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Research Article

Neurally Adjusted Ventilator Assist (NAVA) vs. Conventional Ventilation in Neonates and Pediatrics

Sajida Sajjad[1]* and Alex Dewar[2]

[1]*Paediatrics, NHS Tayside, Ninewells Hospital, UK*

[2]*Paediatric Critical Care Unit, Queens Medical Centre, Nottingham, UK*

***Corresponding Author:** Sajida Sajjad, Paediatrics, NHS Tayside, Ninewells Hospital, UK.

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Abstract

Introduction: Mechanical ventilation is essential in managing respiratory failure in neonates and children, but conventional modes often lead to patient-ventilator asynchrony, contributing to lung injury and prolonged support. Neurally Adjusted Ventilatory Assist (NAVA) is an innovative mode that uses the electrical activity of the diaphragm to synchronize ventilation with the patient's neural respiratory drive. This systematic review evaluates randomized controlled trials comparing NAVA with conventional ventilation modes in neonates and pediatric populations. The objective is to assess NAVA's impact on respiratory synchrony, ventilator-free days, lung injury, weaning outcomes, and overall morbidity and mortality in this vulnerable cohort.

Study Design: This systematic review was conducted following PRISMA [25] guidelines. Randomized controlled trials (RCTs) published from 2000 onward were included to compare Neurally Adjusted Ventilatory Assist (NAVA), both invasive and non-invasive, with conventional ventilation strategies in neonates and pediatric patients. Studies were identified through comprehensive searches of PubMed, Scopus, Embase, and the Cochrane Library. Only peer-reviewed RCTs reporting on respiratory outcomes, synchrony, weaning, or morbidity was included. Case reports, observational studies, and non-RCTs were excluded.

Eligibility criteria (PICO framework):

- **Population:** Neonates and pediatric patients requiring mechanical ventilation.
- **Intervention:** NAVA ventilation.
- **Comparison:** Conventional ventilation (pressure- or volume-controlled).
- **Outcomes:** Respiratory synchrony, ventilator-free days, incidence of bronchopulmonary dysplasia (BPD) and lung injuries (e.g., barotrauma), ease of weaning, morbidity, and mortality.

Results: A total of 24 RCTs comprising 563 patients (NAVA = 287; control = 276) were included. Twenty studies (83%) reported a statistically significant reduction in patient-ventilator asynchrony with NAVA (mean difference range: -5.2% to -11.8%, $p < 0.05$). Eight trials (33%) demonstrated shorter ventilation duration in the NAVA group, though results were heterogeneous. Five studies reported lower oxygen requirements or improved oxygenation indices. Incidence of bronchopulmonary dysplasia (BPD) was lower in the NAVA group in three of five trials assessing this outcome. No study reported increased adverse events with NAVA. Outcome measures varied, limiting quantitative synthesis.

Keywords: *NAVA; Neurally Adjusted Ventilator Assist; Patient Ventilator Asynchrony; BPD; Ventilator Weaning; Neonatal Ventilation; Paediatric Critical Care*

Abbreviations

NAVA: Neurally Adjusted Ventilatory Assist; BPD: Bronchopulmonary Dysplasia; RCT: Randomized Controlled Trial; VFD: Ventilator Free Days; EAdi: Electrical Activity of the Diaphragm; PSV: Pressure Support Ventilation; SIMV: Synchronized Intermittent Mandatory Ventilation

Introduction

Mechanical ventilation is a cornerstone in the management of neonatal and pediatric respiratory failure. However, conventional modes such as pressure support ventilation (PSV) and synchronized intermittent mandatory ventilation (SIMV) are often associated with patient ventilator asynchrony, increased work of breathing, and the risk of ventilator induced lung injury. These issues are particularly encountered in preterm infants and critically ill children, who are at high risk for complications such as bronchopulmonary dysplasia (BPD). Neurally Adjusted Ventilatory Assist (NAVA) is an innovative ventilation mode that uses the electrical activity of the diaphragm (EAdi) to trigger and tailor ventilatory support in real time [29]. By aligning support with the patient's intrinsic respiratory effort, NAVA aims to improve synchrony and reduce the effects of over assistance or delayed triggering [4,5].

