NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Medical technology guidance

Assessment report overview

Ambu aScope2 in unexpected difficult airways management

This assessment report overview has been prepared by the Medical Technologies Evaluation Programme team to highlight the significant findings of the External Assessment Centre report. It includes key features of the evidence base and the cost analysis, any additional analysis carried out, and additional information, uncertainties and key issues the Committee may wish to discuss. It should be read along with the sponsor's submission of evidence and with the External Assessment Centre's assessment report. The overview forms part of the information received by the Medical Technologies Advisory Committee when it develops its recommendations on the technology.

This overview also contains:

- Appendix A: Sources of evidence
- Appendix B: Comments from professional bodies
- Appendix C: Comments from patient organisations
- Appendix D: External Assessment Centre correspondence
- Appendix E: Sponsor's factual check of the assessment report and the External Assessment Centre's responses.

1 The technology

The Ambu aScope2 (Ambu Ltd) is a sterile, flexible, disposable device that is used to overcome difficulties with endotracheal intubation in patients with difficult airways. It is used to visualise the airway and then to aid in the placement of an endotracheal tube, either directly or through an intubating laryngeal mask. It is a portable device that can be used wherever a flexible fibre optic endoscope is needed for airway management (unless an Aintree catheter, through which the current device is too large to pass, is being used). This may be in the anaesthetic room, critical care or emergency departments or in other areas of the hospital where emergency airway management is undertaken. It can also be used to aid percutaneous dilatational tracheostomy and to check the position and patency of airway devices such as endotracheal tubes, double lumen tubes and tracheostomy tubes.

The Ambu aScope2 system consists of 2 components; a single-use aScope and the accompanying aScope monitor for displaying the images. The 2 components are used together and must be available in the same location to generate images. The aScope has an outer diameter of 5.4 mm, a bending section that can be manipulated through an angle of 120° upwards and downwards, a built in camera with 2 light-emitting diodes. It is supplied sterile and ready for use.

The Ambu aScope2 uses video camera technology to create the image which is displayed on the high-resolution aScope monitor. The monitor, which is portable, indicates the rechargeable battery capacity (maximum claimed 2 hours) and also has a video output to transfer images to a larger monitor or recording device. During procedures, the monitor can be powered by either battery or mains and is designed to be connected to the mains at other times.

Other features of the Ambu aScope2 include a clearing membrane that eases removal of secretions from the lens (ClearLens), and a Luer channel of 0.8 mm diameter which can be used for injection of topical anaesthesia or, by attaching a flow connector, to apply an air/oxygen flow. The purpose of this is

to direct secretions away from the tip of the Ambu aScope2; the Ambu aScope2 is not designed for the purpose of oxygenation or ventilation.

2 Proposed use of the technology

2.1 Disease or condition

Approximately 2.9 million general anaesthetics are administered in the NHS each year. Endotracheal intubation is used for airway management in approximately 38% of cases. Difficulties with intubation are expected in approximately 2% of cases and fibre optic intubation while the patient is awake is undertaken in 10% of these (4th National Audit Project [NAP4] Report, published by the Royal College of Anaesthetists and the Difficult Airway Society, 2011). Expert Advisers estimate that approximately 12,000 tracheostomies and 5–8000 percutaneous dilational tracheostomies are carried out in the UK each year.

Difficulties with intubation can arise in people who are obese, have limited mouth opening or cervical spine movements, have experienced trauma to the face or neck, have respiratory tract infections or cancers and in those with tracheostomies.

Difficulties with airways management can be predicted when intubation is undertaken in a planned and elective manner. Difficulties may be encountered, however, in unexpected situations when emergency intubation is needed. Difficulties can also arise because of delayed intubation or the failure to intubate a patient who needs intubation, as a result of the appropriate equipment not being available immediately. Such circumstances may arise, for example, in accident and emergency (A&E) departments or in intensive care units, (ICU) or general wards where multiple-use endoscopes are not necessarily stocked, but where emergency resuscitation is sometimes needed. Problems with airway management can lead to significant consequences for patients ranging from upper airway soft tissue trauma to hypoxic brain damage and death. One of the conclusions of the NAP4 report

was that a lack of essential airway equipment repeatedly contributed to poor outcomes in patients whose tracheostomies became displaced.

2.2 Patient group

The Ambu aScope2 can be used in the management of expected or unexpected difficulties with endotracheal intubation in patients with difficult airways or in assisting with percutaneous dilatory tracheostomy in awake or anaesthetised patients.

For this assessment the Ambu aScope2 is evaluated for patients with unexpected difficult airways needing emergency intubation, including awake or anaesthetised patients with displaced percutaneous dilatory tracheostomies. This device can be used in adults or children who have been clinically evaluated for endotracheal tubes size 6 or above.

No subgroups were identified for this assessment.

2.3 Current management

Placement of an endotracheal tube guided by a multiple-use flexible fibre optic endoscope is the gold standard for managing difficult intubation. Visualisation is currently achieved using fibre optic technology or video technology. Using a fibre optic endoscope or a video scope allows the visualisation and crossing of the vocal chords followed by the accurate placement of an endotracheal tube; this helps secure the difficult airway quickly and minimises the risk to the patient.

The Difficult Airways Society guidelines (Henderson et al., 2004) outline the clinical pathway for unexpected difficult tracheal intubation during routine induction of anaesthesia in adults. The guidelines describe the initial tracheal intubation plan (Plan A) and the secondary tracheal intubation plan (Plan B). With Plan A, standard procedure is to start direct laryngoscopy. After 4 failed intubation attempts, Plan B (in which a supraglottic airway device (SAD) is inserted), should be undertaken. If placement of the SAD is successful and the patient can be ventilated, then either ventilation is maintained via the SAD

or tracheal intubation can begin. If the decision to intubate is made, it can be performed using a multiple-use flexible endoscope, as a conduit for intubation.

Tracheostomy is a surgical procedure performed on the patient's neck to open a direct airway into the trachea. Percutaneous tracheostomy is now considered a standard technique in many ICUs worldwide. The use of the endoscope should reduce the complication rate, by enabling the user to visualise the procedure and, thereby, preventing the needle from penetrating the back of the trachea. The average time needed to perform a percutaneous tracheostomy is 10–15 minutes.

2.4 Proposed management with new technology

For this assessment the aim of the Ambu aScope2 is to provide an alternative device for patients with unexpected difficult airways needing emergency intubation including awake or anaesthetised patients with displaced percutaneous dilatory tracheostomies when a multiple-use fibrescope is not available.

The use of the Ambu aScope2 in planned difficult airways management is not included in this evaluation.

2.5 Equality issues

People at greater risk of airway complications are those with conditions affecting cervical spine mobility. This may include pregnant women, people who are obese, people in whom trauma to the face or neck has occurred, and people with respiratory tract infections or cancers. Groups covered by the Equality Act, 2010, are patients with rheumatoid arthritis with limited spine movements and longer-term tracheostomy patients.

3 Issues for consideration by the Committee

3.1 Claimed benefits

The benefits to patients claimed by the manufacturer are:

- Improved outcomes in emergency and unexpected scenarios of difficult airway management due to the immediate availability of a sterile fibre optic endoscope that does not need calibration.
- Improved safety for patients with tracheostomies due to a reduction in morbidity and mortality associated with the failure to re-establish ventilation if the tracheostomy tube is displaced in a patient with a difficult airway.
- Reduced risk of cross-infection from contaminated fibre optic endoscopes.

The benefits to the health system claimed by the manufacturer are:

- Reduced costs associated with an improvement in clinical outcomes in emergency and unexpected scenarios of difficult airway management including those patients with tracheostomies.
- Reduced costs associated with a reduction in the incidence of cross-infection.
- Reduced time and resources spent on cleaning and repair and internal transfer between hospital departments as the Ambu aScope2 is delivered sterile and ready to use.

4 The evidence

4.1 Summary of evidence of clinical benefit

The sponsor's submission identified 11 studies as relevant to the scope. The External Assessment Centre agreed that all the 11 studies (6 randomised controlled trials (RCTs) and 5 case series reports) were relevant to the scope. One publication (Piepho et al. 2010) comprised two different types of study: a RCT in manikins and an observational case series in patients with expected or unexpected difficult airways. The sponsor submitted these separately (1 as an RCT and 1 as a case series). One RCT was found to have been reported twice (Vijayakumar et al. 2011 and Kumar et al. 2011); therefore the External Assessment Centre only included the results from 1 of these (Vijaykumar et al. 2011). Consequently, 10 studies submitted by the sponsor were considered relevant to the scope.

In addition to the 10 studies identified by the sponsor, the External Assessment Centre found an abstract of a RCT (described as an ongoing study in the sponsor's submission) that compared the Ambu aScope2 with a multiple-use fibre optic bronchoscope in patients with simulated difficult airways (Schoettker et al. 2012). Therefore the clinical evidence is based on a total of 11 studies, 3 evaluating Ambu aScope2 and 8 evaluating Ambu aScope which is the immediate predecessor device (table 1).

Key outcomes identified in the scope were:

- incidence of delayed or failed intubation
- clinical consequences associated with delayed or failed intubation:
  - death
  - hypoxic brain injury
  - Intensive Treatment Unit (ITU) and length of hospital stay
- incidence of successful intubation
- incidence of contamination and cross-infection
- device-related adverse events.

Most studies reported intubation success but reporting of the clinical consequences and the incidence of contamination and cross-infection was limited. Two additional outcomes – image quality of the Ambu aScope2 and the time to intubation – were not part of original decision problem but were considered by the External Assessment Centre because it judged them to be important clinical outcomes.

Table 1 Summary of clinical evidence (adapted from tables 3.1, 3.3, 3.5, 3.6 and 3.7 in the External Assessment Centre report)

Study	Country	Study design	Population	Intervention	Comparator	Outcomes considered
Piepho et al 2010	Germany	RCT	Manikin; (1) a normal airway, (2) an airway with decreased cervical range of movement and pharyngeal oedema. n=21 anaesthetists	Ambu aScope	Storz flexible intubation fiberscope	• incidence of successful intubation • time to intubation • rating of device
Scutt et al 2011	UK	RCT	Manikin; The manikins used were not explicitly revised to simulate difficult airways. n=22	Ambu aScope	Pentax F1 13RBS; with or without a supraglottic airway device (SAD)	• device-related adverse events • time to intubation • rating of device
Vijayakumar et al 2011 (same as Kumar et al 2011)	UK	RCT	Manikin: The manikin was modified by narrowing the airway in 3 places along the path of the endoscope. n=75	Ambu aScope	Olympus multiple-use fibre optic endoscope	• device-related adverse events • time to intubation • rating of device
Kristensen 2011	Denmark	RCT	Patients with expected normal airway and expected difficult airway; n=60	Ambu aScope	Olympus BF160 multiple-use endoscope	• incidence of successful intubation • device-related adverse events • time to intubation • image quality • rating of device

Study	Country	Study design	Population	Intervention	Comparator	Outcomes considered
Lenhardt et al 2011	USA	RCT	Patients with expected difficult airways; n=140	*GlideScope video laryngoscope* (GVL) + Ambu aScope	GVL + Pre-formed stylet (GlideScope)	• incidence of successful intubation • time to intubation • rating of device
Schoettker et al 2012	Switzerland	RCT	Patients with simulated difficult airway; n=100	Ambu aScope2	Fibre optic bronchoscope	• incidence of successful intubation • time to intubation • image quality
Jamadarkhana et al 2011	UK	Case series	Patients who underwent PDT; n=10	Ambu aScope2	None	• time to intubation • device-related adverse events • image quality • rating of device
Perbet et al 2011	France	Case series	Patients needing PDT; n=10	Ambu aScope	None	• rating of device
Piepho et al 2010	Germany	Case series	Patients with expected and unexpected difficult airway; n=5	Ambu aScope	None	• incidence of successful intubation • rating of device
Pujol et al 2010	Spain	Case series	Patients with predicted difficult airways; n=10	Ambu aScope	None	• incidence of successful intubation • time to intubation • image quality • rating of device
Vincent et al 2011	UK	Case series	Patients with expected difficult airways; n=8	Ambu aScope2	None	• incidence of successful intubation • time to intubation • rating of device

Manikin-based RCTs

Piepho et al. (2010) found the time to intubation was slightly longer when using the Ambu aScope compared with the control fibrescope, for both normal and difficult airway scenarios. The mean time to intubation for difficult airways was 63 seconds with the Ambu aScope compared with 56 seconds for the comparator (mean difference 7 seconds; 95% confidence interval [CI] −11.66 to 25.66), which was statistically non-significant. In the difficult intubation scenario, intubation success rate was lower when using the Ambu aScope compared with using control fibrescope (67% versus 81%, p=0.02), which the authors concluded was mainly due to the low image quality. Overall the Ambu aScope scored a rating of 'satisfactory' compared with a rate of 'good' for the comparator.

Scutt et al. (2011) compared the Ambu aScope in 2 simulated settings. In both settings, time to intubation was similar between the use of the Ambu aScope and the control fibrescope (p=0.18). The use of the Ambu aScope was associated with more reported problems than the control fibrescope (32% versus 17%, p=0.04), including manipulation, railroading tubes and picture quality. The Ambu aScope was consistently associated with a lower rating score in terms of ease of use and image quality (mean score 7.7 versus 8.5, 10 being the highest).

