NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Medical Technologies Evaluation Programme

Sponsor submission of evidence:

Evaluation title: Ambu aScope2 for unexpected difficult airways management

Sponsor: Ambu Ltd

Date sections A and B submitted: May 28th 2012

Date section C submitted: June 25th

May 2012

Contents

Instructions for sponsors

This is the template for submission of evidence to the National Institute for Health and Clinical Excellence (NICE) as part of the Medical Technologies Evaluation Programme process for developing NICE medical technologies guidance. Use of the submission template is mandatory.

The purpose of the submission is for the sponsor to collate, analyse and present all relevant evidence that supports the case for adoption of the technology into the NHS in England, within the scope defined by NICE. Failure to comply with the submission template and instructions could mean that the NICE cannot issue recommendations on use of the technology.

The submission should be completed after reading the 'Medical Technologies Evaluation Programme Methods guide' and the 'Medical Technologies Evaluation Programme Process guide' available at www.nice.org.uk/mt. After submission to, and acceptance by, NICE, the submission will be critically appraised by an External Assessment Centre appointed by NICE.

Under exceptional circumstances, unpublished evidence is accepted under agreement of confidentiality. Such evidence includes 'commercial in confidence' information and data that are awaiting publication ('academic in confidence'). When data are 'commercial in confidence' or 'academic in confidence', it is the sponsor's responsibility to highlight such data clearly. For further information on disclosure of information, submitting cost models and equality issues, users should see section 11 of this document 'Related procedures for evidence submission'.

The submission should be concise and informative. The main body of the submission should not exceed 100 pages (excluding the pages covered by the template and appendices). The submission should be sent to NICE electronically in Word or a compatible format, not as a PDF file.

The submission must be a stand-alone document. Additional appendices may only be used for supplementary explanatory information that exceeds the level of detail requested, but that is considered to be relevant to the case for adoption. Appendices will not normally be presented to the Medical Technologies Advisory Committee when developing its recommendations. Any additional appendices should be clearly referenced in the body of the submission. Appendices should not be used for core information that has been requested in the specification. For example, it is not

acceptable to attach a key study as an appendix and to complete the economic evidence section with ‘see appendix X’.

All studies and data included in the submission must be referenced. Identify studies by the first author or trial ID, rather than by relying on numerical referencing alone (for example, ‘Trial 123/Jones et al.[126], rather than ‘one trial[126]’).Please use a recognised referencing style, such as Harvard or Vancouver.

The sponsor should provide a PDF copy of all studies included in the submission. For unpublished studies for which a manuscript is not available, provide a structured abstract about future journal publication. If a structured abstract is not available, the sponsor must provide a statement from the authors to verify the data provided.

If a submission is based on preliminary regulatory recommendations, the sponsor must advise NICE immediately of any variation between the preliminary and final approval.

Document key

Boxed text with a grey background provides specific and/or important guidance for that section. This should not be removed.

Information in highlighted black italic is to help the user complete the submission and may be deleted.

The user should enter text at the point marked ‘Response’ or in the tables as appropriate. ‘Response’ text may be deleted.

List of tables

List of figures

Glossary of terms

Term	Definition
A&E	Accident & Emergency
BMI	Body mass index
CICV	Can't intubate can't ventilate
ENT	Ear, nose and throat
ETT	Endotracheal tube
FOB	Fibreoptic bronchoscope
FOI	Flexible optical intubation
GERD	Gastro-oesophageal reflux disease
ICU	Intensive care unit
IFU	Information for users
ITU	Intensive treatment unit
LED	Light-emitting diode
PDT	Percutaneous dilatational tracheostomy
SAD	Supraglottic airway device
VAS	Visual analogue score
VRS	Verbal rating score

Section A – Decision problem

Section A describes the decision problem, the technology and its clinical context. There is also information about ongoing studies, regulatory information and equality issues.

Sponsors should submit section A before the full submission (for details on timelines, see the NICE document 'Guide to the Medical Technologies Evaluation Programme process', available from www.nice.org.uk/mt

1 Statement of the decision problem

The decision problem is specified in the final scope issued by NICE. The decision problem states the key parameters that should be addressed by the information in the evidence submission. All statements should be evidence based and directly relevant to the decision problem.

Table 1 Statement of the decision problem

	Scope issued by NICE	Variation from scope	Rationale for variation
Population	Patients with unexpected difficult airways requiring emergency intubation including awake or anaesthetised patients with displaced tracheostomies. This device can be used in adults or children who have been clinically evaluated for endotracheal tubes size 6 or above.	N/A	N/A
Intervention	The Ambu aScope2	'The increased rechargeable battery capacity' has been changed to 'the removal of the 30-minute timeout feature'.	This is a more accurate description of the technological enhancements with the aScope2 compared with aScope
Comparator(s)	Multiple-use flexible endoscopes (fibrescopes using fibre optic technology or video scopes using video technology). (see also 'Cost analysis' below)	Olympus, Pentax and Storz, as well as Vision Sciences' disposable sheath for bronchoscopes	These three manufacturers are the three key competitors for aScope in the UK
Outcomes	The outcome measures to be considered in patients undergoing emergency intubation with difficult airways include: • Incidence of delayed or failed intubation • Clinical consequences associated with delayed or failed intubation: o Death o Hypoxic brain injury o ITU and hospital length of stay • Incidence of successful intubation • Incidence of contamination and cross-infection • Device-related adverse events	Studies solely evaluating time to intubation/intubate, intubation time, length of intubation, time to scope position, time to task completion, number of intubation attempts, first time intubation success rate, number of scope attempts, endotracheal intubation success rate, monitor image quality, assessment of insertion cord, assessment of working channel, rating of the device, time spent cleaning and preparing endoscopes, tip surface collision count and ease of use/ease of endoscopy with aScope (AmbuScope, aScope2) were included in addition to outcomes specified in the scope	These additional outcomes were considered relevant for establishing the evidence-base for aScope in difficult airways
Cost analysis	Comparator(s): Multiple-use flexible fibreoptic endoscopes and include stack system costs where required. Costs will be considered from an NHS and personal social services	N/A	N/A

	perspective. The time horizon for the cost analysis will be sufficiently long to reflect any differences in costs and consequences between the technologies being compared. Consideration should be given to: • the costs attached to acute recovery, clinical management, rehabilitation and long-term care of those with hypoxic brain injury • the cost of cleaning/sterilisation of the current multiple-use fibreoptic endoscopes • the repair costs and maintenance of the re-usable endoscopes • the start-up costs of re-usable endoscopes which include the endoscope, light source, camera unit and processor, washer, HEPA filtered system and storage cabinet Sensitivity analysis will be undertaken to address uncertainties in the model parameters, which will include scenarios in which different numbers and combinations of devices are needed, including an analysis of how many monitors are required to allow the use of the Ambu aScope2 in all relevant clinical areas within a typical hospital.		
Subgroups to be considered	None identified	N/A	N/A
Special considerations, including issues related to equality	People at greater risk of airway complications are those with conditions affecting cervical spine mobility, this may include: pregnant women, or people who are obese, people in whom trauma to the face or neck has occurred, and people with respiratory tract infections or cancers. Other groups covered by the disability act are patients with rheumatoid arthritis with limited spine movements and longer term tracheostomy patients.	N/A	N/A

2 Description of technology under assessment

2.1 Give the brand name, approved name and details of any different versions of the same device.

- Approved name: Ambu aScope2.
- Different versions: Ambu aScope (Ambu Ltd) is a hand held single-use flexible intubation videoscope for visual guidance during intubations, which received a CE mark in December 2009. It can be used for difficult and unexpected airway management when a scope is needed immediately. Ambu aScope2 superseded 'aScope' in April 2011. Ambu aScope2 is the same product with a number of enhancements that include an easy clearing membrane, flow connector and the removal of time-out features on the single-use scope that were previously programmed to shut down the camera and light-emitting diodes (LEDs) after 30 minutes of continuous use.

2.2 What is the principal mechanism of action of the technology?

The Ambu aScope2 is a single-patient use, sterile, disposable, flexible intubation scope 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 directly or through an intubating laryngeal mask. It is a portable device that can be used wherever a flexible 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 (PDT) and to check the position and patency of airway devices such as endotracheal tubes and tracheostomy tubes.

The Ambu aScope2 consists of two components; the aScope and the accompanying aScope monitor to display the images. The two 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, and a built in camera with two light-emitting diodes.

The Ambu aScope2 uses video camera technology to create the image that 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 an easy clearing membrane that facilitates removal of secretions from the lens, 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.

The device is delivered sterile and ready for use.

3 Clinical context

3.1 Provide a brief overview of the disease or condition for which the technology is being considered in the scope issued by NICE.

Brief overview of therapeutic area

Ambu aScope2 is indicated for use in the management of expected or unexpected difficulties with endotracheal intubation in patients with difficult airways or in assisting with PDTs in awake or anaesthetised patients. However, under the conditions specified in the scope issued by NICE, the clinical circumstances that are relevant extend only to unexpected difficulties with endotracheal intubation in patients with difficult airways or in assisting with PDT.

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 in 10% of these, awake fibreoptic intubation is undertaken (1). Furthermore, it is estimated that approximately 12,000 tracheostomies and 5,000–8,000 PDTs are carried out in the UK each year (Table 2).

Table 2 Clinical circumstances relevant to the use of aScope2.

Group	Estimated number each year in the UK, based on 4th National Audit Project (NAP4) Report, 2011 and expert advice	Source
Procedures where a general anaesthetic is given	2.9 million	Initial data taken from: 4th National Audit Project (NAP4) Report, 2011 (1)
Proportion of procedures where endotracheal intubation is used for airway management	1.1 million (38% of 2.9 million)	
Management of unexpected difficulties with endotracheal intubation in patients with difficult airways	Difficult intubation: 22,000 (2% of 1.1million), of which 2,200 cases involve awake fibreoptic intubation	
Tracheostomies performed in the UK in one year	12,000 (approximately)	Expert adviser estimates
Assisting with percutaneous dilatory tracheostomy in awake and anaesthetised patients	5,000–8,000 (approximately)	

Difficulties with intubation can arise in patients who are pregnant, obese, have limited mouth opening or cervical spine movements, have experienced trauma to the face or neck, have respiratory tract infections or cancers, as well as in those with tracheostomies. Difficulties with airways management can be predicted, most often, when intubation is undertaken in a planned and elective manner. Difficulties may also be encountered, however, in unexpected and emergency situations when rapid intubation is required. In all settings, respiratory catastrophes resulting from difficult airways are the most common cause of anaesthesia-related brain deaths and deaths (2). Multiple attempts at laryngoscopy (>2 attempts) is associated with an increase in the risk of complications, including a 70% increase in the risk of hypoxia (a 28% increase in severe hypoxia), a 52% increase in oesophageal intubation, a 22% increase in regurgitation, a 13% increase in aspiration and a 11% increase in cardiac arrest (3).

Placement of an endotracheal tube guided by a flexible endoscope is the gold standard for managing patients with difficult intubation (anticipated and unanticipated), as well as being indicated in other clinical settings, such as routine intubations, unanticipated failed intubations, compromised airways, intubation of the conscious patient, patients with a high risk of aspiration or in whom movement of the neck is not desirable, known difficult mask ventilation, and previous tracheostomy or

prolonged intubation (2). The use of a flexible endoscope 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. Visualisation is currently achieved using fibre optic technology (fibrescopes) or video technology (video scopes). The use of flexible endoscopes does require training, and lack of adequate training may result in the failure of the anaesthesiologists to develop and maintain the necessary psychomotor skills to perform the procedure correctly.

3.2 Give details of any relevant NICE or other national guidance or expert guidelines for the condition for which the technology is being used. Specify whether the guidance identifies specific subgroups and make any recommendations for their treatment. If available, these should be UK based guidelines.

There is no related NICE guidance for this technology. However, the Difficult Airway Society published guidelines for the management of unanticipated difficult intubation using flexible fibrescopes (4).

3.3 Describe the clinical pathway of care that includes the proposed use of the technology.

Difficult airway

Prior to managing the airway a thorough pre-anaesthetic evaluation of the patient is performed, and a strategy on the optimal handling of the patient's airway is planned. During the pre-anaesthetic evaluation the clinician will decide on how the anaesthetic procedure should be approached. The choice is either performing an awake/sedated FOI or using general anaesthetic and direct laryngoscopy.

The clinical pathway of unanticipated difficult tracheal intubation during routine induction of anaesthesia in an adult patient is provided in Fig. 1 (see reference (4)). aScope could be used in both Plan A (initial tracheal intubation plan) and Plan B (secondary tracheal intubation plan).

Plan A: Standard procedure is to initiate direct laryngoscopy. After four failed intubation attempts, Plan B needs to be undertaken.

Plan B: A supraglottic airway device (SAD) is inserted. 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 flexible scope, such as the aScope, as a conduit for intubation. The aScope should be preloaded with the endotracheal tube (ETT), and then both the ETT and the aScope directed through the SAD with the aim of optimising the visual view of the vocal cords and thereby optimising the conditions for tube delivery.

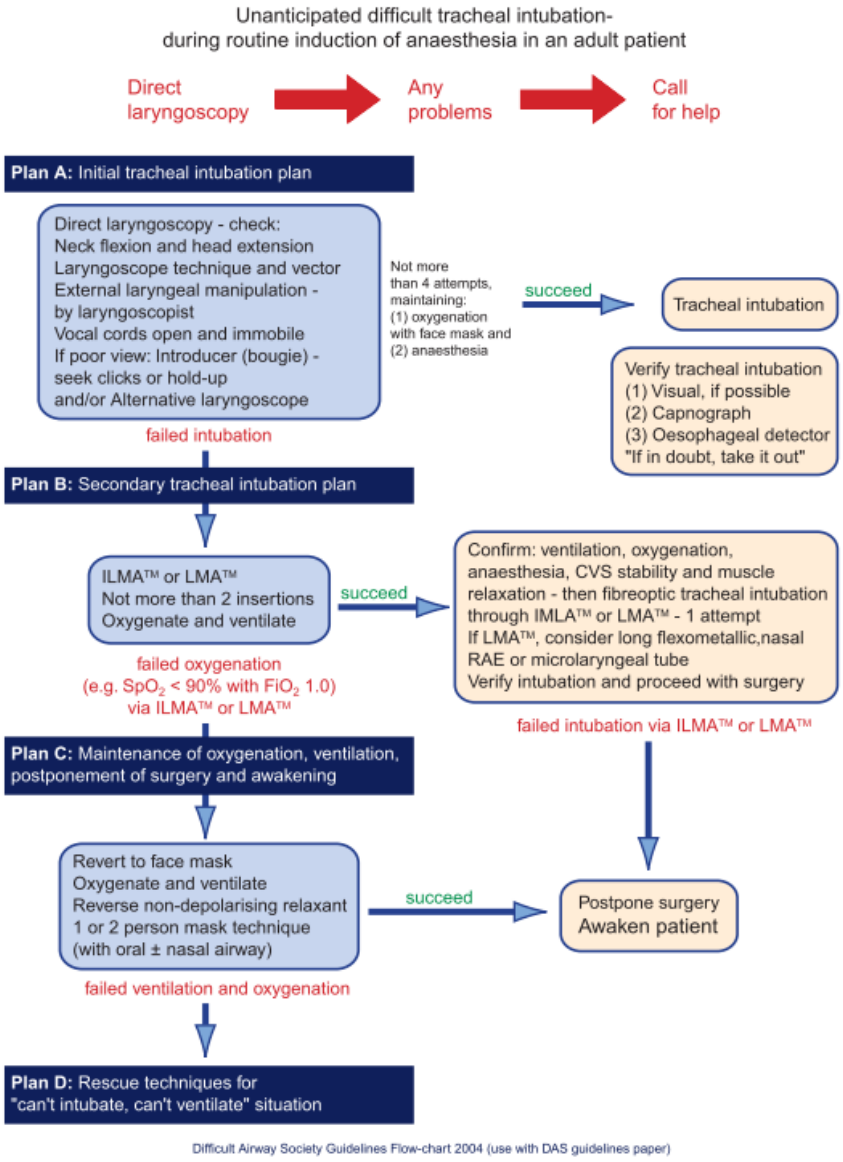


Figure 1 The management of unanticipated difficult tracheal intubation, during routine induction of anaesthesia (4).

If Plan B fails, the clinical pathway for managing failed intubation, increasing hypoxaemia and difficult ventilation in the paralysed anaesthetised patient should commence (Fig. 2; see reference (4)). The clinician will revert to face mask ventilation to obtain oxygenation. If the scenario is not possible to intubate or ventilate the patient, then Plan D (rescue technique for CICV situation) with a cricothyroidotomy, either surgical or using a cannula, will be initiated.

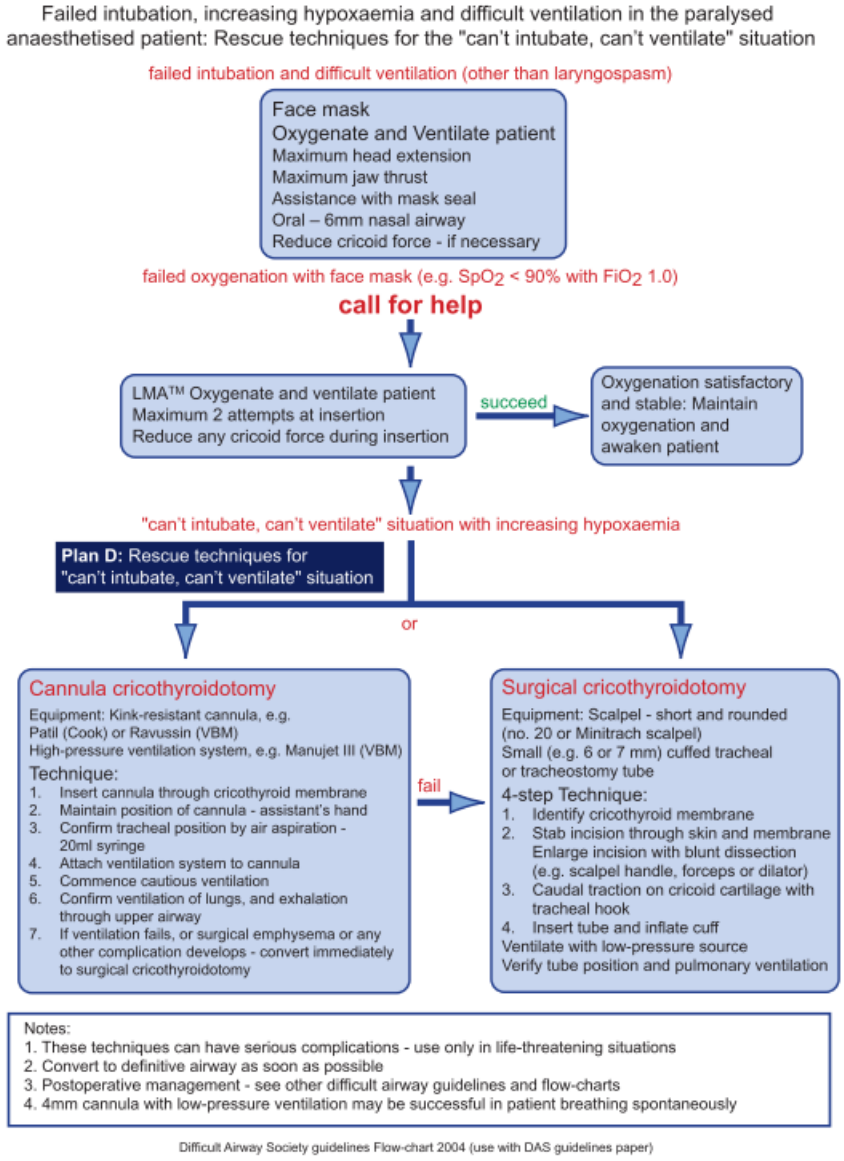


Figure 2 Management of failed intubation, increasing hypoxaemia and difficult ventilation in the paralysed anaesthetised patient (4).

PDT procedure

Tracheostomy is a surgical procedure performed on the patient's neck to open a direct airway into the trachea. Percutaneous tracheostomy has gained widespread

acceptance in recent years and is now considered a standard technique in many ICUs worldwide. The use of the bronchoscope 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, but it has not yet been proven by clinical trials (5-9). Average time required to perform a percutaneous tracheostomy is 10–15 minutes (10).

A survey of 197 general ICUs in the UK showed that percutaneous tracheostomy is favoured over surgical tracheostomy, with ≤8% of ICUs choosing surgical tracheotomies at least 50% of the time (11). In 43% of the units, tracheostomy was performed percutaneously at least 95% of the time. Eighty percent of the ICUs performed all percutaneous tracheostomy under bronchoscopic guidance. Of the 20% of units that performed percutaneous tracheostomy without bronchoscopic guidance: 10% used a fibreoptic bronchoscope (FOB) if a difficult tracheostomy was anticipated; 7% used FOBs >50% time; and 3% never utilized a FOB during insertion of a percutaneous tracheostomy. A common problem is difficulty finding an existing tract down into the trachea. An alternative is to use flexible optical intubation (FOI) to visualize the stoma, which makes it possible to pass a guide wire alongside forceps and into the trachea. The FOI device should be used to verify the correct position of the tracheostomy tube and the tracheostomy tube has adequate clearance of the carina. There is a learning curve when performing percutaneous tracheostomy, and trained users have fewer incidences of complications.

3.4 Describe any issues relating to current clinical practice, including any uncertainty about best practice.

FOI by someone who is experienced in endoscopy is a first-tier tool for the management of unanticipated difficult airway. FOI can be used as an alternative technique for laryngoscopy when intubation using direct laryngoscopy has failed. An orotracheal approach may yield faster access to the trachea in this situation than does the nasotracheal route. However, when presented with a patient with unanticipated difficult airway, the physician has limited time to perform a comprehensive evaluation and preparation of the airway. FOI may not always be the first option in all difficult airway situations, because of the challenges facing physicians to retain their psychomotor skills required for FOI. Many practitioners believe pressures for efficiency in the operating room prevent the frequent use of the FOI device that is required to maintain skills (12). It has been suggested that hesitancy may exist among the general anaesthesia community particularly when awake intubation is indicated (12). Potential reasons for this hesitancy include a lack of personal association with an airway disaster, a feeling that awake intubation is too stressful emotionally and physically for the patient, and that the physician may lack necessary training (12). Cost and unavailability of suitable equipment is likely to contribute to a lack of training in the use of FOBs. In typical training situations, there is a risk that the FOB might be outdated and/or and poorly functioning. Increasing availability of FOBs would enable more physicians to have an opportunity to train and practice in the use of this equipment.

There are no contraindications to FOI, except patients with a documented true allergy to all local anaesthesia and children (but only if the diameter of the scope is larger than the endotracheal tube size). Situations may also arise where the patient is not capable of cooperating, which can aggravate the seriousness of the situation (e.g., children, or mentally challenged, intoxicated or combative patients).

Challenges may be encountered in unexpected and emergency situations when intubation is required. Under these circumstances, failure to achieve adequate ventilation quickly can result in serious clinical consequences, including death and hypoxic brain injury (see sub-sections below for more details). Difficult intubation was found to be the third most common respiratory-related event leading to death and brain damage in a closed-claims analysis by the American Society of Anesthesiologists (ASA) (13). One of the most fundamental reasons for delayed intubation, or indeed the failure to intubate a patient who requires intubation, is the lack of appropriate equipment being available immediately. Lack of essential airway equipment is a major issue, both in context of planned tracheostomies or for management of displaced tracheostomies, that can result in poor outcomes (1). Such circumstances may arise for example in the Accident and Emergency (A&E) department or in Intensive Care Units (ICU) or general wards where multiple use scopes are not necessarily stocked, but where emergency resuscitation is sometimes required. The Fourth National Audit Project (NAP4) Report, published in 2011 by the Royal College of Anaesthetists and the Difficult Airway Society, cited a number of cases (in Section 2 of the report) where awake fibreoptic intubation was indicated but was not used. Although it was not possible to determine the exact reasons behind this, there were examples in which lack of skills, lack of confidence and poor judgement and, in some cases, lack of suitable equipment being immediately available were cited as the potential cause. This latter problem was seen to be particularly prevalent in ICUs (1).

In terms of difficult intubation, it has been suggested that failed intubation occurs in 0.13–0.5% of general anaesthetics (14, 15). The NAP4 report showed that failed intubation represented 16.6% (n=6/36) of all primary airway events in the ICU and 46.6% (n=7/15) in the emergency department (1). The National Patient Safety Agency examined critical incidents relating to airways events in ICUs over a two-year period between 2005 and 2007 (16). The study indicated that there were 453 incidents, 338 of which led to harm and 15 that may have contributed to death. Of these 453 incidents, 276 (60%) involved tracheostomies becoming displaced or blocked.

Having suitable equipment should be standard of care, as it will reduce the risk of tube displacement (1). In the UK, 97% of ICUs that responded to a survey performed some type of percutaneous technique for tracheostomy placement (1). Percutaneous tracheostomy is a routine procedure in ICU and, on occasion, may be required

urgently and out of hours. Therefore, it is vital that the necessary equipment (e.g., capnography or bronchoscopic observation tools) and personnel with appropriate skills are available. Displacement of tracheostomies is the most common lethal problem with this procedure, especially when moving/turning the patient or during routine care. NAP4 reports a number of situations that illustrate the problem of displaced tracheostomies (1). Among 75 cases of unplanned emergency surgical airway, 14 cases of accidental dislodgement of tracheostomies in ICU were reported that lead to death of seven patients and hypoxic brain damage in four patients. Among 25 cases that dealt directly with tracheostomy-specific problems, 12 ended in death of patients. Lack of equipment was considered to be contributory in at least 18 of the 25 cases. Moreover, displaced tracheostomy and, to a lesser extent, displaced tracheal tubes, were identified as the greatest cause of major morbidity and mortality in ICU (1). Obese patients were at particular risk of these events and their associated complications. Since the 'can't intubate can't ventilate' (CICV) situation accounts for at least 25% of all anaesthesia-related deaths (17), having an emergency re-intubation plan on ICU is essential (1).

Hypoxic brain injury

NAP4 showed that hypoxia was a common theme in deaths caused by an airway problem (1). Evaluation of more than 10,000 emergency tracheal intubations at one institution in Connecticut, over a 10-year period, showed that multiple attempts at laryngoscopy were associated with an increased rate of complications, including hypoxia (3). For example, compared with intubation that was achieved on first or second laryngoscopy, intubations requiring more than two laryngoscopies led to a seven-fold increase in hypoxia (14-fold increase in severe hypoxia). The absolute rates of complications are notably high: after more than two attempts at intubation, the rates of hypoxia and severe hypoxia were 70% and 28%, respectively (3). In data collected from 234 cases of difficult intubation from the Thai Anesthesia Incidents Study database (2003–2004), hypoxemia was observed in 54 cases (23.1%) (18).

Death

A study conducted in France reported that the death rate associated with difficult intubation during anaesthesia was 1:176,000 (95% CI 1:714,000 to 1:46,000) in 1999 and 1:46,000 (95% CI 1:386,000 to 1:13,000) in 1978–82 (19). In a study of critically ill adult patients admitted to an ICU, who had been previously intubated, difficult airway at re-intubation was associated with higher mortality (adjusted OR 2.23,

95%CI: 1.01, 4.93, p=0.05) (20). The estimated incidence of death, and/or brain damage, resulting from an airway event during general anaesthesia, as reported in the NAP4 survey, is provided in Table 3 (1).

Table 3 Incidence estimates of major airway complications by airway type for events and death/brain damage (1).

			Events per million cases			Events as fractions 1 in n cases		
Type of event	Numerator	Denominator	Point estimate	Lower CL	Upper CL	Point estimate	Lower CL	Upper CL
Events	133	2,872,600	46.3	38.4	54.2	21,598	26,021	18,461
Deaths	16	2,872,600	5.6	2.8	8.3	179,538	352,033	120,495
Death/brain damage	19	2,872,600	6.6	3.6	9.6	151,189	274,717	104,294
Tracheal tube events	91	1,102,900	82.5	65.6	99.5	12,120	15,254	10,054
Tracheal tube death/ brain damage	10	1,102,900	9.1	3.4	14.7	110,290	290,087	68,089
SAD events	35	1,616,100	21.7	14.5	28.8	46,174	69,051	34,684
SAD death/brain damage	8	1,616,100	5.0	1.5	8.4	202,013	657,942	119,325
FM event	7	154,200	45.4	11.8	79.0	22,029	84,985	12,654
FM death/brain damage	1	154,200	6.5	0.0	19.2	154,200	0	52,095

CL, confidence limits; FM, face mask; SAD, supraglottic airway device.

Prolonged hospital admissions

Prolonged hospital stay, particularly in ICUs, is a recognised consequence of reintubation (21-23). A study investigating the impact of reintubation for events excluding accidental extubation showed that prolonged/increased length of hospital stay was a prominent adverse outcome in 16% of those who needed to be reintubated (21). A recent study showed that among outpatients who had laryngeal mask airway failure during anaesthesia, almost 14% required unplanned hospital admission, 5.6% of whom needed intensive care for persistent hypoxemia (24).

Cross-infection and contamination

A potential, but critical risk of reusable scopes is the possibility of infection and cross-contamination (25, 26). This can be due to a number of factors, including infected bodily fluids from previous patients, failures in the sterilisation/decontamination process or contamination during storage (27).

The problems that lead to inadequate decontamination are inadequate cleaning of hard deposits of organic material on endoscope surfaces caused by damaged and deformed surfaces, perforated instrument channels, part of the instrument not being exposed to the cleaning process because they are closed off by valves or seals

(occluded surfaces), failure to clean intricate areas such as hinge joints, recessed surfaces and long narrow aperture (lumens), ineffective final rinsing and drying, contamination of wash bottles and tubes connected to the endoscope, inappropriate or incomplete decontamination methods e.g. choice of disinfectant and contact time, both of which are critical, continued use of disinfectant diluted below effective concentration or used beyond its recommended shelf life, design faults in automatic endoscope processor system (AERT), allowing the growth or persistence of infectious agents on some parts of the endoscope and/or AERT, water or other fluids of poor microbiological quality for decontamination. All these challenges increase the risk of transmitting infection to a patient (27).

The majority of infection/cross-infection data currently exists for bronchoscopes, where reports of contamination (and true infection) during bronchoscopy have become more frequent over time (25). Although it is difficult to discern the exact number of cases attributable to pathogen transmission, true symptomatic infections caused by bronchoscopy appear to be rare; there are 13 well-documented reports involving 21 patients (25). It is a concern, however, that many of these infections occurred despite thorough decontamination procedures.

