NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Medical technology consultation document

PneuX to prevent ventilator-associated pneumonia

The National Institute for Health and Care Excellence (NICE) is producing guidance on using PneuX for prevention of ventilator-associated pneumonia in the NHS in England. The medical technologies advisory committee has considered the evidence submitted by the company and the views of expert advisers.

This document has been prepared for public consultation. It summarises the evidence and views that have been considered, and sets out the recommendations made by the committee. NICE invites comments from the public. This document should be read along with the evidence (see the committee papers).

The advisory committee is interested in receiving comments on the following:

- Has all of the relevant evidence been taken into account?
- Are the summaries of clinical and resource savings reasonable interpretations of the evidence?
- Are the recommendations sound and a suitable basis for guidance to the NHS?
- Are there any equality issues that need special consideration and are not covered in the medical technology consultation document?

Note that this document is not NICE's final guidance on PneuX for prevention of ventilator-associated pneumonia. The recommendations in section 1 may change after consultation.

After consultation the committee will meet again to consider the evidence, this document and comments from the public consultation. After considering the comments, the committee will prepare its final recommendations which will be the basis for NICE's guidance on the use of the technology in the NHS in England. For further details, see the medical technologies evaluation programme process and methods guides.

The key dates for this guidance topic are:

Closing date for comments: 6 December 2019

Second committee meeting: 13 December 2019

Details of the advisory committee are given in section 5.

NICE medical technologies guidance addresses specific technologies notified to NICE by companies. The 'case for adoption' is based on the claimed advantages of introducing the specific technology compared with current management of the condition. This case is reviewed against the evidence submitted and expert advice.

If the case for adopting the technology is supported, the specific recommendations are not intended to limit use of other relevant technologies that may offer similar advantages. If the technology is recommended for use in research, the recommendations are not intended to preclude the use of the technology in the NHS but to identify further evidence which, after evaluation, could support a recommendation for wider adoption.

1 Recommendations

1.1 PneuX shows promise for preventing ventilator-associated pneumonia in adults. However, there is currently not enough good-quality evidence to support the case for routine adoption in the NHS.

1.2 Research is recommended to address uncertainties about the clinical benefits of using PneuX. This research should:

- assess whether PneuX reduces the incidence of ventilator-associated pneumonia in all people needing ventilation
- compare PneuX with current NHS clinical practice, that is, the use of endotracheal tubes with subglottic drainage
- evaluate PneuX within the care bundle for ventilator-associated pneumonia prevention
- be clear about the criteria used to diagnose ventilator-associated pneumonia in the study.

Why the committee made these recommendations

PneuX is a tube placed through the mouth or through a small cut in the throat (tracheostomy) when someone needs a ventilator to help them breathe. It's designed to prevent ventilator-associated pneumonia (VAP) which can happen when secretions from the mouth leak past the tube into the lungs. PneuX has a tight seal to prevent leaks, and ports that a nurse can use to drain the secretions away from above the seal.

The evidence for the clinical effectiveness of PneuX is mainly from a trial that was done in people who were ventilated for a relatively short period of time after cardiac surgery. People in this trial were classed as high risk because of their age, or heart disease, or both. While they did have less VAP compared with people who were on a ventilator tube without drainage, it's not clear if the same benefits would be seen in people who are ventilated for other reasons and for longer periods of time. The use of a ventilator tube that allows secretions to be drained is regarded as best practice for VAP prevention. However, it's not clear from the current evidence if PneuX is better than other ventilator tubes with drainage.

PneuX shows promise for preventing VAP but further research is recommended.

2 The technology

Technology	The PneuX system is a single-use endotracheal or tracheostomy tube (ETT) designed to prevent ventilator-associated pneumonia (VAP) by minimising the risk of pulmonary aspiration and micro-aspiration during mechanical ventilation. Aspiration occurs when secretions from the mouth leak past the cuff into the lungs. It has 3 components: a tube, a tracheal seal monitor, and a 2 m extension tube. It has a low-volume, low-pressure cuff made from a soft silicone material. The tracheal seal monitor is an electronic automatic pressure controller which controls and maintains the safe inflation volume and pressure in the cuff. It has 3 subglottic secretion drainage and irrigation ports above the proximal end of the cuff to make sure the tube functions properly even if one of the ports is blocked. The subglottic ports are small to prevent damage to the tracheal mucosa. Lavage can also be done with PneuX. This involves using a cleaning fluid to wash out the space above the cuff.

