

Evaluation of nurse-led sedation protocols on clinical outcomes in mechanically ventilated adults within intensive care units: A meta-analysis of randomized controlled trials

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Abstract

Background. Many hospitals worldwide implement nurse-led sedation protocols to prevent both under- and over-sedation and to enhance comfort and safety for mechanically ventilated patients in intensive care units (ICUs); however, definitive conclusions regarding their effectiveness remain limited.

Objectives. To assess the efficacy of nurse-led sedation protocols on clinical outcomes in mechanically ventilated adults within ICUs.

Materials and methods. A systematic search was conducted across 4 electronic databases – PubMed, Embase, Scopus, and the Cochrane Library – to identify relevant studies published in peer-reviewed journals. The standard mean difference (SMD) and risk ratio (RR), along with their corresponding 95% confidence intervals (95% CIs), were calculated. Heterogeneity among studies was assessed using the Cochran's Q test and I² statistic, with significance determined by the appropriate p-value. All statistical analyses were performed using Review Manager (RevMan) v. 5.4.

Results. This meta-analysis of 10 randomized controlled trials (RCTs; n = 1,151 patients) indicates that a nurse-led sedation protocol is significantly more effective than usual care in reducing ICU mortality (RR = 0.34 [95% CI: 0.25 to 0.45]; I² = 38%, p < 0.001), duration of mechanical ventilation (SMD = -1.94 [95% CI: -2.16 to -1.72]; I² = 73%, p < 0.001), length of hospital stay (SMD = -1.70 [95% CI: -1.80 to -1.59]; I² = 79%, p < 0.001), length of ICU stay (SMD = -1.58 [95% CI: -1.76 to -1.40]; I² = 66%, p < 0.001), and incidence of delirium (RR = 0.47 [95% CI: 0.39 to 0.57]; I² = 15%, p < 0.87).

Conclusions. Compared to usual care, nurse-led sedation protocol can improve ICU mortality and other clinical outcomes in mechanically ventilated ICU patients safely and effectively.

Keywords: ICU mortality, intensive care unit (ICU), meta-analysis, mechanical ventilation, nurse-led sedation protocols

Highlights

- Emergency Department (ED) Procedural Sedation and Analgesia (PSA) for patient comfort: PSA in the ED alleviates anxiety, discomfort, and pain during complex procedures, ensuring safety and satisfaction.
- Variable patient responses to ED sedative agents: Despite pre-assessments, trained staff, and adverse-event tracking, individual reactions to procedural sedatives differ widely.
- Limited safety data from small-scale PSA trials: Most research on sedation agents comprises single-center randomized controlled trials (RCTs) or observational studies with fewer than 100 participants, complicating definitive safety conclusions.
- Agent-specific adverse events guide PSA planning: Propofol often triggers respiratory issues, fentanyl and ketamine can cause gastrointestinal disturbances, while ketamine–propofol combinations reduce hemodynamic instability, highlighting the need to tailor sedation by age, comorbidities, and drug risk.

Background

Critically ill patients on mechanical ventilation in intensive care units (ICUs) often require sedation to alleviate pain, anxiety, and agitation. Inadequate sedation can increase sympathetic activity, lead to cardiovascular instability, and cause respiratory complications that compromise patient outcomes.^{1,2} Conversely, inadequate sedation can culminate in delirium, unplanned extubation, and prolonged mechanical ventilation, resulting in lower morbidity, mortality, and healthcare expenditures.^{3,4} The Pain, Agitation/Sedation, Delirium, Immobility, and Sleep Disruption (PADIS) guidelines advocate for the routine utilization of analgesia and sedation in ICUs to minimize discomfort, promote patient-centered care, and diminish the risk of adverse events (AEs).⁵ Despite the critical importance of sedation management in ICUs, ongoing debate surrounds the most effective approach. Traditional physician-led sedation protocols may not consistently achieve optimal sedation levels, potentially resulting in AEs and extended ICU stays. Contemporary controversies in the literature encompass debates on optimal sedation strategies, including physician-led vs nurse-led protocols, ideal depth of sedation, benefits and risks of daily sedation interruptions vs continuous sedation, and concerns regarding the potential long-term effects of sedation on cognitive and psychological outcomes.

In recent years, nurse-led sedation protocols have emerged as a promising alternative, possessing the potential to enhance patient outcomes, reduce healthcare expenditures, and augment patient satisfaction.^{6,7} These protocols involve the utilization of standardized sedation scales, such as the Richmond Agitation-Sedation Scale (RASS) or the Sedation-Agitation Scale (SAS), to assess patient sedation levels and adjust intravenous drip rates accordingly.^{8,9} Many studies^{10–14} have indicated that nurse-led sedation management, guided by specific goals and flowcharts, surpasses traditional methods.

The implementation of a nurse-driven sedation protocol has yielded advantageous results, notably by abbreviating the duration of mechanical ventilation, reducing the length

of stay in the ICU, and minimizing the period of continuous sedation. Furthermore, this approach has enhanced the frequency of spontaneous awakening trials (SATs), ultimately contributing to improved patient outcomes, including diminished morbidity, mortality, and healthcare expenditures. Magner et al. observed in their research that a nurse-led programmed sedation scheme can augment the effectiveness of sedation while concurrently decreasing the occurrence of delirium.¹⁵ In a comparable study, Qi et al. noted that the adoption of a sedation protocol by nursing staff can enhance outcomes, resulting in decreased mortality rates and a reduction in sedation-related AEs among mechanically ventilated patients in ICUs, when contrasted with standard physician-led care.¹⁶

However, Aitken et al. observed no notable disparities in hospital mortality, self-extubation rates, ICU length of stay, and duration of mechanical ventilation when comparing patients subjected to protocol-directed sedation with those undergoing non-protocol-directed sedation.¹⁷ Consequently, the evidence substantiating the efficacy of nurse-led sedation protocols remains inconclusive, as preceding systematic reviews and meta-analyses have been characterized by limited sample sizes and inconsistent results. Moreover, recent investigations have yielded divergent findings, underscoring the necessity for a thorough and contemporary examination of the existing literature.

Objectives

This study seeks to assess the impact of ICU nurse-led sedation protocols on various patient outcomes, such as mechanical ventilation duration, length of stay in the ICU, mortality rates, and AEs related to sedation, in comparison to the traditional physician-led care approach. Our objective was to conduct a thorough assessment of the effectiveness and safety of nurse-led sedation protocols in mechanically ventilated adults in ICUs. This was achieved through a systematic review and meta-analysis of 10 relevant randomized controlled trials (RCTs),^{18–27} selected according

to established inclusion and exclusion criteria, focusing on the impact of nurse-led sedation protocols on various clinical outcomes in ICUs. By synthesizing the available evidence, this study aims to provide a comprehensive and up-to-date evaluation of the efficacy and safety of nurse-led sedation protocols, comparing outcomes with traditional physician-led care, and informing evidence-based practice and future research in sedation management for critically ill patients.

Materials and methods

Eligibility criteria

This study included randomized controlled trials (RCTs) that provided comparative data on the clinical effectiveness of nurse-led sedation protocols for mechanically ventilated adults in ICUs. No restrictions were applied regarding language or publication year. Studies were included if they met the following criteria: 1) RCT design; 2) involved adult ICU patients requiring mechanical ventilation; 3) participants aged 18 years or older; 4) reported outcomes such as ICU mortality, length of hospital stay, duration of mechanical ventilation, incidence of self-extubation, and occurrence of delirium; and 5) full-text articles with sufficient data for constructing a 2 × 2 table.

The following studies were excluded from the evaluation process: 1) studies other than RCTs (e.g., case series, case-control studies, and cohort studies); 2) expert opinions, animal studies, experimental trials, and descriptive reports; 3) studies that did not include ICU patients requiring mechanical ventilation; and 4) bibliographic sources that were anecdotal, methodologically weak, or based solely on expert opinion.