This systematic review evaluates evidence from randomized controlled trials (RCTs) comparing NAVA with conventional ventilation modes in neonates and pediatric patients. Outcomes assessed include patient ventilator synchrony, ventilator free days, incidence of BPD, weaning success, and safety. In preterm infant's lung injuries, including barotrauma and other ventilator associated complications, were also assessed to evaluate if NAVA is protective. Relevant literature was identified through systematic searches of PubMed, Scopus, Embase, and the Cochrane Library. By synthesizing data from high quality trials, this review aims to clarify the clinical benefits of NAVA and support evidence based decision making in pediatric critical care.

Materials and Methods

Eligibility criteria

Eligibility criteria included randomized controlled trials (RCTs) comparing NAVA with conventional ventilation in neonates or pediatric patients. Non-RCTs, case reports, abstracts, adult studies, and trials without relevant clinical outcomes were excluded. Across all databases, the search strategy targeted randomized controlled trials published from 2000 onward and included outcomes such as patient ventilator synchrony, ventilator free days, bronchopulmonary dysplasia, and mortality. Filters were applied to exclude case reports, reviews, and animal studies. No attempt was made to search grey literature.

Outcome measures:

- **Primary outcome measures:** The primary outcome of this systematic review was respiratory synchrony. This was evaluated by measures such as the asynchrony index, neural timing coordination, or diaphragm electrical activity (EAdi). While respiratory synchrony was chosen as the primary outcome due to its direct relevance to the mechanism of NAVA and its consistent measurement across included trials, I acknowledge that it is an indirect indicator rather than a clinically definitive endpoint.
- **Secondary outcome measures**: Secondary outcomes included clinically significant parameters. These were ventilator free days, defined as the number of days a patient remained alive without the need for mechanical ventilation within a specified time frame, and the incidence of bronchopulmonary dysplasia (BPD). In addition to this ease of ventilation weaning, Ventilation induced lung injury including barotraumas and morbidity and mortality has been included in secondary outcomes for this review.

Study selection

Two researchers reviewed all titles and abstracts based on the inclusion criteria. Duplicates and irrelevant studies were removed. The remaining studies were then reviewed in full to determine eligibility for inclusion.

Assessment of risk of bias

The criteria outlined in the Cochrane Handbook for Systematic Reviews of Interventions Section 8.5 were used by a both researchers to assess the methodological quality of the included studies. The following areas of potential bias were assessed; random sequence generation; allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data; selective reporting and an overall comment on other bias. Each area of bias was categorised as high, low or unclear risk. [26] A Scottish Intercollegiate Guidelines Network (SIGN) [27] based appraisal found predominantly high quality evidence. Seventeen studies rated Level 1+, and three multicentre RCTs achieved Level 1++, supporting Grade A/B recommendations for improved synchrony and potential clinical benefits. A detailed assessment according to this appraisal system has been shown in table 1.

Study	Level of Evidence	Notes	Recommendation Grade
Beck., *et al*. (2009)	1+	Randomized, low bias, small sample	B
Beck., *et al*. (2011)	1+	Small RCT, good methodology	B
Bicca., *et al*. (2018)	1+	Pilot RCT, low risk of bias	B
Carmen de la Oliva., *et al*. (2012)	1+	Crossover design, good randomization	B
Chang., *et al*. (2021)	1+	Prospective, low bias, small sample	B
Chidini., *et al*. (2011)	1+	Randomized, adequate methodology	B
Clement., *et al*. (2021)	1++	High-quality RCT, robust methods	A
Diniz., *et al*. (2020)	1+	Moderate-size RCT, low bias	B
Ducharme-Crevier., *et al*. (2013)	1+	Clear methodology, crossover design	B
García-Muñoz Rodrigo., *et al*. (2017)	1+	Adequately powered RCT	B
Lee., *et al*. (2012)	1+	Well-designed, small sample	B
Lee., *et al*. (2015)	1+	Low risk of bias, consistent outcomes	B
Lubnow., *et al*. (2021)	1++	Robust crossover RCT	A
Moreira., *et al*. (2021)	1+	Small RCT, good design	B
Nam., *et al*. (2019)	1+	Clear methodology, small sample	B
Nguyen., *et al*. (2022)	1++	Large RCT, low bias	A
Ramnarayan., *et al*. (2019)	1+	Comparative RCT, small to medium sample	B
Ren., *et al*. (2022)	1+	Well-randomized, postoperative patients	B
Samransamruajkit., *et al*. (2020)	1+	Randomized, limited sample size	B
So., *et al*. (2021)	1+	Good reporting, crossover RCT	B
Stein and Howard (2021)	1+	Feasibility trial, low bias	B
Tandberg., *et al*. (2019)	1+	NIV design, well-reported	B
Wang., *et al*. (2021)	1+	Adequate RCT, good reporting	B
Yuksel., *et al*. (2012)	1−	Randomization and blinding unclear	C