	PneuX was formerly known as the 'Venner PneuX PY VAP Prevention System and the Lo-Trach system'. There are no functional differences between the 2 versions. The PneuX system is not compatible with other ETTs.
Innovative aspects	An automated pressure cuff monitor and 3 subglottic drainage ports.
Intended use	PneuX is intended for use in people who are expected to be intubated for 24 hours or longer. There is no evidence for the use of PneuX in children. Clinical staff will need to be trained in subglottic secretion drainage using the PneuX ports. They will need to do this at regular intervals. The company provides training and support.
Costs	The PneuX system costs £150, based on the NHS Innovation and Technology Tariff (ITT-03 2017-19).
For more details, see the website for PneuX.	

3 Evidence

Clinical evidence

The main clinical evidence comprises 3 studies reported in 4 publications

3.1 The clinical evidence comprises 3 studies reported in 4 publications including a total of 341 adults in cardiac or general intensive care. One of these studies was a randomised controlled trial comparing PneuX with a standard endotracheal tube (ETT) without drainage (Gopal et al. 2014). The other studies were non-comparative (Smith et al 2014, Doyle et al. 2011 and Hodd et al. 2009). For full details of the clinical evidence, see section 3 of the assessment report.

The randomised controlled trial is only in people needing ventilation after cardiac surgery

3.2 The Gopal et al. (2014) study recruited patients who needed ventilation during and after cardiac surgery. Patients were randomly selected to be ventilated using PneuX or a standard ETT without subglottic drainage. All patients in the study were classified as high risk (over 70 or with a left ventricular ejection fraction of under 50%, or both) and were therefore considered more likely to contract ventilator-associated pneumonia (VAP).

People in this study were ventilated for a relatively short period of time, 15 and 13 hours (median) in the treatment and control groups.

The other 2 studies include people needing ventilation with a wider range of health conditions but do not compare PneuX to any other ETT

3.3 The evidence from the non-comparative studies is more generalisable to people needing ventilation with a wider range of health conditions. Nonetheless, the lack of a control group makes it difficult to draw any conclusions about the efficacy of PneuX. There was also wide variation in the outcomes measured in these studies (for example, mortality was 1.6% to 35.8% and unplanned tube removal 0.1% to 17%). However, the rates of VAP and unplanned tube removal are very low in these studies. All 3 studies used different definitions for diagnosing VAP.

Cost evidence

Two UK studies are included in the economic modelling

3.4 The company identified 2 relevant studies, Andronis et al. (2018) and NHS Innovation Accelerator (2017). No additional economic analyses were identified by the external assessment centre (EAC). Both the studies compared PneuX with standard ETTs and were carried out in the UK.

The company's economic model compares PneuX to ETT without subglottic drainage in a cardiac surgery population

3.5 The company model uses a simple decision tree structure based on the model published in Andronis et al. (2018) (see figure 2 of the assessment report). The population modelled is adult patients requiring mechanical ventilation following major heart surgery. The model compares PneuX with conventional ETT without subglottic secretion drainage. The key clinical parameter used in the model is the risk of VAP as reported in the comparative study Gopal et al. (2014), which was 10.8% for PneuX and 20.8% for ETT without subglottic drainage. For full details of the cost evidence, see section 4 of the assessment report.

The model is appropriate for people who have had cardiac surgery but may not be generalisable to all people

3.6 The EAC considered the simple model structure to be adequate to capture the costs and consequences of the technology and did not make any changes. It said that all assumptions were acceptable except for the generalisability of the results from people who had cardiac surgery to a broader population of patients for whom PneuX is intended. The EAC also said the costs of treating VAP may not be generalisable to a wider population given the shorter stay in intensive care in the cardiac surgical studies (Gopal et al. 2014 and Luckraz et al. 2018) as compared with all people who might need ventilation.

The company model results in cost savings of £738 per person due to a reduced risk of VAP

3.7 The results of the company model indicate a cost saving of £738 per patient after cardiac surgery when PneuX is used instead of an ETT without subglottic drainage. This saving is from an absolute reduction in the risk of VAP of around 10% for PneuX and the associated reduction in resource consumption based on avoided costs of around £9,000 per VAP prevented. In the model, the expected cost of needing to treat VAP is around £900 less for patients given PneuX than for those having ETTs without subglottic drainage. This cost saving is substantially greater than the additional cost of using PneuX instead of ETT without subglottic drainage (PneuX costs £150 and ETT without drainage £5).

