was seen 180 min after the intervention commenced.

### 3.3.5. Suction methods

In an RCT, Dastdadeh et al.<sup>60</sup> compared the effectiveness of open and closed endotracheal suction tube systems on 60 mechanically ventilated patients. Patients were randomly allocated to closed suction or open suction systems. The intervention was done once per patient. They found that the type of the suction system used did not affect the level of patient agitation (P < 0.126).

## 4. Discussion

This systematic review aimed to synthesise the best available evidence to identify effective nonpharmacological interventions for agitation in the ICU. An exhaustive search found 11 studies of

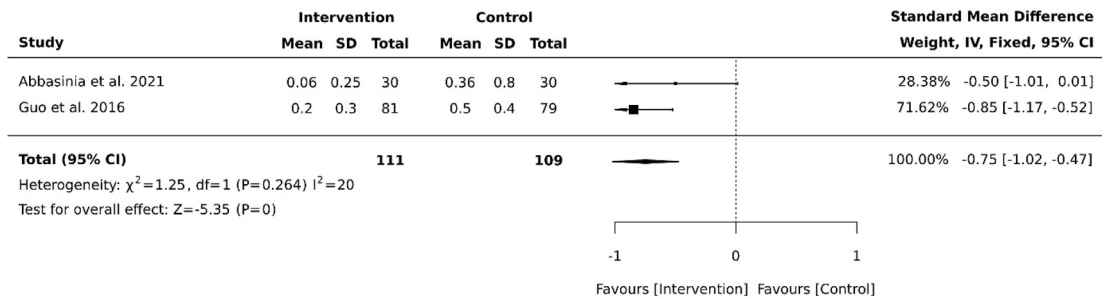


Fig. 2. Synthesis of multicomponeant care interventions. CI, confidence interval; SD, standard deviation.

sufficient quality to be included in this review, five published within the last 3 years.<sup>58,59,62,63,67</sup> Meta-analyses of two studies demonstrated a significant effect of multicomponeant non-pharmacological interventions. Several individual studies showed a significant effect, including nature-based sounds, music, foot reflexology, healing touch, and aromatherapy.

The included studies had several limitations to their designs and were often inadequately described. Issues included allocation concealment, blinding of assessors, groups not being similar at baseline, not clearly outlining the differences between usual care and intervention, and finally not ensuring that outcomes were measured in similar ways. Harms, feasibility, and acceptability by patients and staff were also poorly reported. Overall, sample sizes were small and interventions were short in length, carried out once only, and measured immediately after the intervention. Other systematic reviews on agitation have faced similar issues. Brasure et al.<sup>68</sup> reviewed 125 RCTs on agitation within dementia care and were unable to make conclusions due to the variety of comparisons and low quality of methodological designs. Similarly, a 2019 meta-synthesis<sup>69</sup> of 15 systematic reviews on nonpharmacological interventions for aggressive patients in the emergency department concluded that little and poor-quality evidence existed on effective strategies. The complex nature of agitation combined with the characteristics of nonpharmacological interventions challenges rigorous studies in this area.

Despite missing data and low methodological quality, the included studies may still provide important insight into what may be working. This argument is supported by Cohen-Mansfield et al.,<sup>44</sup> scholars with extensive knowledge on agitation within dementia care. They highlight that while methodological quality is important, researchers must also consider what is meaningful and practically possible. They argue that nonpharmacological interventions are often low-cost, low-risk interventions that even when they are small or prove little effect may be extremely valuable for clinicians and patients for whom the alternative, for example, physical restraints and medication, is associated with much higher risks. It is clear that research on nonpharmacological interventions for agitation in the ICU is in its early stages. While RCTs are ideal, they may not be feasible and ethical and are designs with a higher potential for bias. Researchers may consider observational studies, including prospective and retrospective cohort studies, case-control series, and realist evaluation. Since multiple factors often cause agitation, a multicomponeant approach may be most effective, preferably with a complex intervention approach<sup>70</sup> involving iterative cycles with continuous stakeholder engagement.<sup>71</sup> Other outcomes related to agitation must also be considered, such as the use of physical restraints, use of medication, adverse events, length of mechanical ventilation, patient and staff experiences, workforce injuries. We have developed a list for future researchers to consider when developing studies in this field; please see Table 5.

