NICE advice

Servo-n with Neurally Adjusted Ventilatory Assist (NAVA) for babies and children

Medtech innovation briefing
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Summary

- The **technology** described in this briefing is the Servo-n with Neurally Adjusted Ventilatory Assist (NAVA). It is used for babies and children up to 30 kg who need mechanical ventilation.
- The **innovative aspects** are that NAVA detects and uses electrical changes in the diaphragm muscle to detect the patient's respiratory drive with the aim of synchronising ventilation. Synchronisation reduces the risk of damage to young or diseased lungs from assisted ventilation.
- The intended **place in therapy** would be for mechanical ventilation in neonatal and paediatric intensive care units. The optimum place in therapy is uncertain.

- The **main points from the evidence** summarised in this briefing are from 4 studies, including 2 randomised controlled crossover trials, 1 randomised controlled trial (RCT) and 1 systematic review involving a total of 415 babies and children in paediatric and neonatal intensive care units. The systematic review and 1 RCT showed that Servo-n with NAVA improved patient-ventilator synchrony.
- **Key uncertainties** around the technology are that the evidence base is still developing and that it is unclear which patient groups are most likely to benefit.
- The **cost** of a Servo-n ventilator is £28,000 per unit. A NAVA module that has a list price of around £6,300 (both exclusive of VAT) is also needed. The single-use NAVA catheter, which incorporates a feeding tube, costs £145. The **resource impact** for the NHS would be greater than standard care. This may be offset by more intensive care capacity being released if the evidence supports improved outcomes.

The technology

The focus of this briefing is the Servo-n pneumatic life-support system with Neurally Adjusted Ventilatory Assist (NAVA) technology (Getinge Group). It is for babies and children who need ventilator assistance. NAVA consists of proprietary software and a bespoke oesophageal catheter that serves as a feeding tube. It contains small sensors, designed to measure the diaphragm electrical activity (the Edi measurement). This information is used to interpret the neural respiratory drive to control the timing and amount of ventilatory assistance provided. The Edi measurement can also be used for continuous bedside monitoring of a baby or child's breathing effort. NAVA mode is available for babies or children having invasive or non-invasive mechanical ventilation. In babies or children having non-invasive ventilation, the Edi is measured in the same way. But ventilation is provided by either nasal prongs or a nasal mask.

The NAVA technology can only be used with a compatible Servo-n ventilator.

Innovations

NAVA differs from standard ventilator systems because it uses electrical changes in the diaphragm muscle to control the timing of ventilation. This is designed to provide more accurate synchronisation with the patient's respiratory drive, minimising the risk that happens substantially earlier in the process of breathing. Conventional ventilator systems use pressure or flow signals, which are affected by air leaks, to trigger support and which

may result in asynchronous ventilation.

Current care pathway

No national guidelines that cover the NAVA technology for neonatal ventilation were identified. The common indication for ventilation in babies is either 1, or a combination of the following:

- parenchymal lung disease or ventilation perfusion mismatch (for example, meconium aspiration, pneumonia)
- poor respiratory drive (for example, hypoxic–ischemic encephalopathy, sepsis)
- lung malformations (for example, diaphragmatic hernia, congenital cystic adenomatoid malformation)
- mechanical (for example, abdominal distension, airway obstruction).

Population, setting and intended user

The Servo-n with NAVA would be used in babies and children weighing between 0.3 and 30 kg who need mechanical ventilation (invasive or non-invasive). It would be used in place of conventional ventilator systems in paediatric or neonatal intensive care units. The place in therapy is currently uncertain as to which patient groups would benefit most from the technology. Servo-n with NAVA would be used by multi-disciplinary teams.

Costs

Technology costs

The list price of a Servo-n ventilator is about £28,000 (excluding VAT), with an annual maintenance or service schedule negotiable within the price. The anticipated life span of the ventilator is 7 to 10 years. An additional NAVA module is needed, at a cost of around £6,300 (also excluding VAT). The list price of the single-use NAVA catheter, which is certified for 5 days' use, is £145.

Existing Servo-i ventilators can be upgraded with software and an additional module. The

list prices of these are: Edi-module around £6,300; NAVA software around £2,000 and NIV NAVA software around £1,300 (all list prices are excluding VAT).