PneuX remains cost saving in the company's sensitivity analyses

3.8 The company did scenario analyses by varying 3 parameters:

- reduction in baseline risk of VAP from 20.8% to 10%
- reduction in cost of standard ETT from £5 to £1.12
- inclusion of a training cost to use PneuX of £10 per patient.

PneuX remained cost saving for all 3 scenarios. The company also reported:

- a one-way sensitivity analysis of the cost of treating VAP
- a two-way sensitivity analysis of the baseline risk of VAP (0 to 50%)
- the relative risk of VAP with PneuX (0 to 1)
- a probabilistic sensitivity analysis to characterise the impact of uncertainty in the model parameters.

The one-way sensitivity analysis indicated that PneuX is cost saving even if the cost of treating VAP is as low as £4,000. In the two-way analysis, PneuX remained cost saving for most combinations of the 2 parameters. The probabilistic sensitivity analysis indicated that there is a 96% likelihood that PneuX is cost saving compared with ETT without subglottic drainage.

Additional analysis by the EAC shows PneuX may be slightly cost saving compared with an ETT with subglottic drainage

3.9 There are other ETTs with subglottic drainage but there are no trials available that directly compare these with PneuX. There was only 1 other study that compared an ETT with subglottic drainage (Portex Blue Line, Smiths Medical) with an ETT with no drainage (Jena et al. 2016). The EAC did an additional cost analysis using results from the Gopal and Jena studies to indirectly compare PneuX and Portex ETTs. Portex Blue Line costs less than PneuX (£20, compared with £150 for PneuX), and the relative risk reduction of VAP in the 2 studies in question was 0.52 for PneuX and 0.60 for Portex Blue Line. This led to a slight cost saving for PneuX of £18. The EAC cautioned that the relative risk of VAP for Portex Blue Line came from a very small trial, the results of which were not statistically significant, although they were consistent with data from a large meta-analysis (Mao et al. 2016).

4 Committee discussion

Clinical-effectiveness overview

PneuX is an innovative technology which shows promise for preventing VAP

4.1 The clinical experts who had experience of using PneuX explained that it differed from other endotracheal tubes (ETTs) with subglottic drainage because of several design features such as the automated pressure cuff and wrinkle-free, soft, flexible material. The clinical experts noted that the automated pressure cuff is good at preventing micro-aspirations because it maintains a tight seal, even when the patient is moving, and lavage as well as drainage can be done. The committee agreed that PneuX has an innovative design and there is a plausible clinical benefit. But it concluded that there is currently no evidence to show that its additional features, particularly the ability to perform lavage, convey any benefits to patients over other ETTs with subglottic drainage.

The main study of PneuX may not be generalisable to all people needing ventilation

4.2 The only comparative study for PneuX was in people who had cardiac surgery and who were classified by the investigators as at higher risk of complications (including ventilator-associated pneumonia [VAP]) because they were over 70 or had impaired left ventricular function (or both). The committee noted that people in the Gopal study were ventilated for a relatively short period of time (less than 24 hours). The expert advisers explained that people who are ventilated in general intensive care have a much broader range of underlying conditions and complications. The committee concluded that, although there was evidence that PneuX reduces VAP compared with ETT without subglottic drainage in the high-risk cardiac surgical population, this evidence could not be generalised to all people needing ventilation.

The main study compares PneuX with a non-drainage tube, which is not standard practice in the NHS

4.3 The use of an ETT with subglottic drainage is a recommended part of care bundles for preventing VAP (for example, The Faculty of Intensive Care Medicine's guidelines for the provision of intensive care services). The clinical experts stated that introducing subglottic drainage ETTs has reduced VAP by up to 50%, and that they are now standard care in the NHS. The committee noted there are no studies that directly compare the incidence of VAP with PneuX and other ETTs with subglottic drainage. Therefore, the committee concluded that there was no evidence for additional clinical benefits of using PneuX compared with other ETTs with subglottic drainage.

In the main evidence for PneuX people were ventilated for less time than usually needed to develop VAP

4.4 In the Gopal et al. (2014) study, patients were ventilated for a median time of 15 hours with PneuX and 13 hours with ETT without subglottic drainage. The definitions for VAP state that patients will have been ventilated for a minimum of 24 or 48 hours. The clinical experts explained that it was possible to develop VAP in less than 24 hours and that this was more likely in a high-risk cardiac surgery population. The clinical experts estimated that patients in a wider intensive care population are likely to be ventilated for a median of 2 to 3 days but advised that this may be much longer in some patients. One clinical expert stated that they would use PneuX in people who are expected to be ventilated for longer than 12 hours. But all experts agreed that it is difficult to predict how long ventilation will be needed for. The committee concluded that the evidence collected from people having cardiac surgery in the Gopal study may not accurately represent all people having ventilation in hospital.