Based on the findings in this review, a diverse range of interventions, including multicomponeant interventions, music, nature-based sounds, and sensory interventions, seem promising. The perhaps most promising intervention is the multicomponeant nonpharmacological intervention. Systematic reviews on delirium in the ICU have also demonstrated the impact of multicomponeant nonpharmacological interventions.<sup>72,73</sup> One explanation is that delirium, as with agitation, has multiple causes and, therefore, multicomponeant interventions are more likely to target several risk factors.<sup>74</sup> In this review, the multicomponeant interventions were built on the HELP, a complex intervention focusing on mobilisation, fluids, nutrition, sensory aids, orientation, and therapeutic activities. Originating from the US with a goal to preserve physical and cognitive functioning,<sup>75</sup> this program has successfully reduced the incidences of delirium amongst elderly patients worldwide.<sup>76</sup> However, translation of research can be challenging, and implementation of the HELP in the UK National Health Service was not achievable due to lack of resources.<sup>77</sup> More research is needed to explore the effects of multicomponeant interventions on agitation in the ICU and the feasibility of carrying out such interventions. Furthermore, while such interventions may be effective for agitation, it is still unclear what elements of the nonpharmacological interventions contribute to improvements in clinical outcomes.

Nature-based sounds also showed some effects on agitation. The sounds of nature have shown to have a positive effect on the health and well-being of people in general.<sup>78</sup> The theories of why nature-based sounds create such a powerful reaction in individuals stem back to the theory of evolution. Like mindfulness, one explanation is that nature sounds do not require direct attention and therefore increase our awareness through unconscious and cognitive processes.<sup>78</sup> Another explanation describes how nature is perceived as less threatening and less arousing, thus reducing stress.<sup>78</sup> While Buxton et al.<sup>78</sup> describe how nature sounds can be helpful to reduce stress in noisy urban areas, Minton and Batten<sup>79</sup> explored how such interventions could minimise patient stress and delirium in a hectic ICU environment. They concluded that many nature-based interventions could be implemented, including sounds, views, light, pictures, and posters. Changing patients' physical position changes their views of the environment, and watching nature reminds patients that they are alive and that there is a life beyond the ICU.<sup>79</sup>

Music may be beneficial for agitation, both classical<sup>61,67</sup> and patients' preferred music.<sup>67</sup> Robust literature supports this statement. Music has been used for decades within health. A recent meta-analysis of 12 RCTs showed strong evidence that music can reduce agitation in persons who have dementia.<sup>80</sup> Another systematic review states that music effectively reduces stress.<sup>81</sup> Scholars have described how music decreases physiological arousal and affects stress-related emotional states, including anxiety, worry, and restlessness, by modulating activities in our brain structures.<sup>82</sup> Music, in particular classical music, has been described as effective in reducing pain and levels of stress in the

**Table 5**  
Suggestions for future researchers.

Limitations of included studies	Suggestions for future researchers
Lack of reporting.	Report how several steps are taken to ensure a rigorous study: randomisation, allocation concealment, characteristics of the groups including GCS, levels of sedation, mechanical ventilation, etc. Information on follow-up and detailed information on statistical analysis.
Only RCTs and quasi-experimental studies were identified.	It is challenging to develop rigorous RCTs or quasi-experimental studies on nonpharmacological interventions for agitation in the ICU. Therefore, researchers may want to consider other research designs informed by complex interventions frameworks.
Lack of clear definitions of agitation.	Authors must report how they define agitation. Consensus on what constitute agitated behaviours in the intensive care unit is needed. Such an agreement will ensure consistent observations, measurements, interpretation, and understanding of what may work.
The role of theory in intervention design and evaluation is unclear.	Researchers must be clear about the theoretical framework used to design and evaluate a study.
Limitations to the tools measuring agitation.	Provide solid arguments for the tools used to measure agitation. Identification and verification of tools to measure agitation in the ICU are needed.
Only a few outcomes were considered.	Other outcomes worth exploring: <ul style="list-style-type: none"> <li>- Drug use.</li> <li>- Use of physical restraints.</li> <li>- Adverse events such as unplanned extubations, nosocomial infections, and device removal.</li> <li>- Post-traumatic stress.</li> <li>- Patient experiences and satisfaction.</li> <li>- Family experiences and satisfaction.</li> <li>- Workforce well-being and injuries.</li> <li>- Length of mechanical ventilation.</li> </ul>
Short duration of studies.	Studies that carry out interventions over long periods and follow-up patients over more extended periods would provide more insight into the short- and long-term effects of interventions.
Blinding issues.	Creative blinding methods may be used. For instance, participants may not need to know the precise aim of interventions and when and what outcomes are measured. Researchers can use sham interventions without the active ingredient.
Inter-rater reliability is not ensured.	Ensure that all outcome assessors measure agitation in accurate and consistent ways.
No information about psychoactive medication.	Interventions must describe the type of psychoactive drugs patients receive hours before, during, and after an intervention.
Lack of information about the circumstances and expected active ingredient (who was involved, what was done, when, how often, and in what circumstances were the interventions applied). <i>This information helps the reader understand when and why an intervention may be effective and assist future researchers in developing similar interventions.</i>	Describe the circumstances of an intervention. What could potentially cause agitation in this patient group? Were patients weaning from mechanical ventilation? From drugs? Was the intervention carried out in the morning or evening? After mobilisation? In a quiet room? etc. Ensure that other causes of agitated behaviours are dealt with before an intervention starts, for instance, discomfort due to pain, thirst, or a full bladder.
No studies explored if different sub-groups required different types of treatment.	ICU patient sub-groups may require different nonpharmacological approaches. More research is needed to explore this.
Harms, feasibility, and acceptability by patients, family members, and staff were not reported, making it difficult for clinicians and guideline developers to know if interventions should be recommended.	Interviews and observations may provide valuable insight into the feasibility and acceptability of interventions.