Vijayakumar et al. (2011) found that the mean time to task completion was 63 seconds for the Ambu aScope and 53 seconds for fibrescope, p=0.08 and the estimated 95% CI (1.26 to 18.74) did not overlap with the hypothesized difference of more than 30 seconds. A difference of more than 30 seconds in time to intubation between the Ambu aScope and fibrescope was considered a clinically important minimal difference. The mean number of tip surface collisions was slightly higher with the Ambu aScope at 2.7 compared with fibrescope at 2.5. The ease of use impression was rated at 65 compared with 77 (100 being extremely easy to use)

The External Assessment Centre noted that anaesthetists included in the manikin-based studies had previous experience of using standard fibrescope,

but lacked experience in using the Ambu aScope. Therefore, the differences between the Ambu aScope and conventional fibrescope may have been overestimated in these studies.

Published patient-based RCTs

Schoettker et al 2012 found that the incidence of successful intubation was 100%. The use of the Ambu aScope2 was associated with a longer time to intubation compared with control fibrescope (69.5 versus 49.5 seconds, mean difference of 20 seconds, $p<0.05$). Overall, the image quality provided by the Ambu aScope2 was lower than with the control fibrescope although the quality was judged subjectively to be excellent in 24 out of 50 cases and acceptable in 22 out of 50 cases.

Unpublished patient-based RCTs

In the study by Lenhardt et al. (2011), all patients were successfully intubated and no serious complications were encountered. (A poster presentation regarding this study has been published but some information is still regarded as academic-in-confidence). The time to intubation was similar between the use of the Ambu aScope and a pre-formed rigid stylet (multiple-use endoscope) (−9.0 seconds, [redacted]). The rating for ease of use was found to be similar for the Ambu aScope than the comparator.

In the study by Kristensen (2011), the difference in total intubation time between the Ambu aScope and the control fibrescope was 55 seconds (95% CI 5.8 to 104.4) including lidocaine injection, or 42.5 seconds (95% CI 11.6 to 73.4) without lidocaine injection. Although the difference in time to intubation was statistically significant in favour of the control endoscope ($p<0.05$), the investigators concluded that it was not clinically important because the difference was likely to be less than the hypothesised non-inferiority margin (120 seconds).

[redacted].

However, the External Assessment Centre stated the extent to which the

intubation procedure itself is affected by the poor image quality [redacted] of cases in the Kristensen (2011) study being unaffected. It is stated by the sponsor that the Ambu aScope2 now includes a clearing membrane that eases removal of secretions from the lens (ClearLens).

The External Assessment Centre commented that in Lenhardt et al. (2011), the Ambu aScope was combined with a Glide Scope video laryngoscope (GVL) and compared with a combination of GVL and a preformed rigid stylet. In effect, the Ambu aScope was compared with a rigid stylet, which is not a relevant comparator.

Case series

Piepho et al. (2010) found that typical landmarks such as the uvula, tongue, epiglottis and larynx were adequately identified in all 5 patients. Advancing the tracheal tube was smooth and easy in all 3 nasal route patients. In the oral route patient, airway secretions obstructed vision via the LCD screen. This was resolved following suctioning and cleaning of the Ambu aScope lens using a sterile swab.

In the study by Pujol et al. (2010), 9 of 10 intubations with the Ambu aScope were performed and completed without incident. Intubation could not be accomplished in 1 patient within the 30 minutes allowed. Tube insertion was considered easy in 8 patients and easy but with some manoeuvres needed in 1 patient and impossible in 1 patient. Although the carina was reached, a 7.5 mm tracheal tube could not be advanced through the vocal cords. In all 10 patients, a complete view of the glottis was obtained. The image quality was considered adequate in 5 patients and poor in another 5 patients. Fogging of the lens occurred in 6 patients and was cleared easily by gently touching the airway mucosa in 4 patients and by removing the endoscope and cleaning the tip in the other 2 patients. In 2 cases there were secretions that could not be suctioned but they did not result in difficult tube insertion. Optimal distribution of local anaesthetic over the glottis was achieved in all patients.

The average time to set up the endoscope and monitor was less than 5 minutes in the Jamadarkhana et al. (2011) study. The procedure time from needle puncture of the trachea to tracheostomy tube placement ranged from 5 to 10 minutes. All the anaesthesiologists managing the airway reported easy handling and manoeuvrability because of the light-weight design of the Ambu aScope. The operators performing the procedure scored the clarity and quality of endoscopic view to be between 8 and 10. No complications were reported during use of the Ambu aScope.

Perbet et al. (2011) found that 7 of the 10 participants rated the Ambu aScope 'very satisfactory', and 3 rated it as 'satisfactory' across all parameters. The presence of the screen was deemed useful in all of the cases. The absence of aspiration was missed in 4 cases.

All 8 patients in the Vincent et al. (2011) study were intubated while awake successfully using the Ambu aScope2. The mean (range) time to visualise the carina was 254.5 seconds (62–540 seconds); mean (range) time for confirming the position of the tube in the trachea after visualising the carina was 51.5 seconds (44–60 seconds). Six of the 8 users reported an excellent view of anatomical landmarks, and 2 users reported the view as poor, but sufficient for intubating the trachea. The mean score for manoeuvrability was 6.8 (range 3–9 with 10 classed as extremely manoeuvrable) and the mean score for usefulness of the endoscope was 7.4 (3–10 with 10 classed as extremely useful).

Findings from the case series studies indicate that the Ambu aScope is generally acceptable in practice. However, poor image quality and the need for lens cleaning were reported.

The External Assessment Centre stated that none of the available controlled trials included patients with unexpected difficult airways, and no studies were explicitly conducted in A&E departments. Therefore, it is uncertain whether the results of the included studies could be applied to ‘patients with unexpected difficult airways requiring emergency intubation including awake

or anaesthetised patients with displaced tracheostomies', as specified in the final scope.

The External Assessment Centre commented that the clinical evidence in the sponsor's submission is from studies in manikins or patients with expected (or simulated) difficult airways and from case series of patients needing percutaneous dilatational tracheostomy rather than the population described in the scope.

The External Assessment Centre noted that, in 8 of the 11 studies, the Ambu aScope (the Ambu aScope2 predecessor) was used rather than the Ambu aScope2. However, the sponsor states that the data derived from the studies investigating the Ambu aScope are still relevant and valid for this submission because the Ambu aScope2 has the same mode of action and design as the Ambu aScope, but with certain advancements, such as the easy clearing membrane and no 30-minute time-out feature.

Adverse events

The sponsor found no adverse event reports relating to the Ambu aScope in a search of the FDA's Manufacturer and User Facility Device Experience database. The sponsor also confirmed that no adverse events relating to the Ambu aScope have been reported to the Medicines and Healthcare products Regulatory Agency (MHRA).

4.2 Summary of economic evidence

Three published economic papers were identified by the sponsor (Gupta et al. 2011, Tvede et al. 2012, and Liu et al. 2012). The External Assessment Centre considered these to be relevant to the scope.

The External Assessment Centre found 1 ongoing study by Norris et al. (2010). This study was not included by the sponsor as part of its economic evidence submission. All studies focused on estimating the cost of the Ambu aScope or the multiple-use flexible endoscope. No modelling was included in the studies.

Published evidence

Tvede et al. (2012) compared the Ambu aScope with multiple-use flexible endoscope. Direct costs were estimated associated with both endoscopes in terms of equipment, maintenance, repair and staffing. The other 3 studies (Gupta & Wang 2011, Liu et al. 2012, and Norris et al. 2010) were non-comparative.

Tvede et al. (2012) estimated the total cost of an intubation using either the Ambu aScope or multiple-use endoscope over a 1-year period. The estimated cost of an intubation (the sum of acquisition costs, sterilisation costs and repair costs) for using the Ambu aScope was €204) and for the multiple-use endoscope the cost was €178. The average cost of an intubation using a multiple-use flexible optical endoscope was €177. In comparison the average cost associated with the Ambu aScope2 was estimated at €204.

Gupta et al (2011) compared single-use flexible optical endoscopes (Ambu aScope) and multiple-use for tracheal intubation. A total of 166 intubations were performed during the study time period (1 year). The total cost of intubation for the multiple-use endoscope was estimated at US$119.75 including $20.15 purchasing, $53.48 repair, $33.16 maintenance and $12.96 labour. The repair to intubation ratio was stated as 1:55. Repair costs were $53.48 per intubation and $2,959.44 per instance of repair. This was compared to their single-use price of Ambu aScope, which was $120.00 to $132.00 and stated that the price should range within 10% of the intubation cost per single-use intubation scope.

Liu et al. (2012) estimated the costs associated with multiple-use fibrescopes for tracheal intubation over a 12-month period. Costs included capital acquisition costs, annual repair costs, costs of cleaning and labour for sterilisation. The total cost per fibrescope use was estimated at $94.94 (range $89.79–$98.38) including $13.75 acquisition, $13.12 technical labour, $4.74 consumables and $63.32 repairs and replacements.

The study by Norris et al. (2010) investigated the cost of fibre-optic intubation and its associated costs from maintenance, repair and replacements. They concluded that the cost of fibre optic intubation was £32,000 with 141 procedures performed in 2008 to 2009. This led to an average of £227 per intubation using the fibre optic endoscope.

The comparison study (Tvede et al. 2012) suggests that the net costs per patient intubation are similar in single-use and multiple-use devices, though marginally favouring reusable devices. However, the other studies show that cost estimations are unstable; varying widely from study to study.

New cost analysis

The sponsor submitted a de novo economic model that estimated the costs and consequences associated with the use of the Ambu aScope2 and multiple-use flexible endoscopes (fibrescopes using fibre optic technology or video scopes using video technology). Two decision tree models were developed – 1 for unexpected difficult airway needing emergency intubation and 1 for dislodged tracheostomy:

Figure 1 Model of unexpected difficult airway needing intubation

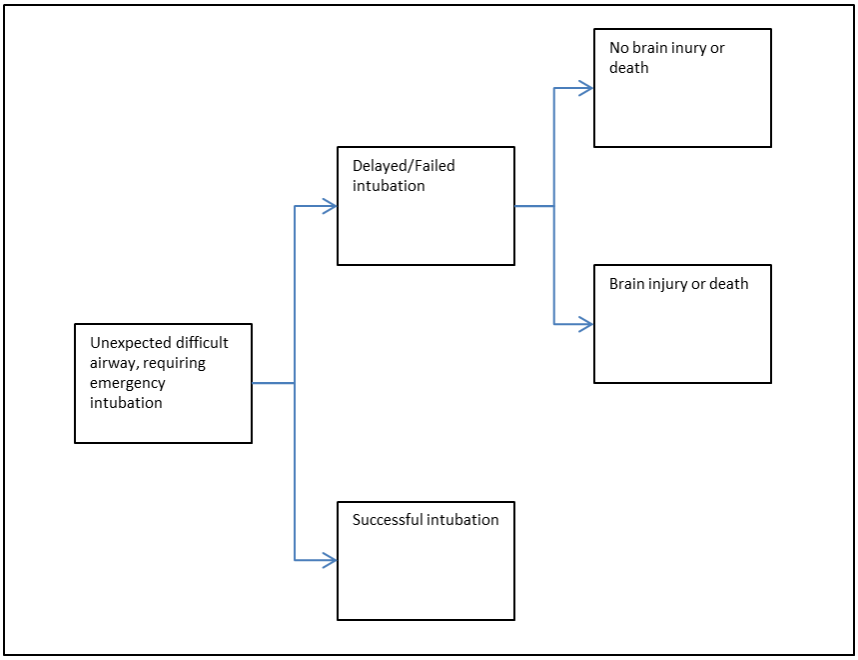
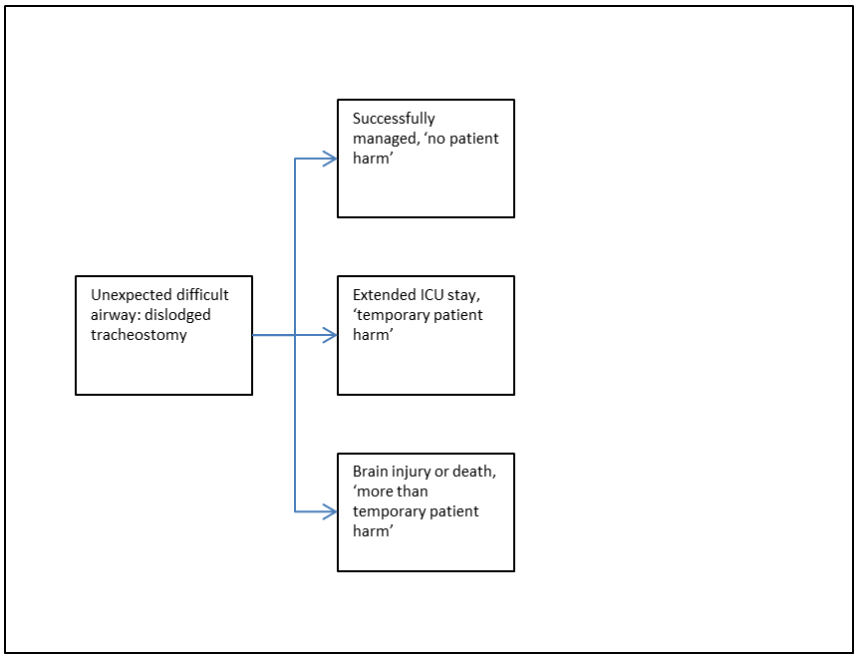


Figure 2 Model of unexpected difficult airway: dislodged tracheostomy



A separate model was designed for dislodged tracheostomy since this is not managed as an 'intubation' and is associated with different costs and outcomes. The decision tree model for unexpected difficult airway needing emergency intubation separated patients according to those who had successful intubations and those who had delayed or failed intubations; this latter group were separated further according to those with no brain injury or death, or those with brain injury or death. The decision tree model for dislodged tracheostomy separated patients into those who were successfully managed, those who had extended ICU stay and those with brain injury or death.