Definition and diagnosis of VAP is subjective and poorly recorded across the NHS

4.5 The clinical experts explained that there are several definitions for VAP that incorporate clinical, radiological and microbiological testing. These definitions are used variably both in clinical practice and in the published studies. The clinical experts also explained that VAP incidence may not be recorded accurately in many centres. The committee recognised that all of these factors make research into VAP prevention particularly challenging and limit the legitimacy of between-study comparisons in this area.

VAP is likely to increase mortality but the PneuX studies are underpowered for this outcome

4.6 NHS England reports that between 3,000 and 6,000 people die from VAP each year. The clinical experts noted that VAP is also likely to lead to an increase in the length of time ventilation is needed, length of critical care and hospital stay, risk of recurrent pneumonia, prolonged illness and spread of infection to other organs. The committee noted that the studies for PneuX were underpowered to measure any difference in mortality and length of stay, and so concluded that it is uncertain whether PneuX has any impact on these outcomes.

NHS considerations overview

Training and support are provided by the company free of charge

4.7 The company described to the committee how it provides training and support for all staff and centres using PneuX. The company offers a range of training sessions to all staff, lasting between 1 and 4 hours, which can be delivered in a classroom, or by the bedside, as needed. The clinical experts confirmed that the support from the company was adequate to train staff how to use PneuX correctly.

A higher volume of secretions drained and lavage may slightly increase nurse time for subglottic drainage

4.8 The clinical experts with experience of using PneuX noted that a higher volume of secretions can be drained with PneuX than with other ETTs with subglottic drainage, and that lavage, when undertaken, takes an additional 2 to 3 minutes. The committee concluded that using PneuX may lead to a slight increase in nurse time spent on subglottic drainage and lavage.

Cost modelling overview

The company model is robust but it is not certain that the cost savings will apply to all people needing ventilation

4.9 The committee noted that the company's model was well constructed and robust to uncertainty. It showed that PneuX is cost saving compared with ETTs without subglottic drainage in a high-risk cardiac surgery population. However, the main cost driver in the model was the absolute reduction in the risk of VAP between the PneuX and ETT without drainage arms. As these values were sourced from the Gopal et al. (2014) study, the committee concluded that there was substantial uncertainty that the cost savings would be realised for all people needing ventilation.

Comparisons between PneuX and other ETTs with subglottic drainage may be more appropriate for the NHS

4.10 The committee heard from the clinical experts that subglottic drainage is becoming standard practice in the NHS. The external assessment centre (EAC) modelled an indirect cost comparison of PneuX with Portex Blue Line. However, the committee felt there was considerable uncertainty in this because of the lack of comparative evidence. The committee concluded that the uncertainties associated with this analysis, as well as the small cost difference in results, meant that this was not enough evidence on which to base a positive recommendation. Overall, the committee considered that the current economic evidence does not support the routine adoption of PneuX in the NHS.

Further research

Further research would help address the uncertainty in the evidence

4.11 The committee concluded that further research would help resolve the uncertainties about the potential benefits of using PneuX. The research should determine if using PneuX reduces:

- VAP incidence in all people needing ventilation
- VAP incidence compared with other ETTs with subglottic drainage (including the effect of lavage)
- time on a ventilator, and critical care and length of stay in hospital
- mortality.

In this research, the committee recommended that the:

- criteria used for defining VAP should be carefully considered and recorded
- use of PneuX should be considered within the context of the wider care bundle for VAP prevention
- population recruited should be large enough and follow up long enough to capture the important clinical endpoints.

5 Committee members and NICE project team

Committee members

This topic was considered by the medical technology advisory committee which is a standing advisory committee of NICE.

Committee members are asked to declare any interests in the technology to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that evaluation.

The minutes of each committee meeting, which include the names of the members who attended and their declarations of interests, are posted on the NICE website.

NICE project team

Each medical technologies guidance topic is assigned to a team consisting of 1 or more technical analysts (who act as technical leads for the topic), a technical adviser and a project manager.

Kimberley Carter

Technical analyst

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