Although the information on infection and cross-contamination is associated with bronchoscopy, it is entirely possible that these complications also have relevance for fibreoptic intubation with flexible scopes. It has, for example, been reported that flexible laryngoscopes can be contaminated with blood, body fluids, organic debris and potentially pathogenic microorganisms during routine clinical use (28). Therefore, unless instruments are reprocessed adequately, using high-level disinfection (i.e., sterilisation), there is a risk of patient-to-patient transmission of pathogenic microorganisms (28, 29). A study by Woodhall and colleagues demonstrated that additional sterility measures (sterile gloves and a sterile surface to receive the endoscope) reduced rates of symptoms associated with infections (30). However, even following the introduction of these measures, a productive cough with green sputum after the procedure was observed in one participant and flu-like symptoms in a further six participants (30). A study investigating the presence of protein deposits on 'cleaned' reusable anaesthetic equipment showed that the cleaning procedures did not remove all proteinaceous material from the surface of previously used and supposedly clean, sterilised laryngeal masks, laryngoscope blades and other equipment (31). Any method of attempted high-level disinfection/sterilisation will likely fail if prior cleaning has been inadequate (29). Furthermore, automated

bronchoscope disinfecting machines may become contaminated with mycobacteria that resist usual disinfection, resulting in a source of bronchoscope contamination (32). The use of an individually packaged disposable sterile sheath on the shaft of a fibreoptic scope can potentially prevent microbes from adhering to the shaft of the scope. However microbial colonisation was still observed in 1/50 scopes using this method in a recent study (33). A single-use, disposable scope eliminates the risk of cross-infection or contamination.

The inability to remove all proteinaceous material from medical devices increases the risk transmitting Creutzfeldt–Jakob disease (vCJD) from one patient to another via contaminated FOBs. The process to clean prions from FOBs requires unique decontamination protocols, because prions resist normal inactivation methods; steam sterilization for at least 30 minutes at 132 °C in a gravity displacement sterilizer is the preferred method (25). However, it is not always known in advance which patients are infected with vCJD. Considering the incubation time of vCJD, many patients could be potential carriers of the prion without knowing. The Department of Health in England has advised that ‘cleaning is of the utmost importance in minimizing the risk of transmission of vCJD via medical devices’ (27). It is recommended that all FOBs should be destroyed if there is any doubt that a FOB has been used on a patient with vCJD, and that, wherever possible, single-use devices should be used, provided that they do not compromise the clinical outcome (27).

The National CJD Surveillance Unit, Western General Hospital in Edinburgh has a pool of dedicated endoscopes that are available if there is a patient with known vCJD. Flexible endoscopes are expensive and if they have to be quarantined, as a result of exposure to a possible case of vCJD, and then subsequently destroyed there is a large cost attached. If it is not possible to identify the instrument with certainty, the relevant instrument cannot be distinguished from identical ones at a centre, which would result in the need to quarantine and possibly destroy the endoscopes (34). A single-use device eliminates this problem.

3.5 Describe the new pathway of care incorporating the new technology that would exist if the technology was adopted by the NHS in England.

Demand for flexible scopes has the potential to exceed availability, due to breakage, loss, contamination and/or cleaning of reusable scopes, even when a difficult airway is anticipated and planned for. Most aScopes used in the NHS today are purchased to complement existing reusable scopes. Therefore, aScope2 fits into the current care pathway alongside existing reusable scopes, but has the advantage of being able to provide a sterile readily available endoscope for immediate use in unexpected or anticipated difficult airways and/or PDT.

3.6 Describe any changes to the way current services are organised or delivered as a result of introducing the technology.

The availability and relatively low cost of disposable equipment, compared with conventional reusable scopes, may facilitate distribution of the aScope to geographical areas where flexible scopes have been previously unavailable (35).

3.7 Describe any additional tests or investigations needed for selecting or monitoring patients, or particular administration requirements, associated with using this technology that are over and above usual clinical practice.

The design, basic functioning principles and clinical use of aScope are equivalent to conventional reusable flexible scopes. Therefore, under normal conditions, no additional tests or investigations are needed for selecting or monitoring patients when using aScope over and above current procedures with reusable scopes.

3.8 Describe any additional facilities, technologies or infrastructure that need to be used alongside the technology under evaluation for the claimed benefits to be realised.

In principle, no other additional facilities, technologies or infrastructure are required for the claimed benefits to be realised.

3.9 Describe any tests, investigations, interventions, facilities or technologies that would no longer be needed with using this technology.

aScope2 is delivered sterile and ready to use, so there is no need for it to be decontaminated or cleaned prior to use. The use of aScope2, therefore, eliminates the need for detergents, running water, disinfectants, alcohol wipes, transportation, storage and sterile bags (36).

In contrast, reusable scopes must undergo a multi-step decontamination and cleaning procedure, which includes washing, inspection, disinfection and/or sterilisation, in order for the instruments to be considered safe for handling and re-use (36). It is necessary to disassemble reusable scopes to ensure each component is adequately cleaned. Therefore, separation and collection of the loose components of disassembled scopes, storage of different loose components, inspection tests and quality control procedures to ensure no leaks and the integrity of the reassembled endoscope would no longer be needed when using aScope. There are also fewer administrative tasks associated with aScope, in terms of keeping records of when an endoscope was last used, cleaned and serviced.

Reusable flexible endoscopes can be difficult to clean, and easy to damage, because of the intricate device design (37). Meticulous cleaning must precede any high-level disinfection or sterilisation procedure of these devices.

When a reusable endoscope is cleaned in a washing machine, the user must follow the procedure recommended by the manufacturer: failure to do so could lead to ineffective cleaning and put patients at risk of infection or cross-contamination. The length of time it takes to thoroughly clean a reusable endoscope varies depending on the type of washing machine available and the type of washing cycle/programme selected. Alternatively, endoscopes can also be cleaned by hand. Reusable scopes

should be decontaminated between patients, i.e., at the end and beginning of each clinic or period of use, if the scope was last decontaminated at least three hours earlier. Although it is acceptable to use a disposable sheath with a reusable scope, the scope must still go through a complete decontamination cycle before use, if it has not been decontaminated within the last three hours, and must go through a complete cycle after being used (36).

3.10 Describe how the NHS in England can disinvest from tests, investigations, interventions, facilities or technologies described in section 3.9 that would no longer be needed with using this technology.

aScope2 is delivered sterile and ready to use; therefore, the NHS in England can disinvest from services and equipment that are associated with reusable scopes, such as cleaning products (detergents, disinfectants, alcohol wipes), staff training in decontamination procedures, servicing, maintenance and repair, transportation, storage, quality control inspections and administrative tasks.

4 Regulatory information

4.1 Provide PDF copies of the following documents:

- instructions for use
- CE mark certificate or equivalent UK regulatory approval such as EC declaration of conformity
- quality systems (ISO 13485) certificate (if required).

4.2 Does the technology have CE mark for the indication(s) specified in the scope issued by NICE? If so, give the date that authorisation was received. If not, state current UK regulatory status, with relevant dates (for example, date of application and/or expected approval dates).

The Ambu aScope received a CE mark in December 2009 and is indicated for use in difficult and unexpected airway management when a fibreoptic endoscope is needed immediately.

In October 2010, aScope 2 was reclassified and approved as a Class IIa medical device following technical file review by BSI, in order to include visual guidance during PDT as part of its indications for use.

Ambu aScope2 superseded 'aScope' in April 2011. It is the same product and is covered by the same CE Mark, with a number of enhancements that include the easy clearing membrane, the oxygen adapter and the removal of the 30-minute timeout feature.

4.3 Does the technology have regulatory approval outside the UK? If so, please provide details.

In the European Union, aScope was approved for use for the PDT procedure in November 2010. The Ambu aScope 2 (for difficult and unexpected airways, and for PDT) has obtained market clearance in the USA and Japan in 2011, and in Canada January 2012.

4.4 If the technology has not been launched in the UK provide the anticipated date of availability in the UK.

N/A. The product has been launched in the UK.

4.5 If the technology has been launched in the UK provide information on the use in England.

Since launch in late 2009, approximately 1600 units of aScope have been purchased in England by approximately 230 NHS departments. These NHS departments are predominantly (70–80%) anaesthesia departments that have purchased aScopes to complement existing stocks of reusable scopes, where availability of these has been highlighted as an issue. The second largest use of aScope is within the ITU where again, the aScope is used to complement inadequate stocks of reusable scopes. However, in the ITU, they are also used to facilitate PDT procedures. In this setting, costly damage frequently occurs when a percutaneous cannula, which is used in the PDT procedure, punctures the scope. Currently, a total of seven A&E departments have purchased aScope for difficult airway management in the UK.

5 Ongoing studies

5.1 Provide details of all completed and ongoing studies on the technology from which additional evidence relevant to the decision problem is likely to be available in the next 12 months.

It is possible that data could be available within the next 12 months from two studies investigating aScope in difficult airways, both of which are currently recruiting patients:

- Evaluation of the Ambu aScope for Tracheal Intubation in Difficult Airways
    - ClinicalTrials.gov Identifier: NCT01467739
    - Study details: randomised, open-label study to evaluate aScope for tracheal intubation in difficult airways due to cervical immobilisation by a cervical collar, and compare it with a conventional reusable fiberscope
    - Estimated primary completion date: December 2011 (Note: Ambu is not aware of the status of completion)
- Video-laryngoscope With a Novel Video-stylet for Difficult Intubation

- ClinicalTrials.gov Identifier: NCT01215695
- Study details: randomised study to evaluate aScope compared with a pre-formed stylet for tracheal intubation in patients that have a predicted difficult airway or an immobilised cervical spine (C-collar in place), who are scheduled for elective or urgent/emergent surgery with general anaesthesia
- Estimated primary completion date: October 2011
- Although this study is still listed on ClinicalTrials.gov website, it refers to Lenhardt2011 (38, 39), parts of which have been published as a congress poster (39)

Ambu are aware of another ongoing study, in which aScope will be used to intubate patients with normal airway, via the Ambu Aura-I supraglottic airway, who are undergoing general anaesthesia. The study will compare the performance of optical intubation with blind intubation. The optical procedure will make use of the Ambu SAD Aura-I in combination with aScope to visualize ETT positioning and the LMA FastTrach will be used for the blind intubation procedure. Data could be available within the next 12 months. Details are as follows:

- Title of study: Flexible optical intubation via the Ambu Aura-I versus blind intubation via the single use intubating LMA – a prospective randomized clinical trial
- Principal investigator: Carin A Hagberg, University of Texas, USA
- Size of the study: 66 patients in the USA (recruitment has begun)

5.2 If the technology is, or is planned to be, subject to any other form of assessment in the UK, please give details of the assessment, organisation and expected timescale.

As far as Ambu is aware, no additional assessments are ongoing or planned with aScope/aScope2 in the UK.

6 Equality

NICE is committed to promoting equality of opportunity and eliminating unlawful discrimination on the grounds of age, disability, gender reassignment, race, religion or belief, sex, and sexual orientation, and to comply fully with legal obligations on equality and human rights.

Equality issues require special attention because of NICE's duties to have due regard to the need to eliminate unlawful discrimination, promote equality and foster good relations between people with a characteristic protected by the equalities legislation and others.

Any issues relating to equality that are relevant to the technology under assessment should be described. This section should identify issues described in the scope and also any equality issues not captured in the final scope.

Further details on equality may be found in section 11.3 of this document.

6.1.1 Describe any equality issues relating to the patient population and condition for which the technology is being used.

The aScope could have particular advantages for people who may be more likely to develop airway complications, such as obese people, pregnant women, patients suffering from conditions affecting cervical spine mobility or who 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. No other potential equality issues have been identified.

6.1.2 Describe any equality issues relating to the assessment of the technology that may require special attention.

The aScope has been assessed mainly in patients with difficult airways, including patients who may be more likely to develop airway complications, such as obese people, pregnant women, patients suffering from conditions affecting cervical spine mobility or who 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.

6.1.3 How will the submission address these issues and any equality issues raised in the scope?

Where available, information from assessments of aScope in patients who may be more likely to develop airway complications has been included in the submission.

Section B – Clinical evidence

7 Published and unpublished clinical evidence

Section B requires sponsors to present published and unpublished clinical evidence for their technology.

Sponsors should read section 6 of the Medical Technologies Evaluation Programme methods guide on published and unpublished evidence, available from www.nice.org.uk/mt

All statements should be evidence-based and directly relevant to the scope. Reasons for deviating from the scope should be clearly stated and explained in table A1.

Sponsors are required to submit section B in advance of the full submission (for details on timelines, see the NICE document 'Guide to the Medical Technologies Evaluation Programme process', available from www.nice.org.uk/mt

7.1 Identification of studies

Published studies

7.1.1 Describe the strategies used to retrieve relevant clinical data from the published literature. Exact details of the search strategy used should be provided in section 10, appendix 1.

A thorough search strategy was designed to retrieve relevant clinical data from published literature, based on principles of the Centre for Reviews and Dissemination (CRD). This search strategy involved searches of relevant literature databases, searches of conference abstracts for the key congresses, and searches of the manufacturer's internal literature databases. Ongoing clinical trials were also identified, with the aim of highlighting future studies that, when published, will provide additional data that addresses the decision problem.

The following databases were interrogated on 02 May 2012 to identify any eligible studies:

- The Cochrane Library (current issue)

- MEDLINE, Ovid SP (1956 to date)
- MEDLINE In Process
- EMBASE, Ovid SP (1982 to date)

When searching the databases, clinical keywords were used to search both the publication titles and the full body of the corresponding abstracts. The MEDLINE search strategy was adapted when searching all other databases, and search strategies used for each database are given in appendix 1.

All relevant studies published since 1992 (i.e. last 20 years) were considered for inclusion. The search was not limited by either language or publication type, in order to maximise search sensitivity. Reference lists of all relevant study publications were also hand searched to identify any additional references.

An electronic search of the abstract databases was performed for the following societies to identify abstracts presented at past meetings:

- American Society of Anaesthesiology (ASA; 2006−2012)
- European Society of Intensive Care Medicine (ESICM; 2006−2012)

Additionally, the websites of the following societies were searched for published abstracts:

- European Society of Anaesthesia (ESA; 2006−2012)
- Society for Technology in Anaesthesia (STA; 2011−2012)

Both the Difficult Airway Society (DAS) and the Society of Airway Management (SAM) were contacted directly to gain access to abstracts from past meetings; however, neither responded to the request in the time period in which this document was being developed.

These electronic congress abstract databases were searched using clinical keywords both subject headings and free text terms, and the search will be extended to all abstracts published since 2006 (i.e. last 5 years; where possible).

Unpublished studies

7.1.2 Describe the strategies used to retrieve relevant clinical data from unpublished sources.

With regard to the unpublished data, our search strategy was three-fold:

Firstly, the manufacturers of the technology under consideration, i.e. Ambu, were contacted to request any relevant unpublished data.

Secondly, after completing the initial review of retrieved published articles, we attempted to contact authors that commented on pending trials, as well as authors of included studies, to identify unpublished data and/or ongoing studies.

Thirdly, ClinicalTrials.gov and the Cochrane Central Register of Controlled Trials (CENTRAL) were searched for relevant ongoing studies and we attempted to contact the key investigators of these studies to identify unpublished or pending data.

Additionally, data from MAUDE was searched to find relevant reports of adverse events. For more information on the search strategy please see section 10.2.5.

7.2 Study selection

Published studies

7.2.1 Complete table B1 to describe the inclusion and exclusion criteria used to select studies from the published literature. Suggested headings are listed in the table below. Other headings should be used if necessary.

Table 4 Selection criteria used for published studies

Inclusion criteria	
Population	Awake, anaesthetised, sedated and asleep/sleeping patients, adults or children/paediatric (>10 years), male or female, with unexpected or expected, difficult, closed or obstructed airway(s) or airway management, tracheostomies/PDT, as well as manikins/mannequins configured to simulate difficult, closed or obstructed airway(s) or airway management
Interventions	Oral, nasal or naso-tracheal intubations with reusable or disposable, single-use or multiple-use, direct or indirect, and portable scope, fibrescope/fibreoptic scope, videoscope/video-assisted, endoscope, bronchoscope or laryngoscope, specifically aScope (AmbuScope, aScope2) and/or Olympus, Pentax and Storz with eyepiece or monitor, as well as Vision Sciences' disposable sheath for bronchoscopes
Outcomes	Studies evaluating incidence, rate or prevalence of delayed or failed intubation, intubation success or failure rate, death, hypoxic brain injury, ITU/hospital length of stay, incidence or rate of successful intubation, incidence, rate or risk of contamination, cross-infection, infection or infectious disease transmission, device-related adverse events, safety concerns, side effects, including hemoptysis and atelectasis specifically, or complaints for aScope (AmbuScope, aScope2) and its key comparators will be included. Studies solely evaluating time to intubation/intubate, intubation time, length of intubation, time to scope position, time to task completion, tip surface collision count and ease of use/ease of endoscopy will only be included if aScope (AmbuScope, aScope2) is being tested either alone or against a comparator
Study design	All types of studies will be included, including randomised controlled trials, retrospective studies, observational studies and case reports, studies and series
Language restrictions	None
Search dates	Published data from 1992 (last 20 years) and congress abstracts from 2007 (last 5 years)
Exclusion criteria	
Population	Patients requiring endoscopy, fibrescopy, videoscopy, bronchoscopy for any clinical reason other than difficult, closed or obstructed airway(s) or airway(s) management or tracheotomies, manikin/mannequin studies outside the setting of difficult, closed or obstructed airway(s) or airway(s) management and all laboratory and animal studies will be excluded
Interventions	Any scope, fibrescope/fibreoptic, videoscope, endoscope, bronchoscope or laryngoscope other than aScope (AmbuScope, aScope2) or Olympus, Pentax and Storz
Outcomes	Studies evaluating any outcomes other those described in the inclusion criteria will be excluded
Study design	All types of studies will be included
Language restrictions	None
Search dates	Published data from before 1992 and congress abstracts before 2007

7.2.2 Report the numbers of published studies included and excluded at each stage in an appropriate format.

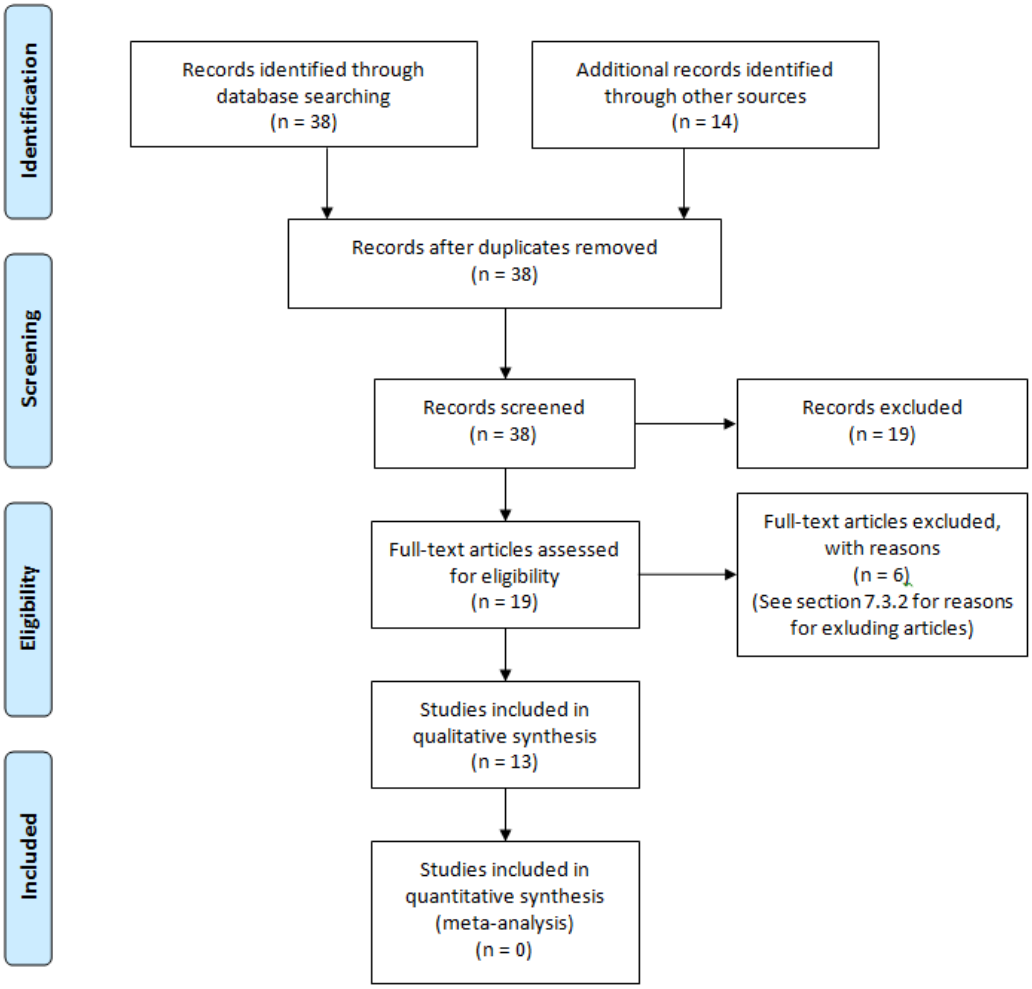


Figure 3 PRISMA statement flow diagram showing the numbers of published studies included and excluded at each stage (40). Source: Moher et al. PLoS Med. 2009;6(7):e1000097.

Unpublished studies

7.2.3 Complete table B2 to describe the inclusion and exclusion criteria used to select studies from the unpublished literature. Suggested headings are listed in the table below. Other headings should be used if necessary.

Table 5 Selection criteria used for unpublished studies

Inclusion criteria	
Population	Awake, anaesthetised, sedated and asleep/sleeping patients, adults or children/paediatric, male or female, with difficult, closed or obstructed airway(s) or airway management, tracheostomies/PDT, as well as manikins/mannequins configured to simulate difficult, closed or obstructed airway(s) or airway management
Interventions	Oral, nasal or naso-tracheal intubations with reusable or disposable, single-use or multiple-use, direct or indirect, and portable scope, fibrescope/fibreoptic scope, videoscope/video-assisted, endoscope, bronchoscope or laryngoscope, specifically aScope (AmbuScope, aScope2) and/or Olympus, Pentax and Storz with eyepiece or monitor, as well as Vision Sciences' disposable sheath for bronchoscopes
Outcomes	Studies evaluating incidence, rate or prevalence of delayed or failed intubation, intubation success or failure rate, death, hypoxic brain injury, ITU/hospital length of stay, incidence or rate of successful intubation, incidence, rate or risk of contamination, cross-infection, infection or infectious disease transmission, device-related adverse events, safety concerns, side effects, including hemoptysis and atelectasis specifically, or complaints for aScope (AmbuScope, aScope2) and its key comparators will be included. Studies solely evaluating time to intubation/intubate, intubation time, length of intubation, time to scope position, time to task completion, tip surface collision count and ease of use/ease of endoscopy will only be included if aScope (AmbuScope, aScope2) is being tested either alone or against a comparator
Study design	All types of studies will be included, including randomised controlled trials, retrospective studies, observational studies and case reports, studies and series
Language restrictions	None
Search dates	Published data from 1992 (last 20 years) and congress abstracts from 2007 (last 5 years)
Exclusion criteria	
Population	Patients requiring endoscopy, fibrescopy, videoscopy, bronchoscopy for any clinical reason other than difficult, closed or obstructed airway(s) or airway(s) management or tracheotomies, manikin/mannequin studies outside the setting of difficult, closed or obstructed airway(s) or airway(s) management and all laboratory and animal studies will be excluded
Interventions	Any scope, fibrescope/fibreoptic, videoscope, endoscope, bronchoscope or laryngoscope other than aScope (AmbuScope, aScope2) or Olympus, Pentax and Storz
Outcomes	Studies evaluating any outcomes other those described in the inclusion criteria will be excluded
Study design	All types of studies will be included
Language restrictions	None
Search dates	Published data from before 1992 and congress abstracts before 2007

7.2.4 Report the numbers of unpublished studies included and excluded at each stage in an appropriate format.

An unpublished study was identified; R-PS-7-2009/Kristensen (41). Please note that the highlighting below indicates that the information should be treated as 'academic in confidence':

- Part 2 of R-PS-7-2009/Kristensen (41) met the inclusion criteria and was included. However, Part 1 of the unpublished R-PS-7-2009/Kristensen (41) study was excluded because it included 20 patients with expected normal airways, who were scheduled for elective Ears, Nose and Throat (ENT) surgery; therefore, these patients did not meet the population criteria as stated in the decision problem (Table 1). The data are awaiting publication; therefore, must be treated as 'academic in confidence' and not be made available to the public

7.3 Complete list of relevant studies

The sponsor should provide a PDF copy of all studies included in the submission. For unpublished studies for which a manuscript is not available, provide a structured abstract about future journal publication. If a structured abstract is not available, the sponsor must provide a statement from the authors to verify the data provided.

7.3.1 Provide details of all published and unpublished studies identified using the selection criteria described in tables B1 and B2.

There are several studies published reporting the use of the disposable Ambu aScope in the intubation of anticipated and unanticipated difficult airways, and in PDT. Moreover, non-clinical models based on manikin simulations of difficult airways have been published to evaluate the learning curve in the use of the device, and to evaluate the performance of aScope in comparison with reusable scopes. The majority of these studies in humans and manikins provide core information that is pertinent to the decision problem (Table 1) and, therefore, have been included in the main body of the submission. Although the majority of data are on aScope, two studies have evaluated aScope2: Vincent2011 (42) in patients with anticipated

difficult airway and Jamadarkhana2011 (43) in patients requiring PDT, and these have been included in the main body of the submission. While a description of the studies is presented in the attached PDFs, their study design, findings and conclusions are summarised in the sections below.

Two studies, Missaghi2011 (44) and Charles2011 (45), were excluded from the submission; and the reasons for this are provided in section 7.3.2. In addition, the unpublished study, R-PS-7-2009/Kristensen (41), investigated awake patients with difficult airway as well as in anaesthetised/sleeping patients with normal airway; data from the latter group have been excluded from the submission (see section 7.3.2).

Of the studies relevant to the scope (Table 1), details of four studies – Kristensen2010 (46), Austin2011 (47), Gernoth2010 (48) and Saumande2010 (49) – have been included in appendices 5–7, as these provide additional supplementary information. Three of these studies – Kristensen2010 (46); Austin2011 (47); Gernoth2010 (48) – are preliminary small-scale case studies each involving four or five patients, and Saumande2010 (49) is a non-clinical randomised study investigating the utility of aScope in combination with a videolaryngoscope. In terms of helping to address potential equality issues, Kristensen2010 (46) reports the usefulness of aScope in difficult airway management of patients with the following:

- Tumour of the hard palate, limited neck-extension and inability to prognath
- Oral cancer
- Suspected oropharyngeal cancer, severely decreased neck extension and thyromental distance of 6 cm
- Intra-thoracic goitre severely compressing the trachea
- Inter-incisor distance of 2.7 cm and inability to prognath

Table 6 List of relevant published studies

Primary study reference	Study name (acronym)	Population	Intervention	Comparator
(38, 39)	Lenhardt2011	Patients with difficult airway scheduled for elective or urgent surgery under general anaesthesia with ETT intubation	aScope	Preformed stylet (from the manufacturers of GlideScope)
(50)	Kumar2011	AirSim Multi manikin (Trucorp Ltd)	aScope	Olympus reusable fibreoptic scope
(42)	Vincent2011	Awake patients with anticipated difficult airways	aScope2	None
(51)	Scutt2011	Three manikins (Airway Trainer [Laerdal]; Bill 1 [VBM]; AirSim [Trucorp Ltd]	aScope	Pentax F1 13RBS
(52)	Vijayakumar2011	AirSim Multi manikin (Trucorp Ltd)	aScope	Olympus LF-GP reusable fibrescope
(53)	Piepho2010	SimMan manikin (Laerdal) and patients with anticipated or unanticipated difficult airways	aScope	Storz flexible intubation fibrescope
(54)	Pujol2010	Patients with predicted difficult intubation	aScope	None
(55)	Perbet2011	Long-term ventilated patients requiring bedside PDT	aScope	None
(43)	Jamadarkhana2011	Patients requiring PDT	aScope2	None
(44)	Missaghi2011	Patients with apparently normal airways	aScope	None
(45)	Charles2011	Patients requiring thoracotomies and thoracoscopies	aScope	Conventional fibrescope (type not stated)
(56)	Seramondi2010	Patients requiring double lumen tubes	aScope	None
(57)	Galindo-Menendez2010	AirSim Multi manikin with normal airway (Trucorp Ltd)	aScope	None
(58)	Kristiansen2011	Patient with difficult airway	aScope	None
(46)	Kristensen2010	Patients with difficult airway	aScope	None
(59)	Laursen2011	Patients with normal airway	aScope	None

(49)	Saumande2010	Intubation trainer mannequin (Storz)	aScope	aScope in combination with Pentax Airwayscope
(47)	Austin2011	Patients requiring PDT	aScope	None
(48)	Gernoth2010	Long-term ventilated patients requiring planned PDT	aScope	None

Table 7 List of relevant unpublished studies

Data source	Study name (acronym)	Population	Intervention	Comparator
(41)	R-PS-7-2009/Kristensen	Awake patients with difficult airway and anaesthetised/ sleeping patients with normal airway	aScope	Olympus BF160 reusable scope

7.3.2 State the rationale behind excluding any of the published studies listed in tables B3 and B4.

- Missaghi et al., (2011) (44) was excluded because the study population, i.e., patients with apparently normal airways, did not meet the population criteria as stated in the decision problem (Table 1)
- Charles et al. (2011) (45) was excluded because the study was undertaken to assess the utility of aScope in controlling distal bronchial structures, which is not related to the decision problem (Table 1)
- Seramondi2010 (56) was excluded because aScope was used in this study to check the position of double lumen tubes and, therefore, is not related to the decision problem (Table 1)
- Galindo-Menendez2010 (57) was excluded because a manikin with normal airway was used in the study and, therefore, did not fulfil the difficult airway criteria stated in the decision problem (Table 1)
- Kristiansen2011 (58) reported a case in which intubation of a difficult airway patient, scheduled for cholecystoscopy, was achieved by inserting aScope through the airway of Aura-I SGA. The procedure was performed by a Clinical Research Specialist at Ambu and, therefore, for fair balance, is excluded from the submission
- Laursen2011 (59) was excluded because aScope was used in patients with normal airway, which does not meet the population criteria as stated in the decision problem (Table 1), and the study was undertaken to evaluate Aura-I

7.4 Summary of methodology of relevant studies

7.4.1 Describe the study design and methodology for each of the published and unpublished studies using tables B5 and B6 as appropriate. A separate table should be completed for each study.