The analysis reported the costs associated with equipment and clinical outcomes, which were delayed or failed intubation and the management of dislodged tracheostomy.

The key assumptions in the sponsor's model are presented in table 2.

Table 2 Key assumptions in sponsor's model (adapted from table 37 in the sponsor's submission)

Variable	Value	Source
Number of procedures performed per annum with multiple-use endoscopes (base case)	150	NHS survey
multiple-use flexible intubation endoscope costs (weighted costs including stack systems, cameras etc.)	£12,105	NHS survey
Number of multiple-use endoscopes available	5	NHS survey
Ambu aScope2 cost per endoscope (and monitor)	£179	Ambu Ltd Note – the monitor has a list price of £799 but is provided with a starter pack to NHS Trust departments free of charge
Rate of delayed/failed intubation in unexpected difficult intubation patients: operating theatre setting – multiple-use endoscopes	6.25%	Rocke (1992)
Rate of delayed/failed intubation in unexpected difficult intubation patients: ICU setting – multiple-use endoscopes	16.6%	Rose (1996)
Rate of brain injury, death in difficult intubation patients where intubation has failed	28%	Thomas and McGrath (2009)
Rate of ICU admission or prolongation of stay because of failed intubation	74%	Thomas and McGrath (2009)
Rate of brain injury or death because of dislodged tracheostomy patients	13%	McGrath and Thomas (2010)
ICU –cost per day	£1,321	Weighted level 2 and 3 critical care cost per day NHS reference costs, 2010/11
Reduction in risk of failed intubation with Ambu aScope2	10%	Exploratory assumption, varied in sensitivity analyses
Reduction in risk of dislodged tracheostomy leading to patient harm	10%	Exploratory assumption, varied in sensitivity analyses

The External Assessment Centre stated that most of the assumptions were acceptable with notable exceptions (see table 4.2 of the External Assessment Centre Report). It did not agree:

- that the costs of the multiple-use endoscopes at £12,105 are accurate due to the great uncertainty associated with the estimated input figures
- that the costs of fibrescopes and video scopes should be estimated together as it believes these would be substantially different.
- with the rate of delayed/failed intubation stated where intubation has failed for the operating theatre (6.25%)
- with the rate of delayed/failed intubation stated where intubation has failed for the ICU setting (16.6%)
- with the rate of brain injury and death in difficult intubation patients where intubation has failed (28%)
- with the assumed reduction in risk of delayed/failed intubation with the Ambu aScope2 leading to patient harm (10%)
- with the assumed reduction in risk of dislodged tracheostomy with the Ambu aScope2 leading to patient harm (10%).

Costs and benefits

The analysis was from the NHS and personal social services perspective.

Evidence from clinical trials of the Ambu aScope and Ambu aScope2, including comparisons with multiple-use flexible endoscope, was not used in the cost analysis because most of the clinical studies took place in planned procedures or manikins rather than in patients with unexpected difficult airways (the patient population in this evaluation). Evidence was not available to show the Ambu aScope2's potential reduction in risk of intubation failure. Neither was there clinical trial evidence to show the associated outcomes of intubation failure or dislodged tracheostomy as a result of Ambu aScope2. Therefore, the sponsor made an exploratory assumption that there would be a

10% reduction in the risk of delayed or failed intubation and a similar reduction in the risk of patient harm in the context of dislodged tracheostomy.

Because limited information about resource use in the NHS in relation to multiple-use flexible endoscopes is available, the sponsor conducted a resource use survey in 20 NHS centres. The survey collected information relating to the costs of equipment and maintenance (see pages 145–146 of the sponsor's submission). The average costs of equipment from the 6 centres who responded were used in the sponsor's model. Unit costs used in the model included the Ambu aScope2, multiple-use endoscopes and ICU and hospital length of stay due to failure of intubation or a dislodged tracheostomy

The External Assessment Centre noted that most of the parameters of the sponsor's model are acceptable. However, it commented that the model is based on a scenario in which urgent intubation or re-siting of a tracheostomy tube is needed and that single-use devices will reduce the chance that the necessary endoscope will not be available. The External Assessment Centre notes that this assumption was not justified by the sponsor.

Results

The sponsor presented the results of base case analysis in 3 settings: unexpected difficult intubation in the operating theatre; unexpected difficult intubation in the ICU; and dislodged tracheostomy. The base-case results assumed that a hypothetical NHS Trust had 5 multiple-use endoscopes that are used 150 times per year. In all the settings, the use of the Ambu aScope2 was cost saving compared with multiple-use endoscopes.

The incremental cost saving of the Ambu aScope2 compared with multiple-use endoscopes was estimated to be £30 per intubation for equipment and staff costs only. This was consistent across the 3 settings. If the Ambu aScope2 was used instead of a multiple-use endoscope and if the equipment and staff costs and the modelled costs associated with hospitalisations were included, then:

- for unexpected and difficult intubation in the operating theatre there are potential incremental cost savings of £68 per patient
- for unexpected difficult airway in the ICU there are potential incremental cost savings of £130.70 per patient
- for dislodged tracheostomy there are potential incremental cost savings of £1,555.80 per patient.

The sponsor included a 1-way deterministic sensitivity analysis to explore parameter uncertainty and the effect of these changes on the cost of the Ambu aScope2. One-way analyses were conducted by varying the failure rate of intubation, reduced risk rates of failed intubation by the Ambu aScope2, length of hospitalisation and the costs associated with multiple-use endoscopes.

The sensitivity analysis showed that the findings were responsive to the parameter changes in all 3 clinical settings. The Ambu aScope2 remained cost saving in most scenarios, with the exceptions being in scenarios of long lifetime equipment or a substantially low equipment cost for the multiple-use endoscope (see pages161 and 162 of the sponsor's submission). The External Assessment Centre confirmed these results.

The sponsor also changed the number of multiple-use endoscopes ranging from 1 to 10 and the number of procedures (frequency of their use) ranging from 50 to 300 (see tables 46–49 of the sponsor's submission). This analysis showed that in hospitals where fewer multiple-use endoscopes are available, the Ambu aScope2 is likely to be cost-incurring for unexpected difficult intubation in the operating theatre and in the ICU. In a large hospital, where more than 5 multiple-use endoscopes are available, the Ambu aScope is likely to be cost saving. For dislodged tracheostomy, using the Ambu aScope2 is likely to prove cost saving regardless of the number of available multiple-use endoscopes or the number of procedures. The External Assessment Centre performed an analysis increasing the number of procedures to 185, which showed that the Ambu aScope becomes cost incurring by £3. If the number of

procedures was changed to 200, the Ambu aScope2 became cost incurring by £14. However this does not consider any other costs in the model.

The External Assessment Centre suggested an alternative model structure with a different scenario in which the Ambu aScope2 is used in a complimentary mode to multiple-use alternatives when multiple-use endoscopes are not immediately available in operating theatres or ICU. This scenario specifically included a comparison of single-use and multiple-use endoscopes, and a more closely specified pathway. It was designed to capture the potential supply chain failure. The model structure is shown on page 64 of the External Assessment Centre report. Unlike the sponsor model, this model did not include the outcomes of death or permanent brain injury should intubation fail. The External Assessment Centre commented that even though these outcomes are possible outcomes of failure of intubation, and are extremely costly, it found no evidence that would enable estimating either the likelihood of such outcomes or the proportion that might be avoided by more timely use of an endoscope to assist intubation. The External Assessment Centre did not model dislodged tracheostomy.

The External Assessment Centre used the following parameters based on the sponsor's model:

- Multiple-use cost per endoscope (£209).
- Ambu aScope2 cost per endoscope (£179).
- Rate of delayed or failed intubation in unexpected difficult intubation in the operating theatre for multiple-use endoscopes and the Ambu aScope2 (6.25%).
- Rate of delayed or failed intubation in unexpected difficult intubation in the ICU for multiple-use endoscopes and the Ambu aScope2 (16.6%).
- ICU length of stay for multiple-use endoscopes and the Ambu aScope2 (6.2 days).
- Rate of ICU admission or prolongation of stay for failed intubation for multiple-use endoscopes and the Ambu aScope2 (74%).

- ICU cost per day (£1,321)

The External Assessment Centre changed 2 parameters based on its interpretation of clinical expert opinion and literature:

- Rate of delayed intubation in unexpected difficult intubation patients in the operating theatre and ICU for multiple-use endoscopes (10%).
- Rate of harm needing extended hospital stay in difficult intubation patients where intubation was delayed (50%)

The External Assessment Centre's base-case analysis in unexpected difficult intubation in an operating theatre indicated a cost saving of £401 when using an Ambu aScope2. The mean cost per patient when using an Ambu aScope2 was £1185 and the mean cost of a multiple-use endoscope was £1524 when used in unexpected difficult intubation in an ICU. This indicates a cost saving of £339 when using an Ambu aScope2 in this setting. However, the External Assessment Centre stated that the results were based on clinical expert opinion and sponsor's assumptions, and the model was presented to illustrate a potential alternative to the sponsor's model only. The External Assessment Centre stated that because of the assumptions used, the model is subject to uncertainty.

The External Assessment Centre stated that there is some uncertainty about the base case presented in the sponsor's model. It models the impact of availability of the Ambu aScope by assuming an exploratory reduction in the risk of delayed or failed intubation and a similar reduction in the risk of patient harm in the context of dislodged tracheostomy. In the base case the sponsor assumed a 10% reduction in risk but acknowledged that at present there is no evidence to validate it. However in its sensitivity analysis it also explored the parameters of 5% and 15%, both of which showed the Ambu aScope2 to be cost saving. Further analysis, by the NICE technical team, showed that (using all the parameters in the sponsor's model) if the rate was reduced to as low as 0.1% the Ambu aScope was still cost saving.

4.3 Main issues

Clinical evidence

The External Assessment Centre noted that the clinical evidence was based on studies in manikins or patients with expected (or simulated) difficult airways and from case series of patients needing percutaneous dilatational tracheostomy. The External Assessment Centre therefore expressed uncertainty as to whether the results of the included studies could be applied to 'patients with unexpected difficult airways needing emergency intubation including awake or anaesthetised patients with displaced tracheostomies', as specified in the final scope.

The External Assessment Centre noted that only 1 RCT and 2 cases series used the current device model: the Ambu aScope2, with other evidence derived from the immediate predecessor device, the Ambu aScope. In its submission, the sponsor stated that the data derived from the studies investigating the Ambu aScope are relevant because they differ only in 2 main design improvements: the easy clearing membrane and the removal of the 30-minute time-out feature.

The External Assessment Centre noted that the outcomes in the clinical evidence were mainly concerned with intubation and some device-related adverse events. It concluded that there is no direct evidence on serious clinical consequences, including death, hypoxic brain injury and length of stay in ICU and hospital with the Ambu aScope or the Ambu aScope2.

Findings from the case series studies indicated that the Ambu aScope is generally acceptable in practice. However, poor image quality and the need for lens cleaning were reported.

Economic evidence

The External Assessment Centre noted that the sponsor's economic model was based on the assumption that using single-use devices will reduce the chance that the necessary scope will not be available. The External

Assessment Centre noted that this assumption was not justified by the sponsor.

The External Assessment Centre expressed particular concerns about a number of parameters in the sponsor's model such as:

- the costs for fibre optic endoscopes and video scopes are different and should be considered separately
- the rate of delayed or failed intubation stated where intubation has failed for the operating theatre setting (based on Rocke et al., 1992)
- the rate of delayed or failed intubation stated where intubation has failed for the ICU setting (based on Rose and Cohen, 1994)
- the rate of brain injury and death in difficult intubation patients where intubation has failed (based on Thomas and McGrath 2009)
- the assumed reduction in risk percentage of failed intubation with the Ambu aScope2 leading to patient harm
- the assumed reduction in risk percentage of dislodged tracheostomy with the Ambu aScope2 leading to patient harm.

The External Assessment Centre suggested an alternative scenario to that suggested by the sponsor. It noted that since the parameters were taken from the sponsor's model or expert opinion, there is uncertainty around the results. The External Assessment Centre noted that further research might be needed to fully inform the parameters.

5 Ongoing research

The External Assessment Centre has proposed an alternative economic model addressing the use of the Ambu aScope2 in a complementary manner to mitigate risks when multiple-use endoscopes are not available. The External Assessment Centre has noted that this could be implemented, but would be hard to populate. Primary research into the numbers, locations, and need for intubating fibrescopes for emergency and difficult airway situations in NHS settings would almost certainly be needed to inform the model. Further

research, which might be both secondary and primary, might be needed to inform parameters around risks attached to endoscope unavailability.

6 Authors

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Sally Doss, Technical Adviser

NICE Medical Technologies Evaluation Programme

October 2012

Appendix A: Sources of evidence considered in the preparation of the overview

A Details of assessment report:

- Shihua Zhu, Fujian Song, Guiqing Lily Yao et al. Ambu aScope2 in unexpected difficult airways management. (August 2012) Birmingham and Brunel consortium External Assessment Centre

B Submissions from the following sponsor:

- Ambu Ltd

C Related NICE guidance

- No related NICE guidance

D References

Austin, P., Crawley, S., Christie, S., and Cole, S. J. (2011). Evaluating the Ambu aScope – an alternative approach to endoscopic monitoring during percutaneous dilational tracheostomy. [Abstract]. Nottingham, UK: Difficult Airways Society Congress.