Information sources

This study adhered to the guidelines set forth by AMSTAR (Assessing the Methodological Quality of Systematic Reviews)²⁸ and PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses),²⁹ and it has been registered in PROSPERO (CRD42025631472). Employing established inclusion and exclusion criteria for the selection of studies, we undertook a systematic review of relevant RCTs that assessed the efficacy and safety of nurse-led sedation protocols in mechanically ventilated adults within ICUs. An extensive search of prominent databases, including Embase, PubMed, Scopus, and Cochrane CENTRAL, was conducted by utilizing specific keywords and search terms, with the search extending up to September 30, 2024.

Search strategy

A comprehensive literature search was conducted across multiple databases to identify relevant studies. The search

terms included: “Nurse-led sedation protocols”, “Sedation”, “Mechanical ventilation”, “Intensive care unit”, “ICU”, “Physician-led usual care”, “Non-protocol-directed sedation”, “Duration of mechanical ventilation”, “Length of stay in ICU”, “Length of hospital stay”, “ICU mortality”, “Incidence of self-extubation”, “Incidence of delirium”, “Systematic review”, “Systematic review and meta-analysis”, “Meta-analysis”, “RCT”, and “Randomized controlled trial”. No language restrictions were applied. Studies published in languages other than English were included when sufficient data could be reliably extracted, and included only RCTs involving mechanically ventilated adults in ICUs, with nurse-led sedation protocols compared against physician-led or non-protocol-directed usual care. The PICO framework guided the selection process: “P” denoted the patient population (mechanically ventilated adults in ICUs), “I” the intervention (nurse-led sedation protocols), “C” the comparator (usual physician-led care or non-protocol-directed sedation), and “O” the outcomes assessed – ICU mortality, length of hospital stay, duration of mechanical ventilation, incidence of self-extubation, and incidence of delirium.³⁰

Selection process

Two reviewers (J.L. and H.L.) conducted an independent evaluation of article titles, abstracts, and full texts to discern potential RCTs. When necessary, a senior researcher (X.H.) was engaged to facilitate the resolution of any discrepancies between the 2 reviewers via discourse. Table 1 provides a comprehensive outline of the search strategy employed.

Data collection process

Two researchers (J.L. and H.L.) independently extracted the demographic information and event data from the selected RCTs using a predefined data collection form. The extracted information included study identification and year, country of origin, sample size, nurse-to-patient ratio, classification of ICU environments, participants' age (mean ± standard deviation (SD)), gender distribution (percentage of male and female patients), intervention specifics, control conditions, and reported outcomes. When data were incomplete or unclear, the original study authors were contacted for clarification or additional details.

Risk of bias assessment of included studies

A standardized questionnaire was utilized to assess the potential for bias in the included RCTs. Two authors (X.H. and J.Z.) conducted independent evaluations of bias potential in individual studies employing the Cochrane risk-of-bias instrument v. 2.³¹ This instrument consisted of 5 components: bias resulting from discrepancies in intended interventions, bias originating from randomization,

Table 1. Database search strategy

Database	Search strategy
Scopus	#1 "Nurse-led sedation protocols" OR "Sedation" OR "Mechanical ventilation" OR "Intensive care unit" OR "ICU" OR "Physician-led usual care" OR "Non protocol directed sedation" OR "Duration of mechanical ventilation" OR "Length of stay in ICU" OR "Length of hospital stay" OR "ICU mortality" OR "Incidence of self extubation" OR "Incidence of delirium". #2 "Systematic review" OR "Systematic review and meta-analysis" OR "Meta-analysis" OR "RCT" OR "Randomized controlled trial" #3 #1 AND #2
PubMed	#1 "Nurse-led sedation protocols" OR "Sedation" OR "Mechanical ventilation" OR "Intensive care unit" OR "ICU" OR "Physician-led usual care"[MeSH Terms] #OR "Non protocol directed sedation," OR "Duration of mechanical ventilation," OR "Length of stay in ICU," OR "Length of hospital stay"[All Fields] OR "ICU mortality" OR "Incidence of self extubation"[All Fields] OR "Incidence of delirium"[All Fields]. #2 "Systematic review," [MeSH Terms] OR "Systematic review and meta-analysis," OR "Meta-analysis," OR "RCT"[All Fields] OR "Randomized controlled trial" #3 #1 AND #2
Embase	#1 "Nurse-led sedation protocols"/exp ⁵ OR "Sedation"/exp OR "Mechanical ventilation"/exp OR "Intensive care unit"/exp OR "ICU"/exp OR "Physician-led usual care"/exp OR "Non protocol directed sedation,"/exp OR "Duration of mechanical ventilation,"/exp OR "Length of stay in ICU"/exp OR "Length of hospital stay"/exp OR "ICU mortality"/exp OR "Incidence of self extubation"/exp OR "Incidence of delirium". #2 "Systematic review"/exp OR "Systematic review and meta-analysis"/exp OR "Meta-analysis"/exp OR "RCT"/exp OR "Randomized controlled trial"/exp #3 #1 AND #2
Cochrane Library	#1 (Nurse-led sedation protocols): ti, ab, kw [®] OR (Sedation): ti, ab, kw OR (Mechanical ventilation): ti, ab, kw OR (ICU): ti, ab, kw OR (Physician-led usual care): ti, ab, kw OR (Non protocol directed sedation): ti, ab, kw OR (: ti, ab, kw OR (Duration of mechanical ventilation): ti, ab, kw OR (Length of stay in ICU) OR (Length of hospital stay): ti, ab, kw OR (ICU mortality): ti, ab, kw OR (Incidence of self extubation): ti, ab, kw OR (Incidence of delirium): ti, ab, kw (Word variations have been searched) #2 (Systematic review): ti, ab, kw OR (Systematic review and meta-analysis): ti, ab, kw OR (Meta-analysis): ti, ab, kw OR (RCT): ti, ab, kw OR (Randomized controlled trial): ti, ab, kw (Word variations have been searched) #3 #1 AND #2

MeSH terms – Medical Subject Headings; ⁵ exp – explosion in Emtree-searching of selected subject terms and related subjects; [®] ti, ab, kw – either title or abstract or keyword fields.

bias due to inadequate outcome data, bias during the assessment of outcomes, and bias in the selection of reported outcomes. Two researchers (X.H. and J.Z.) conducted an evaluation to analyze the possibility of bias. Another reviewer took on the position of an adjudicator to address any outstanding disputes. We assessed potential bias and categorized it as "uncertain risk", "high risk", or "low risk". Publication bias and small-study effects were measured through a comparison-adjusted funnel plot³² and applied Begg's test³³ using MedCalc v. 20.218 (MedCalc Software Ltd., Ostend, Belgium)³⁴ to assess the presence of publication bias and small-study effects, with statistical significance determined at a threshold of $p < 0.05$.

Effect measures

The Review Manager (RevMan) v. 5.4³⁵ (Nordic Cochrane Centre, Copenhagen, Denmark) was employed to assess and scrutinize the impact of various continuous and dichotomous outcomes. The standard mean differences (SMDs), risk ratios (RRs), and 95% confidence intervals (95% CIs) were calculated for each study to evaluate the binary outcomes.³⁶

Statistical analyses

The DerSimonian–Laird method method was employed to compute RR using a 2×2 contingency table containing event data. Forest plots were utilized to visually assess

the impact of various outcome measures. A fixed-effect model was applied when the relative treatment effect was assumed to be consistent across all included studies, while a random-effects model was used when some variability between studies was anticipated. To evaluate heterogeneity among studies, statistical parameters such as the I^2 statistic, χ^2 test value, Z-test statistic, and p-value were used. A result was considered statistically significant when $p < 0.05$. Subgroup analyses were conducted to evaluate the effectiveness of nurse-led sedation protocols in mechanically ventilated ICU patients, focusing on outcomes including the duration of mechanical ventilation, ICU mortality, length of ICU stay, and overall hospital stay. Additionally, RRs were calculated to determine the risk of AEs associated with the nurse-led sedation protocols.^{37–45}