GCS, Glasgow Coma Scale; ICU, intensive care unit; RCT, randomised controlled trial.

ICU.<sup>83</sup> However, clinicians must be aware that since music evokes feelings, playing heavy metal or techno may be ineffective or even harmful.<sup>83</sup>

Lavender aromatherapy may also reduce agitation, although the evidence in this area is sparse. Lavender is said to have antipain, antianxiety, antidepressant effects similar functions of increased benzodiazepines and gamma-aminobutyric acid in the amygdala.<sup>84</sup> A meta-analysis including 15 studies showed some evidence that aromatherapy, including smearing and inhalation, can reduce agitation and aggression in patients suffering from cognitive impairment. A nonrandomised study showed that aromatherapy alleviated stress and improved sleep in the ICU,<sup>85</sup> and an RCT showed a reduction of anxiety, heart rate, and blood pressure after exposure to lavender aromatherapy. These studies support that lavender possibly can be used as a low cost and inexpensive method to prevent or reduce low levels of agitation.

Foot reflexology may reduce agitation in the ICU.<sup>62</sup> The researcher providing this intervention was trained by a professional reflexologist for 1 year prior to the study, which poses a major limitation to the feasibility of this intervention. However, some studies have described how the intervention is easy to learn and apply.<sup>86</sup> A systematic review and meta-analysis reviewing 10 studies of reflexology for anxiety found that reflexology had some positive effect on anxiety amongst patients undergoing cardiac procedures.<sup>87</sup>

Healing touch also showed some effects in this review. Healing touch is believed to reduce stress and promote relaxation work through body–mind communication between the autonomic, endocrine, and immune systems.<sup>59</sup> Limited research has been carried out on the ICU population, but similar to the study by Davis et al.,<sup>59</sup> a pilot study within dementia care also found an effect of healing touch on agitation.<sup>88</sup> An RCT found an effect of healing

touch on anxiety and length of stay in patients undergoing coronary artery bypass.<sup>89</sup> A qualitative Swedish study from the emergency department<sup>90</sup> explored patients' experiences of "caring touch" (a combination of healing touch and tactile massage) and found that the intervention provided trust and consolidation for most acutely ill patients. However, some patients expressed ambivalence towards the "caring touch".<sup>90</sup> When researchers interviewed US nurses about "healing touch", they expressed a desire to provide the intervention. Still, barriers such as lack of time, patient acceptability, and lack of training were common concerns.<sup>91</sup>

Forty-five percent of the included studies were published within the last 3 years, suggesting an increased awareness and need for effective nonpharmacological interventions. While waiting for rigorous evidence, it may be worthwhile to explore how interventions and recommendations from other areas of health may apply to the ICU. For instance, a large body of work has been done on agitation and aggression within psychiatry, and different working groups have developed guideline recommendations.<sup>92–94</sup> It may also be that interventions proven to be effective in other areas of health can be helpful in the ICU context. For instance, a recent network meta-analysis within dementia care, including 65 RCTs, found that massage therapy, animal-assisted intervention, personally tailored activities, and pet robot interventions were the most effective nonpharmacological interventions for agitation.<sup>95</sup> A recent scoping review on the management of the agitated psychiatric patient found that de-escalation techniques, risk assessment and programs involving staff training, patient involvement, and leadership were the most effective interventions and alternatives to physical restraints.<sup>96</sup> We suggest that future research involve relevant stakeholders when developing interventions or guidelines to fully understand what is feasible and acceptable in the ICU context.