Gernoth, C. and Genzwuerke, H.V. (2010) First experiences with the single-use Ambu aScope for fibreoptical monitoring in percutaneous dilatation tracheostomy. [Abstract]. Helsinki, Finland: Euroanaesthesia.

Gupta, D., and Wang, H. (2011). Cost-effectiveness analysis of flexible optical scopes for tracheal intubation: a descriptive comparative study of reusable and single-use scopes. Journal of Clinical Anesthesia; 23(8):632–635.

Henderson, J.J., Popat, M.T., Latto, I.P., and Pearce, A.C., Difficult Airway Society. (2004). Difficult Airway Society guidelines for management of the unanticipated difficult intubation. Anaesthesia; 59(7): 675–694.

Jamadarkhana, S., Mallick, A., and Bodenham, A. (2011). Preliminary Evaluation of Ambu aScope 2 for Endoscopic Guidance During Percutaneous Dilatational Tracheostomy. [Abstract]. London, UK: Intensive Care Society Congress.

Kristensen, M.S., Fredensborg, B.B., Hansen, C.M., and Tvede, M.F. (2010). A disposable flexible intubation videoscope, the Ambu® aScope™, and the first experiences with awake intubation in patients with difficult airways. [Abstract]. Florida, USA: Society for Technology in Anesthesia Annual Meeting.

Kristensen, M. (2011). Clinical Investigation Report (CIR). Post-marketing study: Evaluation and comparison of the new disposable Ambu aScope with the Olympus BF Type 3C160 non-disposable scope for securing the sleeping/awake patients normal and difficult airway. Version 1. 23/09/2011. Ambu A/S (Unpublished).

Kristiansen, A. (2011). The use of the Ambu intubation SGA, Aura-i, in difficult airways. [Abstract].

Kristensen M.S. and Fredensborg. B.B. (2013) "The disposable Ambu aScope vs. a conventional flexible videoscope for awake intubation - a randomized study." Acta Anaesthesiological Scandinavica. doi. 10.1111/aas.12094

Kumar, M., Clarke, A., Wilkes, A.R., Godwin, N., and Hodzovic, I. (2011). Evaluation of the Ambu aScope, a new single-use flexible videoscope. [Abstract].

Lenhardt, R., Sharma, R., and Burkhart, M. (2010). Feasibility of a combined use of a video-laryngoscope with a novel video-stylet for predicted difficult intubation (Version 5-6-2010). [Study Protocol].

Lenhardt, R., Sharma, R., Burkhart, M.T., and Kandadai, S.K. (2011). Feasibility of a combined use of a video-laryngoscope with a novel flexible

video-stylet for predicted difficult intubation. [Abstract]. Chicago, USA: American Society of Anesthesiologists Congress.

Liu, S., Brodsky, J., and Macario, A (unpublished). Cost Identification Analysis of Anesthesia Fiberscope Use for Tracheal Intubation. [Manuscript in preparation].

McGrath B, Thomas A. Patient safety incidents associated with tracheostomies occurring in hospital wards: a review of reports to the UK National Patient Safety Agency. Postgrad Med J. 2010;86(1019):522-5

Norris, A., Wakeling, P., Wiles, M., McCahon, R., and Bennett, M. (2010). Costs associated with a fibrescope inventory: what role for the disposable scope? [Poster]. Nottingham, UK: Difficult Airway Society.

Perbet, S., Jabaudon, M., Cayot-Constantin, S., Guérin, R, Chartier, C., Constantin, J.M., and Bazin, J.E. (2011). The single-use endoscope aScope™ for fibreoptical monitoring in percutaneous dilatational tracheostomy: a feasibility study. [Abstract] Berlin, Germany: European Society of Intensive Care Medicine Congress.

Piepho, T., Werner, C., and Noppens, R. R. (2010). Evaluation of the novel, single-use, flexible aScope for tracheal intubation in the simulated difficult airway and first clinical experiences. Anaesthesia; 65(8): 820-825.

Pujol, E., Lopez, A. M., and Valero, R. (2010). Use of the Ambu® aScope in 10 patients with predicted difficult intubation. Anaesthesia; 65(10): 1037-1040.

Rocke, D.A., Murray, W.B., Rout, C.C., and Gouws, E. (1992). Relative risk analysis of factors associated with difficult intubation in obstetric anesthesia. Anesthesiology; 77(1): 67-73.

Rose, D.K., and Cohen, M.M. (1994) The airway: problems and predictions in 18,500 patients. Canadian Journal of Anaesthesia; 41(5 Pt 1):372-383.

Royal College of Anaesthetists (2011). 4th National Audit Project (NAP4): Major complications of airway management in the United Kingdom. London, UK: The Royal College of Anaesthetists and the Difficult Airway Society. Available from: http://www.rcoa.ac.uk/nap4.

Saumande, B., Wolter, J., Segura, P., Pottecher, T., and Diemunsch, P. (2010). The videolaryngoscope AirwayscopeTM makes the bronchial aScopeTM videoscopy easier. Chicago, USA: Annual Meeting of the American Society of Airway Management.

Schoettker, P., Krugel, V., Frascarolo, P., and Bathory, I. (2012). Comparison of the single-use Ambu aScope2® versus the fiberoptic bronchoscope for tracheal intubation in patients with cervical spine immobilisation by a semi-rigid collar. European Journal of Anaesthesiology; 29(s50): 228-229.

Scutt, S., Clark, N., Cook, T.M., Smith, C., Christmas, T., Coppel, L., and Crewdson, K. (2011). Evaluation of a single-use intubating videoscope (Ambu aScope TM) in three airway training manikins for oral intubation, nasal intubation and intubation via three supraglottic airway devices. Anaesthesia; 66(4):293-299.

Thomas AN, McGrath BA. Patient safety incidents associated with airway devices in critical care: a review of reports to the UK National Patient Safety Agency. Anaesthesia. 2009; 64(4):358-65. Epub 2009/02/04.

Tvede, M., Kristensen, M.S., and Nyhus-Andreasen, M. (2012). A cost analysis of reusable and disposable flexible optical scopes for intubation. Acta Anaesthesiologica Scandinavica; 56(5):577-584.

Vijayakumar, M., Clarke, A., Wilkes, A.R., Goodwin, N., and Hodzovic, I. (2011). Comparison of the manoeuvrability and ease of use of the Ambu aScope and Olympus re-usable fibrescope in a manikin. Anaesthesia. 66(8): 689-693.

Vincent, V., Raval, M., Ong, C., Ahmad, I. et al. (2011). Evaluation of aScope2 in eight patients with anticipated difficult airways having awake fibre-optic intubations. [Abstract]. London, UK: Difficult Airways Society Congress.

Appendix B: Comments from professional bodies

Expert advice was sought from experts who have been nominated or ratified by their Specialist Society, Royal College or Professional Body. The advice received is their individual opinion and does not represent the view of the society.

Dr Brendan McGrath

Consultant Anaesthetist, The Royal College of Anaesthetists

Dr Alistair McNarry

Consultant Anaesthetist, Association of Anaesthetists of Great Britain and Ireland

Dr Ali Diba

Consultant Anaesthetist, Association of Anaesthetists of Great Britain and Ireland

Dr Andrew Bentley

Consultant in Respiratory and Critical Care Medicine, Intensive Care Society

- (Three experts commented at the scope stage). All three experts had direct involvement with the technology.
- All three experts thought that the Ambu aScope device was a significant modification of an existing technology. Two experts commented that it was the disposable nature of the device which was the main modification, whilst another felt that it was related to its use of video and LED.
- Scenarios for use focussed on the device's opportunity for immediate use and included use for emergency intubation or airway inspection in a variety of clinical areas, as well as assisting with percutaneous dilatational tracheostomy in the ICU. One expert felt that the Ambu aScope could be used in hospitals with limited or no access to reusable fibrescopes, or for use in cases of vCJD.

- The main comparators identified were reusable flexible endoscopes (or fibrescopes), but not those used for bronchoscopy or biopsy. Two experts pointed out that the image quality gained from Ambu aScope would not match that of a reusable endoscope but was sufficient and had the additional benefit of immediate use with no additional maintenance.
- No competing disposable flexible endoscopes were identified.
- All three experts felt that main potential benefit of the technology for patients was in its availability. A benefit identified by one expert was a decrease in the risk of cross-contamination as the device is for single use.
- Two experts felt that the relatively low cost of the device should mean there no barriers to its introduction within high-risk clinical areas.
- All three experts thought the potential benefits of the device would be difficult (or even impossible) to measure.
- All experts felt that there could be cost savings associated with use of Ambu aScope compared to the maintenance costs of reusable endoscopes. Two experts felt that the financial benefits were most likely to be felt in smaller hospitals with limited expenditure on endoscopes.
- No obstacles to realising the benefits of the device were identified; two experts said that the benefits should be realised easily.
- All three experts said that no special training would be needed for the safe and effective use of the Ambu aScope.
- All three experts stated that no maintenance would be required for the Ambu aScope. One expert commented that the optical quality and video display is inferior to reusable scopes, however this was an acceptable trade-off for the immediate availability and usability of the device.
- One expert commented that the cost savings of the device would depend on the infrastructure in place for processing reusable scopes.
- None of the experts felt that there would be any controversy around the use of this technology.
- All three experts felt that NICE guidance on the device would be useful.

Appendix C: Comments from patient organisations

Advice and information was sought from patient and carer organisations. The following patient and carer organisations responded:

The following patient organisations were contacted and no response was received.

- Brain and Spinal Injury Charity
- Brain and Spine Foundation
- Brain Injury Rehabilitation Trust
- British Lung Foundation
- Cancer Laryngectomee Trust
- CritPaL - Patient Liaison Committee of the Intensive Care Society
- Get A-Head
- Guillain-Barré Syndrome Support Group
- Headway - The Brain Injury Association
- ICU Steps
- Motor Neurone Disease Association
- Mouth Cancer Foundation
- National Association of Laryngectomee Clubs
- National Obesity Forum
- Neurological Alliance
- Neurosupport
- Ochre
- Oesophageal Patients Association
- Royal College of Anaesthetists Patient Liaison Group
- Royal College of Surgeons Patient Liaison Group
- Stroke Association
- The Overweight and Obesity Organisation
- UK Acquired Brain Injury Forum

Appendix D: External Assessment Centre correspondence

National Institute for Health and Clinical Excellence
External Assessment Centre correspondence

MT158 Ambu aScope for difficult and unexpected airways management

The purpose of this table is to show where the External Assessment Centre relied in their assessment of the topic on information or evidence not included in the sponsors' original submission.

Submission Document Section/Sub-section number	Question / Request Please indicate who was contacted. If an Expert Adviser, only include significant correspondence and include clinical area of expertise.	Response Attach additional documents provided in response as Appendices and reference in relevant cells below.	Action / Impact / Other comments
	Question to Expert Advisors (Consultant anaesthetists / Consultant in Respiratory & Critical Care Medicine): Relative effectiveness of Ambu aScope vs. Standard instruments.	**Expert 1:** No. It feels 'cheaper' but it works just as well. The range of movement is similar and the video screen is good enough. Its advantage is portability without a large 'stack system' to display the images. The images are of course not as good as the expensive alternatives but they are certainly good	Comments taken into account in the EAC's assessment of the clinical effectiveness

Submission Document Section/Sub-section number	Question / Request Please indicate who was contacted. If an Expert Adviser, only include significant correspondence and include clinical area of expertise.	Response Attach additional documents provided in response as Appendices and reference in relevant cells below.	Action / Impact / Other comments
	For the first set of questions, our impression from the literature is that the Ambu aScope2 is a little harder to use than standard equipment. On average it takes longer to complete intubation when an Ambu aScope2 is used to assist the procedure than when standard devices are used. Is this correct in your view?	enough. **Expert 2:** The time differences in both studies were small. It is difficult to make an assertion based on the published evidence that the time difference was clinically significant. Also it is not clear whether the Ambu aScope or the Ambu aScope2 was being evaluated and this may have had a significant bearing on the time to intubation as the slow responsiveness of the screen was one of the problems with the original model. It is certainly true that the aScope2 is a little more awkward to manoeuvre than its reusable counterparts but as the collision study showed there was no difference. **Expert 3:** I am of the view that the Ambu aScope2 should not be considered as a direct comparator and alternative for standard video bronchoscopes. It is an alternative when standard scopes are not immediately available, for example in an emergency situation. I think the concept of it being harder to use is a difficult area as the reasons are multifactorial, including familiarity with the device. However, I feel it	data and the economic model

Submission Document Section/Sub-section number	Question / Request Please indicate who was contacted. If an Expert Adviser, only include significant correspondence and include clinical area of expertise.	Response Attach additional documents provided in response as Appendices and reference in relevant cells below.	Action / Impact / Other comments
		is not as versatile an instrument or as robust as a standard scope and therefore I could anticipate that it may take a little longer to complete an intubation. I do not have direct personal experience to support this. **Expert 4:** You really need to define what you mean by standard equipment. If you are talking about other flexible endoscopes particularly the reusable devices which most commonly for anaesthetics are fiberoptic based, then answer is no aScope is not harder but easier (can expand if required). If you are comparing with a standard retractor type laryngoscope (essentially a bent spoon with a light!) then the answer is a resounding yes, but that is almost a tool aimed at a different task.	
	Question to Expert Advisors (Consultant anaesthetists / Consultant in Respiratory & Critical Care Medicine): Is it unlikely that the Ambu aScope2 is better/more effective than standard	**Expert 1:** It depends what you assessing. Ambu aScope has poorer optics and no suction but will achieve virtually all of what an expensive alternative will. If you have a £20k scope in the washer 10 minutes away and you need a scope in an emergency, I would consider then that the aScope is	Comments taken into account in the EAC's assessment of the clinical effectiveness