Results

Study selection outcomes

Examination of multiple databases was conducted for this investigation, resulting in the identification of 211 papers that fulfilled the inclusion criteria specified in the PICO framework. A total of 190 publications were selected for examination, while 21 papers were removed owing to redundancy. After additional screening, the titles and those articles abstracts of 74 publications were deemed irrelevant and were therefore eliminated. The remaining 105 articles

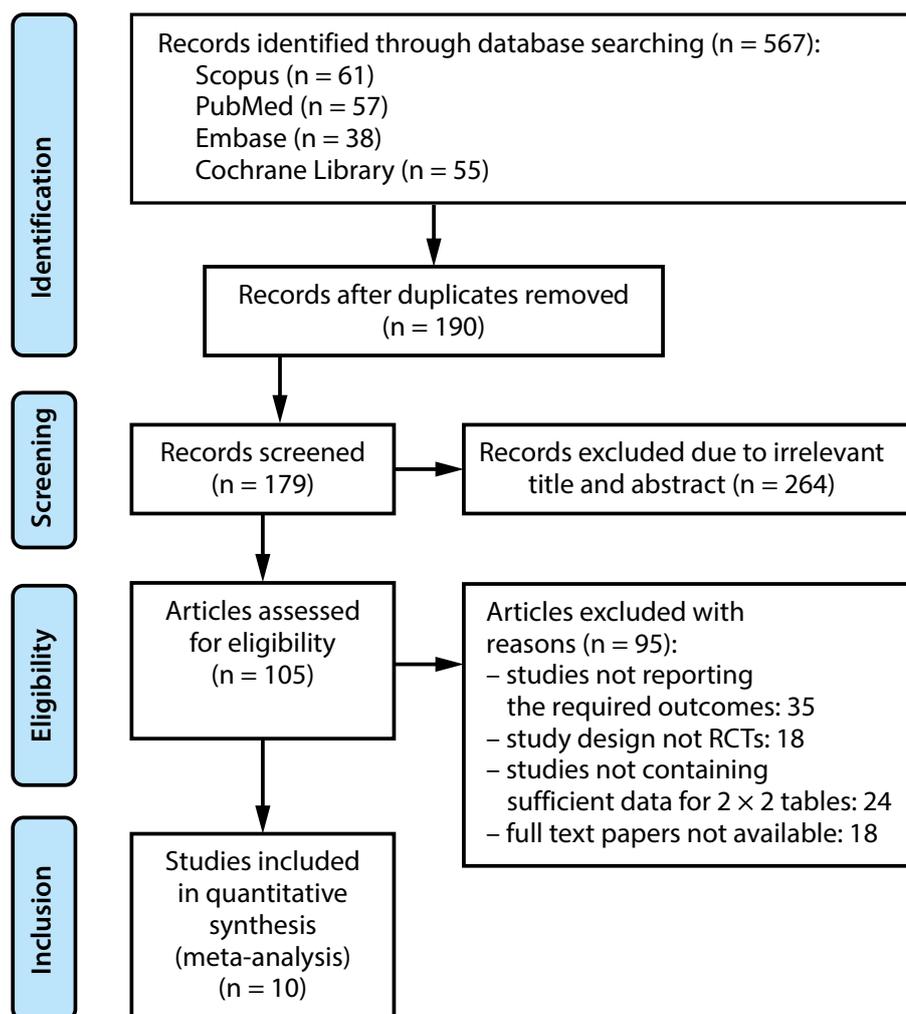


Fig. 1. Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) flow diagram illustrating the study selection process for the systematic review and meta-analysis

RCTs – randomized controlled trials.

underwent further assessment. However, 95 studies were considered ineligible and were consequently excluded following the application of the inclusion-exclusion criteria. This was primarily due to the lack of full-text papers, inadequate data to create 2 × 2 tables, or the absence of necessary outcomes. This meta-analysis included 10 RCTs that met the established inclusion-exclusion criteria, as illustrated in the study flow diagram per PRISMA standards (Fig. 1). This investigation involves a total of 1,151 mechanically ventilated ICU patients that are above the age of 18. Table 2 presents a succinct characteristics and participant demographics of the RCTs included and analyzed in this meta-analysis. Additionally, event data for the 2 × 2 table were acquired from the participating RCTs to do a meta-analysis. Supplementary Table 1 presents the assessment based on the AMSTAR-2 criteria.⁴⁶

Evaluation of potential bias in the selected RCTs

An extensive evaluation of bias risk was undertaken to assess the quality of the studies included in the analysis. The findings of this evaluation, employing a predetermined questionnaire, are delineated in Table 3 for each

of the 10 RCTs incorporated in the meta-analysis. The results of this evaluation, as depicted in the traffic light plot (Fig. 2) and summary plot (Fig. 3), suggest a minimal probability of bias among the studies analyzed. Notably, 8 out of the 10 RCTs were assessed to possess a low risk of bias, indicating a commendable level of methodological rigor. Nevertheless, 1 RCT (Namadian and Taran²⁵) exhibited a moderate risk of bias, chiefly attributable to issues surrounding the randomization process. Furthermore, another RCT (Tobar et al.²³) was recognized as exhibiting a significant risk of bias, chiefly attributable to concerns regarding absent outcome data.

This study assessed the effectiveness and safety of nurse-led sedation protocols for mechanically ventilated adults in the ICU, drawing from 10 RCTs. The analysis of the clinical outcomes within the subgroups produced the results discussed below.

Analysis of subgroups to assess mortality rates in the ICU

To evaluate the influence of the nurse-led sedation protocol on mortality rates in mechanically ventilated adults within the ICU, a comparison was made against standard

Table 2. Characteristics of the included randomized clinical trials (nurse-led protocol-directed sedation vs physician-led non-protocol-directed usual care for all studies)

Study ID and year	Country	Number of participants	Nurse–patient ratio	Types of ICU settings	Age of participants (mean ±SD)	Gender, male/female (%)	Outcomes analyzed
Abdar et al., 2013 ¹⁸	Iran	132	1 : 2–3	3 ICUs of a university affiliated hospital	37.2 ±5.0	58/15	1,2,3,4,5,6
Bucknall et al., 2008 ¹⁹	Australia	312	1 : 1	closed general ICU (24 beds) in a metropolitan teaching hospital	57.1 ±19.8	61.2/38.8	1,2,3,4,5,6
Carraway et al., 2021 ²⁰	USA	110	1 : 2–3	ICU in a level 2 hospital	68.4 ±2.8	58.2/41.8	1,2,3,4,5,6
Mansouri et al., 2013 ²¹	Iran	201	1 : 1	2 mixed ICUs in a university affiliated hospital	52.9 ±20.1	63.2/36.8	1,2,3,4,5,6
Zhang et al., 2019 ²²	China	84	1 : 2–3	ICU in the university affiliated hospital	38.3 ±6.4	58.3/41.7	1,2,3,4,5,6
Tobar et al., 2008 ²³	Chile	40	1 : 1	Clinical Hospital of the University of Chile	65 ±19	58.4/41.6	1,2,3,4,5,6
Taran et al., 2019 ²⁴	Iran	70	1 : 1	ICU in a level 3 hospital	66.8 ±17.7	81.4/18.6	1,2,3,4,5,6
Namadian and Taran, 2021 ²⁵	Iran	78	1 : 2–3	ICU in a university affiliated hospital	54.5 ±11.6	78.2/21.8	1,2,3,4,5,6
Rashidi et al., 2020 ²⁶	Iran	60	1 : 1	ICU in a level 3 hospital	45.7 ±12.9	58.3/41.7	1,2,3,4,5,6
Yousefi et al., 2015 ²⁷	Iran	64	1 : 2–3	ICU in a university affiliated hospital	46.6 ±13.1	57.8/42.2	1,2,3,4,5,6

1 – duration of mechanical ventilation; 2 – length of stay in ICU; 3 – length of hospital stay; 4 – ICU mortality; 5 – incidence of delirium; 6 – incidence of self-extubation; ICU – intensive care unit; SD – standard deviation.