A total of six randomised studies and five observational studies have been included in this section, as these comprise ‘core’ data. Piepho2010 (53) comprised two different types of study: a randomised study in manikins and an observational case

series in patients with anticipated or unanticipated difficult airways. Therefore, for the purposes of this submission, the randomised and observational studies have been captured separately in Tables 9 and 14, respectively. Detailed information on the methodology of each of the studies is provided in the following tables. There is a relatively large variation in the methodology between the studies, which is discussed in more detail in section 7.4.3. It should be noted that this section includes details of R-PS-7-2009/Kristensen (41), which is at present unpublished. Therefore, it is imperative that this information must be treated as ‘academic in confidence’, and must under no circumstances be made available to the public. No manuscript or structured abstract about a future journal publication is available, but the sponsor has provided a statement from the author(s) to verify the data provided (see accompanying document). Similarly, details of Lenhardt2011 (38, 39) provided in this section are based on two sources: a congress poster (39) and additional unpublished information from a study protocol (38). Accordingly, the information from the study protocol must be treated as ‘academic in confidence’ and not be made available for the public. Other than the poster, no manuscript or structured abstract about a future journal publication is available, but the sponsor has provided a statement from the author(s) to verify the data provided (see accompanying document).

Table 8 Summary of methodology for randomised controlled trials; Lenhardt2011 (38, 39)

Study name	Lenhardt2011
Objectives	To test the hypothesis that a combination of video-laryngoscope with a flexible video-stylet is a feasible way to facilitate intubation in patients with a predicted difficult airway
Location	University of Louisville, Louisville, KY, USA
Design	Randomised, prospective
Duration of study	Not stated
Sample size	N=140 patients aged 18–81 years with ASA physical status 1–3
Inclusion criteria	• Body mass index (BMI) >35 • Thyromental distance <6 cm • Sterno-mental distance <12 cm • Mallampati grade 3 and 4 • Interincisor distance <38 mm • Status of dentition: presence of buckteeth • Neck movement <35° • Neck circumference >43 cm [redacted] • Cervical spine pathologies • [redacted]History of difficult intubation [redacted]
Exclusion criteria	• [redacted]
Method of randomisation	Randomisation was stratified as to whether patients were categorized as predicted difficult airway or had an immobilized cervical spine [redacted]

Method of blinding	Not stated
Intervention(s) (n =) and comparator(s) (n =)	aScope vs preformed stylet (from the manufacturers of GlideScope). N-numbers not stated
Baseline differences	Not stated
Duration of follow-up, lost to follow-up information	Not stated
Statistical tests	[redacted]
Primary outcomes (including scoring methods and timings of assessments)	[redacted]
Secondary outcomes	• [redacted]

(including scoring methods and timings of assessments)	[redacted]

Table 9 Summary of methodology for randomised controlled trials; Piepho2010 (53)

Study name	Piepho2010
Objectives	To examine the value of this novel videoscope in simulated difficult (and normal) airways
Location	University Medical Centre of the Johannes Gutenberg-University, Mainz, Germany
Design	Randomised study in a manikin
Duration of study	Not stated
Sample size	N=21 participants
Inclusion criteria	Not stated
Exclusion criteria	Not stated
Method of randomisation	Order of participation by anaesthetists in the scenarios, and the order in which the devices were used, were randomised
Method of blinding	N/A
Intervention(s) (n =) and comparator(s) (n =)	aScope vs Storz flexible intubation fibrescope. Participants used both the intervention and comparator
Baseline differences	All 21 participants had experience of ≥50 tracheal intubations using a fibrescope (ranging from 50 to over 1000) at the time of the investigation: four (19%) anaesthetists had undertaken between 50 and 100 intubations; nine

	(43%) between 100 and 500; seven (33%) between 500 and 1000, and one (5%) participant had undertaken more than 1000 documented intubations using an intubation fibrescope
Duration of follow-up, lost to follow-up information	Not stated
Statistical tests	Time to tracheal intubation was analysed using the t-test; success rates were analysed using the chi-squared test; and rating data were analysed using the Mann-Whitney test. A p-value of <0.05 was considered to be statistically significant
Primary outcomes (including scoring methods and timings of assessments)	• Time required to position the scope (defined as the time period between touching the handle of the scope and passage of its tip through the glottis) • Time for successful tracheal intubation (a failed intubation was defined as an attempt in which the participant resigned or required >180 s)
Secondary outcomes (including scoring methods and timings of assessments)	Rating of the devices (on a scale from 1 to 6: 1, excellent; 2, good; 3, satisfactory; 4, sufficient; 5, inadequate; 6, fail). In addition participants scored the picture quality, rigidity of the flexible insertion tube and the tip articulation for both scopes using the same scale

Table 10 Summary of methodology for randomised controlled trials; Vijayakumar2011 (52)

Study name	Vijayakumar2011
Objectives	To compare the manoeuvrability and ease of use of aScope and Olympus reusable fibrescope in a manikin set to simulate difficult fibrescope placement
Location	• Cardiff and Vale University Health Board, Cardiff, UK • Royal Gwent Hospital, Newport, UK • Cardiff University, Cardiff, UK
Design	Randomised, crossover, non-inferiority study
Duration of study	Not stated
Sample size	75 anaesthetists (34 consultants and 41 trainee anaesthetists) took part in the study

Inclusion criteria	Anaesthetists with >10 fibrescope placements (manikin and patient experience) were eligible
Exclusion criteria	Anaesthetists with <10 fibrescope placements (manikin and patient experience) were not studied
Method of randomisation	Each participant was asked to complete a standardised task on the manikin with both the Ambu aScope and Olympus reusable fibrescope in a computer-generated randomised order
Method of blinding	Two members of the research team, who were blinded to the participant's identity, independently counted the number of tip surface collisions from video recordings
Intervention(s) (n =) and comparator(s) (n =)	aScope vs Olympus LF-GP reusable fibrescope. Participants used both the intervention and comparator
Baseline differences	Participants: the median (interquartile range [range]) number of years of anaesthetic experience of the participants was 9 (5–15 [1–27]) years, and the number of fibrescope placements performed by the participating anaesthetists was 15 (6–30 [0–1000]) on manikins, 20 (11–40 [0–150]) on anaesthetised patients and 10 (4–20 [0–700]) on awake sedated patients
Duration of follow-up, lost to follow-up information	N/A
Statistical tests	The primary outcome measure of time to task completion was analysed using confidence intervals and a one-sided t-test to test the null hypothesis of a difference in time to task completion of at least 30 s against the alternative hypothesis that the difference was <30 s, appropriate for this non-inferiority study. Other data with normal distribution were analysed using paired samples t-tests
Primary outcomes (including scoring methods and timings of assessments)	Time to task completion (defined as the time from picking up the fibrescope to the time the tip of the fibrescope appeared through the manikin's left main bronchus was recorded as the time to completion of the task. Inability to complete the task by either resigning the task or requiring >180 s was considered a failure)
Secondary outcomes (including scoring methods and timings of assessments)	• Number of tip surface collisions (defined as complete or partial red or white out of the screen for any length of time) • Participants' impression on the ease of use (recorded on a 100 mm VAS: 0 mm = extremely difficult and 100 mm = extremely easy)

Table 11 Summary of methodology for randomised controlled trials; Scutt2011 (51)

Study name	Scutt2011
Objectives	To compare aScope with a conventional fibrescope in two simulated settings: paired nasal and oral fibreoptic intubations in three different manikins; intubation of a manikin via three supraglottic airways: classic and intubating laryngeal mask airways and i-gel (a total of 66 intubations)
Location	Royal United Hospital, Combe Park, Bath, UK
Design	The order of fibrescope, manikin and route of intubation were randomised
Duration of study	Not stated
Sample size	• Part 1 (aScope vs. conventional fibrescope for nasal and oral intubation in three manikins): 22 volunteer anaesthetists • Part 2 (aScope vs. conventional fibrescope for intubation via a SAD conduit): 21 volunteer anaesthetists
Inclusion criteria	Not stated
Exclusion criteria	Not stated
Method of randomisation	The order of fibrescope, manikin and route of intubation were randomised
Method of blinding	N/A
Intervention(s) (n =) and comparator(s) (n =)	aScope vs Pentax F1 13RBS. Participants used both the intervention and comparator
Baseline differences	Previous experience in fibreoptic intubation of participants was 0–30 intubations (30% participants), 31–100 (40%) and >100 (30%)
Duration of follow-up, lost to follow-up information	Not stated
Statistical tests	Wilcoxon signed-rank test, two-tailed Fisher's exact test and ANOVA as appropriate. For ANOVA, the outcome measure of interest was treated as the dependent variable and fibrescope type (aScope vs. conventional fibrescope), manikin type (Airway Trainer vs. Bill 1 vs. Airsim) and route (nasal vs. oral or via cLMA vs. via i-gel vs. via ILMA) were the potentially influential factors. Statistical significance was recorded when $p<0.05$
Primary outcomes (including scoring	Time to intubate (from starting endoscopy with a preloaded tracheal tube to first lung ventilation)

methods and timings of assessments)	
Secondary outcomes (including scoring methods and timings of assessments)	• Number of attempts (defined as withdrawal of the fibrescope from the manikin) • Participant-reported problems; ease of endoscopy and ease of railroading as reported by the participant using a verbal rating scale (VRS) scored 0–10 (0=impossible to 10=extremely easy) • Overall usefulness using a VRS score 0–10 (0=no use to10=extremely useful) • On completing all intubations participants rated device quality and image quality (excellent/good/fair/poor/inadequate) and overall performance for fibreoptic intubation (excellent/good/adequate/inadequate/unusable)

Table 12 Summary of methodology for randomised controlled trials; Kumar2011 (50)

Study name	Kumar2011
Objectives	To compare the handling and ease of use of aScope with an Olympus reusable fibreoptic scope during placement (via nasal route) in the trachea of a manikin, modified by narrowing the airway in three places
Location	Cardiff University, Cardiff, UK
Design	Randomised, crossover
Duration of study	Not stated
Sample size	75 volunteer anaesthetists
Inclusion criteria	Not stated
Exclusion criteria	Not stated
Method of randomisation	Not stated
Method of blinding	N/A
Intervention(s) (n =) and comparator(s) (n =)	aScope vs. Olympus reusable fibreoptic scope. Participants used both the intervention and comparator, and were asked to perform the task twice with each scope
Baseline differences	The median (interquartile range) number of years of anaesthetic experience of the participants was 9 (5–15)

	years
Duration of follow-up, lost to follow-up information	Not stated
Statistical tests	Not stated
Primary outcomes (including scoring methods and timings of assessments)	• Time to complete the task (from handling the scope to the time the tip of the scope appeared through the left main bronchus) • User device preference • Participants' impression on the ease of use (VAS: 0 mm = extremely difficult, 100 mm = extremely easy) • Number of tip surface collisions (defined as a complete red out on the screen)
Secondary outcomes (including scoring methods and timings of assessments)	None

Table 13 Summary of methodology for randomised controlled trials; R-PS-7-2009/Kristensen (41)

Study name	R-PS-7-2009/Kristensen
Objectives	Post-marketing study to compare the performance of aScope with the Olympus BF160 reusable scope for securing difficult airway with an ETT in patients scheduled for elective ear nose and throat (ENT) surgery
Location	Copenhagen University Hospital, Rigshospitalet, Denmark
Design	Comparative, randomised controlled trial
Duration of study	First patient included in the randomised part of the study: March 2010 Last patient included in the randomised part of the study: December 2010
Sample size	N=40 patients with anticipated difficult airways
Inclusion criteria	• American Society of Anesthesiologists (ASA) I, II or III • ≥18 years of age

	• Suitable for awake oral endotracheal intubation according to preoperative assessment • Scheduled for elective or acute ENT surgery • Sufficient effect of local anaesthetic is achievable • Placement of Berman airway is possible • Signed consent form
Exclusion criteria	• Massive bleeding in oral cavity or trachea • ASA IV or V • Previous attempts using fibreoptic intubation have failed • Documented allergy to local anaesthesia • Presence of stridor • Dyspnoea
Method of randomisation	StatistiCall produced randomisation lists using ClinStart software (version dated 08.08.1996 from St George's Hospital Medical School). Block randomisation was used. The sponsor prepared envelopes according to the randomisation list. All envelopes were numbered in sequence, and the number matched the patients' trial number. Each time the investigator received a consent form from a patient, they would draw a new envelope – in numbered order
Method of blinding	Not stated
Intervention(s) (n =) and comparator(s) (n =)	aScope (N=20) and Olympus BF160 reusable scope (N=20)
Baseline differences	No significant differences for any demographic parameters (gender, age, weight, height and BMI) between the aScope group and Olympus BF160 group. In addition, no significant differences for preoperative evaluations of the airway (Mallampati scope, mouth opening, thyromental distance, ability to undershoot the tooth row, weight, movement of neck column, previous history of difficult airway and pathology) between the two groups
Duration of follow-up, lost to follow-up information	Not stated
Statistical tests	• All results were included in the statistical report. Statistical analyses were performed for both intention-to-treat (ITT) and per protocol (PP) participants, but the clinical conclusions of the study were based on the PP

	population. All statistical comparisons between groups were carried out with a significance level of 5%, and analysed using SPSS version 17 (or newer) • Two minutes of difference between the groups was defined as the clinically relevant time difference • Student t-test; Wilcoxon test; Chi-square test; Mann-Whitney test; Fisher's Exact test
Primary outcomes (including scoring methods and timings of assessments)	Intubation time, which was divided into four phases: • Scope time upper airway was the time from when the distal end was placed in front of the mouth until it reached the edge of the epiglottis • Injection of lidocaine was measured and the intubation procedure was complete • Scope time to lower airway was the time from when the scope was placed on the edge of the epiglottis until the scope was 5 cm above the carina • Time spent on endotracheal intubation was the time from when the ETT was guided through the mouth until the first CO_2 curve was seen
Secondary outcomes (including scoring methods and timings of assessments)	• Endotracheal intubation success rate • Number of scope attempts • Number of intubation attempts (note that total intubation time, without including injection of lidocaine, should not exceed 8 minutes, otherwise patients were regarded as a dropout) • Total time spent on intubation and local anaesthetic • Assessment of insertion cord, working channel and the quality of monitor image • Time spent on cleaning and preparing the endoscopes • Adverse events and serious adverse events • Adverse device events and serious adverse device events

Table 14 Summary of methodology for observational studies; Piepho2010 (53)

Study name	Piepho2010

<table>
<tr><td>Objective</td><td>To evaluate the utility of aScope to facilitate tracheal intubation in patients with anticipated or unanticipated difficult airways</td></tr>
<tr><td>Location</td><td>University Medical Centre of the Johannes Gutenberg-University, Mainz, Germany</td></tr>
<tr><td>Design</td><td>Case series</td></tr>
<tr><td>Duration of study</td><td>Not stated</td></tr>
<tr><td>Patient population</td><td>Unanticipated or anticipated difficult airway</td></tr>
<tr><td>Sample size</td><td>• N=5 patients
• N=1 anaesthetist</td></tr>
<tr><td>Inclusion criteria</td><td>Unanticipated or anticipated difficult airway</td></tr>
<tr><td>Exclusion criteria</td><td>Not stated</td></tr>
<tr><td>Intervention(s) (n =) and comparator(s) (n =)</td><td>aScope (N=5)</td></tr>
<tr><td>Baseline differences</td><td>Characteristics of patients included in the study as listed here:
<table><tr><th>Number</th><th>Indication</th><th>Age; years</th><th>Sex</th><th>Height; m</th><th>Weight; kg</th><th>Route of intubation</th><th>Internal diameter of tracheal tube; mm</th></tr><tr><td>1</td><td>Unanticipated difficult airway</td><td>65</td><td>Male</td><td>1.79</td><td>87</td><td>oral</td><td>7.5</td></tr><tr><td>2</td><td>Anticipated difficult airway</td><td>53</td><td>Female</td><td>1.72</td><td>82</td><td>nasal</td><td>6.5</td></tr><tr><td>3</td><td>Unanticipated difficult airway</td><td>57</td><td>Male</td><td>1.75</td><td>79</td><td>oral</td><td>7.5</td></tr><tr><td>4</td><td>Anticipated difficult airway</td><td>77</td><td>Male</td><td>1.88</td><td>95</td><td>nasal</td><td>6.5</td></tr><tr><td>5</td><td>Anticipated difficult airway</td><td>45</td><td>Female</td><td>1.63</td><td>55</td><td>nasal</td><td>6.5</td></tr></table>
All five patients were placed supine with their head and neck maintained in a neutral position</td></tr>
<tr><td>How were participants followed-up (for example, through</td><td>Not stated</td></tr>
</table>

pro-active follow-up or passively). Duration of follow-up, participants lost to follow-up	
Statistical tests	None performed
Primary outcomes (including scoring methods and timings of assessments)	Not stated
Secondary outcomes (including scoring methods and timings of assessments)	Not stated

Table 15 Summary of methodology for observational studies; Pujol2010 (54)

Study name	Pujol2010
Objective	To assess the performance of the aScope in patients with predicted difficult tracheal intubations
Location	Hospital Clinic de Barcelona, Barcelona, Spain
Design	Case series
Duration of study	Not stated
Patient population	Patients undergoing general anaesthesia, presenting with a difficult intubation
Sample size	N=10 patients

Inclusion criteria	Predicted difficult intubation
Exclusion criteria	Not stated
Intervention(s) (n =) and comparator(s) (n =)	aScope (N=10 patients)
Baseline differences	For the 10 patients: age range was 35–81 years; median (interquartile range [range]) Arne score was 21.5 (13–36 [11– 41]); five patients had pathology associated with a difficult intubation (intra-oral tumour, maxillary neoplasm, graft reconstruction of the upper lip, acromegaly and Coffin-Lowry syndrome); two patients had a history of difficult intubation and previous awake intubation; and the modified Mallampati score was 3 and 4 in six and four patients, respectively
How were participants followed-up (for example, through pro-active follow-up or passively). Duration of follow-up, participants lost to follow-up	Not stated
Statistical tests	None performed
Primary outcomes (including scoring methods and timings of assessments)	Intubation success
Secondary outcomes (including scoring methods and timings of assessments)	• Ease of use using a three-point scale: 1=difficult insertion/manipulation due to limitation of device manoeuvrability; 2=difficult insertion/advancement due to resistance in passing the scope; and 3 easy insertion • Image quality assessed using a four-point scale: 1=insufficient image to permit intubation; 2=poor; 3=adequate; and 4=excellent

Table 16 Summary of methodology for observational studies; Vincent2011 (42)

Study name	Vincent2011
Objective	To evaluate aScope2 in awake patients with anticipated difficult airway requiring fibreoptic intubation
Location	Guys and St Thomas Hospital NHS Trust, London, UK
Design	Case series
Duration of study	Not stated
Patient population	Patients with anticipated difficult airway requiring elective ENT and maxillofacial surgeries
Sample size	N=8 patients; three consultant anaesthetists with special interest in difficult airway management participated in the study
Inclusion criteria	• Anticipated difficult airway • ENT and maxillofacial surgeries
Exclusion criteria	None stated
Intervention(s) (n =) and comparator(s) (n =)	aScope2 (N=8 patients)
Baseline differences	Mean (range) body mass index (BMI) of the eight patients was 23.75 (17–35)
How were participants followed-up (for example, through pro-active follow-up or passively). Duration of follow-up, participants lost to follow-up	Not stated
Statistical tests	None performed
Primary outcomes (including scoring methods and timings of	• Intubation success • Time for scope position

assessments)	
Secondary outcomes (including scoring methods and timings of assessments)	• Performance of aScope2 (assessed using VRS)

Table 17 Summary of methodology for observational studies; Perbet2011 (55)

Study name	Perbet2011
Objective	To evaluate aScope for guiding PDT in long-term ventilated patients in ICU
Location	University Hospital of Clermont-Ferrand, France
Design	Prospective case study
Duration of study	Not stated
Patient population	Patients requiring a bedside PDT
Sample size	N=10 patients
Inclusion criteria	Long-term ventilated patients requiring PDT
Exclusion criteria	None stated
Intervention(s) (n =) and comparator(s) (n =)	aScope (N=10 patients)
Baseline differences	Median (range) age of patients was 60 (49–70) years, Lymph Gland Cleanse (IGS II; range) was 46 (39–62), and duration of mechanical ventilation from last intubation (range) was 14 (8–22) days
How were participants followed-up (for example, through pro-active follow-up or	Not stated

passively). Duration of follow-up, participants lost to follow-up	
Statistical tests	None performed
Primary outcomes (including scoring methods and timings of assessments)	• Conditions of procedure (duration and visualisation) evaluated by a scale of very unsatisfied/unsatisfied/satisfied/very satisfied
Secondary outcomes (including scoring methods and timings of assessments)	• Costs of fibrescope repair were evaluated retrospectively for the last 5 years

Table 18 Summary of methodology for observational studies; Jamadarkhana2011 (43)

Study name	Jamadarkhana2011
Objective	To assess the feasibility of aScope2 endoscopic guidance during PDT
Location	Leeds General Infirmary, Leeds, UK
Design	Case study
Duration of study	Not stated
Patient population	Patients requiring PDT
Sample size	N=10 patients
Inclusion criteria	Patients requiring PDT
Exclusion criteria	Not stated
Intervention(s) (n =) and comparator(s) (n =)	aScope2 (N=10 patients)

Baseline differences	Average age (range) of patients was 62 (55–80) years, and in 90% of patients PDT was performed between 3 and 6 days after tracheal intubation
How were participants followed-up (for example, through pro-active follow-up or passively). Duration of follow-up, participants lost to follow-up	Not stated
Statistical tests	None performed
Primary outcomes (including scoring methods and timings of assessments)	• Ease of use • Quality of image (brightness, focus, resolution) on a scale of 1 – 10 (1=poor view, 10=best view)
Secondary outcomes (including scoring methods and timings of assessments)	• Arterial blood gases, ventilatory and cardiovascular parameters prior to, during and after the procedure

7.4.2 Provide details on data from any single study that have been drawn from more than one source (for example a poster and unpublished report) and/or when trials are linked this should be made clear (for example, an open-label extension to randomised controlled trial).

Information for Lenhardt2011 (38, 39) was taken from a published congress poster (39) and a study protocol (38). As the information from the study protocol is unpublished it must be treated as 'academic in confidence' and not be made available to the public.

7.4.3 Highlight any differences between patient populations and methodology in all included studies.

A number of differences in terms of study population and methodology exist between the studies, including:

Type of aScope:

Two studies, Vincent2011 (42) and Jamadarkhana2011 (43), investigated aScope2, whereas the remaining studies investigated its predecessor aScope. However, data derived from the studies investigating aScope are still highly relevant and valid for this submission because aScope2 is basically the same product as aScope, but with certain advancements, e.g., easy clearing membrane and no 30-minute time-out feature.

Patient populations:

Different patient populations were included in the studies: patients were considered to either have difficult or normal airway, or be candidates for PDT. In addition, a variety of manikins were used in the studies to simulate different intubation situations.

Baseline differences:

Baseline characteristics were often not reported in the published studies so it is difficult to quantify the differences, but variables included dental status, age, Arne score, pathology, history of difficult intubation, Mallampati score, BMI, and reasons for long-term ventilation and airway management. In addition, differences were also apparent between the different volunteer anaesthetists participating in the studies,

and these included previous experience in performing intubations using a fibrescope and number of years with anaesthetic experience.

Delivery of intervention:

Two different routes of intubation were investigated, i.e., nasal and oral.

Care setting:

Four studies – the ones involving patients requiring PDT (Perbet2011 (55); Jamadarkhana2011 (43); Austin2011 (47); Gernoth2010 (48)) – were undertaken in the ICU. The other studies were carried out in locations other than ICU (e.g., operating rooms).

Comparators:

A range of comparator scopes were included in the studies, including those made by Olympus, Storz and Pentax. In addition, several of the studies did not include a comparator.

7.4.4 Provide details of any subgroup analyses that were undertaken in the studies included in section 7.4.1. Specify the rationale and state whether these analyses were pre-planned or post-hoc.

N/A.

7.4.5 If applicable, provide details of the numbers of patients who were eligible to enter the study(s), randomised, and allocated to each treatment in an appropriate format.

N/A.

7.4.6 If applicable provide details of and the rationale for, patients that were lost to follow-up or withdrew from the studies.

N/A.

7.5 Critical appraisal of relevant studies

7.5.1 Complete a separate quality assessment table for each study. A suggested format for the quality assessment results is shown in tables B7 and B8.

The studies included in this section match those in the previous section, i.e., the six randomised and five observational studies. The unpublished study R-PS-7-2009/Kristensen (41), and information from a study protocol (38) accompanying the Lenhardt2011 (39) poster, are included in this section. Therefore, as the information from the study protocol is unpublished it is imperative that it is treated as 'academic in confidence' and not be made available to the public. Critical appraisal of studies was based on principles of the CRD.

Table 19 and 20 summarise the study question and response for each study included in the submission; however, please see appendix 6 for the details on how the questions were addressed in each of these studies.

Table 19 Critical appraisal of randomised control trials

Study name	Lenhardt2011 (38, 39)	Piepho2010 (53)	Vijayakumar 2011 (52)	Scutt2011 (51)	Kumar2011 (50)	R-PS-7-2009/Kristensen (41)
Study question	**Response (yes/no/not clear/N/A)**	**Response (yes/no/not clear/N/A)**	**Response (yes/no/not clear/N/A)**	**Response (yes/no/not clear/N/A)**	**Response (yes/no/not clear/N/A)**	**Response (yes/no/not clear/N/A)**
Was randomisation carried out appropriately?	Yes	Yes	Yes	Yes	Not clear	Yes
Was the concealment of treatment allocation adequate?	N/A	N/A	N/A	N/A	N/A	N/A
Were the groups similar at the outset of the study in terms of prognostic factors, for example, severity of disease?	Not clear	Yes	Yes	Yes	Yes	Yes
Were the care providers, participants and outcome assessors blind to treatment allocation? If any of these people were not blinded, what might be the likely impact on the risk of bias (for each outcome)?	Not clear	Not clear	Not clear	Not clear	Not clear	Not clear
Were there any unexpected imbalances in drop-outs between groups? If so, were they explained or adjusted for?	No	N/A	N/A	N/A	N/A	N/A
Is there any evidence to suggest that the authors measured more outcomes than they reported?	Not clear	No	No	No	No	No

Did the analysis include an intention-to-treat analysis? If so, was this appropriate and were appropriate methods used to account for missing data?	N/A	N/A	N/A	N/A	N/A	Yes
Adapted from Centre for Reviews and Dissemination (2008) Systematic reviews. CRD's guidance for undertaking reviews in health care. York: Centre for Reviews and Dissemination						

Table 20 Critical appraisal of observational studies

Study name	**Piepho2010 (53)**	**Pujol2010 (54)**	**Vincent2011 (42)**	**Perbet2011 (55)**	**Jamadarkhana2011 (43)**
Study question	**Response yes/no/not clear/N/A)**	**Response yes/no/not clear/N/A)**	**Response yes/no/not clear/N/A)**	**Response yes/no/not clear/N/A)**	**Response yes/no/not clear/N/A)**
Was the cohort recruited in an acceptable way?	Yes	Yes	Yes	Yes	Yes
Was the exposure accurately measured to minimise bias?	N/A	N/A	N/A	N/A	N/A
Was the outcome accurately measured to minimise bias?	N/A	Yes	Yes	Yes	Yes
Have the authors identified all important confounding factors?	Not clear	Not clear	Not clear	Not clear	Not clear
Have the authors taken account of the confounding factors in the design and/or analysis?	N/A	N/A	N/A	N/A	N/A

Was the follow-up of patients complete?	N/A	N/A	N/A	N/A	N/A
How precise (for example, in terms of confidence interval and p values) are the results?	N/A	N/A	N/A	N/A	N/A
Adapted from Critical Appraisal Skills Programme (CASP): Making sense of evidence 12 questions to help you make sense of a cohort study					

7.6 Results of the relevant studies

7.6.1 Complete a results table for each study with all relevant outcome measures pertinent to the decision problem. A suggested format is given in table B9.

Results are reported here from the six randomised studies and five observational studies included in sections 7.4 and 7.5. P-values and 95% confidence intervals are provided, where available. The robustness of data provided in this section is influenced by inherent variability in study methodology, design, number of patients and/or participants and assessments between the studies, which is reflected in the following tables. The unpublished study R-PS-7-2009/Kristensen (41), and unpublished information from a study protocol (38) accompanying the Lenhardt2011 (39) poster, are included in this section. Therefore, information from the study protocol must be treated as ‘academic in confidence’ and not be made available to the public.

Table 21 Outcomes from published and unpublished studies; Lenhardt2011 (38, 39)

Study name		**Lenhardt2011**
Size of study groups	**Treatment**	aScope
	Control	Preformed stylet (from the manufacturers of GlideScope)
Study duration	**Time unit**	N/A
Type of analysis	**Intention-to-treat/per protocol**	N/A
Outcome	**Name**	Intubation attempts
	Unit	Number
Effect size	**Value**	1.1±0.4 (aScope) vs 1.2±0.6 (control)
	95% CI	N/A
Statistical test	**Type**	[redacted]
	p value	0.4

Other outcome	**Name**	Average time to intubation
	Unit	• Seconds • [redacted]
Effect size	**Value**	95±63 (aScope) vs 104±100 (control)
	95% CI	N/A
Statistical test	**Type**	[redacted]
	p value	0.6
Other outcome	**Name**	Time interval of visualisation to intubation
	Unit	Seconds
Effect size	**Value**	61±37 (aScope) vs 69±74 (control)
	95% CI	N/A
Statistical test	**Type**	[redacted]
	p value	0.1
Other outcome	**Name**	Subgroup analysis of patients with a time interval of visualisation to intubation of >60 seconds
	Unit	Seconds

Effect size	**Value**	100±38 (aScope) vs 164±127 (control)
	95% CI	N/A
Statistical test	**Type**	[redacted]
	p value	0.04
Comments		• All patients were successfully intubated • No serious complications were encountered

Table 22 Outcomes from published and unpublished studies; Piepho2010 (53)

Study name		**Piepho2010**
Size of study groups	**Treatment**	aScope
	Control	Storz flexible fibrescope
Study duration	**Time unit**	N/A
Type of analysis	**Intention-to-treat/per protocol**	N/A
Outcome	**Name**	Time to tracheal intubation
	Unit	Seconds
Effect size	**Value**	In the difficult airway scenario (as in the normal airway scenario), the times for passage of the tip of the scopes through the vocal chords and for successful tracheal intubation were similar for both devices (see below) Times for passage of the 'scope tip through the glottis and for placement of the tracheal tube (TT) into the trachea for both normal and difficult airway simulations, using the aScope and the standard fibrescope. Data are expressed as mean (SD). **Passage through glottis; s** / **TT placed in the trachea; s** Normal airway aScope: 14 (9.6) / 32 (15.1) fibrescope: 11 (6.1) / 29 (14.1) Difficult airway aScope: 43 (27.3) / 63 (36.1) fibrescope: 33 (16.1) / 56 (24.5)
	95% CI	N/A
Statistical	**Type**	t-test

test	**p value**	Unknown
Other outcome	**Name**	Intubation success
	Unit	Number
Effect size	**Value**	In the difficult airway scenario, 14/21 (67%) attempts to intubate the trachea were successful using the aScope, compared with 17/21 (81%) using the intubation fibrescope
	95% CI	N/A
Statistical test	**Type**	Chi-squared test
	p value	0.02
Other outcome	**Name**	Rating of the devices
	Unit	Scores
Effect size	**Value**	Compared with the aScope, the standard intubation fibrescope scored more highly on overall assessment ($p<0.0001$), rigidity ($p<0.0001$) and articulation of the tip ($p=0.0032$). The picture quality of the aScope monitor received a lower rating compared with that used for the intubation fibrescope ($p=0.0004$) (see below) Distribution of scores for the aScope and the standard fibrescope.