Submission Document Section/Sub-section number	Question / Request Please indicate who was contacted. If an Expert Adviser, only include significant correspondence and include clinical area of expertise.	Response Attach additional documents provided in response as Appendices and reference in relevant cells below.	Action / Impact / Other comments
	alternatives? Indeed no claim of superiority is made. Can you confirm our impression?	'more effective'. However, in an elective situation, where aScope and an expensive re-useable scope were available to me, I would choose the expensive one usually. **Expert 2:** I would agree, its superiority lies in its disposable nature making it ideal for infected cases. The fact that it comes in a sterile package also means that it could be made rapidly available in areas without storage and cleaning facilities. Also its rapid assembly time is also a potential attraction Its major drawbacks are i) the fact that an Aintree catheter cannot be placed over it [I have discussed this feature with one of the authors of the NAP4 report who underlined the fact that any scope to be used as a rescue device should be compatible with an Aintree catheter and facilitate fibreoptic intubation via a supraglottic airway- ii)the absence of a working channel for the placement of guidewires/ epidural catheters etc –	data and the economic model

Submission Document Section/Sub-section number	Question / Request Please indicate who was contacted. If an Expert Adviser, only include significant correspondence and include clinical area of expertise.	Response Attach additional documents provided in response as Appendices and reference in relevant cells below.	Action / Impact / Other comments
		The Aintree issue is Very Important [I do not refer to the working channel of any fibreoptic laryngoscope as appropriate for suction, so this is not an issue with the aScope2] **Expert 3:** Yes, I would agree with this view. It is has distinct advantages in terms of immediate availability in the management of the emergency airway. I do not believe it is superior to standard scopes. **Expert 4:** This question would suggest you are comparing with, at least now, reusable endoscopes. If that is so then answer is aScope can be better depending on what generation of flexible endoscope is used in that institution and how well it is maintained. E.g. Elderly fiberoptic device with slack control lines on the control lever and or multiple broken fibres or poor light source or poor picture adjustment (all very common scenarios) will be much inferior to aScope.	
	Question to Expert Advisors (Consultant anaesthetists / Consultant in Respiratory	**Expert 1:** To my knowledge, the published data on the use of this scope is that it is comparable in	Comments taken into account in

Submission Document Section/Sub-section number	Question / Request Please indicate who was contacted. If an Expert Adviser, only include significant correspondence and include clinical area of expertise.	Response Attach additional documents provided in response as Appendices and reference in relevant cells below.	Action / Impact / Other comments
	& Critical Care Medicine): Delay in inserting an endotracheal tube is a reasonable surrogate for overall safety; while in an individual case a delay of, say, 10 seconds may not be important but in some cases a delay might be critical. Could you comment on this?	performing intubations in terms of time. 10 seconds is unlikely to be critical and is probably more than compensated by aScope's immediate availability (compared to getting a reusable scope out of a drying cabinet). **Expert 2:** This is a difficult and complex question, and cannot be answered in the same was as when dealing with conventional laryngoscopes The operator must be familiar with the equipment and the technique. The Ascope2 is quick to set up, but people must be familiar with the technique of using it. In an awake patient a delay in the placement of an endotracheal tube is not an issue, as the patient is awake and self oxygenating. It is the adequacy of topicalisation that is important in terms of patient tolerance and this is not a feature that can be attributed to the scope. An asleep fibreoptic intubation should only be attempted when the patient can be adequately oxygenated by an alternative means- or the failed	the EAC's assessment of the clinical effectiveness data and the economic model

Submission Document Section/Sub-section number	Question / Request Please indicate who was contacted. If an Expert Adviser, only include significant correspondence and include clinical area of expertise.	Response Attach additional documents provided in response as Appendices and reference in relevant cells below.	Action / Impact / Other comments
		intubation drill should be in use. Here there are some questions to be answered Because the aScope2 cannot be used with an Aintree catheter, a low-skill fibroptic intubation that all anaesthetists are expected to learn to do during their training is not possible. However, the ready availability (assumed) of the aScope2 may allow the trachea to be intubated in a more timely fashion than having to delay will a conventional reusable scope is sourced (cleaned in certain circumstances) and assembled- The Vijayakumar study showed a clear learning curve with both devices- this was clearly learning the scenario- but the difference between the two devices also narrowed (extrapolation is difficult here as this was not a primary outcome measure) **Expert 3:** I would agree that immediate availability of equipment to support a difficult airway and avoidance of delay is a surrogate to support overall patient safety. A delay in inserting an endotracheal tube could be critical in some situations. Particularly	

Submission Document Section/Sub-section number	Question / Request Please indicate who was contacted. If an Expert Adviser, only include significant correspondence and include clinical area of expertise.	Response Attach additional documents provided in response as Appendices and reference in relevant cells below.	Action / Impact / Other comments
		relevant would be the acutely unwell or emergency patient, for example in an intensive care environment. It is less likely to be as much of a problem in an elective situation with a well pre-oxygenated patient, for example in a intubation prior to a planned operation. Underlying cardiorespiratory disease may have an impact on this situation, by increasing the risk of hypoxia caused by a delay to intubation. The risks would be higher in an acutely unwell patient in an emergency situation who is dependent on high concentration of oxygen. A delay of up to 10 seconds could be of relevance and result in additional morbidity related to hypoxia. **Expert 4:** Disagree that "*inserting an endotracheal tube is a reasonable surrogate for overall safety*," as this is a poor surrogate for safety, though often used. Delays of 10 seconds are probably no significance. "Delay to insertion" is often used as a indicator of ease of use of a device, rather than safety. In truth it's not a delay, but duration of procedure. Depends what papers you are reading.	

Submission Document Section/Sub-section number	Question / Request Please indicate who was contacted. If an Expert Adviser, only include significant correspondence and include clinical area of expertise.	Response Attach additional documents provided in response as Appendices and reference in relevant cells below.	Action / Impact / Other comments
	Question to Expert Advisors (Consultant anaesthetists / Consultant in Respiratory & Critical Care Medicine): Logistical / supply chain issues The second set of questions deal with the claim that conventional scopes are sometimes not available. This may arise if they have been recently deployed and are away for cleaning or if they have not been deployed in a specific location. Since the industry case is based on this scenario we need to know more about this issue. How often does the situation arise that no scope is available when the need arises. How does this vary across locations within a hospital? There may be no data on this rather specific question but some sort of expert impression of the size of the problem would be most helpful. Even anecdote would be useful. For instance have you heard of patient's	**Expert 1:** This depends on your hospital's infrastructure and workload. We have over 120 scopes, and use 4 for our 23 bedded ICU. There is always one available, even if we use 2 out of hours. We had to buy 2 extras though when we went to centralised decontamination to ensure these were always available. A smaller unit with only 1 or 2 scopes may be harder to have 1 available always. Most cleaned scopes are kept in expensive drying cabinets to keep scopes clean for 72 hours. They need monitoring and then re-washing after this (infrastructure required to do this). It is not inconceivable that if you use a scope at midnight on Saturday and then need another immediately for something else, you may have no more scopes available in your area. The cost of providing a few scopes, the cabinet and the people to monitor and decontaminate these scopes is large. If the scopes are there for occasional emergency use (e.g. on an ENT ward or resp ward) then the aScope is a very attractive alternative. Our 2009 and 2010 critical incident reviews included detailed cases of harm occurring due to non availability of equipment. I have	Comments taken into account in the EAC's assessment of the clinical effectiveness data and the economic model

Submission Document Section/Sub-section number	Question / Request Please indicate who was contacted. If an Expert Adviser, only include significant correspondence and include clinical area of expertise.	Response Attach additional documents provided in response as Appendices and reference in relevant cells below.	Action / Impact / Other comments
	coming to harm because a scope was not available?	attached the 2010 paper. We did not report the specific number of scopes here. **Expert 2:** This again is a difficult question. NAP4 [5] is clear that we do not do enough fibreoptic intubations. I have discussed this with a NAP4 editor and he has confirmed that cases were reported to NAP4 where fibreoptic equipment was not available when needed. This was most notable in reports from ICU and the ED. Lack of availability was reported from operating theatres also but it was not a widespread feature. We also know that scope availability varies- in a survey we did in 2010 in England Wales and Northern Ireland, We obtained data from 127 hospitals (53%). Access to FOI equipment was possible in 127 sites (100%), with the mean scope to theatre ratio being 0.4, range 0.09 to 1.0 [6]. In a hospital where there is only one scope, should it become damaged then alternative means of performing a fibreoptic intubation have to be found- Even in a hospital with many scopes, should the	

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		cleaning system develop a fault then all of its reusable scopes are out of commission, unless they have been appropriately stored in a HEPA Cabinet- which is itself a major financial outlay particularly if the number of scopes maintained by an organisation is small. I have certainly been told of difficulty accessing a fibreoptic scope by several individuals because it has to be transported between sites or borrowed from another hospital. I have asked some of my colleagues whether they have actually heard of a specific case of harm because a fibreoptic scope was temporarily unavailable. Another point to consider is the issues surrounding trace-ability and loan scopes- where a company may previously have loaned a replacement scope, now unless they can meet strict trace-ability the hospital may not be able to accept a loan device **Expert 3:** I do not have specific numbers to inform this question but am aware of situations where there	

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		has been a delay in getting hold of a “clean” standard scope quickly. Cases of clinical harm do not come to mind immediately. The issues here relate to the time taken to clean a standard scope or accessing a clean standard scope out of hours in theatre or intensive care. Many hospitals will now have a system of centralised sterilisation of endoscope equipment and therefore do not have the standard scopes immediately available in the place they need to use them. This is based on robust infection control and prevention procedures. They are often packaged, sterilised and stored remotely from the clinical environment. The advantage of the Ambu aScope is its immediate availability in the location it is required, for example in the case of a dislodged tracheostomy in an ICU patient. Standard scopes usually have a separate “stack” for the video equipment which are cumbersome systems to be moved to the bedside in an emergency airway situation compared with the Ambu aScope. **Expert 4:** “*How often does the situation arise*…?” - Can not answer this, at one time this was common,	

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		but now probably few hospitals are without an endoscope for airway use (not sure here about small private hospitals and clinics etc). **It's probably more important to realise that flexible endoscopes (FE) may be available in theory and yet their use untenable** because they are far away, poorly maintained, unfamiliar to staff and seen consequently as a last resort rather than a ready and easy tool. **It may be reasonable to contend that any operating theatre suite which has only one reusable FE should carry some aScopes for when that device is being processed or repaired or even in use**. "*How does this vary…?*" – Hugely. Operating theatres in UK DGH are rarely without at least one FE but obstetric theatres, A+E units, Intensive Care units likely to not have. "…expert impression of the size of the problem…?" – NAP 4 audit looking at theoretically all instances of airway harm in UK has particular references to FE use for airway management. If you are not familiar with this document, may I suggest its perusal or let me know if you need some parts interpreted. For	

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		sure FE not used frequently where it should have been, the reasons for this may be to do with general availability and ease of set up.	
	Question to Expert Advisors (Consultant anaesthetists / Consultant in Respiratory & Critical Care Medicine): Given that sooner or later the situation will arise where a scope is not available when needed, the sponsor argues that Ambu aScope's should be available in locations where *unexpected* difficulties may arise and that standard instruments would not be available there?	**Expert 1:** Where you are expecting difficulties (eg an anaesthetic list with a difficult elective case) one would usually plan to have a high end scope electively available. For unplanned emergencies, a high end scope may be immediately available (usually in a nearby drying cabinet, eg for an ICU or theatre suite) or the aScope may be useful in speeding up the availability issue. For remote sites or wards which do not have the infrastructure to buy the scopes and decontamination facilities, the aScope offers a rapid and effective solution. **Expert 2:** Within the terms provided, the question is challenging, so I must apologise if I stray outside them. The primary purpose of a fibreoptic scope is to facilitate tracheal intubation. In itself it does nothing to oxygenate the patient. The properties of the scope are probably much less important (within certain	Comments taken into account in the EAC's assessment of the clinical effectiveness data and the economic model

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		limits) than the quality of the operator (vide supra). It is certainly true to say that there are many places within a hospital where I would not expect to find a reusable fibrescope unless I had made specific provision for one to be available there. The Ascope2 offers a readily available, rapidly ready to use fibrescope, and if practitioners are experienced in their use then it may be quicker to use it in departments out with a main theatre suite- e.g. to perform a tracheostomy on ICU or to do a fibreoptic intubation in a distant site (intensive care or the emergency department). Access to a low cost scope in these areas may overcome the lack of availability, but only if it is compatible with the guidelines. The Ascope2 is limited in the unexpected difficulty because of the issues with an Aintree catheter- although it could be used effectively to place an endotracheal tube by a skilled operator in an unexpected difficult airway situation- and in a remote site where there would have to be a delay in obtaining the reusable equipment a rapidly available	