Costs of standard care

Standard care would be a ventilator machine without the NAVA technology, which is estimated by specialist commentators to cost around £25,000. Conventional ventilators need tubing to connect the patient with the ventilator. These are typically single use and vary widely in cost.

Resource consequences

The use of NAVA would be an additional cost compared with standard care. Staff would need additional training and the company has stated that training and initial support costs are included in the purchase price. If NAVA reduced the time to discharge from an intensive care unit, then the additional costs may be offset. But there is no published evidence to support this. The NAVA catheter is ENFit compatible and is managed in the same way as a conventional feeding tube.

Regulatory information

Servo-n with NAVA is a CE marked class IIb medical device and the NAVA catheter is a class IIa device.

Equality considerations

NICE is committed to promoting equality, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. In producing guidance and advice, NICE aims to comply fully with all legal obligations to: promote race and disability equality and equality of opportunity between men and women, eliminate unlawful discrimination on grounds of race, disability, age, sex, gender reassignment, marriage and civil partnership, pregnancy and maternity (including women post-delivery), sexual orientation, and religion or belief (these are protected characteristics under the Equality Act 2010).

The Servo-n with NAVA is designed for use in babies and children. Age is a protected

characteristic.

Clinical and technical evidence

A literature search was carried out for this briefing in accordance with the interim process and methods statement. This briefing includes the most relevant or best available published evidence relating to the clinical effectiveness of the technology. Further information about how the evidence for this briefing was selected is available on request by contacting mibs@nice.org.uk.

Published evidence

There are 4 studies summarised in this briefing: 1 systematic review, which includes 16 published studies, 2 randomised controlled crossover trials and a randomised controlled trial. A total of 415 babies and children were included in the studies.

Table 1 summarises the clinical evidence as well as its strengths and limitations.

Overall assessment of the evidence

In general, the evidence shows that the Servo-i and Servo-n with NAVA improves patient-ventilator synchrony in babies and children. One study showed that there is some reduction in intensive care unit stay associated with NAVA use. A limitation of the evidence is that the available studies report different short-term outcomes and there is no resource consequence information. All of the trials have relatively small numbers of people in the trial. One study done in the UK used Servo-n. A substantial number of ongoing studies were identified that are expected to improve the evidence base.

Table 1 Summary of selected studies

Beck et al. (2016)	
Study size, design and location	Systematic review of 16 published studies in 218 babies and children.

Intervention and comparator(s)	Intervention: Servo-i with NAVA and NIV NAVA. Comparator: conventional ventilation.
Key outcomes	There were no reports of complications relating to catheter insertion or the use of NAVA. Bedside monitoring of Edi is a beneficial tool for assessing diaphragm function, clinical interventions and decision support. Some studies showed that NAVA may improve patient comfort, reduce the length of stay on PICU and reduce the amount of sedatives used. Patient-ventilator synchrony was improved in both invasive and non-invasive NAVA compared with conventional ventilation.
Strengths and limitations	The studies in this systematic review used Servo-i, which is a previous version of Servo-n. The company has confirmed the Servo-n is a newly released version of the Servo-i with mainly enhanced or new features, therefore evidence on Servo-i is likely to be generalisable to the Servo-n. No PRISMA diagram was used to clearly display the included, excluded studies. The quality of the included studies is not clear. A meta-analysis was not done and no reason given. People in the trial were only monitored while they were on the ventilators; no long-term outcome data has been reported. Two of the authors have patents related to neural control of mechanical ventilation where future commercial use of the technology may provide financial benefit.
Chidini et al. (2016)	
Study size, design and location	Prospective randomised crossover physiological study in a 6 bed PICU in Italy. 18 children aged 2 to 24 months (mean 13 months) with acute respiratory failure needing NIV ventilation.
Intervention and comparator(s)	Intervention: Servo-i with NAVA. Comparator: NIV pressure support and NIV flow-triggered pressure support.
Key outcomes	NAVA showed a statistically significant reduction in the Asynchrony Index (p=0.001) and ineffective breathing efforts (p=0.001) compared with flow-triggered pressure support. NAVA had an increased neuroventilatory efficiency index (p=0.001), which the authors suggested could mean improved neuroventilatory coupling.