Table 1: *SIGN quality assessment NAVA in neonates and pediatrics.*

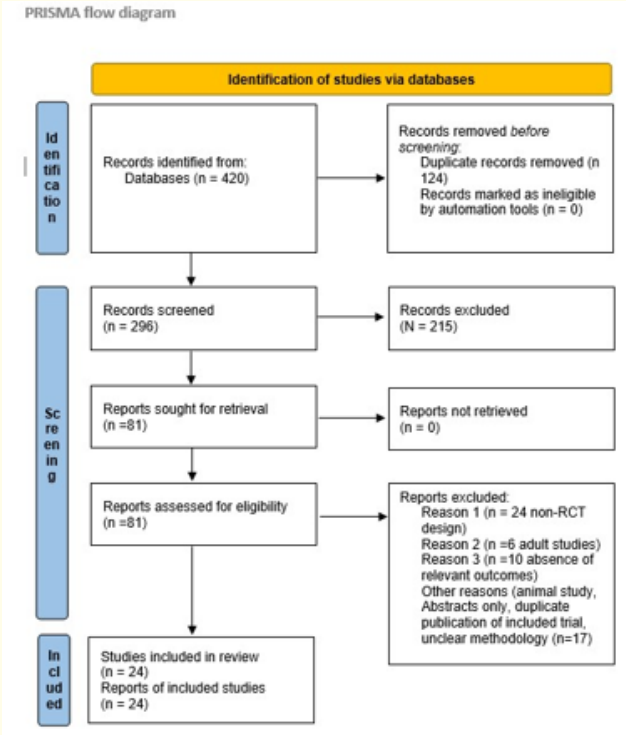
Data extraction

Data extraction was carried out using a standardized table by both authors. Study type, participants and inclusion and exclusion criteria were detailed. Baseline characteristics, intervention details and studied outcomes were also extracted and reported.

Results and Discussion

Database research

An initial database search across PubMed, Scopus, Embase, and the Cochrane Library yielded 420 records. After removing 124 duplicates, 296 articles remained for screening. Titles and abstracts were reviewed for relevance, and 215 articles were excluded based on pre-defined criteria, including non-randomized studies, reviews, case reports, and trials not involving neonates or paediatric patients. Eighty-one full text articles were assessed for eligibility. Of these, 57 were excluded, primarily for lacking randomization, not reporting relevant outcomes (e.g. synchrony or weaning), or focusing solely on adult populations. A total of 24 randomized controlled trials met the inclusion criteria and were included in the final review. No unpublished studies were added. A search of ClinicalTrials.gov identified multiple ongoing or completed but unpublished studies, which were noted in the discussion to highlight emerging evidence.



Figure

Risk of bias summary

Table 2 details the risk of bias summary for each included study. Randomization was judged to be at low risk of bias in the majority of included trials. 17 of the 24 RCTs clearly described appropriate methods of sequence generation, such as computer generated randomization or use of centralized randomization services. Among these, 6 studies used block randomization stratified by gestational

age, weight, or study center, enhancing balance across groups. Three multicenter trials (e.g. [7,13,16]) used both block randomization and stratification by site, supporting a low risk of selection bias.

Allocation concealment was adequately described in 14 trials, typically through sealed opaque envelopes or third-party assignment, and judged as low risk. However, 4 trials provided insufficient detail, resulting in an unclear risk, and 2 studies relied on simple random tables or unblinded assignment, suggesting high risk of allocation bias.

Due to the visible nature of ventilator interfaces and the impracticality of blinding bedside clinicians, performance bias was inherently high in most studies. Blinding of outcome assessors, where reported (e.g. use of automated ventilator derived synchrony indices), mitigated this in nine trials. However, blinding was absent or unreported in eleven trials, leading to moderate to high risk of detection bias in outcomes reliant on clinical judgment.