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		device may be best Importantly, in unexpected difficulty the primary aim is oxygenation rather than intubation and the Ascope2 does not change that. **Expert 3:** I would agree with this view, in environments such as intensive care and theatre recovery areas. **Expert 4:** Probably not an unreasonable comment, although potentially self defeating: if planning to stock areas where an unexpected difficulty may arise then it is not strictly unexpected and perhaps ordinary FE should be available. More generally: from the outset of this NICE evaluation I have repeatedly stated that if there is value in aScope it lies in its making FE available at minimal start up and maintenance costs compared with the reusable devices. This has potentially the effect that it can make reasonable the aim of having FE so widely available that its use as a technique of airway management becomes extremely commonplace and	

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		hence is used earlier and more often. This would match the recommendations of NAP4. The obsession with directing the NICE evaluation / investigation at "unexpected" difficulties is a distraction and complication in an otherwise useful exercise.	
	Question to Expert Advisors (Consultant anaesthetists / Consultant in Respiratory & Critical Care Medicine): Are there any clinical arguments for preferring the Ambu aScope in this situation? To put this another way, if not costs were equal, then would Ambu aScope2s be preferable? We think the answer is 'no', given the above, but would like your opinion.	**Expert 1**: In an emergency, if I was offered an aScope AND a conventional high end scope simultaneously, I would choose the high end scope. In my view, the advantage of the aScope is its immediate availability. **Expert 2:** If costs were equal, the benefit of the Ascope2 is its rapid assembly and availability (plug and play, no white balance required). It also has certain advantages in the ICU where the scope cannot be damaged (like a reusable scope) during the performance of a percutaneous tracheostomy **Expert 3:** If a standard video scope was immediately available in an emergency situation I would choose it	Comments taken into account in the EAC's assessment of the clinical effectiveness data and the economic model

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		over the Ambu aScope. I do not think the Ambu aScope would be preferable compared with a standard scope given a level playing field of access to the equipment. **Expert 4**: There is no reason to prefer the aScope over a well maintained high end reusable FE which these days is likely to have a video chip at the tip and to not rely on fiberoptics for image transmission. These are relatively easy to manage in terms of connecting up to a monitor and generating an image. The picture quality from them would be better and the handling of the device better, however again ready availability is an issue.	
	Question to Expert Advisors (Consultant anaesthetists / Consultant in Respiratory & Critical Care Medicine): Does the standard scope have any other uses apart from facilitating difficult intubation and dislodged tracheostomy?	**Expert 1:** Better optics and suction are usual advantages. The standard scopes are usually thinner and can be used with alternative difficult intubation devices such as the Aintree catheter. The current aScope is too wide for this use. **Expert 2:** This is where the fibreoptic laryngoscope differs from a fibreoptic bronchoscope- Uses are	Comments taken into account in the EAC's assessment of the clinical effectiveness data and the economic model

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		essentially the placement of a tracheal tube or tracheostomy tube and the replacement of same, but I have also used the devices to inspect the airway and check tube placement. Nasendoscopy and tracheoscopy are specifically recommended in NAP4. The latter may be required urgently to confirm tracheal occlusion by blood clot in the absence of detectable CO2. **Expert 3:** The standard video bronchoscopes are diagnostic and therapeutic instruments. They allow inspection of the airways for mucosal and structural abnormalities. They allow diagnostic sampling of the airways in terms of bronchial biopsies, bronchial brushing, washing and bronchoalveolar lavage. This is an essential component particular for the patient intubated and ventilated on an intensive care unit. The standard video bronchoscopes allow suction of the airways with an adequate suction channel to remove secretions and mucus plugs. **Expert 4:** Yes, can be used for assisting percutaneous tracheostomy and diagnostic and or	

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		therapeutic bronchoscopy, including bronchial lavage and biopsy. (note that the devices aimed at working in the bronchi have a much larger external diameter to accommodate the larger working channel and they have a more flexible section above the steerable tip, and are hence less ideal for tracheal intubation).	
	Question to Expert Advisors (Consultant anaesthetists / Consultant in Respiratory & Critical Care Medicine): Are there any particular difficulties in cleaning or sterilising standard scopes?	**Expert 1:** As alluded to above. It takes 1 hour minimum and up to 4 hours for a scope to be taken to the decontamination suite, cleaned, packed up and returned to our local drying cabinet. This service is available in our Trust from 9-6 weekdays and 9-3 weekends. If we use a scope at 3pm on a Saturday, we won't get it back until 11am Sunday for example. This is why we have spares (cost around £10k each). If we use 2 scopes out of hours, we have to then borrow from nearby theatres etc which adds delays in emergency. We have also had a recent incident where the wrong scope was bought from the cabinet in an emergency (a bronchoscope which was too big for intubation, followed by a battery powered scope where the battery was missing. The scope we needed had a small mains powered light	Comments taken into account in the EAC's assessment of the clinical effectiveness data and the economic model

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		source which was eventually located, but we used the aScope in the meantime). These are local examples but I think our ICU is representative of the problems associated with scope availability. **Expert 2:** Standard scopes must be leak tested prior to cleaning, as cleaning a damaged scope will cause further damage. Unless kept appropriately (HEPA Cabinet) a 'clean scope' will be officially unclean after 4 hours whether used or not. Repeated cleaning of reusable scopes will shorten their working lifespan There are infection control issues over prion diseases Regular cleaning of scopes on Difficult Airway Trolleys is therefore necessary even if they are not used. It would be very convenient and probably quite cost effective if we could leave a packaged sterile disposable scope on such a trolley- however such a scope must be compatible with the guidelines.	

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		Expert 3: I do not believe there are any particular difficulties in cleaning or sterilising standard scopes. As described above it is access to a clean scope particularly out of hours. Because of requiring robust infection control and prevention procedures most standard scopes will be cleaned and sterilised in a central cleaning unit for all endoscope equipment. There is usually a reasonable turnaround time of a less than an hour at the point it is required within working hours. Out of hours a standard scope is usually left packaged sterilised and stored in a central store to be collected when required. There would therefore be a potential delay in an emergency situation by not having access to a clean scope in an instant for an emergency airway problem. In all other less urgent situations there is usually time to wait for a standard scope to be collected. **Expert 4:** Just expense, equipment and staff. When used in patients with possible transmissible encephalopathies (e.g. nVCJD) they must be quarantined until diagnosis is certain and then	

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		destroyed.	
	Question to Expert Advisors (Consultant anaesthetists / Consultant in Respiratory & Critical Care Medicine): Are there any material differences between the standard scopes deployed in this country? Is there any particular type that is particularly suitable/unsuitable in use?	**Expert 1:** Yes. Features that vary include: Size Suction Extra working channel (unusual in these small scopes) Optical quality Eye-piece, connected to a 'stack' (lightsource and monitor) or a small screen attached to the 'scope itself Durability – some makes are notoriously easy to damage Support from the company – eg if it breaks, how quickly can we get a replacement / repair. These are delicate and are used (with tracheostomy placement at least) in the vicinity of needles and devices that can puncture or injure it. **Expert 2:** Subtle differences exist but scopes compatible and between video systems and glass fibrescopes however in a recent procurement	Comments taken into account in the EAC's assessment of the clinical effectiveness data and the economic model

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		exercise that I was involved in we specifically rejected the reusable scope that could not be used in conjunction with an Aintree catheter even though the image quality was better. **Expert 3:** Most modern standard scopes are video-scopes with excellent image resolution. They vary in terms of size (diameter) and channel size. This relates to their diagnostic and therapeutic capabilities. In general the thinner scopes allow inspection of more distal airways whereas the larger the channel size allows for improved suction and therapeutic sampling such as larger biopsy forceps. There are still some scopes in use which are fibre-optic and require the operator to look down the scope to see the image or have a camera adaptor to allow projection t a monitor. In the former situation it is not recommended for the operators head to be directly over to avoid splashing of respiratory secretions into the eyes. The use of camera adaptors to slave an image to a monitor results in degradation of the image quality. The fibre-optic scopes therefore should no longer be used. The	

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		video monitor attached to the Ambu a Scope provides an excellent image and does not require the user to “look down” the scope. **Expert 4:** Devices may be fiberoptic based or video chip based, the latter are newer better and more expensive currently. Otherwise little to choose.	
	Question to Sponsor: Question 1: Report Section 4.5 (page 30) mentioned 1600 units of Ambu aScope have been purchased in England since late 2009. **How many units have been sold worldwide?**	**Sponsor:** Please find the overview of our global sales figures for aScope 1 and aScope 2 enclosed (See Appendix 6). It is broken down in our business regions as well, and based on unit sales.	
	Question to Sponsor: Question 2: Literature search strategy seems okay, but it is still unclear whether all unpublished and ongoing studies have been identified. Our rapid review has identified one trial and two	**Sponsor:** The mentioned trial refers to the randomised controlled trial (ACTRN12611001235998), comparing the Ambu aScope with conventional fibreoptic bronchoscope in asleep orotracheal intubation of adult patients undergoing general anaesthesia, as listed on Australian New Zealand Clinical Trial Registry (ANZCTR;	

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	abstracts which were not included in the submission. “Randomised controlled trial comparing the Ambu aScope with conventional fibreoptic bronchoscope in asleep orotracheal intubation of adult patients undergoing general anaesthesia (ACTRN12611001235998)”. The technology is new and most relevant studies may be sponsored or supported by Ambu Ltd. **Can Ambu Ltd please provide us with a complete list of all published, unpublished and ongoing studies of aScope or aScope2 that they have supported or sponsored.**	http://www.anzctr.org.au/trial_view.aspx?id=347774). At the time of the last update in February 2012, the stated date of first participant enrolment was 1st December 2011; however, the recruitment is still not initiated. Therefore, no data are available. Ambu A/S, Denmark, is a secondary sponsor of this study. After having two abstracts handed out at a personal meeting June 15th and sought the cause for not having informed about these publications, we want to clarify that the two abstracts refer to articles by Scutt et al. (Anaesthesia. 2011;66(4):293-9) and Piepho et al. (Anaesthesia. 2010;65(8):820-5) that are included in the submission (See Appendix 4). Since the technology is new, independent investigators do initiate studies without our knowledge; thus, there may appear studies we are not aware of. The list of studies presented in the updated overview, represent to our knowledge, all the studies performed and on-going with Ambu aScope.	

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	Question to Sponsor: The submission identified “six randomised studies and five observational studies”. However, Kumar 2011 and Vijayakumar 2011 reported data from the same study. It is essential that the number of “studies” should not be confused with the number of “publications”. **A check of duplicates and multiple publications of the relevant studies should be conducted.**	**Sponsor:** The two publications, Kumar 2011 (abstract) and Vijayakumar 2011 (full article), do indeed report data from the same randomised crossover study. We are sorry about this mistake. We have checked the rest of the data and have also been informed of two studies “Evaluating the Ambu aScope and alternative approach to endoscopic monitoring during percutaneous dilatational tracheostomy” by Austin and “First experience with the single-use Ambu aScope for fibreoptical monitoring in percutaneous dilatation tracheostomy” by Gernoth sharing some data from the same patients. However, the Austin study has extended the trial with a larger number of cases and endpoints. Additional duplicates/multiple publications have not been identified.	
	Question to Sponsor: Lenhardt 2011 is the largest study of identified studies that used aScope or aScope2 in real patients with difficult airways. The number of patients used	**Sponsor:** Dr. Lenhardt is not interested at the moment to share the raw data of the study due to copyright issues, since he is in the process of submitting the publication to a peer-reviewed journal (Please see our correspondence with Dr. Lenhardt in Appendix 8). Correspondence is initiated in order to	

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	aScope in Lenhardt 2011 (n=70) was much greater than the total number of patients in all other studies (n=43). However, results of Lenhardt 2011 are only reported in an Abstract (plus its protocol). Data reported in the abstract was very limited and no mention of safety and adverse effects. It seems that the Lenhardt study has been completed sometime ago and the internal report has been prepared. It is important for us to have full data from this study. **Can Ambu Ltd please provide us with the full report of Lenhardt et al. 2011 study (published or unpublished, as for the Kristensen study)?**	obtain Dr. Lenhardt's consent to be contacted.	
	Question to Sponsor: Can Ambu Ltd please provide us with the full data on Vincent et al. 2011 (8 patients included)?	**Sponsor:** This is an independent study, and Dr Ahmed, the contact person of the study, has not responded to our request to the full data set (see Appendix 9).	

Please see Appendix 3.1 for additional comments from Expert 2.

Additional comments from Expert 2

Piepho, Werner and Noppens:[1]

1) It is not clear whether it the aScope or the aScope2 that is being evaluated in this article, although the acceptance date of April 2010 and the use lief of 30minutes make it more likely to be the aScope

2) Their choice of a size 8.0 tube in a mannequin is interesting and may have added unduly to the difficulty

3) One of the key differences between the aScope and the aScope2 is the response time on the monitor- one wonders if the slower time with the aScope was at least in part due to the slow response time of the aScope- I have no absolute data for this

4) The failure rates in the diffficult scenario are difficult to understand, this was a mannequin study, the operators have all reported having done a large number of fibreoptic intubations previously and yet they even fail with the reusable scope...

5) small studies like this must be considered in the light of Pandit's editorial [2]

Summary of this study: Small time difference in mannequins which is unlikely to be clinically relevant, identified known features of the scope, some of which - image response time and secretions on the lens may have been corrected for by the aScope2

Vijayakumar, Clarke Wilkes et al [3]

Again, given an abstract of this work was presented in September 2010, unclear whether Ambu aScope or aScope2 being discussed- but again the discussion of a limited chip time to 30 minutes makes the aScope more likely

The correspondence generated by this article merits consideration- to show the present variation in opinion [4]

Although both studies show a time difference between the two scopes, it would not appear to be terribly clinically significant- only 5 real patients were included and their intubations were not timed.