		1 (n) 2 (n) 3 (n) 4 (n) 5 (n) 6 (n) Median (IQR [range]) Overall Rating aScope 1 7 8 4 1 0 3 (2–3.25 [1–5]) fibrescope 4 16 1 0 0 0 2 (1.75–2 [1–2.5])*** Rigidity aScope 0 6 7 5 3 0 3 (2–4 [2–5]) fibrescope 6 11 4 0 0 0 2 (1–2 [1–3])*** Tip Articulation aScope 1 9 7 1 3 0 3 (2–3 [1–5]) fibrescope 3 16 2 0 0 0 2 (2–2 [1–3])* Picture Quality aScope 1 6 7 5 2 0 3 (2–4 [1–5]) fibrescope 4 14 3 0 0 0 2 (1.5–2 [1–3])*** Rating of the intubation fibrescope and the aScope on a scale of 1–6 (1, excellent; 2, good; 3, satisfactory; 4, sufficient; 5, inadequate; 6, fail). *p < 0.01; ***p < 0.0001.
	95% CI	N/A
Statistical test	**Type**	Mann-Whitney test
	p value	See 'Value' box above
Comments		• Overall, three physicians failed to intubate using both scopes • Although none of the participants had experience in using the aScope before the study, the time intervals for both airway simulations were similar to those when using the intubation fibrescope

Table 23 Outcomes from published and unpublished studies; Vijayakumar2011 (52)

Study name		**Vijayakumar2011**
Size of study groups	**Treatment**	aScope
	Control	Olympus reusable fibrescope
Study duration	**Time unit**	N/A
Type of	**Intention-to**	N/A

<table>
<tr><td>analysis</td><td>-treat/per protocol</td><td></td></tr>
<tr><td rowspan="2">Outcome</td><td>Name</td><td>Primary outcome: Time to task completion</td></tr>
<tr><td>Unit</td><td>Seconds</td></tr>
<tr><td rowspan="2">Effect size</td><td>Value</td><td>For the first attempt, there were 73 pairs of data. For the test of non-inferiority, the null hypothesis of a difference of >30 s was rejected and the alternative hypothesis that the difference was <30 s was accepted (see below). A similar result was found when comparing the second attempts. The second attempt for the devices was significantly faster than the first attempt for the time to task completion
Task completion time for Ambu and Olympus fibrescopes when performed by 75 anaesthetists. Values are mean (SD) ([95% CI for the difference between means]).
<table><tr><th></th><th>Ambu</th><th>Olympus</th><th>Difference</th><th>p value*</th></tr><tr><td>Task completion time; s</td><td></td><td></td><td></td><td></td></tr><tr><td>First attempt</td><td>63 (31)</td><td>53 (23)</td><td>10 (3–17)</td><td>0.008</td></tr><tr><td>Second attempt</td><td>48 (23)</td><td>41 (19)</td><td>6 (2–11)</td><td>0.01</td></tr><tr><td>p value†</td><td>< 0.001</td><td>< 0.001</td><td></td><td></td></tr></table>*p value for difference between the devices (first attempt only compared); p < 0.05 rejects the null hypothesis of a difference of more than 30 s.
†p value for difference between first and second attempts.</td></tr>
<tr><td>95% CI</td><td>See ‘Value’ box above</td></tr>
<tr><td rowspan="2">Statistical test</td><td>Type</td><td>One-sided t-test to test the null hypothesis of a difference in time to task completion of at least 30 s against the alternative hypothesis that the difference was <30 s, appropriate for this non-inferiority study. Sample size was calculated using a non-inferiority approach. A sample size of 72 would achieve 90% power to detect non-inferiority using a one-sided t-test when the margin of equivalence is 30 s and the true difference between the mean and the reference value is zero. The data were drawn from a single population with a standard deviation of 77 s for time to task completion. The significance level (alpha) of the test was set at 0.025. A sample size of 75 was chosen to allow for dropouts</td></tr>
<tr><td>p value</td><td>0.001</td></tr>
</table>

<table>
<tr><td rowspan="2">Other outcome</td><td>Name</td><td>Secondary outcome: Tip surface collisions</td></tr>
<tr><td>Unit</td><td>Number</td></tr>
<tr><td rowspan="2">Effect size</td><td>Value</td><td>No significant differences were found in the number of tip surface collisions between the two fibrescopes; and there was no difference between the first and second attempt for the number of tip surface collisions (see below)
Tip surface collision count for Ambu and Olympus fibrescopes when performed by 75 anaesthetists. Values are mean (SD) (95% CI for difference between means).
<table><tr><th></th><th>Ambu</th><th>Olympus</th><th>Difference</th><th>p value*</th></tr><tr><td>Tip collision count</td><td></td><td></td><td></td><td></td></tr><tr><td>First attempt</td><td>2.7 (1.9)</td><td>2.5 (1.8)</td><td>0.2 (−0.4–0.7)</td><td>0.56</td></tr><tr><td>Second attempt</td><td>2.6 (2.0)</td><td>2.6 (1.8)</td><td>0.0 (−0.5–0.4)</td><td>0.89</td></tr><tr><td>p value†</td><td>0.84</td><td>0.43</td><td></td><td></td></tr></table>*p value for comparisons between devices.
†p value for difference between first and second attempts.</td></tr>
<tr><td>95% CI</td><td>See ‘Value’ box above</td></tr>
<tr><td rowspan="2">Statistical test</td><td>Type</td><td>Paired samples t-test</td></tr>
<tr><td>p value</td><td>See ‘Value’ box above</td></tr>
<tr><td rowspan="2">Other outcome</td><td>Name</td><td>Secondary outcome: Participants’ impression on the ease of use</td></tr>
<tr><td>Unit</td><td>VAS (i.e., mm)</td></tr>
<tr><td rowspan="2">Effect size</td><td>Value</td><td>Participants found the Olympus significantly easier to use than the aScope (difference of 12 mm). Mean (SD) visual analogue scores for the perceived ease of use (0 mm=extremely difficult and 100 mm=extremely easy) was 77 (14) mm and 65 (18) mm for the Olympus and aScope, respectively</td></tr>
<tr><td>95% CI</td><td>7–17</td></tr>
<tr><td rowspan="2">Statistical test</td><td>Type</td><td>Paired samples t-test</td></tr>
<tr><td>p value</td><td>0.0001</td></tr>
<tr><td colspan="2">Comments</td><td>• aScope appeared to be an acceptable alternative to the reusable fibrescope</td></tr>
</table>

Table 24 Outcomes from published and unpublished studies; Scutt2011 (51)

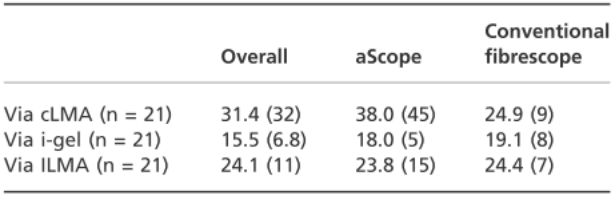
<table>
<tr><td colspan="2">Study name</td><td>Scutt2011</td></tr>
<tr><td rowspan="2">Size of study groups</td><td>Treatment</td><td>aScope</td></tr>
<tr><td>Control</td><td>Pentax F1 13RBS</td></tr>
<tr><td>Study duration</td><td>Time unit</td><td>N/A</td></tr>
<tr><td>Type of analysis</td><td>Intention-to-treat/per protocol</td><td>N/A</td></tr>
<tr><td rowspan="2">Outcome</td><td>Name</td><td>Primary outcome: Time to intubate</td></tr>
<tr><td>Unit</td><td>Seconds</td></tr>
<tr><td>Effect size</td><td>Value</td><td>

Part 1: Neither the type of fibrescope (p=0.18) nor the route (p=0.20) had statistically significant effects on intubation time, but manikin type did (p<0.001) (see below)

Time (s) taken for fibreoptic intubation via three individual manikins. Values are mean (SD).
<table>
<tr><th></th><th>Overall</th><th>aScope</th><th>Conventional fibrescope</th></tr>
<tr><td>Airway Trainer oral (n = 22)</td><td>41.0 (29)</td><td>40.0 (26)</td><td>42.0 (32)</td></tr>
<tr><td>Bill 1 oral (n = 22)</td><td>87.6 (79)</td><td>97.1 (80)</td><td>78.1 (80)</td></tr>
<tr><td>Airsim oral (n = 22)</td><td>53.9 (38)</td><td>61.9 (45)</td><td>45.9 (27)</td></tr>
<tr><td>Airway Trainer nasal (n = 22)</td><td>28.3 (13)</td><td>32.2 (15)</td><td>24.4 (8)</td></tr>
<tr><td>Bill 1 nasal (n = 22)</td><td>50.5 (56)</td><td>40.5 (27)</td><td>60.4 (75)</td></tr>
<tr><td>Airsim nasal (n = 22)</td><td>73.6 (70)</td><td>88.2 (92)</td><td>59.0 (32)</td></tr>
</table>

Part 2: Generally, intubation times were faster when using a conduit (see below) than without (see above). The type of fibrescope had no statistically significant effect on intubation speed (p=0.30), but the type of conduit had (p=0.02)

</td></tr>
</table>

		Time taken for intubation via a supraglottic airway. Values are mean (SD).  cLMA, classic laryngeal mask airway; ILMA, intubating laryngeal mask airway
	95% CI	N/A
Statistical test	**Type**	Wilcoxon signed-rank test, two-tailed Fisher's exact test and ANOVA as appropriate
	p value	See 'Value' box above
Other outcome	**Name**	Secondary outcome: Participant-reported Problems
	Unit	Number
Effect size	**Value**	• Part 1: The frequency of reported problems was highest with the aScope (32% vs 17% with conventional fibrescope; p=0.04) and included problems with manipulation, railroading tubes and picture quality. The frequency of problems in the three manikins was: Airway Trainer 13%; Bill 1 31%; and Airsim 32% (p=0.04). By route, the frequency of problems was nasal 19% and oral 31% (p=0.02). All three variables (fibrescope, manikin and route) were associated with differing rates of problems (p=0.001). There was some evidence of interactions, with the problem rate for oral intubation in Bill 1 manikins being high – particularly with the aScope • Part 2: User-reported problems occurred in 13% of intubations. The frequency with which problems were reported was not statistically significantly affected by fibrescope (p=0.11) or conduit (p=0.14)
	95% CI	N/A
Statistical test	**Type**	Wilcoxon signed-rank test, two-tailed Fisher's exact test and ANOVA as appropriate
	p value	See 'Value' box above

<table>
<tr><td></td><td></td><td></td></tr>
<tr><td rowspan="2">Other outcome</td><td>Name</td><td>Secondary outcome: Ease of endoscopy and railroading</td></tr>
<tr><td>Unit</td><td>VRS</td></tr>
<tr><td rowspan="2">Effect size</td><td>Value</td><td>

Part 1: Mean (SD) VRS for the aScope was 7.2 (2.3) and that for the conventional fibrescope 8.1 (1.6). Regarding the route, mean (SD) VRS for nasal intubation was 8.1 (1.9) and that for oral intubation 7.2 (2.0). Analysis of ease of railroading showed that only manikin type had a statistically significant effect (p<0.0001) with the Airway Trainer having the highest scores (mean (SD) 8.6 (1.7)). Type of fibrescope was not statistically significant (conventional mean (SD) 8.0 (1.8) vs aScope 7.7 (2.0); p=0.15) (see below)

Verbal rating scores of overall usefulness (0–10) for fibreoptic intubation via three individual manikins. Values are mean (SD).
<table>
<tr><th></th><th>aScope</th><th>Conventional fibrescope</th></tr>
<tr><td>Airway Trainer oral (n = 22)</td><td>8.3 (1.63)</td><td>8.75 (0.91)</td></tr>
<tr><td>Bill 1 oral (n = 22)</td><td>6.75 (2.59)</td><td>7.6 (2.62)</td></tr>
<tr><td>Airsim oral (n = 22)</td><td>7.25 (1.89)</td><td>8.58 (1.17)</td></tr>
<tr><td>Airway Trainer nasal (n = 22)</td><td>9.05 (1.19)</td><td>9.5 (0.61)</td></tr>
<tr><td>Bill 1 nasal (n = 22)</td><td>8.2 (1.47)</td><td>8.5 (1.43)</td></tr>
<tr><td>Airsim nasal (n = 22)</td><td>7.6 (2.74)</td><td>8.45 (1.15)</td></tr>
</table>

Part 2: Mean (SD) VRS for the conventional fibrescope was 9.1 (0.9) and for the aScope was 8.9 (1.2). There was no statistically significant difference in VRS for ease of endoscopic intubation between fibrescopes (p=0.22) or conduits (p=0.09). Similarly, mean (SD) VRS for ease of railroading was similar between fibrescopes (conventional 8.8 (1.3), aScope 8.9 (1.2)). There was no statistically significant difference in VRS for ease of railroading between fibrescopes (p=0.72) or between conduits (p=0.29)

</td></tr>
<tr><td>95% CI</td><td>N/A</td></tr>
<tr><td rowspan="2">Statistical test</td><td>Type</td><td>Wilcoxon signed-rank test, two-tailed Fisher’s exact test and ANOVA as appropriate</td></tr>
<tr><td>p value</td><td>See ‘Value’ box above</td></tr>
</table>

<table>
<tr><td rowspan="2">Other outcome</td><td>Name</td><td>Secondary outcome: Overall usefulness</td></tr>
<tr><td>Unit</td><td>VRS</td></tr>
<tr><td rowspan="2">Effect size</td><td>Value</td><td>

Part 1: For overall usefulness, mean (SD) VRS for the conventional fibrescope was 8.5 (1.5) and that for the aScope 7.7 (2.1). Mean (SD) VRS for nasal intubation was 8.5 (1.6) and that for oral intubation 7.7 (2.0). Mean (SD) VRS for the Airway Trainer manikin was 8.8 (1.3), Bill 1 7.7 (2.1) and Airsim 7.8 (1.9). The VRS was affected by all three variables (fibrescope and manikin p<0.001, route p=0.001). The highest usefulness scores were obtained for the conventional fibrescope, the Airway Trainer manikin and the nasal route
Part 2: Mean (SD) VRS for overall usefulness for the conventional fibrescope was 9.2 (0.9) and for the aScope was 9.0 (1.1) (see below). There was no statistically significant difference in VRS for overall usefulness between fibrescope (p=0.12) or between conduits (p=0.28)

Verbal rating scores of overall usefulness (0–10) for intubation via a supraglottic airway. Values are mean (SD).
<table>
<tr><th></th><th>aScope</th><th>Conventional fibrescope</th></tr>
<tr><td>Overall usefulness</td><td></td><td></td></tr>
<tr><td>Via cLMA (n = 21)</td><td>8.75 (1.29)</td><td>9.3 (0.8)</td></tr>
<tr><td>Via i-gel (n = 21)</td><td>9.3 (1.03)</td><td>9.3 (1.08)</td></tr>
<tr><td>Via ILMA (n = 21)</td><td>8.85 (1.09)</td><td>9.1 (0.91)</td></tr>
</table>
cLMA, classic laryngeal mask airway; ILMA, intubating laryngeal mask airway
</td></tr>
<tr><td>95% CI</td><td>N/A</td></tr>
<tr><td rowspan="2">Statistical test</td><td>Type</td><td>Wilcoxon signed-rank test, two-tailed Fisher’s exact test and ANOVA as appropriate</td></tr>
<tr><td>p value</td><td>See ‘Value’ box above</td></tr>
<tr><td colspan="2">Comments</td><td>

Part 1: The majority (88%) of intubations were successful on initial attempt. The lowest rates of first attempt successes were via the oral route (83%) and using the Bill 1 manikin (80%)

</td></tr>
</table>

	• Part 1: There were four failures of first intubation attempt in 126 attempts (3%) • Part 1 and 2: Twenty-one participants completing both parts of the study rated performance subjectively. Responsiveness and manipulation were rated on a scale excellent/good/fair/poor/unacceptable: 4/7/6/4/0 for the aScope and 11/8/1/1/0 for the conventional fibrescope. Image quality rated on the same scale for the aScope was 2/8/6/5/0 and for the conventional fibrescope it was 14/6/1/0/0. Overall, aScope performance was rated as: excellent 6; good 12: adequate 2; inadequate 1; and unusable 0

Table 25 Outcomes from published and unpublished studies; Kumar2011 (50)

Study name		**Kumar2011**
Size of study groups	**Treatment**	aScope
	Control	Olympus reusable scope
Study duration	**Time unit**	N/A
Type of analysis	**Intention-to-treat/per protocol**	N/A
Outcome	**Name**	Time to complete task
	Unit	Seconds
Effect size	**Value**	There was a significant difference in the time to task completion between the aScope and Olympus reusable scope (see below) Values are mean (SD), proportion (%) as appropriate. (n = 75) Olympus / Ambu / Diff [95% CI] / P-value Completion time; s 1st attempt 53 (23) / 63 (31) / 10 [3 to 17] / 0.008 2nd attempt 41 (19) / 48 (23) / 6 [2 to 11] / 0.010
	95% CI	See 'Value' box above

<table>
<tr><td rowspan="2">Statistical test</td><td>Type</td><td>Unknown</td></tr>
<tr><td>p value</td><td>See ‘Value’ box above</td></tr>
<tr><td rowspan="2">Other outcome</td><td>Name</td><td>Tip collisions</td></tr>
<tr><td>Unit</td><td>Number</td></tr>
<tr><td rowspan="2">Effect size</td><td>Value</td><td>There was no significant difference in the number of tip surface collisions between the aScope and Olympus reusable scope (see below)
Values are mean (SD), proportion (%) as appropriate. (n = 75)
<table><tr><th></th><th>Olympus</th><th>Ambu</th><th>Diff [95% CI]</th><th>P-value</th></tr><tr><td>Tip collisions</td><td></td><td></td><td></td><td></td></tr><tr><td>1st attempt</td><td>2.5 (1.8)</td><td>2.7 (1.9)</td><td>0.2 [-0.4 to 0.7]</td><td>0.56</td></tr><tr><td>2nd attempt</td><td>2.6 (1.8)</td><td>2.6 (2.0)</td><td>0.0 [-0.4 to 0.5]</td><td>0.89</td></tr></table></td></tr>
<tr><td>95% CI</td><td>See ‘Value’ box above</td></tr>
<tr><td rowspan="2">Statistical test</td><td>Type</td><td>Unknown</td></tr>
<tr><td>p value</td><td>See ‘Value’ box above</td></tr>
<tr><td rowspan="2">Other outcome</td><td>Name</td><td>Ease of use</td></tr>
<tr><td>Unit</td><td>VAS (i.e., mm)</td></tr>
<tr><td rowspan="2">Effect size</td><td>Value</td><td>Participants found the Olympus reusable scope significantly easier to use than aScope (see below)
Values are mean (SD), proportion (%) as appropriate. (n = 75)
<table><tr><th></th><th>Olympus</th><th>Ambu</th><th>Diff [95% CI]</th><th>P-value</th></tr><tr><td>Ease of use VAS; mm</td><td>77 (14)</td><td>65 (18)</td><td>-12 [-7 to -17]</td><td><0.001</td></tr></table></td></tr>
<tr><td>95% CI</td><td>See ‘Value’ box above</td></tr>
<tr><td rowspan="2">Statistical test</td><td>Type</td><td>Unknown</td></tr>
<tr><td>p value</td><td>See ‘Value’ box above</td></tr>
<tr><td>Other</td><td>Name</td><td>Preference</td></tr>
</table>

outcome	**Unit**	Participants' opinion
Effect size	**Value**	Participants preferred the Olympus reusable scope to aScope (see below). The reasons for this were familiarity and ease of manoeuvring the tip of the scope Values are mean (SD), proportion (%) as appropriate. (n = 75) Olympus / Ambu / Diff [95% CI] / P-value Preference: 57 (76%) / 18 (24%) / <0.001
	95% CI	N/A
Statistical test	**Type**	Unknown
	p value	See 'Value' box above
Comments		

Table 26 Outcomes from published and unpublished studies; R-PS-7-2009/Kristensen (41)

Study name		**R-PS-7-2009/Kristensen**
Size of study groups	**Treatment**	aScope (N=20)
	Control	Olympus BF160 reusable scope (N=20)
Study duration	**Time unit**	March 2010 (first patient included) to December 2010 (last patient included)
Type of analy	**Intention-to -**	N/A

sis	**treat /per prot ocol**	
Outc ome	**Nam e**	Primary outcome: Total intubation time
	Unit	Seconds (mean and standard deviation)
Effec t size	**Valu e**	• [redacted]
	95% CI	N/A
Stati stical test	**Type**	• [redacted]
	p valu e	[redacted]
Othe r outc ome	**Nam e**	[redacted]
	Unit	[redacted]
Effec t size	**Valu e**	○ [redacted]

		[redacted]
	95% CI	[redacted]
Statistical test	Type	[redacted]
	p value	[redacted]
Other outcome	Name	[redacted]
	Unit	[redacted]
Effect size	Value	[redacted]
	95% CI	[redacted]
Statistical test	Type	[redacted]
	p value	[redacted]
Other outcome	Name	[redacted]
	Unit	[redacted]
Effect size	Value	[redacted]
	95% CI	[redacted]
Stati	Type	[redacted]

stical test	**p value**	[redacted]
Other outcome	**Name**	[redacted]
	Unit	[redacted]
Effect size	**Value**	[redacted]
	95% CI	[redacted]
Statistical test	**Type**	[redacted]
	p value	<0.0005
Comments		• Overall, intubation success rates were 100% at first attempt for aScope and Olympus BF160

Table 27 Outcomes from published and unpublished studies; Piepho2010 (53)

Study name		**Piepho2010 (case series)**
Size of study groups	**Treatment**	aScope (N=5 patients with unanticipated or anticipated airway)
	Control	N/A
Study duration	**Time unit**	N/A
Type of analysis	**Intention-to-treat/per protocol**	N/A
Outcome	**Name**	N/A
	Unit	N/A
Effect size	**Value**	N/A
	95% CI	N/A
Statistical test	**Type**	N/A
	p value	N/A
Other outcome	**Name**	N/A
	Unit	N/A
Effect size	**Value**	N/A
	95% CI	N/A
Statistical test	**Type**	N/A
	p value	N/A
Comments		• Tracheal intubation was possible in all five patients • Awake fibreoptic intubations, via a nasal route, were performed in three adult patients with predicted difficult airway who required general anaesthesia. Typical landmarks such as the uvula, tongue, epiglottis and larynx were adequately identified. In two cases the videoscope had to be removed during the procedure to allow the lens to be cleaned with a sterile swab. Application of 4 ml lidocaine onto the glottis

	via the built-in channel of aScope was fast and controlled under direct vision. Advancing the tracheal tube was smooth and easy in all three cases • aScope was also used in the management of two patients, via an oral route, with unanticipated difficult airways for whom fibreoptic intubation was indicated. In one case, airway secretions obstructed vision via the LCD screen. This was resolved following suctioning and cleaning of the aScope lens using a sterile swab. All anatomical landmarks were identified and the videoscope was advanced smoothly through the glottis following which the tube was advanced into the trachea

Table 28 Outcomes from published and unpublished studies; Pujol2010 (54)

Study name		**Pujol2010**
Size of study groups	**Treatment**	aScope (N=10 patients with predicted difficult intubation)
	Control	N/A
Study duration	**Time unit**	N/A
Type of analysis	**Intention-to-treat/per protocol**	N/A
Outcome	**Name**	N/A
	Unit	N/A
Effect size	**Value**	N/A
	95% CI	N/A
Statistical test	**Type**	N/A
	p value	N/A
Other outcome	**Name**	N/A
	Unit	N/A
Effect size	**Value**	N/A

	95% CI	N/A
Statistical test	**Type**	N/A
	p value	N/A
Comments		• All the patients underwent oral tracheal intubation (see below), except two who required nasal intubation to enable maxillofacial surgery. It should be noted that all intubations were performed by anaesthetists experienced in awake fibreoptic tracheal intubation and difficult airway management. Nine of 10 intubations with aScope were performed and completed without incident. Intubation could not be accomplished in one patient within the 30 min permitted. Although an adequate view of the glottis was obtained with the aScope and the carina was reached, a 7.5 mm tracheal tube could not be advanced through the vocal cords. Patients' details and outcome of use of Ambu® aScope™.

Patient	Age; years	BMI; (kg.m^{-2})	Arné score	Mallampati score	Clinical details	Comments
1	61	31	11	3	Limited cervical movement	Fogging and secretions that impeded view of glottis; difficulty in advancing device; multiple attempts to advance tracheal tube; device 'lifetime' exceeded
2	81	22.9	41	4	Jaw tumour with previous resection and radiotherapy; limited mouth opening; several previous awake intubations	Nasal intubation; good vision
3	81	22.0	38	4	Maxillary neoplasm; limited mouth opening	Fogging cleared by touching mucosa
4	78	29.4	30	4	Graft reconstruction of upper lip; limited mouth opening, several previous awake intubations	Nasal intubation; fogging that did not interfere with vision
5	48	27.3	23	3	Limited mouth opening	Fogging that did not interfere with vision
6	48	35.9	11	3	Thyromental distance < 6.5 cm	Fogging; poor vision; removal of device to clean the lens; intubation after induction of general anaesthesia
7	69	23.8	13	3	Cervical disk herniation	Good vision
8	37	25	39	4	Coffin–Lowry Syndrome	Good vision
9	60	38.0	13	3	Severe obesity; limited cervical spine movement	Good vision
10	35	32.3	20	3	Acromegaly; thyromental distance < 6.5 cm	Fogging; removal of device to clean the lens

- The device was easy to insert in nine of 10 patients and difficult to advance due to resistance in one patient (the same patient in whom difficulty in passing the tracheal tube into the trachea was experienced). In all 10 patients, a complete view of the glottis was obtained. The image quality was considered adequate in five patients and poor in five. Fogging of the lens occurred in six patients and was cleared easily by gently touching the airway mucosa in four and by removing the scope and cleaning the tip in two. In two 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. Tube insertion was easy in eight patients and easy but with some manoeuvres needed in one patient and impossible in one patient

Table 29 Outcomes from published and unpublished studies; Vincent2011 (42)

Study name		**Vincent2011**
Size of study groups	**Treatment**	aScope2 (N=8 patients with difficult airway)
	Control	N/A
Study duration	**Time unit**	N/A
Type of analysis	**Intention-to-treat/per protocol**	N/A
Outcome	**Name**	N/A
	Unit	N/A
Effect size	**Value**	N/A
	95% CI	N/A
Statistical test	**Type**	N/A
	p value	N/A
Other outcome	**Name**	N/A
	Unit	N/A
Effect size	**Value**	N/A
	95% CI	N/A
Statistical test	**Type**	N/A
	p value	N/A
Comments		• Primary outcome; intubation success: All eight patients were intubated awake successfully using aScope2; six of eight patients were intubated at the first attempt and the other two patients at the second attempt; seven of eight patients were intubated by the nasal route and one patient orally • Primary outcome; time for scope position: Mean (range) time to visualize the carina (Tp) was 254.5 s (62–540 s); mean (range) time for confirming position of the tube in the trachea after visualizing carina

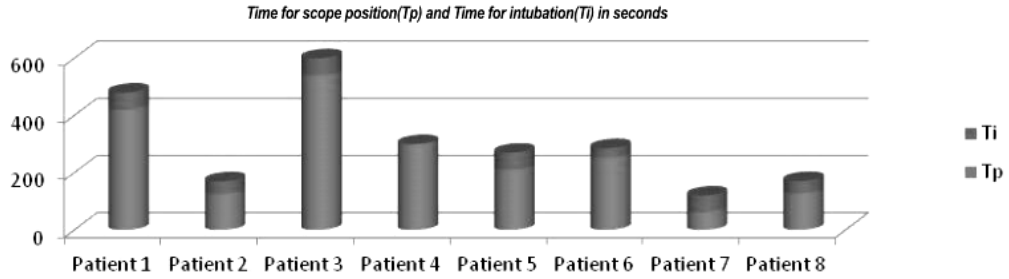
	(Ti) was 51.5 s (44–60 s) (see below)  • Secondary outcome; performance: In six of the eight uses, an excellent view of anatomical land marks was reported, and in two uses the view was reported as poor, but sufficient for intubating the trachea. Mean score for manoeuvrability was 6.8 (range 3–9). During one use the scope could not be removed from the ETT, but could be removed very easily after the other seven uses. Mean score for the usefulness of the scope was 7.4 (3–10)

Table 30 Outcomes from published and unpublished studies; Perbet2011 (55)

Study name		**Perbet2011**
Size of study groups	**Treatment**	aScope (N=10 patients requiring PDT)
	Control	N/A
Study duration	**Time unit**	N/A
Type of analysis	**Intention-to-treat/per protocol**	N/A
Outcome	**Name**	N/A
	Unit	N/A
Effect size	**Value**	N/A
	95% CI	N/A
Statistical test	**Type**	N/A
	p value	N/A
Other outcome	**Name**	N/A
	Unit	N/A
Effect size	**Value**	N/A
	95% CI	N/A
Statistical test	**Type**	N/A
	p value	N/A
Comments		• A PDT was achieved in 10 patients • Seven of 10 participants rated the aScope ‘very satisfactory’, and three rated it as ‘satisfactory’ (see below)

	Very unsatisfactory	Unsatisfactory	Satisfactory	Very satisfactory
Implementation			1	9
Interest for anatomical tracking			2	8
Guidewire entry in the trachea			2	8
Endotracheal placement of the tracheotomy tube			2	8
Brightness quality		2	2	6
picture quality	1	2	5	2
Global interest			5	5
Overall satisfaction			3	7

- The majority of participants rated aScope ‘very satisfactory’ or ‘satisfactory’ across all of the parameters investigated, including guidewire entry into the trachea and endotracheal placement of the tracheostomy tube (see above)
- The presence of the screen was deemed useful in all of the cases
- The absence of aspiration was missed in four cases
- In one case, the endoscope was turned off before the end of the procedure and the control of the cannula placement in the trachea had to be done with a standard endoscope

Table 31 Outcomes from published and unpublished studies; Jamadarkhana2011 (43)

Study name		**Jamadarkhana2011**
Size of study groups	**Treatment**	aScope2 (N=10 patients requiring PDT)
	Control	N/A
Study duration	**Time unit**	N/A
Type of analysis	**Intention-to-treat/per protocol**	N/A
Outcome	**Name**	N/A
	Unit	N/A
Effect size	**Value**	N/A
	95% CI	N/A
Statistical test	**Type**	N/A
	p value	N/A
Other outcome	**Name**	N/A
	Unit	N/A
Effect size	**Value**	N/A
	95% CI	N/A
Statistical test	**Type**	N/A
	p value	N/A
Comments		• The average time to set up the scope and monitor was <5 minutes • The procedure time from needle puncture of the trachea to tracheostomy tube placement ranged from 5 to 10 minutes • In one patient, the procedure time was 45 minutes due to a tracheal ring fracture and cuff damage of the

	tracheostomy tube • All the anaesthesiologists managing the airway reported easy handling and manoeuvrability because of the light-weight design of aScope • The operators performing the procedure scored the clarity and quality of endoscopic view (of needle, guidewire, stomal dilatation and tracheostomy tube placement) to be between 8 and 10 • Cardiovascular and ventilatory parameters were not significantly changed during the procedure in any patient • No complications were reported during use of aScope

7.6.2 Justify the inclusion of outcomes in table B9 from any analyses other than intention-to-treat.

7.7 Adverse events

In section 7.7 the sponsor is required to provide information on the adverse events experienced with the technology being evaluated in relation to the scope.