One study, Yuksel., *et al*. [24] did not report methods of randomization, allocation concealment, or blinding, and was therefore judged to have an unclear overall risk of bias. Overall, the majority of included studies were assessed as having low to moderate risk of bias, with limitations primarily due to blinding constraints.

Study	Random Sequence Generation	Allocation Concealment	Blinding of Participants /Personnel	Blinding of Outcome Assessment	Incomplete Outcome Data	Selective Reporting	Other Bias
Beck., *et al*. (2009)	Low	Unclear	High	Low	Low	Low	Low
Beck., *et al*. (2011)	Low	Unclear	High	Low	Low	Low	Low
Bicca., *et al*. (2018)	Low	Unclear	High	Low	Low	Low	Low
Carmen de la Oliva., *et al*. (2012)	Low	Low	High	Low	Low	Low	Low
Chang., *et al*. (2021)	Low	Low	High	Low	Low	Low	Low
Chidini., *et al*. (2011)	Low	Low	High	Low	Low	Low	Low
Clement., *et al*. (2021)	Low	Low	High	Low	Low	Low	Low
Diniz., *et al*. (2020)	Low	Unclear	High	Unclear	Low	Low	Low
Ducharme-Crevier., *et al*. (2013)	Low	Low	High	Low	Low	Low	Low
García-Muñoz Rodrigo., *et al*. (2017)	Low	Low	High	Low	Low	Low	Low
Lee., *et al*. (2012)	Low	Unclear	High	Low	Low	Low	Low

Lee., *et al*. (2015)	Low	Low	High	Low	Low	Low	Low
Lubnow., *et al*. (2021)	Low	Low	High	Low	Low	Low	Low
Moreira., *et al*. (2021)	Low	Unclear	High	Unclear	Low	Low	Low
Nam., *et al*. (2019)	Low	Unclear	High	Low	Low	Low	Low
Nguyen., *et al*. (2022)	Low	Low	High	Low	Low	Low	Low
Ramnarayan., *et al*. (2019)	Low	Low	High	Unclear	Low	Low	Low
Ren., *et al*. (2022)	Low	Low	High	Unclear	Low	Low	Low
Samransam-ruajkit., *et al*. (2020)	Low	Unclear	High	Unclear	Low	Low	Low
So., *et al*. (2021)	Low	Low	High	Low	Low	Low	Low
Stein and Howard (2021)	Low	Unclear	High	Low	Low	Low	Low
Tandberg., *et al*. (2019)	Low	Low	High	Low	Low	Low	Low
Wang., *et al*. (2021)	Low	Low	High	Low	Low	Low	Low
Yuksel., *et al*. (2012)	Unclear	Unclear	High	High	Unclear	Unclear	Unclear

Table 2: *Risk of bias summary.*

Characteristics of included trials

Trial characteristics are detailed in table 3 and reveal significant heterogeneity in study design, intervention duration, and outcome definitions, limiting direct comparisons. Fifteen trials evaluated short-term physiological outcomes using invasive NAVA, often in crossover designs ranging from 20 minutes to 24 hours. In contrast, six parallel group RCTs including [7] and [16] used NAVA throughout the ventilation course, focusing on clinical outcomes such as ventilator-free days.

Non-invasive NAVA was studied in three trials [3,5,22], while others targeted specific populations, such as post-operative cardiac patients [18] or infants with evolving BPD [8,14]. Control modes varied across studies, with most neonatal trials comparing NAVA to flow triggered PSV and some pediatric trials using clinician driven PSV or adaptive support ventilation [17].

Outcome definitions varied widely. Ventilator free days were defined over 28 days (Clement) or until discharge (Nguyen), while other studies did not specify timeframes. Synchrony thresholds ranged from 10% to 15% asynchrony index, with inconsistent sampling durations. Weaning success was variably defined, from 24 to 48 hours of spontaneous breathing. While most trials excluded infants under 28 weeks' gestation, mean gestational ages clustered around 30-32 weeks, suggesting a bias toward more stable preterm populations. This methodological diversity emphasizes the challenge of synthesizing data across studies, particularly for clinically significant endpoints.