Table 3. Risk assessment for included studies

Study ID and year	Abdar et al., 2013 ¹⁸	Bucknall et al., 2008 ¹⁹	Carraway et al., 2021 ²⁰	Mansouri et al., 2013 ²¹	Zhang et al., 2019 ²²	Tobar et al., 2008 ²³	Taran et al., 2019 ²⁴	Namadian and Taran, 2021 ²⁵	Rashidi et al., 2020 ²⁶	Yousefi et al., 2015 ²⁷
Was a consecutive or random sample of patients enrolled?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Did the study avoid inappropriate exclusions?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Did all patients receive the same reference standard?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Were all patients included in the analysis?	N	N	N	N	N	N	N	N	N	N
Was the sample frame appropriate to address the target population?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Were study participants sampled in an appropriate way?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Were the study subjects and the setting described in detail?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Were valid methods used for the identification of the condition?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Was the condition measured in a standard, reliable way for all participants?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y

Y – yes; N – no.

care. The RR was calculated for both the intervention and control groups, utilizing event data obtained from the selected RCTs,^{18–27} as depicted in Fig. 4. The forest plot (Fig. 4A) demonstrates that the nurse-led sedation

protocol significantly reduces the risk of ICU mortality when juxtaposed with usual care (RR = 0.34 (95% CI: 0.25 to 0.45); $\chi^2 = 18.20$, degrees of freedom (df) = 9, Z = 7.50, $I^2 = 38\%$, and $p < 0.001$). Furthermore, the symmetrical



Fig. 2. Traffic light plot depicting the risk of bias assessment

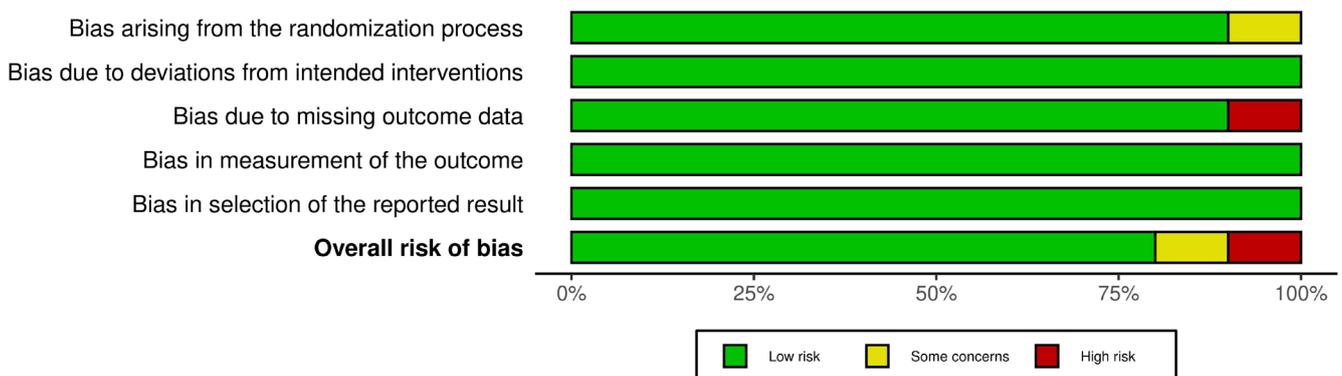


Fig. 3. Summary plot of the risk of bias assessment

funnel plot (Fig. 4B) and the statistically nonsignificant p-value for Begg’s test ($p = 0.134$), which surpasses the established significance threshold of 0.05, suggest a minimal likelihood of publication bias.

Analysis of subgroups to assess the duration of ICU admission

In order to assess the impact of the nurse-led sedation protocol on the length of ICU stay for mechanically

ventilated adults in comparison to standard care, the SMD was calculated for both the intervention and control groups, utilizing event data sourced from the included RCTs,^{18–27} as illustrated in Fig. 5. The forest plot (Fig. 5A) illustrates that the nurse-led sedation strategy yields a reduced length of stay in ICUs when contrasted with standard care (SMD = -1.58 (95% CI: -1.76 to -1.40); $\chi^2 = 26.30$, $df = 9$, $Z = 17.16$, $I^2 = 66\%$, and $p < 0.001$). The symmetrical funnel plot (Fig. 5B) and the nonsignificant p-value for Begg’s test ($p = 0.176$), which exceeds the established

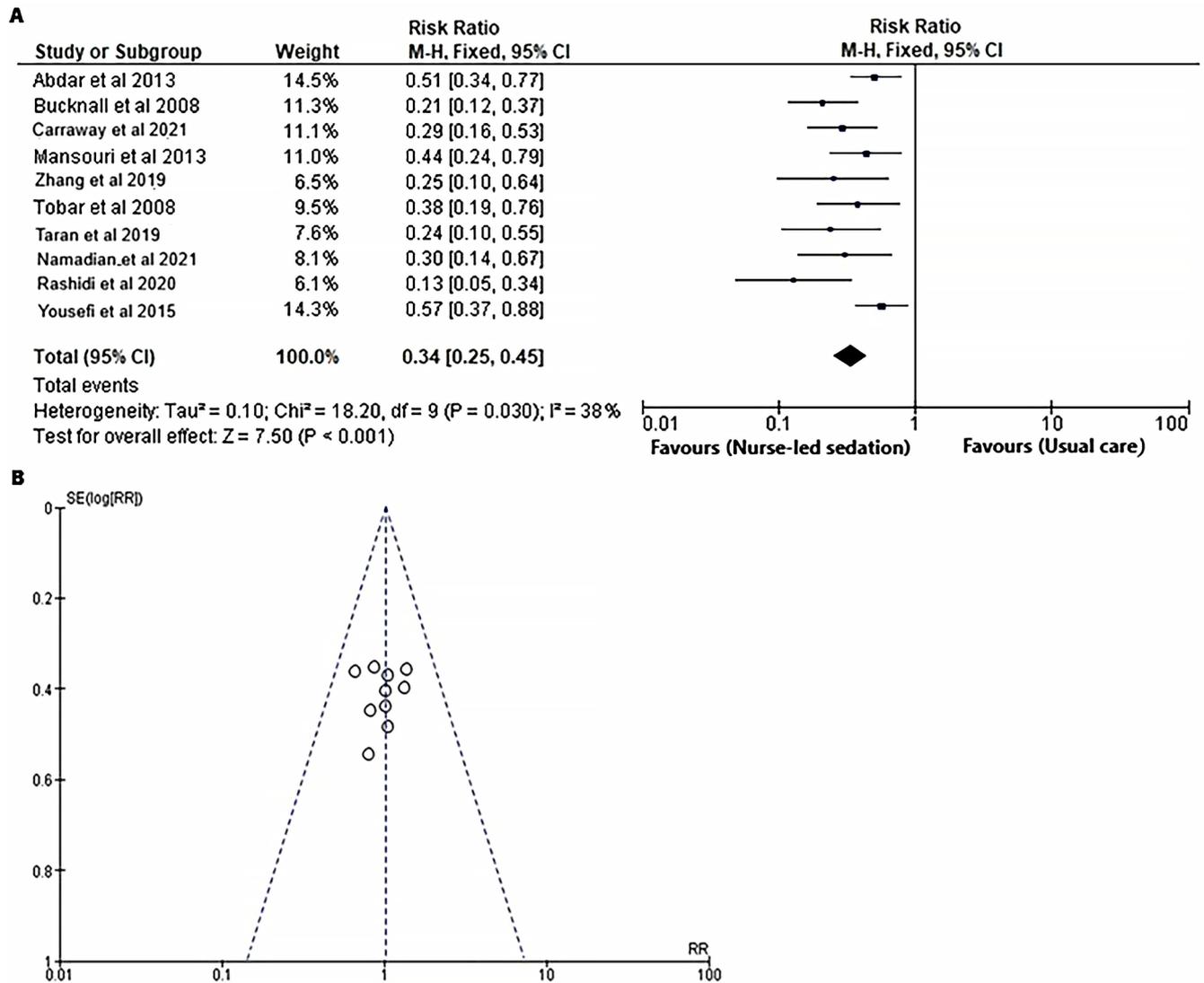


Fig. 4. Subgroup analysis for intensive care unit (ICU) mortality. A. Forest plot; B. Funnel plot

significance threshold of 0.05, indicate a minimal probability of publication bias.