For example, post-marketing surveillance data may demonstrate that the technology shows a relative lack of adverse events commonly associated with the comparator.

7.7.1 Using the previous instructions in sections 7.1 to 7.6, provide details of the identification of studies on adverse events, study selection, study methodologies, critical appraisal and results.

None of the studies included in sections 7.1 to 7.6 of the submission were designed primarily to assess safety outcomes or detect significant differences between treatments, with respect to adverse events. In addition, as far as Ambu is aware, aScope has not caused or contributed to any adverse events (see declaration from Ambu signed and dated May 11, 2012 that accompanies this submission). Therefore, none of the studies included in sections 7.1 to 7.6 are reported in this section.

7.7.2 Provide details of all important adverse events reported for each study. A suggested format is shown in table B10.

N/A.

7.7.3 Describe all adverse events and outcomes associated with the technology in national regulatory databases such as those maintained by the MHRA and FDA (Maude).

No adverse events associated with aScope are listed on MAUDE (date accessed 15 May, 2012).

7.7.4 Provide a brief overview of the safety of the technology in relation to the scope.

N/A.

7.8 Evidence synthesis and meta-analysis

When more than one study is available and the methodology is comparable, a meta-analysis should be considered.

Section 7.8 should be read in conjunction with the 'Medical Technologies Evaluation Programme Methods Guide', available from www.nice.org.uk/mt

7.8.1 Describe the technique used for evidence synthesis and/or meta-analysis. Include a rationale for the studies selected, details of the methodology used and the results of the analysis.

N/A (see section 7.8.2).

7.8.2 If evidence synthesis is not considered appropriate, give a rationale and provide a qualitative review. The review should summarise the overall results of the individual studies with reference to their critical appraisal.

Data are available from several comparative studies investigating aScope versus a conventional reusable flexible scope. However, a large heterogeneity in methodology exists between the studies (discussed in more detail in section 7.4.3), particularly in terms of the population being investigated (e.g., age, indication and route of intubation), clinical setting, type of comparator scope and participants' experience of performing intubations. For a full description of the methodologies of the studies included in this analysis, please see Section 7.3.1. Therefore, a meta-analysis is unwarranted.

A total of six randomised studies (Lenhardt2011 (38, 39); Piepho2010 (53); Vijayakumar2011 (52); Kumar2011 (50); Scutt2011 (51); R-PS-7-2009/Kristensen (41)) and five observational studies (Piepho2010 (53); Pujol2010 (54); Vincent2011 (42) Perbet2011 (55) Jamadarkhana2011 (43)) investigating aScope have been included in this evaluation, as these comprise 'core' data for the technology in question. A critical appraisal of the methodology of these studies is included in Section 7.5.1.

A detailed overview of the clinical evidence for aScope is given in Section 7.9.1. In brief, similarly high rates of intubation success and times to intubation were observed between aScope and conventional reusable scopes. In addition to providing acceptable visualisation of anatomical structures, aScope was considered easy to use and manoeuvre, as well as being useful. aScope is, therefore, a suitable alternative to reusable scopes for facilitating tracheal intubation in patients with difficult airway and for those requiring PDT. This ready-to-use, single-use device negates the issue of availability, minimises the risk of infection and cross-contamination, and eliminates the delays and possible damage associated with reprocessing of reusable scopes.

7.9 Interpretation of clinical evidence

7.9.1 Provide a statement of principal findings from the clinical evidence highlighting the clinical benefit and any risks relating to adverse events from the technology.

Overview of clinical evidence and benefits of aScope

Data are available from several published studies, and an unpublished post-market surveillance study, investigating aScope in a range of clinical settings, in the same way that conventional reusable scopes are typically used. The utility of aScope for intubation of anticipated and unanticipated difficult airways, via nasal and oral routes, and during PDT was demonstrated.

Similarly high rates of intubation success and times to intubation were observed between aScope and conventional reusable scopes. In addition to providing acceptable visualisation of anatomical structures, aScope was considered easy to use and manoeuvre, as well as being useful. aScope is, therefore, a suitable

alternative to reusable scopes for facilitating tracheal intubation in patients with difficult airway and for those requiring PDT. This ready-to-use, single-use device negates the issue of availability, minimises the risk of infection and cross-contamination, and eliminates the delays and possible damage associated with reprocessing of reusable scopes. aScope2 is the same product as aScope, but offers several advancements including removal of the 30-minute timed lifespan and incorporating an easy clearing membrane to help improve image quality. These modifications have been included in aScope2 to overcome limitations of aScope reported in the clinical studies.

The design and basic functioning principles of aScope are equivalent to conventional reusable flexible scopes, and the clinical use of the device is the same as the reusable scopes. Therefore, when used under normal conditions, aScope will not compromise the clinical condition or the safety of patients and does not present other risks than those associated with reusable flexible scopes.

The following subsections provide a summary of the key clinical evidence from studies in patients with difficult airway, patients who require PDT, and from manikin simulations.

Difficult airway

Results from the case series Vincent2011 (42) of eight patients showed that aScope2 can be used to facilitate tracheal intubation in anticipated difficult airways. Intubation success rate was 100% within two attempts, and 75% for the first attempt. Manoeuvrability score was 6.8 (3−9 scale), and usefulness of the scope was 7.4 (3−10) by consultant anaesthetists with special interest in difficult airway. The authors reported that they did not have to interrupt the use of aScope2 to clear the tip of secretions in any of their cases. The image quality was adequate to identify the anatomical landmarks to enable tracheal intubation.

Data from the case series Pujol2010 (54), involving 10 patients with predicted difficult tracheal intubations, including one with severe obesity and limited cervical spine movement, showed that the majority of intubation procedures were easy and successful. Intubation at first attempt was achieved in nine of 10 patients. The authors of the article commented that the main advantages of aScope are that it is always ready to use and it avoids the risk of infectious disease transmission.

Findings from the unpublished randomised study R-PS-7-2009/Kristensen (41) comparing the performance of aScope versus Olympus BF160 in 40 patients with predicted difficult airways elected for ENT surgery showed that all patients in both groups were successfully intubated at first attempt. There was no statistical significant difference between the scopes in terms of endoscopy times and intubation times, when clinical relevance was taken into account (defined as a difference of >2 minutes).

Findings from the case series Piepho2010 (53), involving three patients with anticipated and two patients with unanticipated difficult airways, showed that nasal and oral intubations could be performed successfully with aScope. Successful intubation was achieved in all cases and anatomical structures were identified during the procedures.

Data from the randomised Lenhard2011 (39) study involving 140 patients showed that aScope in combination with a video laryngoscope (VLS) may further increase the success rate of intubation and decrease time spent intubating patients with difficult airway. The number of intubation attempts, the average intubation time and ease of handling were similar for the two devices. However, the difference in time to intubation of 10 seconds (1.1±0.4 [aScope] vs. 1.2±0.6 [control]) was deemed to be significant. Four patients could not be intubated with the VLS, but successful intubation was achieved with the aScope. In terms of addressing potential equality issues, patients with BMI >35, neck circumference >43 cm, neck movement <35°, cervical spine pathologies and/or immobilisation, as well as other predictive measures of difficult airway (e.g., Mallampati grade and status of dentition), were included in Lenhard2011 (39).

PDT

Jamadarkhana2011 (43) and Perbet2011 (55) investigated aScope2 and aScope, respectively, in patients who required PDT. The data from these studies demonstrated that aScope2 and aScope are viable devices for visualising PDT. The light-weight design of aScope2 made it easy to handle and enabled the observer to have a clear endoscopic view of the needle, guidewire and tracheostomy tube. Cardiovascular parameters (heart rate, mean arterial pressure) were measured in both studies prior to use, as well as during and after the procedure, and no significant changes were noted during the PDT procedure. The Perbet2011 study (55) concluded that aScope is a good alternative to conventional endoscopes in this

setting, and notes that it use can reduce costs, based on the observation that the cost/year for the repair of conventional endoscope was 3000 euros (25 PDT/year) compared with the cost of a disposable endoscope of 160–200 euros.

Manikin simulations

Results from Piepho2010 (53) showed that successful intubation rates were higher for the standard intubating Storz fibrescope than aScope in the difficult intubation scenario (14/21 [67%] attempts to intubate the trachea were successful using the aScope compared with 17/21 [81%] using the intubation fibrescope); however, intubation times were similar for both flexible scopes and aScope provided an acceptable view of the anatomical land marks. It is worthwhile noting that all study participants had prior experience of using a fibrescope (at least 50 tracheal intubations at the time of the investigation), whereas none had prior experience with the aScope. This suggests that the aScope may be easier to learn to use than the fibrescope, given intubation times were similar for the two devices. Vijayakumar2011 (52) confirmed that both devices were associated with comparable manoeuvrability, despite participants having no prior experience with aScope; however, interestingly, subjectively, participants did report finding the Olympus reusable fibrescope easier to use, possibly as a consequence of familiarity with the device. The findings of Scutt2011 (51) mirrored that of the two above studies and additionally indicated that a subjective measure of performance marginally favoured the conventional Pentax fibrescope. Nevertheless, overall, the aScope was shown to perform well in both nasal and oral simulated fibreoptic intubation.

7.9.2 Provide a summary of the strengths and limitations of the clinical evidence base of the technology.

There are a number of limitations and strengths of the clinical evidence base associated with aScope2 in the management of difficult airways.

Strengths

The evidence base for aScope is derived from a total of six randomised studies (Lenhardt2011 (38, 39); Piepho2010 (53); Vijayakumar2011 (52); Kumar2011 (50); Scutt2011 (51); R-PS-7-2009/Kristensen (41)) and five observational studies (Piepho2010 (53); Pujol2010 (54); Vincent2011 (42) Perbet2011 (55) Jamadarkhana2011 (43)). The combination of human and manikin studies has established that aScope offers comparable or superior rates of successful intubation, as well as similar intubation time when compared with other flexible, but reusable, endoscopes commonly used in clinical practice in the UK. In addition, aScope has been largely shown to be easy to use, manoeuvrable and useful by those using the device, with similar levels to other flexible endoscopes despite the fact that, in many of the studies, participants had prior experience with the comparator endoscopes, but not aScope. This suggests that users in the clinical setting are likely to learn how to use aScope quickly, and familiarity with the device has been shown in the published literature to have an impact on patient outcomes. It is noteworthy that in the Lenhardt (39) study, four patients who could not be intubated with the VLS and rigid stylet were successfully intubated using aScope. The randomised studies evaluating aScope were generally well designed, with clearly defined endpoints and assessments, giving the results a level of robustness and credibility. Moreover, the results of the randomised trials, which have been published as full articles, appear to have been reported in a transparent and unbiased manner, and limitations of the studies taken into consideration.

Limitations

There are a limited number of randomised controlled trials investigating aScope, and none evaluating aScope2. Therefore, much of the clinical evidence base for aScope2 relies on two preliminary case series involving patients with difficult airway (Jamadarkhana2011 (43)) and patients who require PDT (Vincent2011 (42)), as well as the randomised controlled and observational studies that have investigated its predecessor aScope. The case series lack statistical analyses and inclusion/exclusion criteria, and have an inherent risk of bias either towards or against aScope. Nevertheless, the case series provide the opportunity to evaluate aScope in 'real-world' clinical practice settings.

The relatively low numbers of patients and heterogeneity among patient populations included in the clinical studies could be considered a limitation of the clinical evidence base. The heterogeneity of the patients across studies means it is difficult to draw cross-study comparisons or perform any meaningful meta-analyses of their findings. However, it could also be argued that this heterogeneity indicates that aScope was shown to perform well in a variety of different patients and that therefore the findings of the studies better reflect the wide range of patients in whom the technology will be used in clinical practice.

Moreover, several studies evaluated the performance of aScope versus a reusable scope in manikins. A limitation of using manikins is that the settings from such studies cannot be extrapolated to airway management in clinical practice. Nevertheless, there are advantages of using manikins since they enable a large number of procedures and comparison of devices to be evaluated in a consistent environment, in a large number of clinicians. Furthermore, the use of manikins leads to large statistical power as the airway devices can be tested in one identical test arrangement and crossover studies are more easily designed. Indeed, a range of commonly used reusable scopes from the key manufacturers (Olympus, Storz and Pentax) were used as comparators to aScope in the manikin studies.

7.9.3 Provide a brief statement on the relevance of the evidence base to the scope. This should focus on the claimed patient- and system-benefits described in the scope.

The clinical evidence base is relevant to the scope issued by NICE, for example:

- aScope was shown to be an effective device for the intubation of patients with unexpected (and expected) difficult airways, including awake or anaesthetised patients, and those requiring PDT
- aScope has been evaluated against multiple-use flexible endoscopes and shown to perform well in simulated fibreoptic intubation
- Timely and successful intubation with aScope was achieved in the majority of patients (and manikins)
- aScope is delivered in a sterile package and, therefore, eliminates the potential risk of contamination and cross-infection associated with reusable scopes
- No device-related adverse events have been reported with aScope

7.9.4 Identify any factors that may influence the external validity of study results to patients in routine clinical practice.

Data from clinical studies indicate that aScope is a viable alternative to conventional reusable scopes for intubating difficult airways. Results from clinical trials cannot be extrapolated directly to routine daily practice, but the cases indicate that aScope can be used successfully in practice situations. As far as possible, the vital endpoints, such as intubation time and success rates, and number of intubation attempts, as well as manoeuvrability, ease of use and handling were assessed in patients. However, manikin simulation studies were also used to assess these endpoints and provided a valuable approach for investigating a large number of procedures. While manikin studies are considered surrogates for the clinical environment, they cannot entirely reflect conditions found during routine clinical practice. Nevertheless, results from Piepho2010 (53), Scutt2011 (51) and Vijayakumar2011 (52), investigating aScope in manikins and patients, indicated that, for anaesthetists with experience in

performing fibreoptic intubations, additional training was not required when using the aScope for the first time. This likely reflects the ease of use of aScope and that its use is the same as with conventional reusable scopes. The skills and techniques required to use a reusable scope appear to be transferrable to the aScope.

7.9.5 Based on external validity factors identified in 7.9.4 describe any criteria that would be used in clinical practice to select patients for whom the technology would be suitable.

The criteria used in clinical practice to select patients for intubation with a conventional flexible fibrescope will not differ for aScope, i.e., criteria are patients with unexpected (or expected) difficult airway and those requiring PDT. Clinical areas where a flexible scope are indicated include ENT procedures, pregnancy, a swollen airway (e.g., due to burns or carbon monoxide poisoning), obesity, position of the patient (e.g., prone), occluded airway (e.g., due to infection, tumour, or growth), protruding front teeth, receding chin, overshot jaw, and having a short, thick or stiff neck.

Since aScope is used in the same way as conventional reusable scopes, an anaesthetist with experience of intubating with reusable scopes should be able to use the aScope in a patient with difficult airway without requiring additional training (53). After receiving adequate training with aScope, anaesthetists who have less experience of intubating with flexible fibrescopes should also be able to use this device in patients with difficult airway.

Section C – Economic evidence

Section C requires sponsors to present economic evidence for their technology.

All statements should be evidence-based and directly relevant to the decision problem.

The approach to the de novo cost analysis expected to be appropriate for most technologies is cost-consequence analysis. Sponsors should read section 7 of the Medical Technologies Evaluation Programme Methods guide on cost-consequences analysis, available from www.nice.org.uk/mt

Sponsors are requested to submit section C with the full submission. For details on timelines, see the NICE document 'Guide to the Medical Technologies Evaluation Programme process', available from www.nice.org.uk/mt

8 Existing economic evaluations

8.1 Identification of studies

8.1.1 Describe the strategies used to retrieve relevant health economics studies from the published literature and to identify all unpublished data. The search strategy used should be provided as in section 10, appendix 3.

A search strategy was developed to identify cost studies and other forms of economic evaluation from the published literature. The search strategy focused on relevant literature databases and searches of the manufacturer's internal literature databases including unpublished studies where a draft report or manuscript was available.

The following databases were interrogated to identify any eligible studies:

- Medline 1946 to present (Ovid)
- Embase 1974 to 2012 (Ovid)

- Medline (R) In-Process (Ovid)
- NHS EED.

Keywords were used to search both the publication titles and the full body of abstracts. Full details of the search strategies used for each database are given in appendix 1.

In order to maximise the sensitivity of the search, a minimal number of restrictions were included in the search strategy. Searches were limited to the last 10 years (2002 onwards) and were restricted to English language. The search was not limited by publication type. Reference lists of all relevant study publications were also hand searched to identify any additional references.

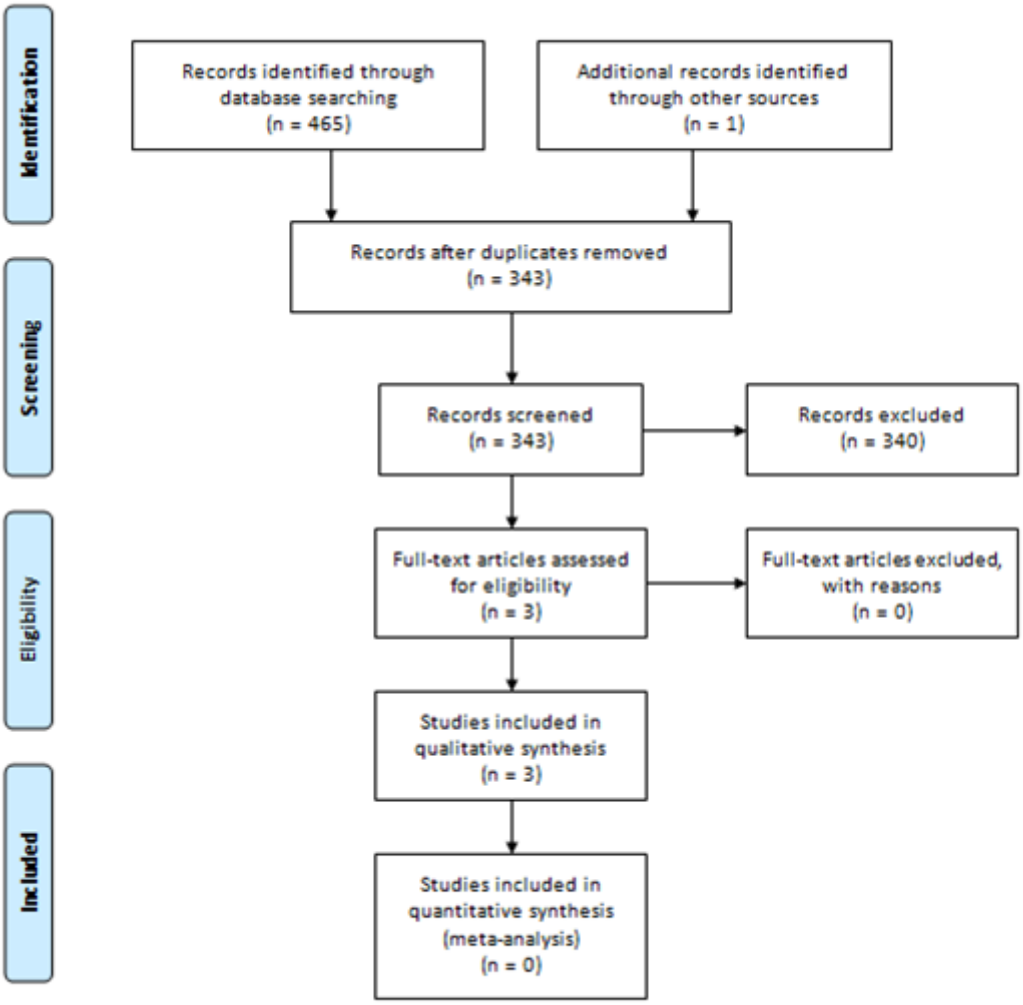
8.1.2 Describe the inclusion and exclusion criteria used to select studies from the published and unpublished literature. Suggested headings are listed in the table below. Other headings should be used if necessary.

Table 32 Selection criteria used for health economic studies

Inclusion criteria	
Population	Awake, anaesthetised, sedated and asleep/sleeping patients, adults or children/paediatric (>10 years), male or female, with unexpected or expected, difficult, closed or obstructed airway(s) or airway management, tracheostomies/PDT, as well as manikins/mannequins configured to simulate difficult, closed or obstructed airway(s) or airway management
Interventions	Oral, nasal or naso-tracheal intubations with reusable or disposable, single-use or multiple-use, direct or indirect, and portable scope, fibrescope/fibreoptic scope, videoscope/video-assisted, endoscope, bronchoscope or laryngoscope, including but not limited to aScope2 (AmbuScope, aScopeaScope2) and/or Olympus, Pentax and Storz with eyepiece or monitor, as well as Vision Sciences' disposable sheath for bronchoscopes
Outcomes	Studies reporting costs and/or resource utilisation; studies reporting results of cost-effectiveness analyses
Study design	All cost studies including cost-effectiveness analysis, cost-minimisation, cost-consequences analysis, cost analysis and any other form of economic evaluation.
Language restrictions	English language
Search dates	2002-2012
Exclusion criteria	
Population	Patients requiring endoscopy, fibrescopy, videoscopy, bronchoscopy for any clinical reason other than difficult, closed or obstructed airway(s) or airway(s) management or tracheotomies, manikin/mannequin studies outside the setting of difficult, closed or obstructed airway(s) or airway(s) management and were excluded
Interventions	None
Outcomes	None
Study design	Studies other than costing studies as described in the inclusion criteria
Language restrictions	Languages other than English
Search dates	Studies prior to 2002

8.1.3 Report the numbers of published studies included and excluded at each stage in an appropriate format.

Figure 4 PRISMA for economic studies



8.2 Description of identified studies

8.2.1 Provide a brief review of each study, stating the methods, results and relevance to the scope.

Table 33 Summary list of all evaluations involving costs

Study name (year)	**Location of study**	**Summary of model and comparators**	**Patient population *(key characteristics, average age)***	**Costs *(intervention and comparator)***	***Patient outcomes (clinical outcomes, utilities, life expectancy, time to recurrence for intervention and comparator)***	***Results (annual cost savings, annual savings per patient, incremental cost per QALY)***
Gupta D et al. (2011) (61)	Detroit, USA	No modelling was included in the study. A costing analysis was conducted comparing reusable and single-use flexible optical scopes for tracheal intubation	All intubations over a period of 1 year were included in the study. A total of 166 intubations were performed during the study time period	Acquisition costs for reusable fibrescopes, total repair costs as well as sterilisation costs were included in the analysis	No patient outcomes were included	Total cost of intubation was estimated at $119.75 [US dollars] 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
Tvede M et al. (2012) (35)	Copenhagen, Denmark	No modelling was included in the study. Costs incurred during intubations	All intubations using flexible optical scopes performed during a 1 year period	Cost per intubation was estimated as the sum of acquisition costs,	No patient outcomes were included	The average cost of an intubation using a reusable flexible optical scope was 177 Euros. In comparison the average cost

		using flexible optical scopes were identified and compared with a series of intubations using aScope2		sterilisation costs and repair costs		associated with the aScope2 was estimated at 204.4 Euros. Costs were expected to be equivalent where the number of intubations per month was 22.5. If only video scopes were considered, aScope and reusable scopes were at similar costs (204.4 vs. 204.5 Euros)
Liu S et al. (62)	Stanford, USA	No modelling was included in the study. The study estimated the costs associated with reusable fibrescopes for tracheal intubation	All fibrescope intubations performed over a 12 month period	Costs included capital acquisition costs, annual repair costs, costs of cleaning and labour for sterilisation	No patient outcomes were included	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

8.2.2 Provide a complete quality assessment for each health economic study identified. A suggested format is shown in table C3.

Table 34 Quality assessment; Gupta et al. 2011 (61)

Study name Cost-effectiveness analysis of flexible optical scopes for tracheal intubation: a descriptive comparative study of reusable and single-use scopes		
Study design	*Costing Study*	
Study question	**Response (yes/no/not clear/N/A)**	**Comments**
1. Was the research question stated?	Yes	
2. Was the economic importance of the research question stated?	Yes	Justification of new technology to replace reusable scopes for intubation
3. Was/were the viewpoint(s) of the analysis clearly stated and justified?	No	
4. Was a rationale reported for the choice of the alternative programmes or interventions compared?	Yes	Current practice data collected for comparison with hypothetical costs for single-use scope
5. Were the alternatives being compared clearly described?	Yes	
6. Was the form of economic evaluation stated?	No	Termed cost-effectiveness analysis, but no measure of effect included
7. Was the choice of form of economic evaluation justified in relation to the questions addressed?	No	
8. Was/were the source(s) of effectiveness estimates used stated?	N/A	
9. Were details of the design and results of the effectiveness study given (if based on a single study)?	N/A	
10. Were details of the methods of synthesis or meta-analysis of estimates given (if based on an overview of a number of effectiveness studies)?	N/A	
11. Were the primary outcome measure(s) for the economic evaluation clearly stated?	N/A	
12. Were the methods used to value health states and other benefits stated?	N/A	

13. Were the details of the subjects from whom valuations were obtained given?	N/A	
14. Were productivity changes (if included) reported separately?	N/A	
15. Was the relevance of productivity changes to the study question discussed?	N/A	
16. Were quantities of resources reported separately from their unit cost?	Yes	Some description of unit costs and quantities included in the methods
17. Were the methods for the estimation of quantities and unit costs described?	Yes	
18. Were currency and price data recorded?	Yes	
19. Were details of price adjustments for inflation or currency conversion given?	N/A	
20. Were details of any model used given?	N/A	
21. Was there a justification for the choice of model used and the key parameters on which it was based?	N/A	
22. Was the time horizon of cost and benefits stated?	N/A	
23. Was the discount rate stated?	N/A	
24. Was the choice of rate justified?	N/A	
25. Was an explanation given if cost or benefits were not discounted?	N/A	
26. Were the details of statistical test(s) and confidence intervals given for stochastic data?	N/A	
27. Was the approach to sensitivity analysis described?	N/A	
28. Was the choice of variables for sensitivity analysis justified?	N/A	
29. Were the ranges over which the parameters were varied stated?	N/A	
30. Were relevant alternatives	No	No data collection was included and

compared? (That is, were appropriate comparisons made when conducting the incremental analysis?)		no direct comparison with aScope2 was made.
31. Was an incremental analysis reported?	N/A	
32. Were major outcomes presented in a disaggregated as well as aggregated form?	N/A	
33. Was the answer to the study question given?	No	Objective was stated as a comparative estimation of costs, but this was not performed, only a price range statement for aScope2
34. Did conclusions follow from the data reported?	Yes	Since conclusions related to the necessary price for aScope2 to be cost-neutral
35. Were conclusions accompanied by the appropriate caveats?	Yes	Some discussion of limitations
36. Were generalisability issues addressed?	No	
Adapted from Drummond MF, Jefferson TO (1996) Guidelines for authors and peer reviewers of economic submissions to the BMJ. The BMJ Economic Evaluation Working Party. British Medical Journal 313 (7052): 275–83. Cited in Centre for Reviews and Dissemination (2008) Systematic reviews. CRD's guidance for undertaking reviews in health care. York: Centre for Reviews and Dissemination		

Table 35 Quality assessment; Tvede et al. 2012 (35)