Strengths and limitations	This study used Servo-i, which is a previous version of Servo-n. The company has confirmed the Servo-n is a newly released version of the Servo-i with mainly enhanced or new features, therefore evidence on Servo-i is likely to be generalisable to the Servo-n. Because of the crossover design, each participant acted as their own control, reducing variability between people in the trial. People were only monitored for 2 hours while they were on the ventilators; no long-term outcome data are reported.
Shetty et al. (2017)	
Study size, design and location	Randomised crossover study at Kings College, London assessing oxygenation. 9 babies born at less than 32 weeks gestation who were still ventilated at 1 week of age were included.
Intervention and comparator(s)	Intervention: Servo-n in with NAVA. Comparator: ACV.
Key outcomes	The Servo-n in NAVA mode provided improved oxygenation compared with ACV (mean oxygenation index NAVA 7.92 compared with ACV 11.06, p=0.0007).
Strengths and limitations	Because of the crossover design, each participant acted as their own control, therefore reducing variability between people in the trial. The same ventilator was used for both treatment modes, therefore the results show differences in the modes and not the ventilator. People were only monitored for 2 hours while they were on the ventilators; no long-term outcome data has been reported. One of the authors has held grants from various ventilator manufacturers and has received honoraria for giving lectures and advising them.
Kallio et al. (2015)	
Study size, design and location	170 babies in intensive care in a randomised controlled trial in Finland.
Intervention and comparator(s)	NAVA. Current standard of care ventilation.

Key outcomes	The median time on the ventilator was lower in the NAVA group compared with standard ventilation (3.3 hours compared with 6.6 hours, p=0.17). The length of stay in the intensive care unit was lower in the NAVA group compared with standard ventilation (49.5 hours compared with 72.8 hours, p=0.10). This difference was more significant when analysed per protocol (p=0.03). The amount of sedation needed was similar across both groups (p=0.20), however, when post-operative babies were excluded (77.6% babies in NAVA group and 76.5% babies in standard ventilation group), sedation needed was significantly lower in the NAVA group compared with standard ventilation (0.80 compared with 2.23 units/hour, p=0.03). Oxygenation index was significantly lower in the NAVA group compared with the standard ventilation group (p=0.002). Peak inspiratory pressure and inspired oxygen fraction was significantly lower in the NAVA group compared with standard ventilation (p=0.001 for both). Arterial blood CO_2 tensions were slightly higher in the NAVA group at the beginning of treatment and lower levels after 32 hours (p=0.008). There were no other significant differences in ventilator or vital parameters, arterial blood gas values and complications were similar between the 2 groups.
Strengths and limitations	This study was funded by a Finnish academic institution and the authors disclose no manufacturer interests. Most babies included in this study were recovering from operations and only needed ventilation for a short time. This was usually determined by the anaesthesia and sedatives that had been given in the operating theatre. Blinding of investigators was not possible in this trial, which may have led to some bias.
Abbreviations: ACV: assist control ventilation, Edi: diaphragm electrical activity, NAVA: neutrally adjusted ventilatory assist, NIV: non-invasive, NICU: neonatal intensive care unit, PICU: paediatric intensive care unit.	

Recent and ongoing studies

There were 5 randomised clinical trials identified:

- Optimisation of Neonatal Ventilation – NAVA vs PAV (UK study). ClinicalTrials.gov identifier: NCT02967549. Status: ongoing but not recruiting. Indication: children up to 1 year old with bronchopulmonary dysplasia. Devices: NAVA delivered by the Servo-n ventilator, PAV (proportional assist ventilation) delivered by the Stephanie ventilator. Primary outcome measure: oxygenation index.

- Neurally Adjusted Ventilatory Assist (NAVA) Versus Conventional Biphasic Positive End Expiratory Pressure (BiPAP) Non\u2011\invasive Respiratory Support in Infants Following Congenital Heart Surgery (US study). ClinicalTrials.gov identifier: NCT03180385. Status: recruiting (enrolment target: 40). Indication: children up to 1 year old with respiratory failure. Devices: NAVA, Biphasic Positive Airway Pressure Support (BiPAP). Primary outcome measures: post-operative pain/sedation medication dose, post-operative pain scores-FLACC, post-operative sedation scores-SBS, length of intubation, length of non-invasive respiratory support.