The important features when doing an awake fibreoptic intubation are

1) Patient Preparedness (adequacy of topcialisation)

2) Skilled assistance

3) View

4) Operator skill

5) Attributes of the scope

What would appear to be missing for the Ascope2 is a large patient series in the literature from which conclusions might be drawn.

References

1. Piepho, T., et al. (2010). Anaesthesia; 65: 820-825. doi: 10.1111/j.1365-2044.2010.06406.x.
2. Pandit, J. J. (2012). Anaesthesia; 67: 578–583. doi: 10.1111/j.1365-2044.2012.07155.x.
3. Vijayakumar, M. (2011). Anaesthesia; 66: 689–693. doi: 10.1111/j.1365-2044.2011.06761.x.
4. Anaesthesia. (2011). Comparison of Ambu aScope and Olympus re-usable fibrescope: Responses. Available at: http://www.respond2articles.com/ANA/forums/thread/902.aspx?vol=66&iss=8&art=320772 (accessed 19th July 2012).
5. 4th National Audit Project of the Royal College of Anaesthetists and The Difficult Airway Society. (2011). Major complications of airway management in the United Kingdom. Report and findings, March 2011. Cook, T.M., et al. (editors). Available at: http://www.rcoa.ac.uk/node/4211 (accessed 19th July 2012).
6. Jeffrey, A. S., et al. (2011). European Journal of Anaesthesia; 28: P232P.

Appendix E: Sponsor's factual check of the assessment report and the External Assessment Centre's responses

National Institute for Health and Clinical Excellence

Centre for Health Technology Evaluation Assessment Report fact check response

Ambu aScope2 in unexpected difficult airways management

The External Assessment Report was reassessed so there are two fact checks from **July 30th 2012** and **October 1st 2012**

July 30th 2012

Issue 1

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC Action
Page 5, section 1.1. "The population was patients with unexpected difficult airways requiring emergency intubation	We propose that the last sentence: "The evidence submitted therefore may not apply to the scope population." is removed or rephrased.	The intended use of Ambu aScope2 is "*as an aid in the placement of an Endotracheal Tube (ETT) directly or through an intubating laryngeal mask during non-difficult and difficult intubation procedures or for a tracheostomy tube during percutaneous tracheostomy procedures*". Therefore the clinical evidence presented for	We agree that it is difficult, if not impossible, to conduct clinical studies of patients with unexpected difficult airways or patients with displaced tracheostomies. Because of a lack of directly relevant research evidence,

including awake or anaesthetised patients with displaced tracheostomies", and "adults or children evaluated for endotracheal tubes size 6 or above." Later, it is written: "The clinical evidence came from studies of manikins or patients with expected (or simulated) difficult airways and from case series of patients requiring percutaneous dilatational tracheostomy. The evidence submitted therefore may not apply to the scope population."		tracheotomy consists of cases series where aScope was used to visualize PDT procedures. While the data submitted does not present specific cases of displaced tracheotomy, the use of flexible endoscopes to check position of tracheal/ tracheostomy tubes and assist with fibreoptic intubation or percutaneous tracheostomy placement is recommended by the NAP4 report as one of the means to decrease the risk of complications [1]. Thus, we believe that the clinical data submitted for PDT is still relevant, and in any case, a fair clarification of why clinical evidence of displaced tracheotomies is not available shall be allowed. Moreover, we would like to remind that the incidence of complications for both surgical and percutaneous tracheostomies are reported to be as high as 5% during insertion, and include displacement, bleeding, pneumothorax and, later infection [1]. Thus, running a prospective clinical investigation of unexpected difficult airways is problematic. [1] Report and findings of the 4th National Audit Project of The Royal College of Anaesthetists. 2011, page 128	subjective judgment is required to decide whether evidence from studies of manikins, patients with expected difficult airways, or patients requiring PDT is completely relevant to patients with unexpected difficult airways or patients with displaced tracheostomies. The last sentence is appropriately evidence based. However, it may be revised as: "The evidence submitted therefore may not fully apply to the scope population".

Issue 2

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC Action
Page 5, section 1.1 "The clinical evidence came from studies of manikins or patients with expected (or simulated) difficult airways and from case series of patients requiring percutaneous dilatational tracheostomy. The evidence submitted therefore may not apply to the scope population."	We propose that the last sentence: "The evidence submitted therefore may not apply to the scope population." is removed or rephrased.	The case series of Phiepo et al. (2010) reports two unexpected difficult airways, which were satisfactorily intubated with Ambu aScope. While the number of unexpected difficult airways might be considered low by the reviewers, we would like to remind that the incidence of expected difficult airways is low, and the incidence of unexpected difficult airways is even lower (See note). Thus, running a prospective clinical investigation including large amount of unexpected difficult airways is problematic. To our knowledge, there have not been published large prospective studies involving unexpected difficult airways and studies based on expected difficult airways are considered a fair representation of unexpected difficult airways. Thus, the sponsor considers that the provided clinical data regarding performance and safety of Ambu aScope does apply to the scope population. ____ Note: NAP4 (1) reports difficulty with tracheal intubation to be expected in 1% cases of general population (Page 56). It is also reported that from the 133 anaesthesia reports analyzed, difficulty with airway management was expected in 66 and not expected in 67 (Page 139). 1. Report and findings of the 4th National Audit Project of The Royal College of Anaesthetists. 2011.	See EAC Action about Issue 1.

Issue 3

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC Action
Page 5, section 1.1. Page 6, section 1.3. Page 14, section 2.3.4 "The outcomes measured were mainly concerned with intubation, and there was no direct evidence regarding clinical consequences or safety issues associated with the use of Ambu aScope."	We propose the following: "The outcomes measured were mainly concerned with intubation, but in some studies data of clinical consequences and safety issues associated with the use of Ambu aScope is provided."	Kristensen et al (2011) (being prepared for publication), measured hemodynamic data before and after the intubation procedure (blood pressure, heart rate, SpO2, FiO2), the occurrence of adverse events during the procedure (emergency airway, larynx and bronchospasm, coughing), injuries related to the intubation procedure (blood in trachea, visible injury on airway mucosa), and events after the endoscopic procedure (coughing, injury to the tong, injury to the lips, damages to the teeth). In the sponsor's opinion, these are end points related to clinical consequences and safety associated to the use of aScope. Moreover, end points such as intubation success and intubation attempt have been measured in several of the studies reported. In the opinion of the sponsor, these parameters are also related to safety.	According to the final scope, the relevant outcomes include clinical consequences associated with delayed or failed intubation, including death, hypoxic brain injury, and length of stay in ICU and hospital. There is no direct evidence on these clinical consequences, although some studies provided data on device-related adverse events. To provide further details, the (pg 5) sentence can be revised as: "The outcomes measured were mainly concerned with intubation, and some device-related adverse events. However, there is no direct evidence regarding serious clinical consequences, including death, hypoxic brain injury, length of stay in Intensive Care Unit (ICU) and hospital associated with the use of Ambu aScope". The (pg 6) sentence can be revised as: "There is no direct evidence on serious clinical consequences, including death,

			hypoxic brain injury, length of stay in Intensive Care Unit (ICU) and hospital with the use of Ambu aScope." The (pg 14) sentence can be revised as: "However, there is no direct evidence regarding serious clinical consequences, including death, hypoxic brain injury, length of stay in Intensive Care Unit (ICU) and hospital, associated with the use of Ambu aScope."

Issue 4

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC Action
Page 6, section 1.3. It is written: "Very few patients with unexpected difficult airways were included in the studies, thus failing to demonstrate applicability of results to such patients"	We propose to delete: "thus failing to demonstrate applicability of results to such patients."	(See Issue 2).	This statement is evidence based.

Issue 5

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC Action
Page 6, section 1.3. "…the EAC found two additional RCTs that compared Ambu aScope2 with a reusable fibreoptic bronchoscope. One, which was published as an abstract, studied 100 patients with simulated difficult airway…while the second study is still ongoing." Same inaccuracy is written in: page 12, section 2.2 page17, section 3.1.1.2 page 19, section 3.1.3 page 20, section 3.3.1 page 23, table 3.1 page 24, section 3.3.3 page 27, section 3.5 page 32, section 3.6.2 page 33, table 3.6	We propose that the first sentence is rephrased to: "the EAC found one additional RCT which was a study still ongoing".	The first RCT being referred to is the study performed by Schoettker et al. (2012), presented at ESA June 12th 2012. On June 15th at the meeting between EAC and Ambu hosted by NICE, the poster was personally handed to the EAC by Ambu (Clinical Research Specialist Sanne Wille). For reference, please also refer to email correspondence sent 25-06-2012 at 12:45 to Joanne Burnett with the EAC members as cc. Additional information: At ESA Ambu's Clinical Research Specialist, Torben Frost, spoke to the author, which Ambu had not been in contact with previously since the study was driven independently without Ambu's knowledge. The author is in the process of preparing a manuscript with the purpose of submitting for publication, and at the moment is not interested in sharing for publication reasons.	The abstract by Schoettker et al was identified by EAC before the meeting on June 15th 2012. The sentence can be revised as: "…the EAC identified one additional RCT, which was a study still ongoing. In addition, the EAC found an abstract of a RCT (described as an ongoing study in the sponsor's submission) that compared Ambu aScope2 with a reusable fibreoptic bronchoscope in patients with simulated difficult airway."

Issue 6

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC Action
Page 6, section 1.4. "The cost of Ambu aScope2 was £179 per single use scope, and the cost of a reusable scope was £174 per patient/treatment"	We propose the sentence is rephrased to: "The cost of Ambu aScope2 was £179 per single use scope, and the cost of a reusable scope was £209 per patient/treatment"	It is not an appropriate comparison, since the costs for reprocessing have been omitted from the reusable scope estimate. The appropriate figure for this comparison is as per table 4.3 of the EAC report which presents costs for the base case as £179 for aScope2 and £209 for reusable scopes	The sentence revised as: "The cost of Ambu aScope2 was £179 per single use scope, and the estimated mean cost of a reusable scope from NHS survey was £209 per patient/treatment"

Issue 7

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC Action
Page 7, section 1.6 "The clinical evidence is limited in terms of patients included, interventions evaluated, and outcomes measured".	We propose that the sentence is rephrased or eliminated.	Patients: When studies involving patients with difficult airways are considered, the total amount of clinical data reported is from 300 patients (table 3.1 and 3.2 of the assessment report). Considering the incidence of difficult airways (see issue 2), the sponsor considers this as a fair amount of clinical data for the mentioned patient population.	This sentence is appropriate. There is a lack of studies of patients with unexpected difficult airways. The revised version Ambu aScope2 was evaluated in only one controlled study (n=50) and

		Interventions: The interventions evaluated as relevant for this submission are 2: intubation and PDT. Studies related to other interventions (e.g. verification of DLT position, combination with SGA, combination with VLS) were considered not applicable by the reviewers since the interventions do not apply to the submission. Thus, it is not clear for the sponsor, what other interventions should have been included. Outcomes: Outcomes related to intubation performance, safety and clinical consequences of using aScope have been measured (see issue 3).	in two case series (total N=18). There is no direct evidence regarding the use of Abmu aScope2 on serious clinical consequences, including death, hypoxic brain injury, length of stay in ICU and hospital.

Issue 8

Description of factual inaccuracy	**Description of proposed amendment**	**Justification for amendment**	**EAC Action**
Page 11, section 2.1. "One drawback of the	We propose the following: "Due to its insertion	1. Misspelling: 'Aintree' not 'Ainslee' 2. All manufacturers of fiberscopes have scopes of different diameters. We are aware that aScope2 cannot be used with an Aintree catheter. [redacted]. However, aScope2 can be used with most difficult airway intubation devices as SAD for intubation, stylets and videolaryngoscopes.	The sentence was revised as: "Due

Ambu aScope, however, is that given its size, it cannot be used with other difficult intubation devices. For example, an Ainslee catheter cannot be placed over the Ambu aScope, meaning that a low-skill fibreoptic	cord diameter, the Ambu aScope 2, cannot be used with an Aintree catheter.”	In addition, I the sponsor’s opinion using an Aintree catheter for intubation is not ‘low skill’ since it is introducing another piece of equipment in the procedure.	to the insertion cord diameter the Ambu aScope2 cannot be used with some other intubation devices. For example it cannot be used with the Aintree

intubation, which is learnt by all anaesthetists, cannot be used”			catheter, a relatively low-skill intubation device.”

Issue 9

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC Action
Page 12, section 2.2 **“**During searches of the European Society of Anaesthesiologists meeting abstracts the EAC also identified an abstract in which the results of trial NCT01467739 were presented (Schoettker et al. 2012). Therefore, there would appear to be some results available for both of the two ongoing trials identified by	We propose to delete both sentences.	- NCT01467739, please see issue 5 - NC01215695. As documented in the submission of clinical evidence the author, Dr. Lenhardt was contacted but is not interested in sharing his data due to publication copyright reasons.	The two sentences are accurate. Also see response to issue 5.

the sponsor, together with an additional study which they did not identify".			