Study name A cost analysis of reusable and disposable flexible optical scopes for intubation		
Study design	*Cost Analysis*	
Study question	**Response (yes/no/not clear/N/A)**	**Comments**
1. Was the research question stated?	Yes	
2. Was the economic importance of the research question stated?	Yes	Introduction of disposable flexible scope merits scrutiny of total costs versus reusable scopes
3. Was/were the viewpoint(s) of the analysis clearly stated and justified?	No	
4. Was a rationale reported for the choice of the alternative programmes or interventions compared?	Yes	
5. Were the alternatives being compared clearly described?	Yes	aScope2 versus reusable flexible optical intubation scopes
6. Was the form of economic	Not clear	A cost analysis is described without

evaluation stated?		clear reference to the form of evaluation
7. Was the choice of form of economic evaluation justified in relation to the questions addressed?	No	
8. Was/were the source(s) of effectiveness estimates used stated?	N/A	
9. Were details of the design and results of the effectiveness study given (if based on a single study)?	N/A	
10. Were details of the methods of synthesis or meta-analysis of estimates given (if based on an overview of a number of effectiveness studies)?	N/A	
11. Were the primary outcome measure(s) for the economic evaluation clearly stated?	N/A	
12. Were the methods used to value health states and other benefits stated?	N/A	
13. Were the details of the subjects from whom valuations were obtained given?	N/A	
14. Were productivity changes (if included) reported separately?	N/A	
15. Was the relevance of productivity changes to the study question discussed?	N/A	
16. Were quantities of resources reported separately from their unit cost?	No	
17. Were the methods for the estimation of quantities and unit costs described?	Yes	
18. Were currency and price data recorded?	Yes	
19. Were details of price adjustments for inflation or currency conversion given?	N/A	
20. Were details of any model used given?	N/A	
21. Was there a justification for the choice of model used	N/A	

and the key parameters on which it was based?		
22. Was the time horizon of cost and benefits stated?	N/A	
23. Was the discount rate stated?	N/A	
24. Was the choice of rate justified?	N/A	
25. Was an explanation given if cost or benefits were not discounted?	N/A	
26. Were the details of statistical test(s) and confidence intervals given for stochastic data?	N/A	
27. Was the approach to sensitivity analysis described?	Yes	An attempt was made to explore the relationship between frequency of intubation and cost
28. Was the choice of variables for sensitivity analysis justified?	No	
29. Were the ranges over which the parameters were varied stated?	N/A	
30. Were relevant alternatives compared? (That is, were appropriate comparisons made when conducting the incremental analysis?)	Yes	No incremental analysis was included, but total costs were compared between aScope2 and reusable scopes
31. Was an incremental analysis reported?	No	
32. Were major outcomes presented in a disaggregated as well as aggregated form?	Yes	Cost per intubation was broken down into component parts – expenditure, repair etc
33. Was the answer to the study question given?	Yes	
34. Did conclusions follow from the data reported?	Yes	
35. Were conclusions accompanied by the appropriate caveats?	Yes	
36. Were generalisability issues addressed?	Yes	
Adapted from Drummond MF, Jefferson TO (1996) Guidelines for authors and peer reviewers of economic submissions to the BMJ. The BMJ Economic Evaluation Working Party. British Medical Journal 313 (7052): 275–83. Cited in Centre for Reviews and Dissemination (2008) Systematic reviews. CRD's guidance for undertaking reviews in health care. York: Centre for Reviews and Dissemination		

Table 36 Quality assessment; Liu et al. (unpublished) (62)

Study name Cost Identification Analysis of Anesthesia Fiberscope Use for Tracheal Intubation		
Study design	*Costing Study*	
Study question	**Response (yes/no/not clear/N/A)**	**Comments**
1. Was the research question stated?	Yes	
2. Was the economic importance of the research question stated?	Yes	Better understanding of costs needed to manage and allocate healthcare resources
3. Was/were the viewpoint(s) of the analysis clearly stated and justified?	Yes	Hospital perspective
4. Was a rationale reported for the choice of the alternative programmes or interventions compared?	Yes	Only included reusable flexible intubation fibrescopes
5. Were the alternatives being compared clearly described?	N/A	
6. Was the form of economic evaluation stated?	Yes	Termed cost-identification analysis
7. Was the choice of form of economic evaluation justified in relation to the questions addressed?	No	
8. Was/were the source(s) of effectiveness estimates used stated?	N/A	
9. Were details of the design and results of the effectiveness study given (if based on a single study)?	N/A	
10. Were details of the methods of synthesis or meta-analysis of estimates given (if based on an overview of a number of effectiveness studies)?	N/A	
11. Were the primary outcome measure(s) for the economic evaluation clearly stated?	N/A	
12. Were the methods used to value health states and other benefits stated?	N/A	
13. Were the details of the subjects from whom valuations were obtained given?	N/A	

14. Were productivity changes (if included) reported separately?	N/A	
15. Was the relevance of productivity changes to the study question discussed?	N/A	
16. Were quantities of resources reported separately from their unit cost?	No	Some description of unit costs and quantities included in results, but limited
17. Were the methods for the estimation of quantities and unit costs described?	Yes	
18. Were currency and price data recorded?	Yes	
19. Were details of price adjustments for inflation or currency conversion given?	N/A	
20. Were details of any model used given?	N/A	
21. Was there a justification for the choice of model used and the key parameters on which it was based?	N/A	
22. Was the time horizon of cost and benefits stated?	N/A	
23. Was the discount rate stated?	N/A	
24. Was the choice of rate justified?	N/A	
25. Was an explanation given if cost or benefits were not discounted?	N/A	
26. Were the details of statistical test(s) and confidence intervals given for stochastic data?	N/A	
27. Was the approach to sensitivity analysis described?	N/A	
28. Was the choice of variables for sensitivity analysis justified?	N/A	
29. Were the ranges over which the parameters were varied stated?	N/A	
30. Were relevant alternatives compared? (That is, were appropriate comparisons made when conducting the incremental analysis?)	No	Data was only collected for fibrescopes

31. Was an incremental analysis reported?	N/A	
32. Were major outcomes presented in a disaggregated as well as aggregated form?	N/A	
33. Was the answer to the study question given?	Yes	Cost per use was reported
34. Did conclusions follow from the data reported?	Yes	
35. Were conclusions accompanied by the appropriate caveats?	Yes	Some discussion of limitations
36. Were generalisability issues addressed?	Yes	
Adapted from Drummond MF, Jefferson TO (1996) Guidelines for authors and peer reviewers of economic submissions to the BMJ. The BMJ Economic Evaluation Working Party. British Medical Journal 313 (7052): 275–83. Cited in Centre for Reviews and Dissemination (2008) Systematic reviews. CRD's guidance for undertaking reviews in health care. York: Centre for Reviews and Dissemination		

9 De novo cost analysis

Section 9 requires the sponsor to provide information on the de novo cost analysis.

The de novo cost analysis developed should be relevant to the scope.

All costs resulting from or associated with the use of the technology should be estimated using processes relevant to the NHS and personal social services.

Note that NICE cites the price of the product used in the model in the Medical Technology guidance.

9.1 Description of the de novo cost analysis

9.1.1 Provide the rationale for undertaking further cost analysis in relation to the scope.

A simple cost analysis has been developed to estimate the costs and consequences associated with the use of aScope2 and the comparator identified in the decision problem for this MTAC assessment – namely, multiple-use flexible endoscopes (fibrescopes using fibre optic technology or video scopes using video technology).

No costing analysis comparing these technologies in the NHS setting is currently available and the de novo analysis reported here has therefore been undertaken to inform an assessment of the relative costs and effects associated with the technologies in question.

In particular, a further detailed cost analysis is required as the costs of aScope2 are easily identifiable – i.e. the current average price to the NHS cost is £179 per single-use scope, whereas the costs associated with the use of reusable scopes are more complex to estimate.

Costs associated with reusable scopes comprise the equipment costs, maintenance costs, and costs associated with reprocessing and storing the equipment prior to use.

As well as the costs associated with equipment, the analysis reported here has explored costs associated with clinical outcomes – namely delayed or failed intubation and the management of dislodged tracheostomy. This is a crucial aspect of the economic assessment for aScope2 since it relates to a key potential benefit compared to conventional reusable scopes. Immediate availability of equipment is clearly essential during emergencies but it has been widely reported that it is frequently difficult to access relevant equipment rapidly, particularly on ICU. Specifically in relation to fibrescopes the NAP4 report (1) states the following: *"There was clear evidence that some ICUs do not have access to adequate difficult airway equipment. Prompt access to a fibrescope for airway inspection or for difficult airway management was a recurrent problem."*

There is limited evidence with regard to the scale of this problem. However, NAP4 reported that equipment contributed to or was a causal factor in roughly one quarter (26 per cent) of all major airway complications. On the ICU equipment was found to have contributed in over one third (36 per cent) of major airway complications. In another report on patient safety incidents associated with airway devices (63) equipment factors were said to have contributed to delayed/failed intubation in adults/children in almost two thirds of cases (62 per cent).

In a recent report on tracheostomy incidents in the NHS (16), 176 of the 453 incidents directly affecting patients involved equipment (39 per cent). It is therefore clear that problems with equipment, including multiple-use flexible endoscopes, play a major role in many cases of complicated emergency airway.

Since aScope2 is a single-use scope and is supplied in sterile packaging, ready for use, it effectively eliminates important availability issues associated with multiple-use flexible endoscopes for tracheal intubation. No evidence is available in relation to the proportion of events that could be avoided with aScope2 through its immediate availability. Therefore we have only been able to model the impact of availability by assuming an exploratory reduction in the risk of delayed/failed intubation and a similar reduction in the risk of patient

harm in the context of dislodged tracheostomy. In the base case we have assumed a 10 per cent reduction in risk. In view of the substantial proportion of events that relate to equipment, we believe that this is a reasonable assumption, but acknowledge that at present there is simply no evidence to validate it.

Patients

9.1.2 What patient group(s) is (are) included in the cost analysis?

The cost analysis has been conducted specifically in relation to the population identified in the decision problem – namely, patients with unexpected difficult airways requiring emergency intubation including awake or anaesthetised patients with displaced tracheostomies, including adults or children who have been clinically evaluated for endotracheal tubes size 6 or above.

Technology and comparator

9.1.3 Provide a justification if the comparator used in the cost analysis is different from the scope.

The comparator selected for the costing analysis is multiple-use flexible endoscopes (fibrescopes using fibre optic technology or video scopes using video technology).

This is an appropriate comparator for the assessment of aScope2 and is in line with the decision problem. In reality the comparator represents a wide range of technologies – with different configurations and costs and this is a significant challenge with respect to developing a cost analysis to inform assessments that are generalisable to the NHS.

In order to overcome this, we have estimated the average cost per reusable scope using a survey of NHS centres to collect available information relating to the costs of equipment and maintenance. Videoscopes are substantially more expensive compared to fibrescopes. We have not been able to present separate analyses for these two types of technologies, but sensitivity analyses reflect uncertainty around the cost of equipment.

Model structure

9.1.4 Provide a diagram of the model structure you have chosen.

Two diagrams are presented to reflect the consideration of intubation and dislodged tracheostomy separately.

Figure 5 Model of unexpected difficult airway requiring intubation

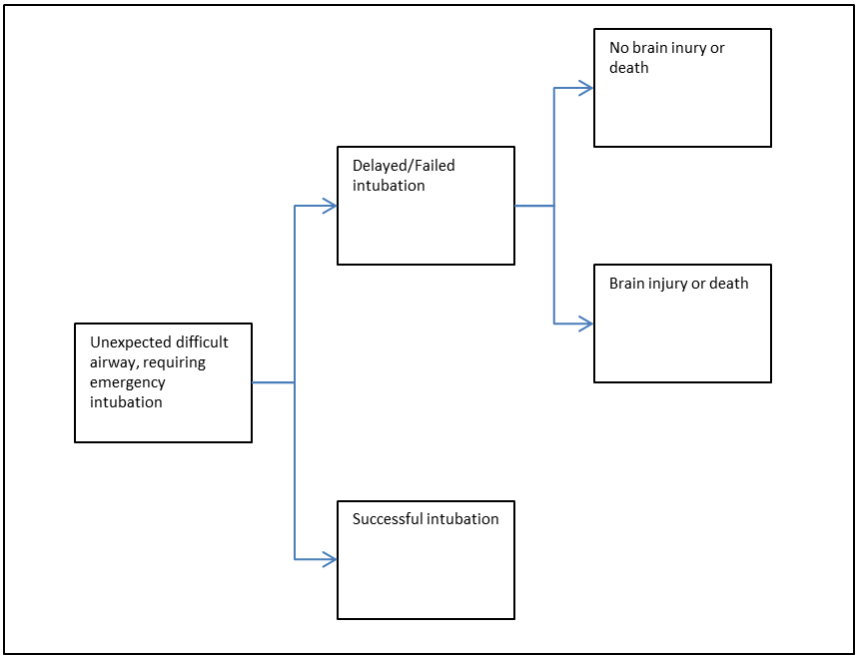
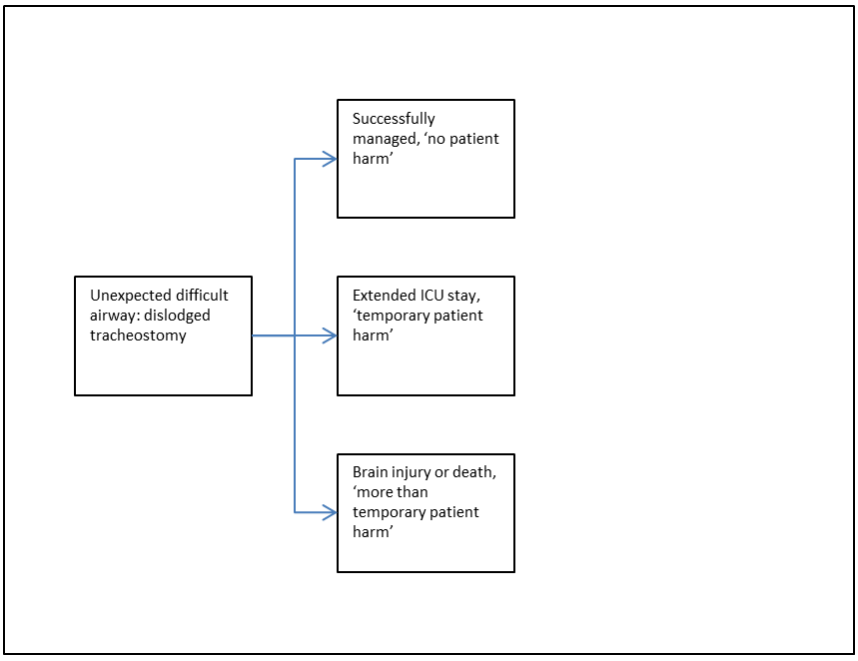


Figure 6 Model of unexpected difficult airway – dislodged tracheostomy



9.1.5 Justify the chosen structure in line with the clinical pathway of care identified in response to question 3.3.

The clinical pathway of care identified in response to question 3.3 describes the position of aScope2 in unanticipated difficult tracheal intubation. This pathway includes the key outcome of interest for the decision analysis – i.e. delayed/failed intubation. A simple decision analysis was selected in order to

capture costs and consequences in line with the decision problem. Outcomes identified in the decision problem for patients undergoing emergency intubation with difficult airways were delayed or failed intubation, death, hypoxic brain injury, ICU and hospital length of stay, successful intubation. A decision model was designed to capture these outcomes for the alternative technologies. A separate decision analysis was included for the specific clinical event – dislodged tracheostomy since this is not managed as an 'intubation' and is associated with different costs and outcomes.

9.1.6 Provide a list of all assumptions in the cost model and a justification for each assumption.

Table 37 List of cost model assumptions

Assumption	Value	Justification
Number of procedures performed per annum with reusable scopes (basecase)	150	The number of procedures performed with reusable equipment is a key variable in the cost analysis since it determines the cost per use of a reusable scope. However this varies widely by NHS institution and setting. A base-case was selected to reflect data collected in a survey of NHS centres and this assumption was varied in sensitivity analyses (64)
Reusable flexible intubation scope costs (weighted costs including stack systems, cameras etc)	£12,105	Each NHS centre has a unique set up in terms of reusable equipment. An NHS survey was used to estimate the average cost per reusable scope,

		including the acquisition costs for scopes and related equipment such as stack systems and cameras. This cost is varied in sensitivity analyses (64)
Annual Reusable flexible intubation scope maintenance & repair costs – proportion of equipment acquisition costs	0.21	Maintenance costs (including any repair costs) were collected using the NHS survey (64). Data on maintenance and repair was very difficult to collect, however in one centre good information was available. This was used to estimate the proportion of a piece of equipment's acquisition cost that is spent on maintenance and repair on an annual basis (64)
Number of reusable scopes available	5	The base-case number of scopes reflects the results of a survey in NHS centres and is varied in sensitivity analyses (64)
Assumed lifetime of reusable scope equipment (years)	5	This reflects the literature (65) and is varied in sensitivity analyses
Endoscopic Reprocessing costs (per scope reprocessed)	£35	The majority of NHS centres surveyed (4/6) used a central reprocessing centre. A

		standard cost is charged per item reprocessed. In the base case we have used the mid-point of the costs quoted for central reprocessing. Other centres reprocess scopes locally – for example in the department. This has been considered in sensitivity analyses using NHS survey data on the staff and time involved in reprocessing as well as the costs for equipment (64)
Rate of delayed/failed intubation in unexpected difficult intubation patients: Operating Theatre setting – reusable scopes	0.0625	Available trial data suggests that there are no significant differences between scopes in terms of intubation outcomes. However, the available trial data does not correspond to the setting defined in the decision problem – i.e. unexpected difficult airways. Rates of intubation failure in difficult intubation patients were therefore identified in the literature (66) and varied in sensitivity analyses
Rate of delayed/failed intubation in unexpected difficult intubation patients:	0.166	Estimates for failed intubation in difficult intubation patients on the

ICU setting – reusable scopes		ICU were not available. The upper estimate of the range for general anaesthesia was used in the base case (67)
Rate of brain injury, death in difficult intubation patients where intubation has failed	0.28	No data on outcomes related to delayed/failed intubation were available from clinical trials for any of the technologies. Data on rates of brain injury and death in the relevant population and settings were taken from the literature and varied in sensitivity analyses (63)
ICU length of stay_failed intubation	6.2 days	HES data (Hospital Episode Statistics) was investigated to identify relevant patient episodes and associated length of stay estimates. Failed intubation data were reviewed and ICU stays were estimate from available data (68)
Rate of ICU admission or prolongation of stay_failed intubation	0.75	A published survey (63) of patient safety incidents was used to estimate the rate of ICU admission (or patients where ICU stay was prolonged)

Rate of brain injury or death in patients with dislodged tracheostomy	0.13	A published survey (63) of patient safety incidents was used to estimate the rate of brain injury or death.
Rate of ICU stay or prolongation of stay_dislodged tracheostomy	0.75	The rate of ICU stay with dislodged tracheostomy was based on a recently conducted survey of tracheostomies (16)
ICU length of stay_dislodged tracheostomy	15.4 days	HES data was investigated to identify relevant patient episodes and associated length of stay estimates. Revised tracheostomy data were reviewed and ICU stays were estimate from available data (68)
Assumed reduction in events with aScope2	10 per cent	Exploratory assumption, varied in sensitivity analyses

9.1.7 Define what the model's health states are intended to capture.

Not applicable - a health state model has not been included.

9.1.8 Describe any key features of the cost model not previously reported. A suggested format is presented below.

Table 38 Key features of model not previously reported

Factor	Chosen values	Justification	Reference
Time horizon of model	1 year	Costs and outcomes associated with unexpected difficult airways are anticipated to be captured within a 1 year time period. It is possible that certain clinical outcomes associated with failed intubation (namely hypoxic brain injury) could have costs and outcomes extending considerably beyond 1 year. However, there is very limited evidence relating to rates of brain injury following failed intubation and limited information relating to the prognosis or management of patients. Given the considerable uncertainty, a conservative approach has been taken, to limit consideration of costs to a 1 year horizon.	
Discount of 3.5% for costs	N/A	Costs modelled within 1 year. The only exception here relates to equipment costs where an Equivalent Annual Cost approach by annuitization	Drummond et al. (2005) (65)
Perspective (NHS/PSS)	NHS	As per the decision problem.	
Cycle length	N/A		
NHS, National Health Service; PSS, Personal Social Services			

9.2 Clinical parameters and variables

9.2.1 Describe how the data from the clinical evidence were used in the cost analysis.

Evidence from clinical trials of aScope, including comparisons with reusable flexible intubation scopes, has not been used in the cost analysis. There is very limited trial evidence in patients with unexpected difficult airways as per

the decision problem. The majority of the available clinical studies of aScope were designed to measure time to intubation as a primary outcome in planned procedures or manikins. Where other outcomes were included such as intubation success or the number of intubation attempts required, these are likely to reflect a variety of factors including familiarity of the physician with aScope. In the largest available trial for aScope in patients no failed intubations were reported (see pages 70-71, section 7.6.1) (39).

Overall, the clinical trial evidence is supportive of aScope2 providing similar results to reusable flexible scopes of various forms including videoscopes and fibrescopes (see pages 99-100, section 7.9.1). In real clinical practice, intubation failure/success is likely to be a function of a range of other factors not captured in clinical trials – such as the availability of equipment in a timely manner. As described earlier in section 2.1.1, immediate access to necessary equipment in the event of an unexpected difficult airway is crucial but there are frequent reports of equipment problems and delays in access to equipment including fibreoptic scopes (69). Evidence relating to the potential reduction in risk of intubation failure and associated outcomes, as well as outcomes in the event of a dislodged tracheostomy, as a result of immediate availability of aScope2, is not available in clinical trials or in the literature. In order to model this important feature of difficult airway management, it is necessary to make an assumption about the potential reduction in risk associated with aScope2, guided by available evidence on the proportion of delayed/failed intubations as well as dislodged tracheostomy events that are contributed to by equipment issues.

Definitions of intubation failure, delayed intubation and difficult intubation vary across published studies and the reporting of particular outcomes also varies. As a result rates of delayed/failed intubation in the unexpected difficult airway setting are difficult to estimate accurately from the literature. NAP4 reports that rates of failed intubation range from 1 in 300 to 1 in 800 among general anaesthesia patients (1). This range is widely reported and relies on a number of large studies airway complications in general anaesthesia patients.

The low overall rates of intubation failure in these studies are unlikely to be relevant to the current decision problem since they relate to all general anaesthesia patients in these studies and not specifically those with unexpected difficult airways. However, two of these large cohort studies, that inform the range of intubation failure quoted in NAP4, also allow estimation of the rate of failed intubation conditional on difficult intubation – i.e. of those patients where intubation was reported to be difficult, the proportion that resulted in failed intubation. This appears to be the most relevant rate of failed intubation for the aScope2 decision problem since it is more likely to relate to the unexpected difficult airway scenario.

Rose and Cohen report the outcomes of airways management in 18,500 patients attended by anaesthetists over a period of 27 months (67). Difficult intubations among 18,205 of these patients following direct laryngoscopy were reported in 326 patients (1.8 per cent). Of these difficult intubations, 54 were categorised as failed intubations (16.6 per cent).

Rocke and colleagues report the results of a study on difficult intubation in 1,500 patients undergoing emergency and elective caesarean section under general anaesthesia (66). A total of 32 tracheal intubations were reported to be difficult and 2 of these difficult intubations failed. This implies a failed intubation rate among difficult intubations of 6.25 per cent.

These two studies appear to reflect the range of overall failed intubation reported by the authors of NAP4 and we believe this represents the best available evidence in relation to failed intubation among difficult intubation patients. However, it is possible that other relevant evidence has been overlooked. These studies in general anaesthesia do not report rates of delayed intubation and we have therefore had to rely on estimates specifically for failed intubation among difficult intubations for the cost analysis. In the base case cost analysis, we have assumed a failure rate of 6.25 per cent among unexpected difficult airways in the general anaesthesia (operating theatre) setting.

In the intensive care setting it is generally recognised that risks of complications and outcomes such as brain injury or death are much higher. This is a theme throughout the NAP4 report (69). Unfortunately, while the NAP4 report does provide very useful information on events occurring in ICU, no census (denominator) data was collected in this setting and it is not possible to estimate rates of outcomes to inform this cost analysis.

Other literature is available and reports that rates of complications among patients undergoing emergency intubation in ICU are substantially higher than in general anaesthesia. For example, a number of studies report rates of difficult intubations in the ICU in the range 10 to 13 per cent (3, 70, 71). Whilst these rates of difficult intubation are certainly much higher than those reported in general anaesthesia, the studies do not report rates of failed intubation among these difficult cases. In the ICU setting, we have used the higher estimate of failed intubation (16.6%) from the difficult intubations in the general anaesthesia setting.

In the dislodged tracheostomy setting, the best available evidence is currently a study of tracheostomies conducted by McGrath and Thomas (16). They report the proportion of dislodged tracheostomy cases categorised as either no patient harm, some patient harm or more than temporary patient harm. Some (temporary) patient harm is defined as increased length of ICU or hospital stay; more than temporary harm is defined as ‘intervention needed to sustain life, reaction may have caused or contributed to death’. In the absence of more specific outcomes data, we have used the McGrath and Thomas study to estimate rates of ICU stay/prolongation of stay and rates of brain injury or death. 19 of 147 displaced tube incidents resulted in more than temporary harm to patients. In 75 per cent of patients there was some harm.

As discussed earlier, evidence is not available regarding the potential reduction in rates of failed intubation with aScope2 or the impact that the immediate availability of aScope2 would have on management of dislodged tracheostomy. For the purposes of this decision analysis, we have therefore relied upon an exploratory assumption regarding the reduction in risk of failed intubation.

Since aScope2 would be immediately available in the event of an unexpected difficult airway, it has the potential to eliminate commonly occurring issues with reusable scopes such as availability, delays in locating equipment or problems with broken or unusable equipment. Whilst the reduction in risk with aScope2 is unknown, it seems reasonable to expect a meaningful risk reduction would be potentially achievable – particularly in higher risk situations such as ICU or in the dislodged tracheostomy scenario where immediate access to scope equipment is of utmost importance.

Rates of brain injury and death are also specified in the decision problem for aScope2. There are reports of deaths in a number of studies including NAP4 which reports that of the 36 cases of major airway complications on the ICU, 50 per cent resulted in death and a further 11 per cent resulted in brain damage (69). However, it is likely that the rates in NAP4 reflect the inclusion criteria for cases in this study as a whole. An alternative source of evidence in this regard is the report by Thomas and McGrath which reports rates of harm to patients where intubation has been delayed or has failed (63). 'More than temporary harm' was reported in 28 per cent of adults and children in this study. Whilst this outcome does not specify brain injury or death, it is likely to reflect outcomes where there was a permanent injury to patients and includes cases where the incident was judged to have potentially caused or contributed to death. In the dislodged tracheostomy setting a similar approach has been taken on the basis of the report by McGrath and Thomas (16). In patients with dislodged tracheostomies, more than temporary harm was reported in 19 of 147 incidents (12.9 per cent).

9.2.2 Are costs and clinical outcomes extrapolated beyond the study follow-up period(s)? If so, what are the assumptions that underpin this extrapolation and how are they justified?

Not applicable – outcomes from clinical trials were not considered in the cost analysis.

9.2.3 Were intermediate outcome measures linked to final outcomes (for example, was a change in a surrogate outcome linked to a final

clinical outcome)? If so, how was this relationship estimated, what sources of evidence were used and what other evidence is there to support it?

Not applicable

9.2.4 Were adverse events such as those described in section 7.7 included in the cost analysis? If appropriate, provide a rationale for the calculation of the risk of each adverse event.

Not applicable

9.2.5 Provide details of the process used when the sponsor's clinical advisers assessed the applicability of available or estimated clinical model parameter and inputs used in the analysis.

Given the simple nature of the cost analysis conducted, limited input from clinical advisers was required. Many of the parameters and assumptions in the model are driven by local NHS factors – in other words the specifics of a particular NHS unit in terms of equipment, processes and clinical activity (number of procedures etc).

Advice from clinicians was sought in relation to the issue of equipment availability and how in turn this might impact upon rates of intubation failure and other outcomes. Clinical advisers were approached individually via telephone interview and presented with a description of the decision problem for the MTAC assessment. Evidence from NAP4 and other related literature on rates of intubation failure, and the proportion of events related to equipment, was also discussed. Advisers were asked to comment on the assumption that aScope2 had the potential to reduce rates of intubation failure and to improve rates of successful management of displaced tracheostomy by improving the immediate availability of equipment for the management of unexpected difficult airways. Clinical advisers were selected based upon their experience and seniority, their familiarity with aScope2.

Ultimately the advice received was that the best available evidence on potential risk reduction with aScope2 is to be found in the recently published reports that estimate the proportion of events where equipment contributed (16, 63, 69). No definitive estimates of the proportion of events that could be avoided with aScope are therefore available. As exploratory assumption has been used and tested in sensitivity analyses.

9.2.6 Summarise all the variables included in the cost analysis. Provide cross-references to other parts of the submission. A suggested format is provided in table C5 below.

Table 39 Summary of variables applied in the cost model

Variable	Value	Source
Number of procedures performed per annum with reusable scopes (base case)	150	NHS survey (64)
Reusable flexible intubation scope costs (weighted costs including stack systems, cameras etc)	£12,105	NHS survey (64)
Annual Reusable flexible intubation scope maintenance & repair costs – proportion of equipment acquisition costs	0.21	NHS survey (64)
Number of reusable scopes available	5	NHS survey (64)
Assumed lifetime of reusable scope equipment (years)	5	Drummond et al. (2005) (65); a range tested in sensitivity analyses to reflect uncertainty with

		manufacturer estimates at the upper end
aScope2 cost per scope	£179	Ambu Ltd
aScope2 monitor	£0	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
Endoscopic Reprocessing costs (per scope reprocessed)	£30	NHS survey (64)
Rate of failed intubation in unexpected difficult intubation patients: Operating Theatre setting – reusable scopes	0.0625	Rocke (1992) (66)
Rate of failed intubation in unexpected difficult intubation patients: ICU setting – reusable scopes	0.166	Rose (1996) (67)
Rate of brain injury, death in difficult intubation patients where intubation has failed	28%	Thomas and McGrath (2009) (63)
ICU length of stay_failed intubation	6.2 days	HES data (68)
Rate of ICU admission or prolongation of stay_failed	0.74	Thomas and McGrath (2009) (63)

intubation		
Rate of brain injury or death_dislodged tracheostomy patients	0.13	McGrath and Thomas (2010) (16)
Rate of ICU stay or prolongation of stay_dislodged tracheostomy	0.75	McGrath and Thomas (2010) (16)
ICU length of stay_dislodged tracheostomy	15.4 days	HES data (68)
ICU_cost per day	£1,321	Weighted level 2 and 3 critical care cost per day NHS reference costs, 2010/11 (72)
Reduction in risk of failed intubation with aScope2	10 per cent	Exploratory assumption, varied in sensitivity analyses
Reduction in risk of dislodged tracheostomy leading to patient harm	10 per cent	Exploratory assumption, varied in sensitivity analyses

9.3 Resource identification, measurement and valuation

NHS costs

9.3.1 Describe how the clinical management of the condition is currently costed in the NHS in terms of reference costs and the payment by results (PbR) tariff.

Patients with unexpected difficult airways who suffer a failed intubation episode, particularly on the ICU, represent a very wide range of underlying conditions. Their hospitalisation and length of stay are therefore to a large

degree independent of the event of interest in this analysis. However, failed intubation is known to lead to ICU admission or prolongation of ICU for patients already being treated in this setting. We determined that the most appropriate way to estimate costs associated with failed intubation episodes was to focus on the ICU activity for patients with a failed intubation and to identify those episodes within this data set that were most relevant to the tracheal intubation setting.

To identify fibrescopic tracheal intubation we used a diagnosis code - T884 Failed / difficult intubation – and searched for this in every diagnostic position in the Hospital Episode Statistics dataset. Code T884 was associated with a very wide range of HRGs. Failed intubation is not therefore associated with specific reference costs or PbR tariffs and its costs are assumed to be captured within the HRG for a patient's primary condition.