Analysis of subgroups to assess the duration of hospitalization

In order to assess the influence of the nurse-led sedation protocol on the duration of hospital stay for mechanically ventilated adults in the ICU, a SMD was calculated for both the intervention and control groups, utilizing event data obtained from the relevant RCTs,^{18–27} as illustrated in Fig. 6. The forest plot (Fig. 6A) illustrates that the nurse-led sedation protocol is associated with a reduced duration of hospital stay when contrasted with standard care (SMD = -1.70 (95% CI: -1.80 to -1.59); $\chi^2 = 21.74$, df = 9, Z = 31.94, I² = 79%, and p < 0.001). Moreover, the symmetrical funnel plot (Fig. 6B) and the statistically insignificant p-value for Begg's test (p = 0.185), which surpasses the designated significance threshold of 0.05, suggest a minimal probability of publication bias.

Analysis of subgroups to assess the length of mechanical ventilation

In order to evaluate the effect of the nurse-led sedation protocol on the duration of mechanical ventilation in adults receiving mechanical ventilation in the ICU, the SMD was calculated for both the intervention and control groups, utilizing event data obtained from the relevant RCTs,^{18–27} as illustrated in Fig. 7. The forest plot (Fig. 7A) illustrates that the nurse-led sedation protocol led to a reduction in the duration of mechanical ventilation when contrasted with standard care practices as evidenced by a SMD of -1.94 (95% CI: -2.16 to -1.72); tau² = 0.09, $\chi^2 = 33.91$, df = 9, Z = 17.54, I² = 73%, and p < 0.001). Moreover, the symmetrical funnel plot (Fig. 7B), along with the statistically insignificant p-value for Begg's test (p = 0.105), exceeding the established significance threshold of 0.05, indicates a minimal likelihood of publication bias.

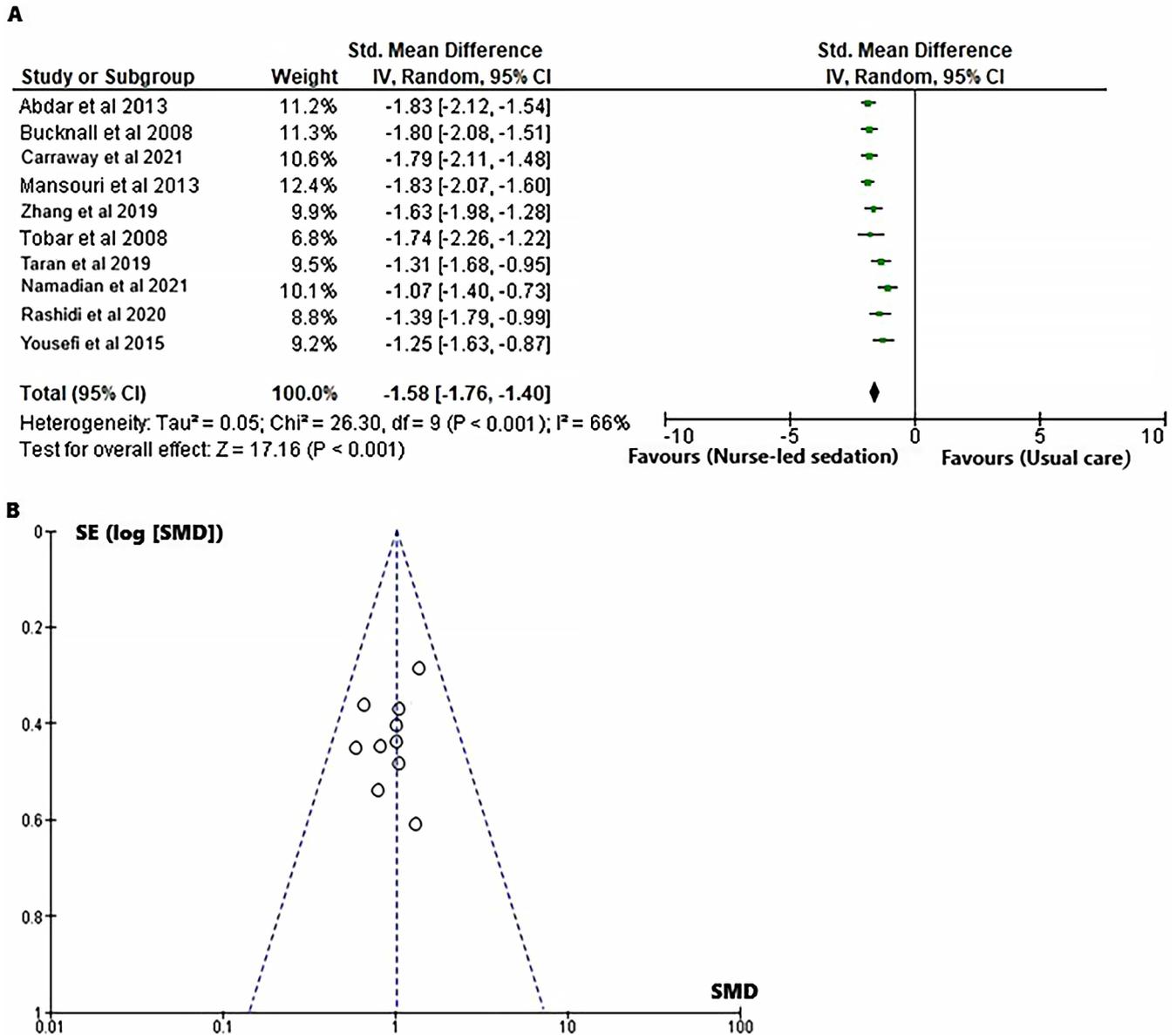


Fig. 5. Subgroup analysis for length of intensive care unit (ICU) stay. A. Forest plot; B. Funnel plot

Analysis of subgroups to evaluate the occurrence of self-extubation

A meta-analysis was performed to evaluate the impact of nurse-led sedation protocols on the occurrence of self-extubation among mechanically ventilated adults in ICUs, utilizing data from 10 RCTs.^{18–27} The RR was computed for both the intervention and control groups, as illustrated in Fig. 8. The forest plot (Fig. 8A) indicates that there was no statistically significant difference in the incidence of self-extubation between the 2 groups, as evidenced by a RR of 1.02 (95% CI: 0.25 to 4.45, $\chi^2 = 8.08$, df = 9, Z = 0.16, I² = 0%, and p = 0.877). Moreover, the symmetrical funnel plot (Fig. 8B), along with the nonsignificant p-value for Begg’s test (p = 0.166), indicates a minimal probability of publication bias, given that the p-value surpasses the established significance threshold of 0.05.

Analysis of subgroups to evaluate the occurrence of delirium

To assess the impact of nurse-led sedation protocols on the incidence of delirium in mechanically ventilated adults in ICUs, the RR was calculated using event data extracted from 10 RCTs, as illustrated in Fig. 9. The results presented in Fig. 9A indicate that the RR for delirium was significantly lower in the nurse-led sedation protocol group compared to the usual care group, with an RR of 0.47 (95% CI: 0.39–0.57; $\chi^2 = 10.60$; df = 9; Z = 7.68; I² = 15%; p < 0.001). Furthermore, the funnel plot (Fig. 9B) demonstrates symmetry, and Begg’s test for publication bias yielded a nonsignificant p-value (p = 0.190), suggesting that the results are unlikely to be influenced by publication bias.