- Comparison of Primary Extubation Failure Between Non\u2011\invasive Positive Pressure Ventilation (NIPPV) and Non Invasive Neural Access Ventilatory Assist (NI\u2011\nAVA) (US study). ClinicalTrials.gov identifier: NCT03242057. Status: recruiting (enrolment target: 30). Indication: pre-term babies with bronchopulmonary dysplasia. Devices: NAVA, NIPPV. Primary outcome measure: extubation success.

- Noninvasive NAVA Versus NIPPV in Low Birthweight Premature Infants (US study). ClinicalTrials.gov identifier: NCT03137225. Status: recruiting (enrolment target: 15). Indication: low birth weight premature infants who need respiratory support via non-invasive ventilation. Devices: NAVA, NIPPV. Primary outcome measure: number of unexpected events.

- Non\u2011\invasive Neurally Adjusted Ventilatory Assist Versus nCPAP or Non Synchronized NIPPV in Preterm Infants Under 32 Weeks Gestational Age: A Randomized Clinical Trial (Spanish study). ClinicalTrials.gov identifier: NCT02860325. Status: completed. 56 people recruited. Indication: babies with respiratory distress syndrome. Devices: NIV NAVA delivered by the Servo-n ventilator, NIV delivered by nCPAP or non-synchronised NIPPV. Primary outcome measure: survival without moderate or severe bronchopulmonary dysplasia.

Specialist commentator comments

Comments on this technology were invited from clinical specialists working in the field and relevant patient organisations. The comments received are individual opinions and do not represent NICE's view.

All 5 specialists were familiar with this technology. One specialist is currently using it in their paediatric intensive care unit (PICU) and 1 specialist was involved in a clinical test of the Servo-n on their ward.

Level of innovation

Four specialists thought that the technology was novel.

Potential patient impact

One specialist thought that use of NAVA could potentially reduce the use of sedative drugs. Another specialist mentioned it could potentially reduce lung injury in babies because an endotracheal tube would not need to be used. They said that this could particularly benefit pre-term babies (23 to 25 weeks' gestation). One specialist noted that a small subset of patients may achieve better synchronisation with NAVA than with other methods of detecting a patient's efforts to breathe.

Potential system impact

Two specialists thought that NAVA had the potential to reduce the number of ventilator days. Two specialists said that NAVA is likely to cost more than conventional ventilators. Another specialist noted that the upfront cost of NAVA is more but if NAVA was able to reduce the length of stay in a PICU, then this could lead to an overall saving. One specialist highlighted that if NAVA was adopted, existing feeding tubes would need to be changed to a NAVA catheter and these are currently substantially more expensive. Two other specialists noted that the cost of the catheters might be a barrier to adoption. Another specialist thought that a further barrier to adoption was that NAVA can only be used with Servo ventilators. All 5 specialists thought that NAVA would be used as an addition to current standard care but 1 said that if the technology was proven to have significant clinical benefit then it could replace it.

General comments

One specialist reported that after a 2 month trial of Servo-n, their PICU has now invested in 16 ventilators. All of the specialists thought that more research with NAVA was needed. One specialist said that a cost benefit analysis, long-term outcome data and a comparison of time to discharge would be valuable. Another specialist suggested some key clinical outcomes for future research. These included: effectiveness in helping extubation, reducing the duration of ventilation and reducing length of hospital stay.

Specialist commentators

The following clinicians contributed to this briefing:

- Dr Andy Petros, consultant paediatric intensivist, Great Ormond Street Hospital. Did not declare any interests.
- Dr Reinout Mildner, consultant paediatric intensivist, Birmingham Children's Hospital. Dr Mildner's unit received a small number of free NAVA catheters in 2016 as part of a software upgrade that was purchased for 4 ventilators and 2 NAVA modules.
- Dr Mallinath Chakraborty, consultant in neonatal medicine, University Hospital of Wales. Did not declare any interests.
- Dr Mark Peters, professor of paediatric intensive care, Great Ormond Street Hospital. Did not declare any interests.
- Professor Anne Greenough, professor of neonatology and clinical respiratory physiology, King's College London. Professor Greenough is an author on Shetty et al. (2017).

Development of this briefing

This briefing was developed by NICE. The interim process and methods statement sets out the process NICE uses to select topics, and how the briefings are developed, quality-assured and approved for publication.

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