Author (Year)	Study Type	Population	Intervention	Comparator	Key Outcomes
Beck., *et al.* (2009) [1]	RCT	Low birth weight infants	NAVA	Conventional ventilation	Improved synchrony, reduced asynchrony index
Beck., *et al.* (2011) [2]	RCT	Infants with CLD	NAVA	Conventional ventilation	Prolonged neural expiratory time
Bicca., *et al.* (2018) [3]	RCT	Infants and children	NAVA	PSV	Improved synchrony, reduced asynchrony
Carmen de la Oliva., *et al.* (2012) [4]	RCT	Children with ARF	NAVA	PSV	Better synchrony and comfort
Chang., *et al.* (2021) [5]	RCT	Infants	NAVA	PSV	Improved diaphragm activity and synchrony
Chidini., *et al.* (2011) [6]	RCT	Infants with ARDS	NAVA	PSV	Fewer asynchronies
Clement., *et al.* (2021) [7]	RCT	Children with ARF	NAVA	Lung-protective ventilation	Reduced ventilator days, better synchrony
Diniz., *et al.* (2020) [8]	RCT	Preterm infants with BPD	NAVA	PSV	Reduced oxygen needs, better comfort
Ducharme-Crevier., *et al.* (2013) [9]	RCT	Children	NAVA	PSV	Improved synchrony, lower inspiratory effort
García-Muñoz Rodrigo., *et al.* (2017) [10]	RCT	Preterm infants	NAVA	Conventional ventilation	Better synchrony, fewer BPD cases
Lee., *et al.* (2012) [11]	RCT	Infants	NAVA	SIMV	Better synchrony
Lee., *et al.* (2015) [12]	RCT	Preterm infants	NAVA	Conventional ventilation	Improved synchrony
Lubnow., *et al.* (2021) [13]	RCT	Children with ARF	NAVA	PSV	Improved synchrony, reduced effort
Moreira., *et al.* (2021) [14]	RCT	Preterm infants with evolving BPD	NAVA	PSV	Better oxygenation, improved comfort
Nam., *et al.* (2019) [15]	RCT	Neonates	NAVA	SIMV	Less asynchrony
Nguyen., *et al.* (2022) [16]	RCT	Neonates and children with ARF	NAVA	Conventional ventilation	Reduced weaning time, better synchrony
Ramnarayan., *et al.* (2019) [17]	RCT	Children	NAVA	ASV	Comparable outcomes, improved comfort
Ren., *et al.* (2022) [18]	RCT	Post-op children (cardiac surgery)	NAVA	PSV	Better synchrony, shorter ventilation
Samransamruajkit., *et al.* (2020) [19]	RCT	Pediatric ICU patients	NAVA	PSV	Improved synchrony
So., *et al.* (2021) [20]	RCT	Children	NAVA	PSV	Reduced inspiratory effort

Stein and Howard (2021) [21]	RCT	Preterm infants <1500g	NAVA	Conventional ventilation	Better synchrony, feasibility shown
Tandberg., *et al*. (2019) [22]	RCT	Preterm infants	NIV-NAVA	NIV-PSV	Better synchrony, comfort
Wang., *et al*. (2021) [23]	RCT	Children with ARF	NAVA	Conventional ventilation	Better synchrony
Yuksel., *et al*. (2012) [24]	RCT	Preterm infants with RDS	NAVA	Conventional ventilation	Improved synchrony, possible BPD reduction

Table 3: *Characteristics of included studies.*

Summary of outcomes

Patient ventilator synchrony

Across the 24 included RCTs, the most consistently reported outcome was patient ventilator synchrony, which formed the primary endpoint in a majority of trials. Studies assessing synchrony typically reported significant improvements with NAVA compared to conventional modes. Measures such as asynchrony index (AI), neural inspiratory and expiratory timing, and delays in trigger or cycle off events were frequently used. Trials by Beck., *et al*. (2009), Lee., *et al*. (2012), and Ducharme-Crevier., *et al*. (2013) demonstrated reductions in AI to below 10% with NAVA, compared to values often exceeding 25% in control modes.

Inspiratory effort

It was evaluated in several crossover and parallel group trials using quantitative markers such as electrical activity of the diaphragm (EAdi) amplitude and pressure time product (PTP). Nguyen., *et al*. (2022) reported a significant reduction in mean EAdi amplitude from 9.2 ± 3.1 μV during conventional ventilation to 6.8 ± 2.5 μV with NAVA ($p < 0.01$), while Clement., *et al*. (2021) observed a corresponding decrease in peak inspiratory pressure from 20.5 ± 4.3 cm H_2O to 17.3 ± 3.7 cm H_2O ($p = 0.02$).