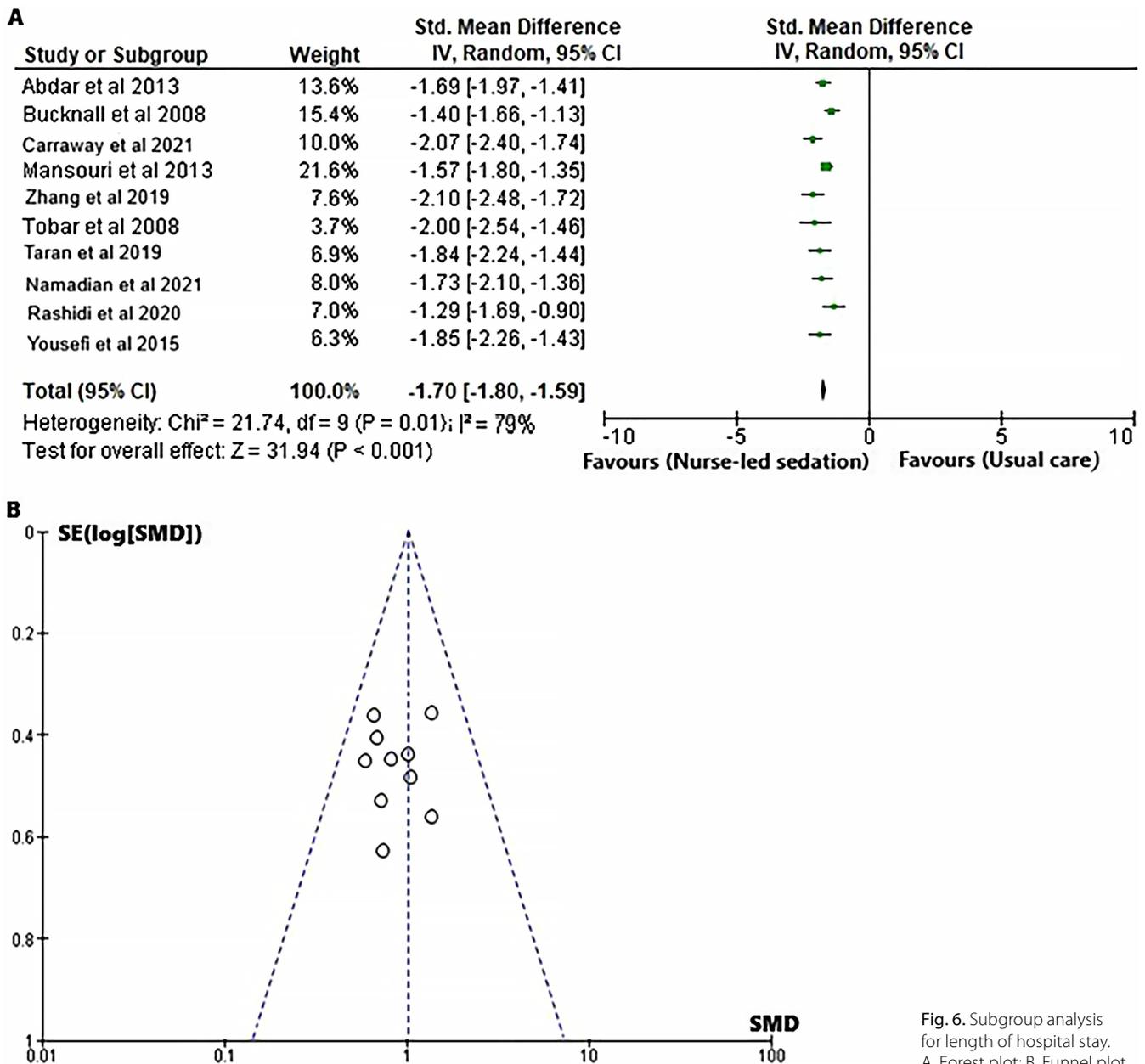


Fig. 6. Subgroup analysis for length of hospital stay. A. Forest plot; B. Funnel plot

Discussion

This systematic review and meta-analysis of 10 RCTs aimed to provide a comprehensive overview of the current evidence on nurse-led sedation protocols. The results of this analysis demonstrate that nurse-led sedation protocols can significantly improve patient safety outcomes. In ICUs where physicians are not consistently present at the bedside, effective communication between nurses and physicians is essential for ensuring timely treatment modifications and facilitating timely modifications to treatment instructions.^{47,48} However, this communication often results in delayed implementation of treatment instructions, which can compromise patient care.⁴⁹ To address this challenge, the implementation of a nurse-led sedation protocol can empower ICU nurses to adjust sedation

doses in real-time based on patients' sedation scores, without requiring physician input. This approach can prevent complications arising from excessive or inadequate sedation, such as respiratory depression, cardiac instability, and prolonged mechanical ventilation.^{50–52} By delegating sedation management to nurses, nurse-led sedation protocols can expedite clinical decision-making, reduce delays in treatment, and ensure standardized medical management. This is particularly crucial in ICUs, where timely and effective management of sedation is essential to prevent complications and improve patient outcomes. The nurse-to-patient ratio in ICUs is a critical determinant of nursing workload, particularly in the management of mechanically ventilated patients.^{53,54} Nurse-led sedation protocols in mechanically ventilated patients in ICUs involve a multidisciplinary approach to optimize sedation management.

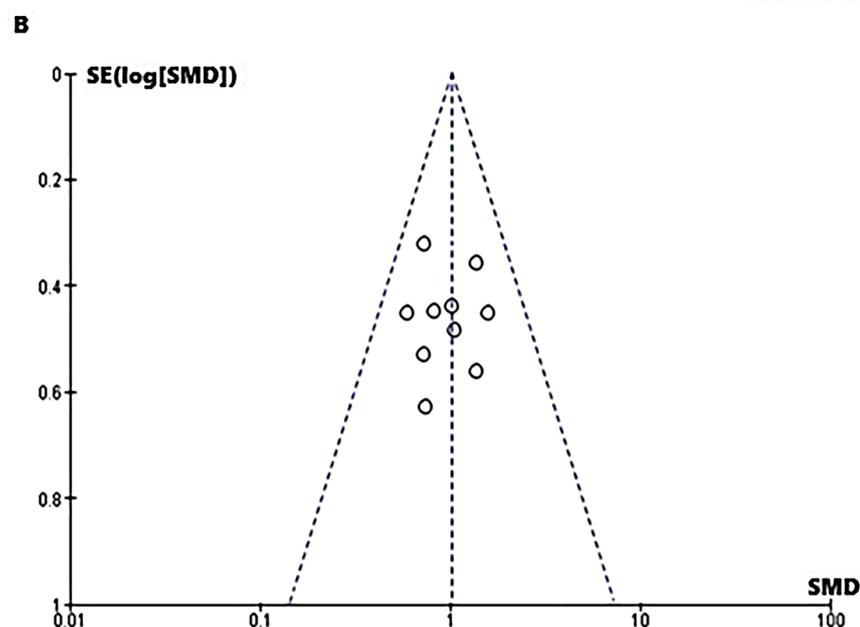
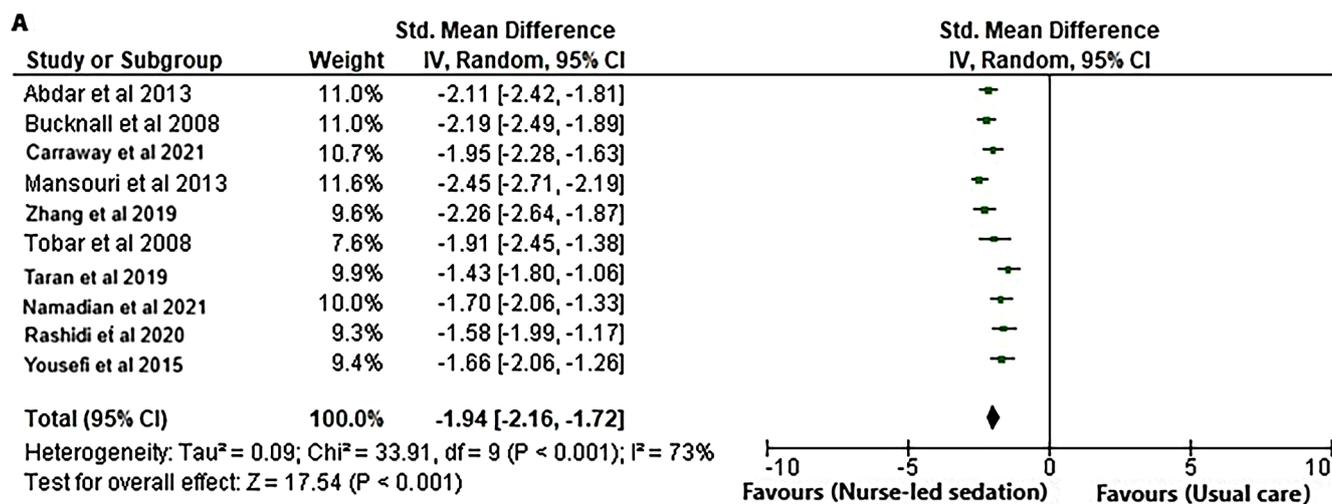