Failed/difficult intubation data was investigated to estimate the average length of critical care stay associated with this event. We excluded patients with overall general hospital stays below 5 days in order to focus on the most relevant activity – since code T884 was also associated with a large amount of activity in areas such as gastroenterology with patients undergoing exploratory investigations in a completely different clinical context to difficult airway management. For this subgroup of episodes we then estimated the average stay in critical care (6.2 days) (68). This estimate has been used in modelling to represent the average length of stay/prolongation of stay in ICU as a result of failed intubation. Uncertainty has been explored in sensitivity analyses varying this ICU length of stay.

9.3.2 State the Office of Population, Censuses and Surveys Classification of Surgical Operations and Procedures (OPCS) codes for the operations, procedures and interventions relevant to the use of the technology for the clinical management of the condition.

Failed/difficult intubations appear to be mainly captured using diagnosis code T884 which is associated with a very wide range of OPCS codes for

operations, procedures and so on that relate to the patient's underlying condition rather than difficult airway management. However, for dislodged tracheostomy there is a group of OPCS codes – the most relevant of which is code E424 – revised tracheostomy.

As with failed intubation, patients with dislodged tracheostomy are hospitalised for a very broad range of underlying conditions. Therefore as with failed intubation we have focused on the critical care activity – estimating the average critical care length of stay for episodes coded with E424 and using this in the model to reflect the length of stay or prolongation of stay in ICU for patients with dislodged tracheostomies. Uncertainty around the mean length of stay in HES data (15.4 days) was tested in sensitivity analyses (68).

Resource identification, measurement and valuation studies

9.3.3 Provide a systematic search of relevant resource data for the NHS in England. Include a search strategy and inclusion criteria, and consider published and unpublished studies.

Data on NHS resource use associated with the management of unexpected difficult airways including equipment costs and reprocessing costs is not available in the literature.

A systematic review of cost studies in relevant therapeutic settings revealed no NHS studies. Reflecting this, data on resource utilisation and associated costs was collected directly from NHS centres via a survey.

A further systematic review to identify resource use data for the NHS relevant to the decision problem was not considered relevant.

9.3.4 Provide details of the process used when clinical advisers assessed the applicability of the resources used in the model[1].

In general very little is known about resource use in the NHS in relation to reusable flexible scopes. We conducted a resource use survey in order to gather information about available reusable scope equipment in terms of the quantity of equipment as well as costs for acquisition and maintenance.

This data is very difficult to collect – in most centres clinical advisers are not immediately able to provide this information and a range of other staff including theatre managers or technicians may be better placed to provide information. The most detailed information was available from one of the centres surveyed (Nottingham, Queen's Medical Centre) where a detailed study of costs and resource use associated with intubation is underway.

We approached NHS centres using a standard survey form and asked for information on the number of procedures performed using reusable equipment, the number of reusable intubation scopes available, their costs for acquisition and maintenance. We discussed the MTAC submission for aScope2 and the relevance of resource use data within this submission. We also asked for information regarding the reprocessing of scope equipment.

For centres where scopes were reprocessed centrally we asked for an estimate of the cost per scope reprocessed. Where reprocessed locally, we collected data on the staff and time associated with reprocessing using the approach employed by Tvede et al. (35). We also asked for information regarding equipment used for reprocessing including acquisition and maintenance costs.

Surveys were sent to approximately 20 NHS centres. Data was available from 6 centres. Precision of estimates was variable. Estimates regarding the number of scopes available and acquisition costs were provided by all centres. Accurate data on resource use associated with reprocessing was

[1] Adapted from Pharmaceutical Benefits Advisory Committee (2008) Guidelines for preparing submissions to the Pharmaceutical Benefits Advisory Committee (Version 4.3). Canberra: Pharmaceutical Benefits Advisory Committee.

very difficult to collect. The majority of centres (4 of 6) reprocessed scopes centrally and where this was the case an estimate of the recharge or cost charged to the department for each item reprocessed was provided.

Costs for maintenance and repair were not generally available. Detailed data was available from one centre (Nottingham QMC) with regard to repair and maintenance costs. On this basis we estimated that annual repair costs could equate to around 21 per cent of the acquisition cost for the scope equipment.

A summary of survey results is presented below. Uncertainty around survey results is considered in sensitivity analyses.

Table 40 Summary of survey data on reusable equipment

Centre	Number of scopes	Acquisition cost per scope, including additional equipment	Maintenance cost per scope (annual)	Total acquisition cost	Total Maintenance (annual)
1	9	9,962	2,119	89,661	19,067
2	8	8,000	1,701	64,000	13,610
3	1	30,000	6,380	30,000	6,380
4	3	18,000	3,828	54,000	11,483
5	3	8,500	1,808	25,500	5,423
6	6	16,667	3,544	100,000	21,265
Sum	30	91,129	19,379	363,161	77,227
Average per centre	5			60,527	12,871

A number of centres reported centralised reprocessing was in place. Reported costs per item reprocessed ranged from £30 to £40. We also attempted to collect data on the staff and time associated with reprocessing where this was conducted locally in a department. We followed the approach set out by

Tvede et al. (35). Only 2 of the 6 centres reprocessed scopes locally. This data is summarised below.

Table 41 Summary of survey data on local reprocessing resource use

Resource item	Staff involved	Resource description	Mean	Min	Max
Preparation for intubation	Nurse, day ward	Draping assistance table, lining up utensils, locating scope in storage cupboard, moving table to operating room	9.50	4.00	15.00
Immediate rinsing after scope use	Nurse, day ward	Rinsing scope in soapy water, rinsing with saline, pulling bottlebrush through channel, moving assistance table to washing room	5.00	5.00	5.00
Clearing up and inserting FOS into washer	Nurse, day ward	Mounting hose between scope and washer, inserting scope into washer, starting washer, cleaning up and moving table to prep room	4.00	3.00	5.00
Emptying washer, prep FOS	Nurse, day ward	Remove scope from washer, rinsing channels with alcohol, blow-drying, place scope in storage cupboard, complete log	5.00	5.00	5.00
Daily control of washer	Nurse, day ward	Checking and refilling cleaning and disinfection solutions, checking equipment, emptying filters, filling in log	0.71	0.43	1.00
Monthly sample collection for microbiology analysis	Nurse, day ward	Locate scopes, collect samples, place scope in storage cupboard, filling forms/labels, packing and sending samples, log results	2.70	1.80	3.60
Transport to/from external departments	Clinical support worker	Locate scope in storage cupboard, place in transport tray, transfer to external department, collect from department and return to wash room	13.00	6.00	20.00

Data on resource use for local reprocessing was combined with published data on unit costs for staff in the NHS (73). Data on automatic endoscope reprocessing costs – acquisition cost, maintenance and operating costs was very difficult to establish. One publically available NHS business case

provided estimates for a particular AER that has been mentioned in the survey and costs from this business case were used as the best available estimate for equipment costs (74).

Technology and comparators' costs

9.3.5 Provide the list price for the technology.

Ambu aScope2 is available at a list price varying from £149 to £199. The mid-point of this range is £179. The price depends on the size of an order and the current effective price (current average selling price) is £179.

The Ambu aScope2 monitor has a list price of £799. However, a monitor is supplied free of charge within a starter pack, along with any initial order of aScope2s. In practice, there is therefore currently no cost associated with acquiring the aScope2 monitor. In the event of a fault with the monitor or damage, the monitor is replaced at no cost by the manufacturer.

9.3.6 If the list price is not used in the de novo cost model, provide the alternative price and a justification.

As stated above, the current average selling price of aScope2 to the NHS is £179 and the list price range that is transparently available to all NHS customers as per Ambu's official marketing materials. We have used £179 in the model base case and vary this in sensitivity analyses.

The list price for the aScope2 monitor has not been used in the de novo model since in practice monitors are currently supplied to the NHS free of charge, alongside initial orders of the aScope2. Where additional monitors are required, for example where a number of departments within a hospital use the equipment, a further starter pack is provided including the monitor, free of charge. The decision problem stipulates consideration of the impact of the number of aScope monitors required. Our assumption is that a single aScope monitor per hospital department will be sufficient in the context of unexpected difficult airway management and that this is therefore available free of charge.

9.3.7 Summarise the annual costs associated with the technology and the comparator technology (if applicable) applied in the cost model.

A suggested format is provided in tables C6 and C7. Table C7 should only be completed when the most relevant UK comparator for the cost analysis refers to another technology.

Costs for reusable flexible scopes comprise the acquisition cost, the maintenance and repair costs and the costs associated with reprocessing scopes prior to their use.

The acquisition cost for reusable scope equipment is a one-off purchase, but in a comparison between aScope2 and reusable equipment, the cost for a reusable scope should include its acquisition cost, spread over its useful lifetime. This approach is standard in health economic evaluation and the method described by Drummond et al. to estimate an annual equivalent cost has been used (65). We estimate the average cost per intubation by dividing the annuitized cost per scope by its annual frequency of use. A discount rate of 3.5% has been used.

We have also included an estimate for maintenance and repair costs in relation to reusable scopes. Using available data we estimate that these costs represent approximately 21 per cent of the equipment acquisition cost on an annual basis.

Finally we have included a cost for reprocessing in the estimated cost for reusable scopes. Tvede et al. (35) estimated costs for reprocessing using a detailed macro-costing exercise and identified resource use in a hospital department in Denmark. We attempted to collect similar data from NHS centres but it where reprocessing was conducted locally in a hospital department, estimates of staff and time were difficult to collect with precision. In fact the majority of centres surveyed (4 of 6) stated that reprocessing was available centrally in their Trust. Where this is the case there tends to be a standard reprocessing charge per item. We have used the mid-point of these estimates in the base case to reflect reprocessing costs in sensitivity analyses.

Table 42 Costs per treatment/patient associated with the technology in the cost model

Items	Value	Source
Price of the technology per treatment/patient	£179	Ambu
Total cost per treatment/patient	£179	

Table 43 Costs per treatment/patient associated with the comparator technology in the cost model

Items	Value	Source
Cost of the comparator per treatment/patient	£174.1	NHS survey (64)
Consumables (if applicable)		NHS survey (64)
Maintenance cost		NHS survey (64)
Training cost		
Reprocessing costs per scope (central reprocessing)	£35	NHS survey (64)
Total cost per treatment/patient	£209.1	NHS survey (64)
** the cost per intubation with reusable equipment varies according to the number of scopes available and the number of procedures performed as well as the lifetime of the equipment.*		

Health-state costs

9.3.8 If the cost model presents health states, the costs related to each health state should be presented in table C8. The health states should refer to the states in section 9.1.7. Provide a rationale for the choice of values used in the cost model.

Not applicable

Adverse-event costs

9.3.9 Complete table C9 with details of the costs associated with each adverse event referred to in 9.2.4 included in the cost model. Include all adverse events and complication costs, both during and after longer-term use of the technology.

Not applicable

Miscellaneous costs

9.3.10 Describe any additional costs and cost savings that have not been covered anywhere else (for example, PSS costs, and patient and carer costs). If none, please state.

Not applicable

9.3.11 Are there any other opportunities for resource savings or redirection of resources that it has not been possible to quantify?

There are two other important considerations with respect to potential resource savings associated with aScope2. Firstly, since aScope2 is supplied in sterile packaging, this eliminates important risks of cross-contamination that exist for reusable equipment. Section 3.4 of the clinical submission reviews the available evidence on infection as a result of contamination. There is not sufficient evidence to incorporate these aspects into the modelling. However, the potential reduction in risks of infection should be considered in the context of infection control as a major focus for the NHS. The Healthcare-Associated Infection (HCAI) Research Network reports that as well as affecting patients, HCAI is also a serious burden on the NHS (75). These infections are costing the NHS an estimated £1 billion a year and they are having a major impact on the availability of beds because infected patients have to spend, on average, an extra 11 days in hospital. Furthermore, infected patients cost 3 times more to treat than uninfected patients and infections are becoming difficult to treat because of an increase in antimicrobial resistance (75). The potential risk of Creutzfeldt–Jakob disease (vCJD) transmission from one patient to another via contaminated medical equipment is also recognised as a major consideration with respect to reprocessing and decontamination methods. Further details regarding vCJD issues are discussed in the clinical evidence submission (see section 3.4, page 25).

Secondly, aScope2 has the potential to reduce litigation costs for NHS Trusts through reducing rates of failed intubation as well as brain injury and death for patients suffering either failed intubation or a displaced tracheostomy. Cook et al. conducted a review of claims notified to the NHS Litigation Authority in England between 1995 and 2007 and found that the total cost of (non-dental)

airway claims was £4.9 million (84% closed, median cost £30 000) and that of respiratory claims was £3.3 million (81% closed, median £27 000) (76). Airway and respiratory claims account for 12% of anaesthesia related claims, 53% of deaths, 27% of cost and ten of the 50 most expensive claims in the dataset. Whilst the potential cost of claims is an important consideration in relation to aScope2 and the potential to reduce the occurrence of failed intubation and other outcomes, it is not possible to include this aspect directly into the modelling.

9.4 Approach to sensitivity analysis

Section 9.4 requires the sponsor to carry out sensitivity analyses to explore uncertainty around the structural assumptions and parameters used in the analysis. All inputs used in the analysis will be estimated with a degree of imprecision. For technologies whose final price/acquisition cost has not been confirmed, sensitivity analysis should be conducted over a plausible range of prices.

Analysis of a representative range of plausible scenarios should be presented and each alternative analysis should present separate results.

9.4.1 Has the uncertainty around structural assumptions been investigated? State the types of sensitivity analysis that have been carried out in the cost analysis.

Structural uncertainty was not considered. The model employs a very simple structure to determine the relevant costs and outcomes. More complex model structures were not considered relevant and it was felt that data would not have been available to populate more complex models.

A range of univariate sensitivity analyses were conducted to explore the sensitivity of results to all important parameters in the model including costs and outcomes.

9.4.2 Was a deterministic and/or probabilistic sensitivity analysis undertaken? If not, why not? How were variables varied and what was the rationale for this? If relevant, the distributions and their sources should be clearly stated.

A univariate, deterministic sensitivity analysis has been conducted. A probabilistic analysis was not considered applicable particularly given the limited availability of data. It was concluded that in this case a univariate sensitivity analysis would be sufficient to explore the uncertainty around the base case results.

Base case parameters were varied mainly by simple percentage adjustment. For certain parameters where data was available a specific range was tested – for example, reprocessing costs were varied from a minimum value of £20 per item reflecting the local resource use available, to an upper value of £40 per item, reflecting the highest cost per item reported in the NHS survey (64). The price for aScope2 was varied from £149 to £199 specifically to reflect the available range of per unit prices officially available to the NHS, depending on quantity of aScope2 products ordered.

9.4.3 Complete table C10.1, C10.2 and/or C10.3 as appropriate to summarise the variables used in the sensitivity analysis.

Table 44 Variables used in one-way scenario-based deterministic sensitivity analysis

Variable	Base-case value	Range of values
Cost of reusable scope equipment, average per scope	£12,105	+/- 25%; £9,078 to £15,131
Maintenance costs per year (as proportion of equipment acquisition cost)	0.21	+/-25%; 0.16 to 0.26
Equipment lifetime (years)	5	10 to 3 years
Rate of ICU admission/prolongation of stay for failed intubation	0.74	+/-25% 0.50 to 1
Length of stay in ICU for failed intubation	6.2 days	+/-50%; 3 to 9 days
Rate of failed intubation_Operating Theatre	0.062	+/-50%; 0.032 to 0.093
Rate of failed intubation_ICU	0.17	+/-50%; 0.085 to 0.255
Reprocessing costs per item reprocessed	£35	Local reprocessing estimated to higher of central estimates; £20 to £40
Length of stay in ICU for dislodged tracheostomy	15.4 days	+/-50%; 7.7 to 23.1 days
Rate of ICU admission/prolongation of stay for dislodged tracheostomy	0.75	+/-50%; 0.50 to 1
Reduction in risk of failed intubation with aScope2	10 per cent	5 to 15 per cent
Reduction in risk of dislodged tracheostomy leading to patient harm with aScope2	10 per cent	5 to 15 per cent
Cost per day ICU	£1,321	Level 2 to level 3 critical care reference cost; £1,226 to £1,440
Price per unit, aScope2	£179	Discount range offered by Ambu; £199 to £149

9.4.4 If any parameters or variables listed in section 9.2.6 were omitted from the sensitivity analysis, provide the rationale.

Costs for the aScope2 monitor were not included in the sensitivity analyses since costs for these items are controlled by Ambu and are fixed.

9.5 Results of de novo cost analysis

Section 9.5 requires the sponsor to report the de novo cost analysis results. These should include the following:

- costs
- disaggregated results such as costs associated with treatment, costs associated with adverse events, and costs associated with follow-up/subsequent treatment
- a tabulation of the mean cost results
- results of the sensitivity analysis.

Base-case analysis

9.5.1 Report the total costs associated with use of the technology and the comparator(s) in the base-case analysis. A suggested format is presented in table C11.

In the base case we present results for three settings – unexpected difficult intubation in the Operating Theatre, unexpected difficult intubation in the ICU and dislodged tracheostomy. Base case results are presented for a hypothetical NHS Trust with 5 reusable scopes that are used in total 150 times per year.

Since the cost per intubation is in part a function of the number of scopes available and the frequency of use of scope equipment, additional tables are provided reporting the incremental cost by number of scopes available and annual number of procedures using scopes.

Table 45 Base-case results

	Total per patient cost (£)
Unexpected difficult intubation, operating theatre setting	
aScope2	£520
Reusable scope	£588
Unexpected difficult airway, ICU setting	
aScope2	£1,085
Reusable scope	£1,215
Dislodged tracheostomy	
aScope2	£13,911
Reusable scope	£15,467

Table 46 Base-case results: aScope2 incremental cost per intubation (£s), unexpected difficult airway [equipment and staffing costs only] – Operating theatre, ICU and dislodged tracheostomy settings

	50	***100***	***150***	***200***	***250***	***300***
1	39.5	91.8	109.2	117.9	123.1	126.6
2	-64.9	39.5	74.4	91.8	102.2	109.2
3	-169.4	-12.7	39.5	65.7	81.3	91.8

4	-273.8	-64.9	4.7	39.5	60.4	74.4
5	-378.3	-117.1	-30.1	13.4	39.5	57.0
6	-482.7	-169.4	-64.9	-12.7	18.7	39.5
7	-587.2	-221.6	-99.7	-38.8	-2.2	22.1
8	-691.6	-273.8	-134.5	-64.9	-23.1	4.7
9	-796.1	-326.0	-169.4	-91.0	-44.0	-12.7
10	-900.5	-378.3	-204.2	-117.1	-64.9	-30.1

Incremental costs per intubation are presented by number of reusable scopes available (vertical axis) and number of procedures performed annually with reusable equipment (horizontal axis)

Table 47 Base-case results: aScope2 incremental cost per intubation (£s), unexpected difficult airway in the operating theatre [equipment, staffing and hospitalisation costs]

	50	***100***	***150***	***200***	***250***	***300***
1	1.7	53.9	71.3	80.0	85.2	88.7
2	-102.8	1.7	36.5	53.9	64.3	71.3
3	-207.2	-50.6	1.7	27.8	43.4	53.9
4	-311.7	-102.8	-33.2	1.7	22.6	36.5
5	-416.1	-155.0	-68.0	-24.4	1.7	19.1
6	-520.6	-207.2	-102.8	-50.6	-19.2	1.7
7	-625.0	-259.5	-137.6	-76.7	-40.1	-15.7
8	-729.5	-311.7	-172.4	-102.8	-61.0	-33.2
9	-834.0	-363.9	-207.2	-128.9	-81.9	-50.6
10	-938.4	-416.1	-242.1	-155.0	-102.8	-68.0

Incremental costs per intubation are presented by number of reusable scopes available (vertical axis) and number of procedures performed annually with reusable equipment (horizontal axis)

Table 48 Base-case results: aScope2 incremental cost per intubation (£s), unexpected difficult airway in the ICU [equipment, staffing and hospitalisation costs]

	50	***100***	***150***	***200***	***250***	***300***
1	-61.1	-8.8	8.6	17.3	22.5	26.0
2	-165.5	-61.1	-26.2	-8.8	1.6	8.6
3	-270.0	-113.3	-61.1	-34.9	-19.3	-8.8
4	-374.4	-165.5	-95.9	-61.1	-40.2	-26.2
5	-478.9	-217.7	-130.7	-87.2	-61.1	-43.7
6	-583.3	-270.0	-165.5	-113.3	-82.0	-61.1
7	-687.8	-322.2	-200.3	-139.4	-102.8	-78.5
8	-792.2	-374.4	-235.1	-165.5	-123.7	-95.9
9	-896.7	-426.6	-270.0	-191.6	-144.6	-113.3
10	-1001.1	-478.9	-304.8	-217.7	-165.5	-130.7

Incremental costs per intubation are presented by number of reusable scopes available (vertical axis) and number of procedures performed annually with reusable equipment (horizontal axis)

Table 49 Base-case results: aScope2 incremental cost per intubation (£s), dislodged tracheostomy [equipment, staffing and hospitalisation costs]

	50	***100***	***150***	***200***	***250***	***300***
1	-1486.2	-1434.0	-1416.6	-1407.9	-1402.6	-1399.2
2	-1590.7	-1486.2	-1451.4	-1434.0	-1423.5	-1416.6
3	-1695.1	-1538.4	-1486.2	-1460.1	-1444.4	-1434.0
4	-1799.6	-1590.7	-1521.0	-1486.2	-1465.3	-1451.4
5	-1904.0	-1642.9	-1555.8	-1512.3	-1486.2	-1468.8
6	-2008.5	-1695.1	-1590.7	-1538.4	-1507.1	-1486.2
7	-2112.9	-1747.3	-1625.5	-1564.5	-1528.0	-1503.6
8	-2217.4	-1799.6	-1660.3	-1590.7	-1548.9	-1521.0
9	-2321.8	-1851.8	-1695.1	-1616.8	-1569.8	-1538.4
10	-2426.3	-1904.0	-1729.9	-1642.9	-1590.7	-1555.8

Incremental costs per intubation are presented by number of reusable scopes available (vertical axis) and number of procedures performed annually with reusable equipment (horizontal axis)

9.5.2 Report the total difference in costs between the technology and comparator(s).

In the base case, for a hypothetical NHS Trust with 5 reusable scopes that are used 150 times per annum, the incremental cost of aScope2 compared to reusable scopes is estimated at -£30 per intubation (cost-saving) in the unexpected difficult airway managed in the operating theatre setting (equipment and staff costs only). Inclusion of modelled costs associated with hospitalisations results in an incremental cost of -£68.

In the ICU setting base case, the incremental cost of aScope2 compared to reusable scopes is estimated at -£30 per intubation (equipment and staff costs only) and -£131 when modelled costs associated with hospitalisations are included.

In the dislodged tracheostomy setting the incremental cost of aScope2 compared to reusable scopes is estimated at -£30 per dislodged tracheostomy managed and -£1,556 when modelled costs associated with hospitalisations are included.

Results presented in tables Table 46 to Table 49 report incremental costs across a range of permutations for numbers of reusable scopes (vertical axis) and their frequency of use (horizontal axis).

9.5.3 Provide details of the costs for the technology and its comparator by category of cost. A suggested format is presented in table C15.

Three separate tables are presented to report base case results for the settings of interest – Table 50; unexpected difficult intubation in the operating theatre, Table 51; unexpected difficult intubation in the ICU and Table 52; dislodged tracheostomy.

Table 50 Summary of costs by category of cost per intubation (£s); unexpected difficult airway in the operating theatre setting

Item	Cost *reusable scope*	Cost aScope2	Increment
Scope equipment costs including annual maintenance	174.1	179.0	4.9
Costs associated with sterilisation procedures	35.0	0.0	-35.0
Total equipment and staff costs	**209.1**	**179.0**	**-30.1**
Hospitalisation costs for failed/complicated intubation	378.8	340.9	-37.9
Total costs including hospitalisation costs	**587.9**	**519.9**	**-68.0**

Table 51 Summary of costs by category of cost per intubation (£s); unexpected difficult airway in the ICU setting

Item	Cost *reusable scope*	Cost aScope2	Increment
Scope equipment costs including annual maintenance	174.1	179.0	4.9
Costs associated with sterilisation procedures	35.0	0.0	-35.0
Total equipment and staff costs	**209.1**	**179.0**	**-30.1**
Hospitalisation costs for failed/complicated intubation	1006.1	905.5	-100.6

Total costs including hospitalisation costs	**1215.2**	**1084.5**	**-130.7**

Table 52 Summary of costs by category of cost per intubation (£s); dislodged tracheostomy

Item	**Cost *reusable scope***	**Cost aScope2**	**Increment**
Scope equipment costs including annual maintenance	174.1	179.0	4.9
Costs associated with sterilisation procedures	35.0	0.0	-35.0
Total equipment and staff costs	**209.1**	**179.0**	**-30.1**
Hospitalisation costs for failed/complicated intubation	15257.6	13731.8	-1525.8
Total costs including hospitalisation costs	**15466.6**	**13910.8**	**-1555.8**

9.5.4 If appropriate, provide details of the costs for the technology and its comparator by health state. A suggested format is presented in table C13.

Not applicable

9.5.5 If appropriate, provide details of the costs for the technology and its comparator by adverse event. A suggested format is provided in table C14.

Not applicable

Sensitivity analysis results

9.5.6 Present results of deterministic one-way sensitivity analysis of the variables described in table C10.1.

The cost analysis including equipment and staff costs only is consistent across the three settings of interest (operating theatre, ICU and dislodged tracheostomy setting). Sensitivity analyses for these costs are presented below in Table 53. Further sensitivity analyses including hospitalisation costs are presented separately for each setting – difficult intubation in the operating theatre Table 54, difficult intubation in the ICU Table 55 and finally the dislodged tracheostomy setting in Table 56.

Table 53 Sensitivity analysis; unexpected difficult airway in the operating theatre setting (equipment and staff costs only) incremental cost per intubation (£) operating theatre, ICU and dislodged tracheostomy setting

Base case incremental cost per intubation	-£30.1	
Variable for sensitivity analysis	**Lower value**	**Upper value**
Cost of reusable scope equipment, average per scope	13.4	-73.6
Maintenance costs per year	-9.9	-50.3
Equipment lifetime	10.8	-84.7
Reprocessing costs per item reprocessed	-15.1	-35.1
Price per unit aScope2	-10.1	-60.1

Table 54 Sensitivity analysis; unexpected difficult airway in the operating theatre setting (equipment, staff and hospital costs) incremental cost per intubation (£)

Base case incremental cost per intubation	-£68.0	
Variable for sensitivity analysis	**Lower value**	**Upper value**
Cost of reusable scope equipment, average per scope	-87.2	-82.87
Maintenance costs per year	-47.8	-88.1
Equipment lifetime	-27.1	-122.6
Rate of ICU admission/prolongation of stay for failed intubation	-55.7	-81.3
Length of stay in ICU for failed intubation	-48.4	-85.1
Rate of failed intubation_Operating Theatre	-49.5	-86.5
Reprocessing costs per item reprocessed	-52.9	-73.0
Reduction in risk of failed intubation with aScope2	-49.0	-86.9
Cost per day ICU	-65.2	-71.4
Price per unit aScope2	-48.0	-98.0

Table 55 Sensitivity analysis; unexpected difficult airway in the ICU setting (equipment, staff and hospital costs) incremental cost per intubation (£)

Base case incremental cost per intubation	-£130.7	
Variable for sensitivity analysis	**Lower value**	**Upper value**
Cost of reusable scope equipment, average per scope	-87.2	-174.2
Maintenance costs per year	-110.5	-150.9
Equipment lifetime	-89.8	-185.4
Rate of ICU admission/prolongation of stay for failed intubation	-98.1	-166.0
Length of stay in ICU for failed intubation	-78.8	-176.1
Rate of failed intubation_ICU	-81.6	-184.6
Reprocessing costs per item reprocessed	-115.7	-135.7
Reduction in risk of failed intubation with aScope2	-80.4	-181.0
Cost per day ICU	-123.5	-139.8
Cost per unit aScope2	-110.7	-160.7

Table 56 Sensitivity analysis; dislodged tracheostomy setting, (equipment, staff and hospital costs) incremental cost per dislodged tracheostomy (£)

Base case incremental cost per intubation	-£1,555.8	
Variable for sensitivity analysis	**Lower value**	**Upper value**
Cost of reusable scope equipment, average per scope	-1,512.3	-1,599.4
Maintenance costs per year	-1,535.7	-1,576.0
Equipment lifetime	-1,515.0	-1,610.5
Rate of ICU admission/prolongation of stay for dislodged tracheostomy	-1,047.3	-2,064.4
Length of stay in ICU for dislodged tracheostomy	-793.0	-2,318.7
Reprocessing costs per item reprocessed	-1,540.8	-1,560.8
Reduction in risk of failed tracheostomy leading to patient harm with aScope2	-793	-2,318.7
Cost per day ICU	-1,446.1	-1,693.3
Cost per unit aScope2	-1,535.8	-1,585.8

9.5.7 Present results of deterministic multi-way scenario sensitivity analysis described in table C10.2.

Not applicable

9.5.8 Present results of the probabilistic sensitivity analysis described in table C10.3.

Not applicable

9.5.9 What were the main findings of each of the sensitivity analyses?

In the three settings (operating theatre setting and ICU for difficult intubation; and dislodged tracheostomy) the incremental cost per intubation with aScope2 was sensitive to a number of variables. Results were sensitive to assumptions about the cost of reusable scope equipment, the cost of maintenance for reusable scopes and the rate of failed intubation among difficult intubations in the operating theatre. Results were also sensitive to assumptions about the potential reduction in the rate of failed intubation with aScope2. Results remained broadly cost-saving across the range of sensitivity analyses conducted and only became cost incurring with optimistic assumptions about the longevity of reusable equipment and substantially lower equipment costs for reusable scopes.

In analyses including hospitalisation costs, aScope remained cost-saving for all the conducted sensitivity analyses.

9.5.10 What are the key drivers of the cost results?

Key drivers of the results are the average cost of reusable equipment, its assumed lifetime, the assumed level of costs for maintenance and repair and costs associated with reprocessing scopes.

In the wider analysis including hospitalisation, results are driven by assumptions regarding rates of outcomes, hospital stay as well as assumed risk reduction with aScope2.

Miscellaneous results

9.5.11 Describe any additional results that have not been specifically requested in this template. If none, please state.