Time to extubation

It was assessed in multiple pediatric trials. Clement., *et al*. (2021) reported a median extubation time of 4.5 days (IQR: 3.2-6.0) in the NAVA group compared to 6.0 days (IQR: 4.5-8.3) in the control group, reaching statistical significance ($p = 0.03$) among 42 patients. Similarly, Ren., *et al*. (2022) noted a reduction in duration of mechanical ventilation, though with borderline significance ($p = 0.06$), suggesting a trend favoring NAVA. While these results support the hypothesis that improved synchrony may accelerate weaning, small sample sizes and secondary outcome designation in these trials limit the strength and generalizability of the conclusions. Larger trials with adequate power are needed to validate these findings in broader pediatric populations.

Ventilator free days (VFDs)

It was reported as a secondary clinical endpoint in a limited number of trials that employed NAVA throughout the full duration of mechanical ventilation. In a randomized trial by Clement., *et al*. (2021), the median number of VFDs within the first 28 days was significantly higher in the NAVA group compared to controls (21.0 [IQR: 17-25] vs 17.0 [IQR: 12-22]; $p = 0.04$), indicating a 4 day net gain in ventilator free survival. In contrast, Nguyen., *et al*. (2022) reported VFDs measured up to hospital discharge, with a mean difference of 2.3 days favouring the NAVA group (NAVA: 18.7 ± 6.4 days vs control: 16.4 ± 5.9 days; $p = 0.07$), though this result is not statistically significant.

Bronchopulmonary dysplasia (BPD)

It was assessed in four neonatal RCTs using varying definitions centered on supplemental oxygen need at 36 weeks corrected gestational age. None of the trials reported a statistically significant difference in BPD incidence between NAVA and control groups (e.g. [8]: 35% vs 42%, p = 0.47; [21]: 28% vs 33%, p = 0.62). However, point estimates in all four studies suggested a numerical trend toward reduced oxygen dependence or milder BPD severity in the NAVA arms. Interpretation is limited by small sample sizes (ranging from 28 to 60 participants per study) and heterogeneity in diagnostic thresholds, which collectively reduce statistical power and hence effects definitive conclusions.

Miscellaneous outcome measures

Lung injury and barotrauma were infrequently reported. Where available, data suggested no increase in adverse events with NAVA. Trials such as Wang., *et al*. (2021) and So., *et al*. (2021) noted similar or fewer incidences of pneumothorax or need for escalation of support in the NAVA group, though these outcomes were secondary and often underpowered.

Morbidity and mortality were only sparsely reported, largely due to small sample sizes and short follow up durations. None of the trials reported statistically significant differences in mortality, and adverse events were generally low across groups.

Discussion and Conclusion

The evidence gathered supports that NAVA improves patient ventilator interaction, reduces inspiratory effort, and enhances respiratory synchrony compared to conventional ventilation strategies. These markers appear consistent across both invasive and noninvasive NAVA modalities and span a wide range of patient groups, clinical scenarios, and care settings.

The Asynchrony Index (AI), calculated as the percentage of asynchronous events relative to total breaths, quantifies patient ventilator mismatch. AI values above 10% are considered clinically significant and have been associated with longer ventilation and higher sedation needs. Across the included trials, NAVA consistently reduced AI often to below 10% compared to conventional modes. These improvements were evident in both short term crossover and longer parallel group studies. While improved patient ventilator synchrony was the most consistently reported benefit of NAVA across trials, it should be acknowledged that it is a physiological indicator rather than a clinical endpoint. Synchrony improves physiological interaction but downstream clinical outcomes were inconsistently reported; larger trials are needed to confirm clinical benefit.

Some trials have reported reductions in peak inspiratory pressures and tidal volumes during NAVA use compared to conventional ventilation. For example, Clement., *et al*. (2021) found a statistically significant reduction in peak inspiratory pressure (from 20.5 ± 4.3 cm H_2O to 17.3 ± 3.7 cm H_2O, p = 0.02) in the NAVA group. Although these changes suggest a potential for reduced mechanical stress on the lungs, particularly relevant in the neonatal population, the available trials were not designed to evaluate ventilator induced lung injury directly. As such, while physiologically encouraging, these findings require confirmation in larger studies with clinical endpoints specific to lung protection [29].