Fig. 7. Subgroup analysis for duration of mechanical ventilation. A. Forest plot; B. Funnel plot

Nurses regularly assess patients' sedation levels using standardized scales, such as the RASS or SAS, and adjust sedation medications accordingly. Vital signs and pain levels are continuously monitored, and sedation medications are titrated to maintain optimal sedation levels. Daily sedation interruptions and SATs are performed to assess patients' ability to breathe spontaneously and reduce sedation-related AEs. Nurses also implement pain management strategies, such as administering analgesics or using non-pharmacological interventions. Collaboration with physicians, respiratory therapists, and other healthcare professionals ensures consistent sedation management and clear communication with patients and families promotes informed care. Regular review and updates of sedation protocols ensure consistency with current evidence-based practices, and quality metrics monitoring evaluates protocol effectiveness and identifies areas for improvement. A 2016 survey revealed that approx. 1/3 of nurse respondents perceived that optimal nurse-to-patient ratios (1:1 or 1:2) significantly impacted sedation practices,⁵⁵ while 45%

of respondents reported administering sedative medications to facilitate completion of other nursing tasks. Notably, ICUs with higher nurse-to-patient ratios tend to exhibit more standardized and efficient sedation management for mechanically ventilated patients, which may contribute to improved patient outcomes, including shorter durations of mechanical ventilation and ICU lengths of stay. Furthermore, nursing behavior is a pivotal factor in sedation management, and increased nursing workload can compromise adherence to nurse-led sedation protocols.⁵⁶⁻⁵⁸ Conversely, the implementation of nurse-led sedation protocols has been shown to enhance patient safety, as evidenced by reduced ICU mortality rates, which can be attributed to improved sedation management and practice, thereby mitigating the risk of AEs related to excessive sedation, such as nosocomial infections and delirium.⁵⁹ Hernandez et al.⁶⁰ presented findings from their study, which revealed that protocolized sedation, whether implemented through algorithmic approaches or daily interruptions, is a safe and effective strategy compared to standard management

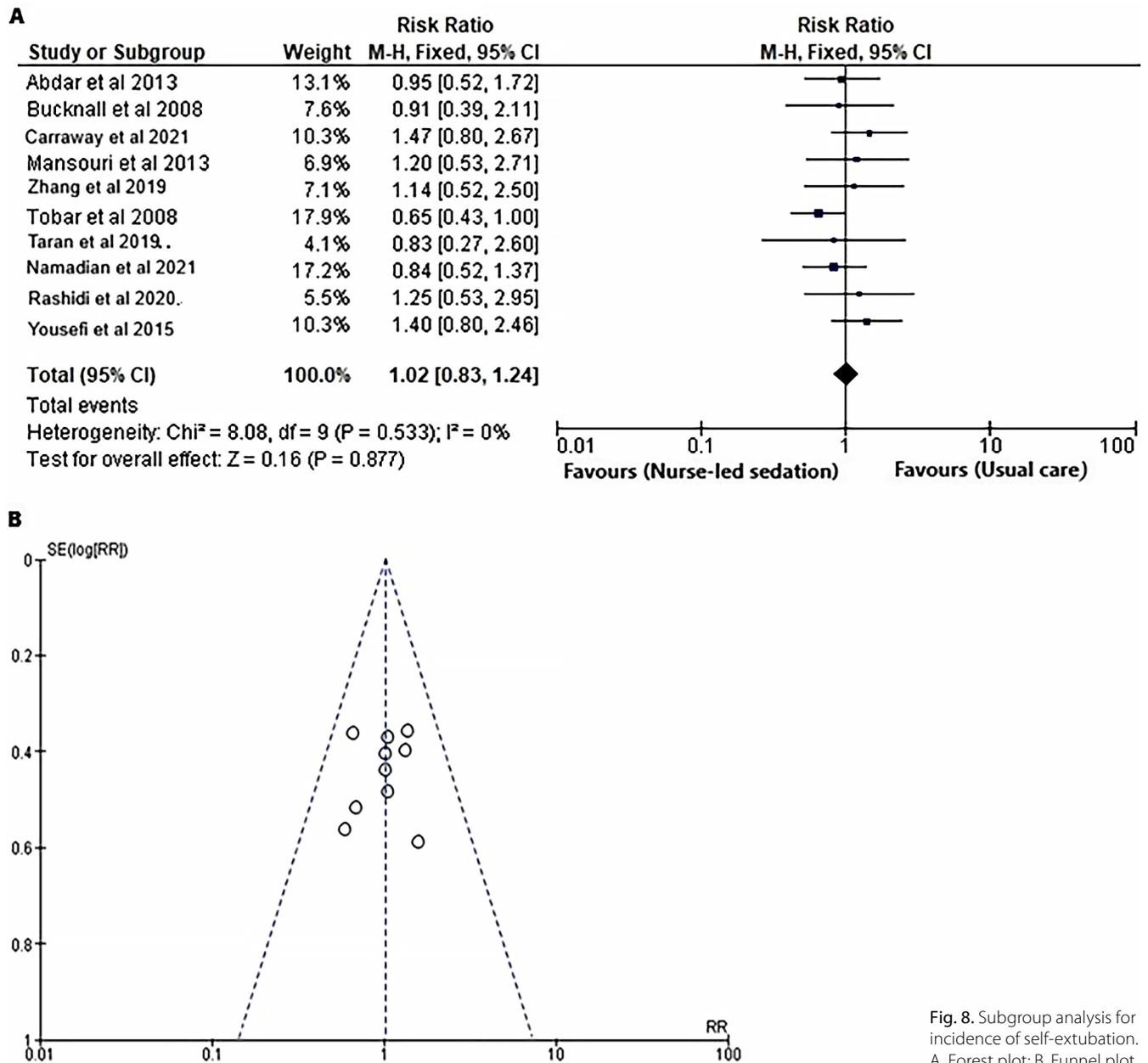


Fig. 8. Subgroup analysis for incidence of self-extubation. A. Forest plot; B. Funnel plot

in ventilated ICU patients. The results demonstrated that protocolized sedation is associated with a reduced RR for mortality (0.80 and a 95% CI of 0.68 to 0.93). Additionally, protocolized sedation resulted in a decrease in ventilation days, with a SMD of -1.12 days (95% CI: -2.11 to -0.14), and a notable reduction in ICU stay with a SMD of -2.24 days (95% CI: -3.59 to -0.89). However, the incidence of self-extubation did not exhibit a significant difference, with an RR of 1.20 and a 95% CI of 0.49 to 2.94. The findings from this study provide valuable insights to inform evidence-based practices in sedation management for critically ill patients in ICUs. Minhas et al.⁶¹ conducted a systematic review and meta-analysis of RCTs to evaluate the effects of protocolized sedation, utilizing either algorithms or daily interruptions, in comparison to standard care without protocolized sedation, on clinical outcomes in mechanically ventilated adult patients

in ICUs. The findings of the present meta-analysis indicate that, in mechanically ventilated adults treated in closed, non-specialized ICUs, the implementation of protocolized sedation is associated with a significant reduction in overall mortality (15%), as well as decreased lengths of stay in both the ICU (1.73 days) and hospital (3.55 days), and a lower incidence of tracheostomy (31%), when compared to standard care without protocolized sedation. Our findings indicate that nurse-led sedation protocols are capable of reducing the duration of mechanical ventilation and the length of stay in the ICU when compared to standard care practices. Nonetheless, the variability of these outcomes was considerable, aligning with the results of earlier meta-analyses. Our findings elucidate that these protocols are associated with a significant reduction in ICU mortality (RR = 0.34 (95% CI: 0.25 to 0.45); $I^2 = 38\%$, and $p < 0.001$), duration of mechanical ventilation (SMD = -1.94 (95% CI:

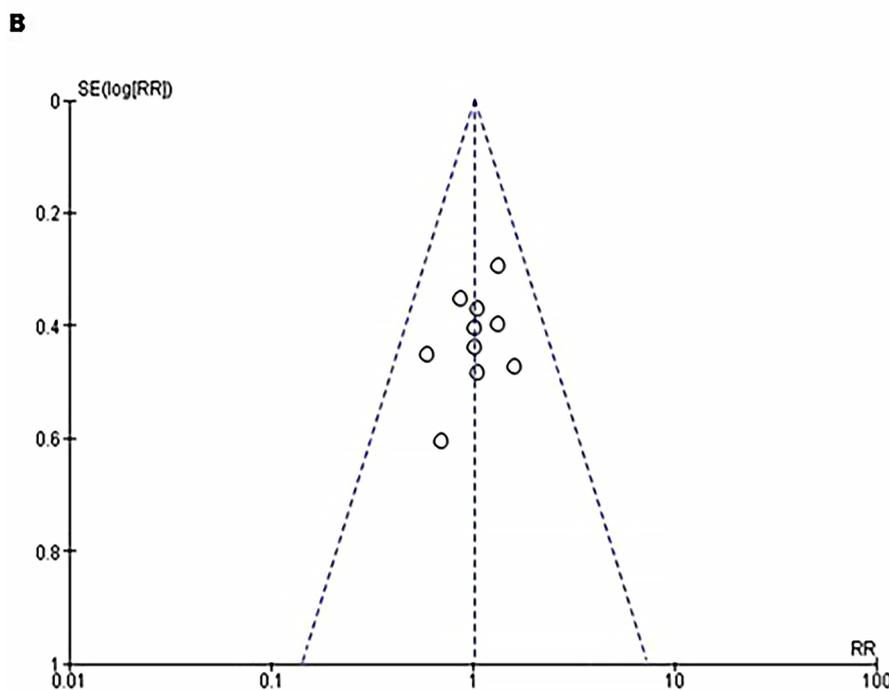
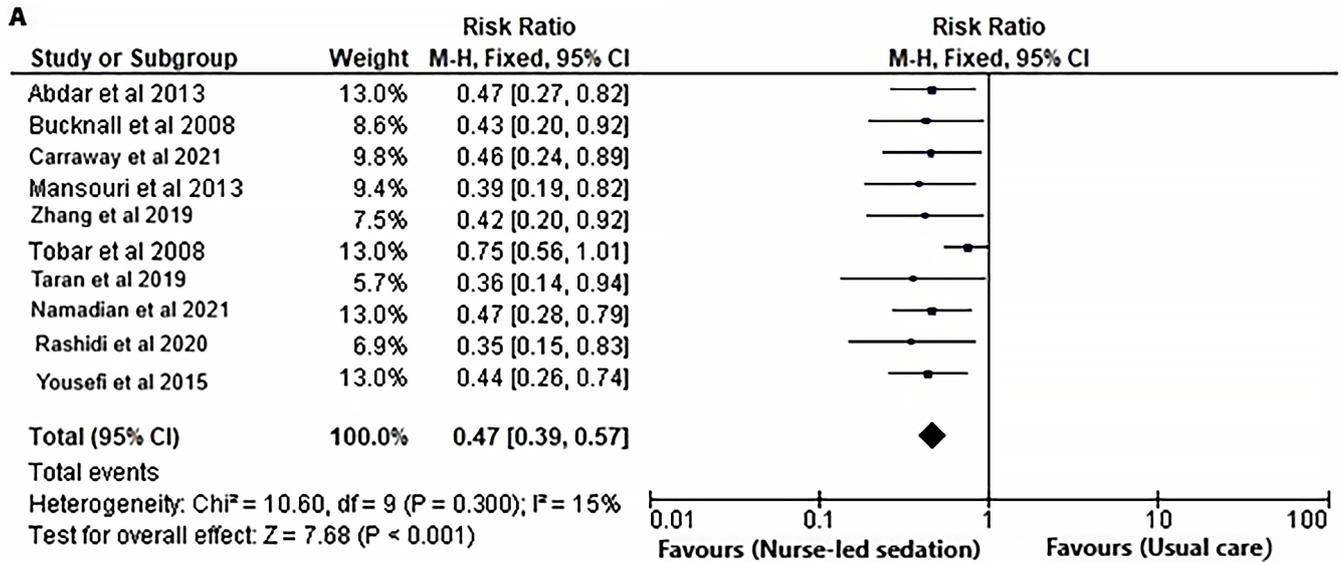


Fig. 9. Subgroup analysis for incidence of delirium. A. Forest plot; B. Funnel plot

-2.16 to -1.72); $I^2 = 73\%$, and $p < 0.001$), length of hospital stay (SMD = -1.70 (95% CI: -1.80 to -1.59); $I^2 = 79\%$, and $p < 0.001$), length of ICU stay [SMD = -1.58 (95% CI: -1.76 to -1.40); $I^2 = 66\%$, and $p < 0.001$), and incidence of delirium (RR = 0.47 (95% CI: 0.39 to 0.57); $I^2 = 15\%$, and $p < 0.001$). Nevertheless, the examination revealed no notable disparity in the occurrence of self-extubation (RR = 1.02 (95% CI: 0.83 to 1.24); $I^2 = 0\%$ and $p = 0.87$) when comparing the nurse-led sedation protocol to standard care. The subgroup analysis of RCTs demonstrated ongoing heterogeneity, potentially stemming from differences in protocol quality, patient demographics, and sedation methodologies across various ICUs. A multitude of factors could have played a role in the observed heterogeneity, encompassing disparities in sedation protocols and assessment scales, variations in the sedative agents utilized along

with their dosages, and differing modalities of mechanical ventilation employed in ICUs.

Additionally, the quality of the sedation protocols, the experience and training of the nurses, and the availability of resources and equipment may have also influenced the outcomes. Therefore, future studies should aim to standardize sedation protocols, minimize variability in sedation practices, and control for potential confounding factors to provide more generalizable findings.

Limitations

However, it is essential to acknowledge the study's limitations. Selection bias may exist because we excluded studies that did not meet the inclusion criteria. Second, this meta-analysis includes only 10 RCTs with small sample

sizes, limiting precise comparisons. Third, the included trials varied in patient populations and usual care practices. Lastly, the evaluated outcomes are based on subjective data only. Consequently, future long-term follow-up RCTs with larger sample sizes, varied patient demographics, and standardized usual care interventions are essential to validate the enduring efficacy and safety of nurse-led sedation protocols on clinical outcomes in mechanically ventilated adults in ICUs, with the objective of enhancing patient care.

Conclusions

This systematic review and meta-analysis provide compelling evidence that nurse-led sedation protocols can safely enhance clinical outcomes for mechanically ventilated adults in ICUs. Implementation of these protocols was associated with significant reductions in ICU mortality, duration of mechanical ventilation, length of ICU and hospital stays, and the incidence of sedation-related AEs. Despite these promising results, further research is necessary to confirm the long-term efficacy and generalizability of nurse-led sedation protocols, particularly in light of the methodological limitations and relatively small sample sizes of the included studies. Future investigations employing rigorous designs and larger cohorts will be critical to advancing evidence-based practice, optimizing ICU management, and improving patient outcomes.

Supplementary data

The supplementary materials are available at <https://doi.org/10.5281/zenodo.15655332>. The package contains the following files:

Supplementary Table 1. Quality assessment based on the AMSTAR-2 criteria.

Consent for publication

Not applicable.

Use of AI and AI-assisted technologies

Not applicable.

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