Issue 10

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC Action
Page 13, section 2.3.1 "None of the available trials included patients with unexpected difficult airways, and no studies were explicitly conducted in Accident and Emergency (A&E) departments. Therefore, it is uncertain whether the results of the included studies could be applied to	We propose to replace the sentence underlined, with the following sentence: "The case series of Phiepo et al (2010) presents evidence of 2 unexpected difficult airways." Moreover, we propose to delete the sentence: "Therefore, it is uncertain whether the results of the included studies could be	See issue 2 for discussion of data of unexpected difficult airways and the validity of predicted difficult airways data. It is correct that none of the studies were performed in A&E Departments. However, this does not mean in the sponsor's opinion, that patients with unexpected difficult airways cannot be considered an emergency, despite there are intubated at the operating room.	The sentence underlined is accurate, but it can be revised as: "None of the available controlled trials included patients with unexpected difficult airways, and no studies were explicitly conducted in Accident and Emergency (A&E) departments." The last sentence is appropriate and evidence based.

“patients with unexpected difficult airways requiring emergency intubation including awake or anaesthetized patients with displaced tracheostomies”, as specified in the final scope”.	applied to “patients with unexpected difficult airways requiring emergency intubation including awake or anaesthetized patients with displaced tracheostomies”, as specified in the final scope.”		

Issue 11

Description of factual inaccuracy	**Description of proposed amendment**	**Justification for amendment**	**EAC Action**
Page 13, section 2.3.3 “The final scope by NICE specified the comparators as “multiple-use flexible endoscopes (fibrescopes using fibre-optic technology or video scopes using video technology)”. In the controlled trials obtained, the comparators used were reusable flexible optical	We propose to delete the final sentence: “Thus, only two RCTs are relevant (Kristensen 2011; Schoettker et al. 2012).” Furthermore, we	Lenhardt’s description of the clinical problem addressed in his study is that, in difficult airway cases (expected or unexpected) intubation may fail even with a VLS despite the use of rigid or malleolable stylets. “The reason is that the inflexible tip of these stylets may make it difficult to position the tube in front of the glottic opening. Thus, the operator may visualize the glottis, but may be unable to pass the tube through the vocal cords.” [Text extracted from Lenhardt poster ASA 2011]. The hypothesis of Lenhardt et al. (2011) is that the combined use of a VLS and a flexible scope may provide a higher intubation	The final sentence accurately reflects the fact that the comparator used in Lenhardt trial (preformed rigid stylet) was different from the relevant

scopes that are commonly used in the UK (manufactured by Storz, Pentax or Olympus). However, in one of the studies included in the submission (Lenhardt et al. 2011) Ambu aScope was combined with a GlideScope video laryngoscope (GVL), and compared with a combination of GVL and a pre-formed rigid stylet. In effect, the Ambu aScope was compared to a rigid stylet, which is not the relevant comparison as set out in advance. Thus, only two RCTs are relevant (Kristensen 2011; Schoettker et al. 2012)".	propose that the study of Lenhardt et al. is taken into consideration as clinical relevant evidence.	success. In fact, his results showed that 4 patients could not be intubated with the VLS and rigid stylet, and were subsequently intubated using the flexiblescope (aScope). In the sponsor's opinion, this is a relevant clinical application of the aScope (or any flexible scope) and a clinical relevant investigation, since any procedure that may increase the intubation success in difficult airways is of high importance. This study includes 140 difficult airways, which is one of the largest studies published on the field involving difficult airway patients, and it does provide valuable evidence of the use of aScope in the population scope of this submission.	comparators (multiple use flexible endoscopes) described in the final scope.

Issue 12

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC Action
Page 16,		In our experience, when developing a search strategy that includes very broad key	

section 3.1.1.1. "The decision not to use index terms such as MeSH Medical subject headings is not explained."		words, such as 'endoscope' and 'difficult airways', it is important to develop a search string that will find all of the relevant papers without giving rise to a vast amount of irrelevant results that will require manual screening. This manual process is prone to human error and key papers may be missed. When initially developing the search strategy, we tested a number of different search strings, including and excluding various search terms, and found that using generic terms, such as 'endoscope' gave rise to too many results to be feasible to manually process within the timeframe allotted. We therefore spent time crafting a search string, with appropriate wild-cards and truncations (i.e. *), to strike the right balance between ensuring that we captured the information we were looking for and minimising redundancies. We are pleased that the EAC found our search terms choice to be appropriate and that they have noted that truncation has been employed to capture a range of word endings and thus broaden the search.	

Issue 13

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC Action
Page 17, section 3.1.1.2 "However, the sponsor did not conduct a search of the UK Medicines and Healthcare Products Regulatory Agency (MHRA) safety database, as	We propose to delete the final sentence	MHRA safety database was searched, and in the original declaration from Ambu Regulatory affairs it is stated:" Ambu aScope System has not caused nor contributed to any adverse events nor has Ambu aScope System been subject to any recalls as evaluated according to EU MEDDEV 2.12/1 rev-7 Medical devices vigilance system". Pdf-document was submitted together with the clinical evidence. Above is identical with FDA and MHRA due to being	Proposed amendment accepted. Final sentence deleted.

recommended by the NICE template".		aligned with Meddev.	

Issue 14

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC Action
Page 17, section 3.1.2. "However, the sponsor did not provide the individual search strategies for MEDLINE, EMBASE, MEDLINE In Process, and Cochrane's CENTRAL in the appendix – instead there is only a combined strategy for MEDLINE and EMBASE.		The same search terms were used for MEDLINE, MEDLINE In Process and EMBASE: all of which were searched using an Ovid search algorithm (details of which were provided in the Appendix of the NICE submission). The simultaneous searching of MEDLINE and MEDLINE In Process was based on the search strategy documented in appendix.	

Issue 15

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC Action
Page 22, table 3.1.	We propose the	Ambu provided the trial with aScope's and the	Proposed amendment accepted.

“Sponsor, unclear”	following: “Equipment partly provided by Ambu”.	SAD “Aura-I”, but did not support with FastTrach from LMA.	Thank you for clarifying the sponsorship for this ongoing study.

Issue 16

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC Action
Page 47, section 4.7.4, figure 4.3 The model presents two arms and labels one arm as 'Reusable aScope'. Having discovered this error, we also note that the model appears to contain further errors. In fact the EAC proposed model is incomplete and apparently illogical.		Where reusable scopes are available in the EAC model, outcomes of successful intubation and failed intubation are modelled with failed intubation leading to harm or no harm to patients. However, in the event that a scope is not available, the EAC model does not include intubation outcomes. This appears to be an error – since where a fibrescope is not available, other methods of intubation would be certainly be attempted in order to ventilate the patient.	Thank you to the sponsor for pointing out the error. It has been re-labelled as "reusable scope". We accepted the model was not clearly labelled and described, which caused confusion. It is actually that when a scoped is not immediately available, and it caused delayed intubation. A clearer labelled schematic diagram has replaced the original one.

Issue 17

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC Action
Page 49, section 4.7.6.1 "In the sponsor model	We propose the sentence is rephrased to: "..they were not able to present separate analyses for the two types of	There appears to be a typo in this sentence – we were not able to distinguish between fibrescopes and videoscopes	Thanks for this. We corrected the typo. "In the sponsor model the sponsor stated that they were not able to present separate

the sponsor stated that they were able to present separate analyses for these two types of technologies. Average costs of equipment over the survey centres were used in their model. This uncertainty was explored in sensitivity analyses".	technologies, fibrescopes and videoscopes".		analyses for the two types of technologies, fibrescopes and videoscopes. Average costs of equipment over the survey centres were used in their model. This uncertainty was explored in sensitivity analyses".

October 1st 2012

Issue 1

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC Action
Page 19, section 3.1.1.2 "Searches by the EAC identified an additional item (Schoettker et al. 2012) via the ESA annual meetings online, which does not appear to be listed by the sponsor." Same inaccuracy is written in: Page 21, section 3.1.3 Page 22, section 3.3.1 Page 25, section 3.3.1, table 3.1 Page 26, section 3.3.3 Page 27, section 3.4 Page 29, section 3.5.1 Page 35, section 3.6.2, table 3.6	We propose the sentence is eliminated	It is our understanding from answer to issue 5 of previous EAC report, that EAC acknowledges Ambu identified and delivered the Schoettker study; however, it is still stated in several sections that EAC identified the study. The study was presented at ESA June 12th 2012. June 15th at the meeting with EAC and Ambu hosted by NICE, the poster was personally handed to the EAC by Ambu (Clinical research Specialist Sanne Wille). For reference, please also refer to email correspondence sent 25-06-2012 at 12:45 to Joanne Burnett with the EAC members as cc.	Text on noted pages changed to include the fact that the sponsor subsequently provided the abstract, due to the presentation being made after the initial submission of evidence.

Issue 2

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC Action
Page 8, section 1.6 "It is possible that Ambu aScope2 will be more readily available because they do not need to be cleaned or linked to a monitor."	"It is possible that Ambu aScope2 will be more readily available because they do not need to be cleaned. It only needs to be connected to the corresponding monitor".	The aScope device in itself doesn't have possibility of visualization. It is mandatory that it is connected to a monitor.	Accepted and changed as proposed.

Issue 3

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC Action
Page 13, section 2.2 "The sponsor is also aware of a further ongoing study (Hagberg, University of Texas), which is detailed in Section 5.1 and which compares performance of optical intubation with blind intubation. The trial is not listed in ClinicalTrials.gov, ISCTRN database, or WHO ICTRP and thus the EAC assumes this information is only available in-house to the sponsor."	We propose: "The sponsor is also aware of a further ongoing study (Hagberg, University of Texas), which is detailed in Section 5.1 and which compares performance of optical intubation with blind intubation (listed in ClinicalTrials.gov identifier NCT011656967)."	Now registered. Please refer to an update of clinical evidence send to NICE's contact persons August 15th 2012.	Accepted and changed as underlined: "The sponsor is also aware of a further ongoing study (Hagberg, University of Texas), which is detailed in Section 5.1 and which compares performance of optical intubation with blind intubation (this is now listed in ClinicalTrials.gov, identifier NCT011656967)."

Issue 4

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC Action
Page 23, section 3.3.1 "Furthermore, the sponsor submission mentioned three ongoing studies that were relevant (ClinicalTrials.gov Identifier: NCT01467739, ClinicalTrials.gov Identifier: NCT01215695, and Hagberg's on-going study)."	Furthermore, the sponsor submission mentioned three ongoing studies that were relevant (ClinicalTrials.gov Identifier: NCT01467739, ClinicalTrials.gov Identifier: NCT01215695, and NCT011656967.	Now registered. Please refer to an update of clinical evidence send to NICE's contact persons August 15th 2012.	Accepted and changed as underlined: "Furthermore, the sponsor submission mentioned three ongoing studies that were relevant (ClinicalTrials.gov Identifier: NCT01467739, ClinicalTrials.gov Identifier: NCT01215695, and ClinicalTrials.gov Identifier: NCT011656967 [now registered])."

Issue 5

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC Action
Page 23, table 3.1. Patient-based studies, Kristensen,2011,(R-PS-7-2009) Setting(country): "Unclear, Denmark"	Setting (country): "OR, Denmark"	The setting is OR.	Accepted and changed as proposed.

Issue 6

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC Action
Page 23, section 3.3.1, table 3.1. Patient-based studies, Kristensen,2011,(R-PS-7-2009) Subjects: “N=40 Patients for elective or acute ENT surgery: awake patients with difficult airway and anaesthetised/ sleeping patients with normal airway.”	Subjects in total: N= 60 All patients for elective or acute ENT surgery. Part 1: 20 anaesthetised patients with expected normal airway Part 2: 40 awake patients with expected difficult airways	In total the study investigated 60 patients, 20 normal airways and 40 patients with difficult airways	Accepted and changed as proposed.

Issue 7

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC Action
Page 26, section 3.3.2 “The procedure was performed by a specialist at Ambu (Kristiansen 2011).”	“The report was written by a specialist at Ambu (Kristiansen 2011), and therefore, it was excluded from the submission.”	Please note that there was no procedure performed by the Ambu specialist. This is a white paper written by the Ambu Clinical Department (Author: Kristiansen), where we report the use of aScope in 3 difficult airways. Two expected and one unexpected difficult airway (a 59 years-old patient	Accepted and changed as proposed.

		scheduled for cholecystoscopy). We excluded the report from our clinical evidence, since the document was written by Ambu. The veracity of these cases can be confirmed.	

Issue 8

Description of factual inaccuracy	**Description of proposed amendment**	**Justification for amendment**	**EAC Action**
Page 35, section 3.6.2, table 3.6 Study: Kristensen, 2011 Patients with expected difficult airways, including anaesthetised/sleeping patients with normal airway: Ambu aScope N=20 Olympus N=20	Study: Kristensen, 2011 Sleeping patients with normal airways N=20/ all aScope Awake patients with expected difficult airways N=40: Ambu aScope N=20 Olympus N=20	We would like to clarify that it is a total of 40 cases of difficult airway, and 20 patients with normal airways	Accepted and changed as proposed.

Issue 9

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC Action
Page 47, section 4.3, table 4.1 "Study: Liu et al."	"Study: Liu et al. (2012)."	This study is published now in: Anesthesia & Clinical Research, Volume 3, Issue 5, 2012. Please refer to an update of economic evidence send to NICE's contact persons September 2012.	Accepted and changed as proposed. (Has also been changed throughout document.)

Issue 10

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC Action
Page 51, section 4.7.4 "However, stock control is not perfect at hospital or operating theatre/ward level, and so reusable devices equally might not be available after disposal."	"However, stock control is not perfect at hospital or operating theatre/ward level, and so single-use devices equally might not be available after disposal."	Statement contradicts pervious argument. If reusable devices are equally not available after disposable, then both device types face similar challenge.	Accepted and changed as proposed.