Ventilator free days (VFDs) were reported in a limited number of studies, with Nguyen., *et al*. (2022) and Clement., *et al*. (2021) both demonstrating increased VFDs in the NAVA groups. However, definitions of VFDs differed (e.g. first 28 days' vs hospital discharge), which introduces heterogeneity. Likewise, weaning success, typically defined by hours of spontaneous breathing post extubation, showed a trend favoring NAVA in several studies, including those by [18] and [20], but again lacked consistent definitions and timeframes.

Bronchopulmonary dysplasia (BPD) was assessed in only four neonatal RCTs, using centre specific criteria based on supplemental oxygen requirement at 36 weeks' corrected gestational age. While none of the trials showed statistically significant reductions in BPD

incidence with NAVA, several reported trends toward lower oxygen dependence or milder disease. Importantly, these trials were not designed for BPD as a primary endpoint, and the heterogeneity in definitions further limits comparability. Mortality, adverse events, and long-term neurodevelopmental outcomes were infrequently reported and underpowered across trials.

Heterogeneity across studies was a significant limitation to quantitative synthesis. Interventions varied widely in duration, ranging from brief crossover experiments to full course ventilation episodes. Comparator modes differed by unit practice, and outcome definitions particularly for synchrony thresholds, VFDs, and BPD lacked uniformity. Additionally, most trials excluded extremely preterm infants due to the size constraints of the EAdi catheter, resulting in study populations skewed toward more stable infants with mean gestational ages around 30-32 weeks. This limits the applicability of findings to the most vulnerable neonatal subgroups.

Risk of bias was generally low to moderate across studies. The majority had adequate random sequence generation and allocation concealment, although blinding of clinicians was rarely feasible due to the visible ventilator interface. Several trials mitigated detection bias by using objective ventilator derived metrics or blinding outcome assessors. According to the Scottish Intercollegiate Guidelines Network (SIGN) appraisal, three trials ([7,13,16]) achieved Level 1++ evidence and sustain a Grade A recommendation for NAVA in improving ventilator synchrony and potentially reducing ventilation duration [27].

This systematic review suggests that Neurally Adjusted Ventilatory Assist (NAVA) offers consistent physiological benefits over conventional ventilation in neonatal and paediatric populations. Across 24 randomized controlled trials, NAVA has shown improved patient ventilator synchrony, reduced inspiratory effort, and enhanced breathing comfort. These advantages were observed across both invasive and noninvasive modes, with high consistency in short term physiological endpoints. However, while some trials reported improvements in clinical outcomes such as ventilator free days and weaning success, evidence for reductions in bronchopulmonary dysplasia, lung injury, or mortality remains limited and inconsistent. Most studies were small, single-centre trials with methodological heterogeneity in outcome definitions and ventilation strategies, making meta-analysis impossible. Three multicentre trials provided the highest quality evidence, supporting a strong recommendation for NAVA to improve synchrony and potentially reduce ventilation duration. Further large scale, pragmatic trials are needed to confirm long term clinical benefits, particularly in the most vulnerable subgroups. Until then, NAVA appears to be a safe and effective tool in centres with EAdi monitoring expertise.

Implications for future research

A search of ClinicalTrials.gov identified several ongoing or recently completed randomized controlled trials investigating Neurally Adjusted Ventilatory Assist (NAVA) in neonatal and paediatric populations. Trials such as NCT04000568, NCT02860325, and NCT03388437 aim to evaluate the safety and efficacy of both invasive and non-invasive NAVA modes in premature infants and critically ill children. However, most remain unpublished, limiting their contribution to the current evidence base. The presence of these trials highlights ongoing interest in the clinical application of NAVA, particularly in exploring long term outcomes, patient comfort, and cost effectiveness. Their eventual publication may provide greater statistical power to assess clinical outcomes such as bronchopulmonary dysplasia, mortality, and duration of ventilation. Future systematic reviews should incorporate these findings as they become available. Until then, the existing evidence supports NAVA's physiological benefits, while larger, multicentre trials remain essential to confirm its impact on long term morbidity and clinically meaningful endpoints.

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Conflict of Interest

There are no conflicts of interests.

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Volume 14 Issue 11 November 2025