#### 4.1. Limitations to the RASS scale when measuring levels of agitation

All studies, except one, used the RASS scale, a scale that has been said to be valid and reliable<sup>97</sup> and that has been used in several studies measuring the effectiveness of pharmacology on agitation.<sup>98</sup> However, there are several limitations to this scale that was originally developed to measure levels of sedation. First, on the scale,  $-4$  to  $-1$  describe levels of sedation, not levels of agitation. If RASS scores increase in sedated patients, it is an indication of a more awake patient rather than increased levels of agitation. This makes it challenging to ensure accurate analysis and interpretation of research results. For example, in the study by Davis et al.,<sup>59</sup> the authors claim that levels of agitation decreased from a mean of  $-0.59 \pm 1.25$  to a mean of  $-0.86 \pm 1.16$ . One could argue that patients were simply more awake after the HT sessions. Second, issues arise with the RASS scale when patients are sedated/unconscious and agitated. Other scholars have pointed out the difficulties of rating two constructs, sedation and agitation, in one scale.<sup>99</sup> We recommend that authors pay special attention to inter-rater reliability and scales that more precisely measure agitation and are able to capture the breadth of these behaviours. Multiple and more nuanced scales, such as the Overt Agitation Severity Scale<sup>100</sup> and the Cohen-Mansfield Agitation Inventory,<sup>101</sup> exist outside the ICU setting that can potentially be modified and tested to suit the ICU environment. Related to levels of agitation, the included studies did not provide information about the frequency and duration of agitation, and no authors discussed what constitutes clinically meaningful changes in levels of agitation, making it difficult to fully understand the reported statistically significant differences.

#### 4.2. Strengths and limitations of the review

We conducted an exhaustive search and rigorously evaluated studies to ensure reliability in study inclusion and quality ratings. We reduced bias by excluding studies of low quality and by only including studies that used validated tools to measure agitation. However, there are limitations to this review. Only studies in English were included, which may have excluded some relevant studies. Although we followed the GRADE approach for grading the certainty of the evidence, this assessment is a subjective process, and even though the reviewers in this article agreed about the ratings, others may not. However, we have attempted to provide transparent and explicit explanations for our judgements throughout this review.

### 5. Conclusion

Despite an urgent need to identify effective nonpharmacological interventions, this review found insufficient evidence to draw firm conclusions on ways to reduce agitation in the ICU. Multi-component nonpharmacological interventions, nature-based sounds, music, foot reflexology, healing touch, and aromatherapy may offer some benefits but need to be further studied. While this study calls out for rigorous research designs, it also encourages researchers to consider alternative methodological research approaches. RCTs are at the top of the evidence hierarchy but may not be meaningful, feasible, and ethical when researching agitation in a complex and ever-changing critical care environment. In addition to the effect on agitation, future research should also consider other important patient-centred, family-centred, and clinician outcomes.

It is a concern that no consensus exists on what non-pharmacological strategies should be recommended for agitation in the ICU. As a result, agitation is more likely to be managed pharmacologically or with methods that may not be effective or person-centred. While waiting for rigorous evidence, clinicians and researchers need to continuously discuss the role of non-pharmacological approaches while also considering how high-quality care for this vulnerable population can be ensured internationally.

#### Conflict of interest

The authors have no conflict of interest to declare.

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#### CRedit authorship contribution statement

**Anne Mette Adams:** Conceptualisation, Methodology, Validation, Investigation, Analysis, Writing – original draft, Writing – review & editing. **Diane Chamberlain:** Methodology, Validation, Writing – review & editing. **Mette Grønkjær:** Writing – review & editing. **Charlotte Brun Thorup:** Writing – review & editing. **Tiffany Conroy:** Conceptualisation, Methodology, Validation, Writing – review & editing, Supervision.

All authors have given final approval of the final version of the manuscript to be published, agree to be accountable for all aspects of the work, and acknowledge that those who are entitled to authorship are listed as authors.

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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.2022.02.005>.

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