Evidence with regard to relevant clinical outcomes as set out in the decision problem is very limited. Results for outcomes of interest are presented as an illustrative analysis based on the available evidence. Rates of successful intubation and brain injury/death were estimated in the difficult intubation setting. In the dislodged tracheostomy setting, rates of successfully managed patients as well as rates of brain injury/death were estimated. Results are summarised in Table 57 for the three settings of interest.

Table 57 Model results for clinical outcomes of interest, base case

Model setting	Reusable Scopes	aScope2	Incremental
Unexpected difficult airway, operating theatre setting			
Successful intubations per 1000 procedures	938	944	6
Brain injury/deaths per 1000 procedures	18	16	-2
Unexpected difficult airway, ICU setting			
Successful intubations per 1000 procedures	834	851	17
Brain injury/deaths per 1000 procedures	46	42	-5
Displaced tracheostomy setting			
Successfully managed patients per 1000 cases of displaced tracheostomy	250	325	75
Number of deaths/brain injuries per 1000 cases	129	116	-13

9.6 Subgroup analysis

For many technologies, the capacity to benefit from treatment will differ for patients with differing characteristics. Sponsors are required to complete section 9.6 in accordance with the subgroups identified in the scope and for any additional subgroups considered relevant.

Types of subgroups that are not considered relevant are those based solely on the following factors.

- Subgroups based solely on differential treatment costs for individuals according to their social characteristics.
- Subgroups specified in relation to the costs of providing treatment in different geographical locations within the UK (for example, if the costs of facilities available for providing the technology vary according to location).

9.6.1 Specify whether analysis of subgroups was undertaken and how these subgroups were identified. Cross-reference the response to the decision problem in table A1 and sections 3.2 and 7.4.4.

Not applicable

9.6.2 Define the characteristics of patients in the subgroup(s).

Not applicable

9.6.3 Describe how the subgroups were included in the cost analysis.

Not applicable

9.6.4 What were the results of the subgroup analysis/analyses, if conducted? The results should be presented in a table similar to that in section 9.5.1 (base-case analysis).

Not applicable

9.6.5 Were any subgroups not included in the submission? If so, which ones, and why were they not considered?

Not applicable

9.7 Validation

9.7.1 Describe the methods used to validate and cross-validate (for example with external evidence sources) and quality-assure the model. Provide references to the results produced and cross-reference to evidence identified in the clinical and resources sections.

There are very limited data in the literature to support a validation of the modelling undertaken. Modelling relies in particular on assumptions regarding the potential for aScope2 to reduce the risks of failed intubation and other

outcomes, as a result of being immediately available for use in emergency clinical situations.

No attempts have previously been made that we are aware of to model reductions in the rates of events such as failed intubation, brain injury or death. The model detailed costing analysis available, published recently in Denmark is consistent with the results of our modelling – in relation to the findings that the costs of aScope2 are dependent to a significant extent on the frequency of use of scope equipment.

Whilst it is difficult to validate the model at present, a study is on-going in a major UK centre (Nottingham, Queen's Medical Centre) which will provide detailed costings and draw comparisons between costs for reusable equipment and aScope2. Evidence from this ongoing study was made available to Ambu, which increases the validity of some important model parameters – in particular, the cost of equipment and maintenance for reusable scopes.

9.8 Interpretation of economic evidence

9.8.1 Are the results from this cost analysis consistent with the published economic literature? If not, why do the results from this evaluation differ, and why should the results in the submission be given more credence than those in the published literature?

As above, the results of the modelling are broadly consistent with the existing published studies where these are comparable. The analysis by Tvede and colleagues found that costs for aScope and reusable scopes were similar and that, beyond a threshold level of clinical activity per year, aScope would become cost-saving (35). This is in line with our modelling approach – as represented in the results tables reporting incremental costs by number of scopes available and number of annual procedures with reusable equipment. As discussed above however, to our knowledge no other modelling work has been undertaken in relation to outcomes in this area.

9.8.2 Is the cost analysis relevant to all groups of patients and NHS settings in England that could potentially use the technology as identified in the scope?

Yes

9.8.3 What are the main strengths and weaknesses of the analysis? How might these affect the interpretation of the results?

One of the main strengths of the analysis is the NHS survey data (64). We were able to gather useful information on the costs of reusable equipment and maintenance costs for this equipment. This data is hard to find and often lacking in precision. In particular, the availability of data from a large on-going study in Nottingham at QMC has aided the accuracy of the cost data included in the model.

One weakness in the cost analysis relates to the fact that we have been unable to distinguish between fibreoptic and video scopes. However, videoscope equipment is significantly more costly than the fibreoptic alternative. To some extent we have tested this in the sensitivity analysis.

A key weakness relates to the accuracy of data on maintenance and repair costs for reusable scopes. Data were available for one centre and indicated that repair costs were likely to equate to around 21 per cent of the acquisition cost of scope equipment on annual basis. Other information, albeit anecdotal suggests that we may have underestimated repair and maintenance costs. Three studies have looked specifically at costs in the area of bronchoscopy and have found that repair costs represent a significant component of costs in bronchoscopy units (77-79). Base case assumptions in the modelling presented here may well represent an underestimate of the true costs associated with repair and maintenance for reusable scope equipment.

The main weakness in the analysis relates to the outcomes data. Clinical trials for aScope2 demonstrate the efficacy of the product but do not address the outcomes defined in to the decision problem such as failed intubation in unanticipated difficult airway. Evidence in the literature for failed intubation is

variable – both in terms of the way failed intubation is defined and the consistency of reporting across multiple studies. As a result the analyses relying on outcomes, hospital activity and reductions in risk associated with aScope2 are highly uncertain. There is a clear logic supporting the rationale that having aScope2 immediately available on the NHS – particularly in areas where patients are at higher risk such as ICU on patients with tracheostomies on wards in remote locations in a hospital – has significant potential to reduce the risk of events such as failed intubation, brain injury or death. NAP4 as well as the reports by McGrath and Thomas highlight the fact that availability of equipment during emergencies is a key issue in the NHS. However, quantifying the extent to which aScope2 will reduce risks is very difficult at present and therefore the approach taken here is to rely on an illustrative base case assumption to estimate the potential benefits and cost savings.

9.8.4 What further analyses could be undertaken to enhance the robustness/completeness of the results?

A wider survey of NHS centres may improve the accuracy of costing data with regard to equipment and maintenance costs. The results of the on-going study in Nottingham are likely to be available soon and will provide further useful information on the real costs of reusable equipment on the NHS.

References

1. Royal College of Anaesthetists. 4th National Audit Project (NAP4); Major complications of airway management in the UK2011. Available from: http://www.rcoa.ac.uk/nap4.
2. Benumof J. Management of the difficult airway. Ann Acad Med Singapore. 1994;23(4):589-91.
3. Mort T. Emergency tracheal intubation: complications associated with repeated laryngoscopic attempts. Anesth Analg. 2004;99(2):607-13.
4. Henderson JJ, Popat MT, Latto IP, Pearce AC. Difficult Airway Society guidelines for management of the unanticipated difficult intubation. Anaesthesia. 2004;59(7):675-94.
5. Paw H, Bodenham A. Percutaneous tracheostomy: A practical handbook: Greenwich medical Media Ltd; 2004.
6. Datta D, Onyirimba F, McNamee M. The utility of chest radiographs following percutaneous dilatational tracheostomy. Chest. 2003;123(5):1603-6.
7. Engels P, Bagshaw S, Meier M, Brindley P. Tracheostomy: from insertion to decannulation. Can J Surg. 2009;52(5):427-33.
8. Rana S, Pendem S, Pogodzinski M, Hubmayr R, Gajic O. Tracheostomy in critically ill patients. Mayo Clin Proc. 2005;80(12):1632-8.
9. Popat M. Practical Fibreoptic Intubation. Boston: Butterworth Heinmann; 2001.
10. Petros S. Percutaneous tracheostomy. Crit Care. 1999;3(2):R5-10.
11. Veenith T, Ganeshamoorthy S, Standley T, Carter J, Young P. Intensive care unit tracheostomy: a snapshot of UK practice. Int Arch Med. 2008;1(1):21.
12. Benumof J, Hagberg C. Benumof's Airway Management: Principles and Practice (2nd Edition). Missouri: Mosby; 2007.
13. Cheney F. The American Society of Anesthesiologists Closed Claims Project: what have we learned, how has it affected practice, and how will it affect practice in the future? Anesthesiology. 1999;91(2):552-6.
14. Crosby E, Cooper R, Douglas M, Doyle D, Hung O, Labrecque P, et al. The unanticipated difficult airway with recommendations for management. Can J Anaesth. 1998;45(8):757-76.
15. Voyagis G, Kyriakis K, Roussaki-Danou K, Bastounis E. Evaluating the difficult airway. An epidemiological study. Minerva Anestesiol. 1995;61(12):483-9.
16. 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.
17. Nagaro T, Yorozuya T, Sotani M, Adachi N, Tabo E, Arai T, et al. Survey of patients whose lungs could not be ventilated and whose trachea could not be intubated in university hospitals in Japan. J Anesth. 2003;17(4):232-40.
18. Chanchayanon T, Suraseranivongse S, Chau-in W. The Thai Anesthesia Incidents Study (THAI Study) of difficult intubation: a qualitative analysis. J Med Assoc Thai. 2005;88(Suppl 7):S62-8.

19. Auroy Y, Benhamou D, Péquignot F, Bovet M, Jougla E, Lienhart A. Mortality related to anaesthesia in France: analysis of deaths related to airway complications. Anaesthesia. 2009;64(4):366-70.
20. Menon N, Joffe A, Deem S, Yanez N, Grabinsky A, Dagal A, et al. Occurrence and Complications of Tracheal Reintubation in Critically Ill Adults. Respir Care. 2012;Epub ahead of print.
21. Beckmann U, Gillies D. Factors associated with reintubation in intensive care: an analysis of causes and outcomes. Chest. 2001;120(2):538-42.
22. Epstein S, Ciubotaru R, Wong J. Effect of failed extubation on the outcome of mechanical ventilation. Chest. 1997;112(1):186-92.
23. Daley B, Garcia-Perez F, Ross S. Reintubation as an outcome predictor in trauma patients. Chest. 1996;110(6):1577-80.
24. Ramachandran S, Mathis M, Tremper K, Shanks A, Kheterpal S. Predictors and Clinical Outcomes from Failed Laryngeal Mask Airway Unique™: A Study of 15,795 Patients. Anesthesiology. 2012:Epub ahead of print.
25. Culver D, Gordon S, Mehta A. Infection control in the bronchoscopy suite: a review of outbreaks and guidelines for prevention. Am J Respir Crit Care Med. 2003;167(8):1050-6.
26. Ramsey A, Oemig T, Davis J, Massey J, Török T. An outbreak of bronchoscopy-related Mycobacterium tuberculosis infections due to lack of bronchoscope leak testing. Chest. 2002;121(3):976-81.
27. Medical Devices Agency. Device Bulletin: Decontamination of endoscopes (MDA DB2002 [05])2002. Available from: http://www.mhra.gov.uk/home/groups/dts-bi/documents/publication/con007330.pdf.
28. Muscarella L. Prevention of disease transmission during flexible laryngoscopy. Am J Infect Control. 2007;35(8):536-44.
29. Cowen A. The clinical risks of infection associated with endoscopy. Can J Gastroenterol. 2001;15(5):321-31.
30. Woodall N, Harwood R, Barker G. Complications of awake fibreoptic intubation without sedation in 200 healthy anaesthetists attending a training course. Br J Anaesth. 2008;100(6):850-5.
31. Miller D, Youkhana I, Karunaratne W, Pearce A. Presence of protein deposits on 'cleaned' re-usable anaesthetic equipment. Anaesthesia. 2001;56(11):1069-72.
32. Fraser V, Jones M, Murray P, Medoff G, Zhang Y, Wallace Jr R. Contamination of flexible fiberoptic bronchoscopes with Mycobacterium chelonae linked to an automated bronchoscope disinfection machine. Am Rev Respir Dis. 1992;145(4 pt 1):853-5.
33. Elackattu A, Zoccoli M, Spiegel J, Grundfast K. A comparison of two methods for preventing cross-contamination when using flexible fiberoptic endoscopes in an otolaryngology clinic: disposable sterile sheaths versus immersion in germicidal liquid. Laryngoscope. 2010;120(12):2410-6.
34. Health Service Circular Series number: HSC 1999/178 Issue date: 13th August 1999 Review data: 13 August 2002 Category Public Health Status: Action.
35. Tvede M, Kristensen M, Nyhus-Andreasen M. A cost analysis of reusable and disposable flexible optical scopes for intubation. Acta Anaesthesiol Scand. 2012;56(5):577-84.

36. Jones P, Malik T, Ridgway G, Bates G. Summary of guidelines for decontaminating ENT fibreoptic scopes. 2005. Available from: https://entuk.org/docs/prof/publications/summary_guidelines_cleaning_fibreoptic_laryngosopes.
37. Rutala W, Weber D, Healthcare Infection Control Practices Advisory Committee (HICPAC). Guideline for Disinfection and Sterilization in Healthcare Facilities. 2008. Available from: http://www.cdc.gov/hicpac/Disinfection_Sterilization/acknowledg.html.
38. Lenhardt R, Sharma R, Burkhart M. Study Protocol: Feasibility of a combined use of a video-laryngoscope with a novel video-stylet for predicted difficult intubation. 2010;Version 5-6-2010.
39. Lenhardt R, Sharma R, Burkhart M, Kandadai S. Feasibility of a combined use of a video-laryngoscope with a novel flexible video-stylet for predicted difficult intubation. American Society of Anesthesiologists Congress. 2011:Chicago, USA.
40. Moher D, Liberati A, Tetzlaff J, Altman D, PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS Med. 2009;6(7):e1000097.
41. Ambu A/S. R-PS-7-2009; 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.
42. Vincent V, Raval M, Ong C, Ahmad I. Evaluation of the Ambu aScope2 in eight patients with anticipated difficult airways having awake fibre-optic intubations. Nottingham, UK: 2011.
43. Jamadarkhana S, Mallick A, Bodenham A. Preliminary Evaluation of Ambu aScope 2 for Endoscopic Guidance During Percutaneous Dilatational Tracheostomy. Intensive Care Society Congress. 2011:London, UK.
44. Missaghi S, Krasser K, Zadrobilek E. Ambu aScope: a New Disposable Flexible Video Laryngoscope. Internet Journal of Airway Management. 2010;6.
45. Charles C, Schmidt W, Diemunsch P. Fiberscope Versus Single Use Ambu aScope Bronchoscope For Control of Double-lumen Tubes and Bronchial Sutures. American Society of Anesthesiologists Congress. 2011:Chicago, 2011.
46. Kristensen M, Fredensborg B, Hansen C, Tvede M. A disposable flexible intubation videoscope, the Ambu® aScope™, and the first experiences with awake intubation in patients with difficult airways. Society for Technology in Anesthesia Annual Meeting. 2010:Florida, USA.
47. Austin P, Crawley S, Christie S, Cole S. Evaluating the Ambu aScope – an alternative approach to endoscopic monitoring during percutaneous dilational tracheostomy. Difficult Airways Society Congress. 2011:Nottingham, UK.
48. Gernoth C, Genzwuerke H. First experiences with the single-use Ambu aScope for fibreoptical monitoring in percutaneous dilatation tracheostomy. Euroanaesthesia. 2010:Helsinki, Finland.
49. Saumande B, Wolter J, Segura P, Pottecher T, Diemunsch P. The videolaryngoscope Airwayscope makes the bronchial aScope videoscopy

easier. Annual Meeting of the American Society of Airway Management. 2010:Chicago, USA.
50. Kumar M, Clarke A, Wilkes A, Goodwin N, Hodzovic I. Evaluation of the Ambu aScope, a new single-use flexible videoscope. Anaesthesia. 2011;66(8):689-93.
51. Scutt S, Clark N, Cook T, Smith C, Christmas T, Coppel L, et al. Evaluation of a single-use intubating videoscope (Ambu aScope ™) in three airway training manikins for oral intubation, nasal intubation and intubation via three supraglottic airway devices. Anaesthesia. 2011;66(4):293-9.
52. Vijayakumar M, Clarke A, Wilkes A, Goodwin N, Hodzovic I. Comparison of the manoeuvrability and ease of use of the Ambu aScope and Olympus re-usable fibrescope in a manikin. Anaesthesia. 2011;66(8):689-93.
53. Piepho T, Werner C, Noppens R. Evaluation of the novel, single-use, flexible aScope® for tracheal intubation in the simulated difficult airway and first clinical experiences. Anaesthesia. 2010;65(8):820-5.
54. Pujol E, López A, Valero R. Use of the Ambu(®) aScope™ in 10 patients with predicted difficult intubation. Anaesthesia. 2010;65(10):1037-40.
55. Perbet S, Jabaudon M, Cayot-Constantin S, Guérin R, Chartier C, Constantin J, et al. The single-use endoscope aScope™ for fibreoptical monitoring in percutaneous dilatational tracheostomy: a feasibility study. European Society of Intensive Care Medicine Congress. 2011:Berlin, Germany.
56. Seramondi R, Roze H, Germain A, Perrier V, Gallon P, Regnier P, et al. Interet du aScope pour la mise en place d'une sonde d'intubation selective a double lumiere. Société Française d'Anesthésie et de Réanimation Congress. 2010:Paris, France.
57. Galindo-Menéndez S, López-García A. The learning curve for using Ambu® aScope™. Publication submitted to the Spanish Magazine of Anaesthesiology. 2010.
58. Kristiansen A. The use of the Ambu intubation SGA, Aura-i, in difficult airways. 2011.
59. Laursen S, Jensen F, Kristiansen A, Mazzaro N. The use of the Ambu Aura-i SupraGlottic airway in an iSGA-first rescue strategy. American Aociety of Anaesthesiologists. 2011;Abstract A560.
60. Cormack R, Lehane J. Difficult tracheal intubation in obstetrics. Anaesthesia. 1984;39(11):1105-11.
61. Gupta D, Wang H. Cost-effectiveness analysis of flexible optical scopes for tracheal intubation: a descriptive comparative study of reusable and single-use scopes. Journal of clinical anesthesia. 2011;23(8):632-5. Epub 2011/12/06.
62. Liu S, Brodsky J, Macario A. Cost Identification Analysis of Anesthesia Fiberscope Use for Tracheal Intubation. Manuscript in preparation.
63. 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.
64. Ambu A/S. NHS survey. Data on file.
65. Drummond M, Sculpher M, Torrance G, O'Brien B, Stoddart G. Methods for the Economic Evaluation of Health Care Programmes. Third ed: Oxford University Press; 2005.

66. Rocke DA, Murray WB, Rout CC, Gouws E. Relative risk analysis of factors associated with difficult intubation in obstetric anesthesia. Anesthesiology. 1992;77(1):67-73. Epub 1992/07/01.
67. Rose DK, Cohen MM. The airway: problems and predictions in 18,500 patients. Can J Anaesth. 1994;41(5 Pt 1):372-83. Epub 1994/05/01.
68. Ambu A/S. Hospital Episode Statistics. Data on file.
69. Cook TM, Woodall N, Harper J, Benger J. Major complications of airway management in the UK: results of the Fourth National Audit Project of the Royal College of Anaesthetists and the Difficult Airway Society. Part 2: intensive care and emergency departments. Br J Anaesth. 2011;106(5):632-42. Epub 2011/03/31.
70. Jaber S, Amraoui J, Lefrant JY, Arich C, Cohendy R, Landreau L, et al. Clinical practice and risk factors for immediate complications of endotracheal intubation in the intensive care unit: a prospective, multiple-center study. Critical care medicine. 2006;34(9):2355-61. Epub 2006/07/20.
71. Griesdale DE, Bosma TL, Kurth T, Isac G, Chittock DR. Complications of endotracheal intubation in the critically ill. Intensive care medicine. 2008;34(10):1835-42. Epub 2008/07/08.
72. Department of Health. NHS reference costs, 2010-112011. Available from: http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_131140.
73. Curtis L. Unit Costs of Health & Social Care 2011: Personal Social Services Research Unit (PSSRU), University of Kent, Canterbury, UK; 2011.
74. Ambu A/S. NHS business case. Data on file.
75. Healthcare-Associated Infections (HCAI) Research Network. About Healthcare-Associated Infections2012. Available from: http://www.hcainetwork.org/about%20hcai.htm.
76. Cook TM, Scott S, Mihai R. Litigation related to airway and respiratory complications of anaesthesia: an analysis of claims against the NHS in England 1995-2007. Anaesthesia. 2010;65(6):556-63. Epub 2010/03/30.
77. Rozman A, Duh S, Petrinec-Primozic M, Triller N. Flexible bronchoscope damage and repair costs in a bronchoscopy teaching unit. Respiration; international review of thoracic diseases. 2009;77(3):325-30. Epub 2009/01/06.
78. Choure A, Manali E, Krizmanich G, Gildea T, Mehta A. High Price of Bronchoscopy. J Bronchol. 2005;12(3):147-50.
79. Lunn W, Garland R, Gryniuk L, Smith L, Feller-Kopman D, Ernst A. Reducing maintenance and repair costs in an interventional pulmonology program. Chest. 2005;127(4):1382-7. Epub 2005/04/12.
80. Boet S, Bould M, Schaeffer R, Fischhof S, Stojeba N, Naik V, et al. Learning fibreoptic intubation with a virtual computer program transfers to 'hands on' improvement. Eur J Anaesthesiol. 2010;27(1):31-5.

10 Appendices

10.1 Appendix 1: Search strategy for clinical evidence (section 7.1.1)

The following information should be provided:

10.1.1 The specific databases searched and the service provider used (for example, Dialog, DataStar, OVID, Silver Platter), including at least:

- Medline
- Embase
- Medline (R) In-Process
- The Cochrane Library.

For identifying any eligible studies, the following electronic databases were searched: the Cochrane Library (current issue), MEDLINE, Ovid SP (1956 to date), MEDLINE In Process and EMBASE, Ovid SP (1982 to date).

10.1.2 The date on which the search was conducted.

The search was conducted on 02 May 2012.

10.1.3 The date span of the search.

All relevant studies published since 1992 (i.e. last 20 years) were considered for inclusion.

10.1.4 The complete search strategies used, including all the search terms: textwords (free text), subject index headings (for example, MeSH) and the relationship between the search terms (for example, Boolean).

The search strategy for Embase and Medline is given below:

Table 58 Example search strategy for Embase and Medline

Search	Search term	Results
Indication		
1	Unexpect* or expect* or anticipat* or unanticipat* or emergenc* or predict* or unpredict* or difficult or closed or obstruct*	2101315
2	airway* OR airway*-management OR trache* OR dilat* OR PDT OR intubat* OR translaryngeal OR laryngeal* OR tracheal OR endotrach* OR emergency-resuscitation OR foreign-body	390832
Technology		
3	aScope* OR Ambu OR Ambuscope	456
4	Scope* OR fibre* OR video* OR endoscope* OR bronchoscope* OR laryngoscope* OR sheath*	217714
5	#1 AND #2 AND #3 AND #4	25

10.1.5 Details of any additional searches, such as searches of company or professional organisation databases (include a description of each database).

An electronic search of the abstract databases was performed for the following societies to identify abstracts presented at past meetings:

- American Society of Anaesthesiology (ASA; 2006−2012)
- European Society of Intensive Care Medicine (ESICM; 2006−2012)

The databases were searched using the following terms: "*scope*", "difficult airway", "tracheostomy" and "Ambu". All abstracts were hand-searched for relevance to the decision problem and the duplicate records removed.

Additionally, the websites of the following societies were searched for published abstracts:

- European Society of Anaesthesia (ESA; 2006−2012)
- Society for Technology in Anaesthesia (STA; 2011−2012)

The databases were searched using the following terms: "*scope*", "difficult airway", "tracheostomy" and "Ambu". All abstracts were hand-searched for relevance to the decision problem and the duplicate records removed.

Both the Difficult Airway Society (DAS) and the Society of Airway Management (SAM) were contacted directly to gain access to abstracts from past meetings;

however, neither responded to the request in the time period in which this document was being developed.

The ClinicalTrials.gov website was searched for ongoing and completed clinical trials using the search terms “*scope*”, “Ambu” and “difficult airway”.

10.1.6 The inclusion and exclusion criteria.

Table 59 Inclusion and exclusion criteria for clinical evidence

Inclusion criteria	
Population	Awake, anaesthetised, sedated and asleep/sleeping patients, adults or children/paediatric (>10 years), male or female, with unexpected or expected, difficult, closed or obstructed airway(s) or airway management, tracheostomies/PDT, as well as manikins/mannequins configured to simulate difficult, closed or obstructed airway(s) or airway management
Interventions	Oral, nasal or naso-tracheal intubations with reusable or disposable, single-use or multiple-use, direct or indirect, and portable scope, fibrescope/fibreoptic scope, videoscope/video-assisted, endoscope, bronchoscope or laryngoscope, specifically aScope (AmbuScope, aScope2) and/or Olympus, Pentax and Storz with eyepiece or monitor, as well as Vision Sciences’ disposable sheath for bronchoscopes
Outcomes	Studies evaluating incidence, rate or prevalence of delayed or failed intubation, intubation success or failure rate, death, hypoxic brain injury, ITU/hospital length of stay, incidence or rate of successful intubation, incidence, rate or risk of contamination, cross-infection, infection or infectious disease transmission, device-related adverse events, safety concerns, side effects, including hemoptysis and atelectasis specifically, or complaints for aScope (AmbuScope, aScope2) and its key comparators will be included. Studies solely evaluating time to intubation/intubate, intubation time, length of intubation, time to scope position, time to task completion, tip surface collision count and ease of use/ease of endoscopy will only be included if aScope (AmbuScope, aScope2) is being tested either alone or against a comparator
Study design	All types of studies will be included, including randomised controlled trials, retrospective studies, observational studies and case reports, studies and series
Language restrictions	None
Search dates	Published data from 1992 (last 20 years) and congress abstracts from 2007 (last 5 years)
Exclusion criteria	
Population	Patients requiring endoscopy, fibrescopy, videoscopy, bronchoscopy for any clinical reason other than difficult, closed or obstructed airway(s) or airway(s) management or tracheotomies, manikin/mannequin studies outside the setting of difficult, closed or obstructed airway(s) or airway(s) management and all laboratory and animal studies will be excluded
Interventions	Any scope, fibrescope/fibreoptic, videoscope, endoscope, bronchoscope or laryngoscope other than aScope (AmbuScope, aScope2) or Olympus, Pentax and Storz

Outcomes	Studies evaluating any outcomes other those described in the inclusion criteria will be excluded
Study design	All types of studies will be included
Language restrictions	None
Search dates	Published data from before 1992 and congress abstracts before 2007

10.1.7 The data abstraction strategy.

All citations were first screened by hand based on the title supplied with each citation. Each citation was screened by two independent reviewers with any discrepancies resolved by a third reviewer. All of the citations that clearly did not meet the eligibility criteria were excluded at this stage.

The abstracts associated with the citations that passed this first screening were then downloaded into a MS Excel database. Again each abstract was screened by two independent reviewers with any discrepancies resolved by a third reviewer. All of the abstracts that did not meet the eligibility criteria were excluded at this stage and reasons for exclusion noted in the database. Full text copies of all the references that were, at this stage, determined to potentially meet all of the eligibility criteria, were then ordered.

Data from the eligible trials were then extracted independently by two reviewers, with any discrepancies resolved by a third reviewer. All data were then included in the relevant tables in Section B of this document.

10.2 Appendix 2: Search strategy for adverse events (section 7.7.1)

The following information should be provided.

10.2.1 The specific databases searched and the service provider used (for example, Dialog, DataStar, OVID, Silver Platter), including at least:

- Medline
- Embase
- Medline (R) In-Process

- The Cochrane Library.

For identifying any eligible studies, the following electronic databases were searched: the Cochrane Library (current issue), MEDLINE, Ovid SP (1956 to date), MEDLINE In Process and EMBASE, Ovid SP (1982 to date).

10.2.2 The date on which the search was conducted.

The search was conducted on 02 May 2012.

10.2.3 The date span of the search.

All relevant studies published since 1992 (i.e. last 20 years) were considered for inclusion.

10.2.4 The complete search strategies used, including all the search terms: textwords (free text), subject index headings (for example, MeSH) and the relationship between the search terms (for example, Boolean).

The search strategy for Embase and Medline, as described above, was designed to identify all publications involving the technology under consideration. This therefore included all publications in which information about adverse events, side effects or complications was given.

10.2.5 Details of any additional searches (for example, searches of company databases [include a description of each database]).

An electronic search of the abstract databases was performed for the following societies to identify abstracts presented at past meetings:

- American Society of Anaesthesiology (ASA; 2006−2012)
- European Society of Intensive Care Medicine (ESICM; 2006−2012)

The databases were searched using the following terms: "*scope*", "difficult airway", "tracheostomy" and "Ambu". All abstracts were hand-searched for relevance to the decision problem and the duplicate records removed.

Additionally, the websites of the following societies were searched for published abstracts:

- European Society of Anaesthesia (ESA; 2006−2012)
- Society for Technology in Anaesthesia (STA; 2011−2012)

The databases were searched using the following terms: "*scope*", "difficult airway", "tracheostomy" and "Ambu". All abstracts were hand-searched for relevance to the decision problem and the duplicate records removed.

Additionally, a search of the MAUDE database was performed. MAUDE data represents reports of adverse events involving medical devices. The data consists of voluntary reports since June 1993, user facility reports since 1991, distributor reports since 1993, and manufacturer reports since August 1996. MAUDE may not include reports made according to exemptions, variances, or alternative-reporting requirements granted less than 21 CFR 803.19. The MAUDE database was searched using the following search terms: intubation scopes, bronchoscopes and aScope.

10.2.6 The inclusion and exclusion criteria.

Table 60 Inclusion and exclusion criteria for adverse events

Inclusion criteria	
Population	Awake, anaesthetised, sedated and asleep/sleeping patients, adults or children/paediatric (>10 years), male or female, with unexpected or expected, difficult, closed or obstructed airway(s) or airway management, tracheostomies/PDT, as well as manikins/mannequins configured to simulate difficult, closed or obstructed airway(s) or airway management
Interventions	Oral, nasal or naso-tracheal intubations with reusable or disposable, single-use or multiple-use, direct or indirect, and portable scope, fibrescope/fibreoptic scope, videoscope/video-assisted, endoscope, bronchoscope or laryngoscope, specifically aScope (AmbuScope, aScope2) and/or Olympus, Pentax and Storz with eyepiece or monitor, as well as Vision Sciences' disposable sheath for bronchoscopes
Outcomes	Studies evaluating device-related adverse events, safety concerns, side effects, including hemoptysis and atelectasis specifically, or

	complaints for aScope (AmbuScope, aScope2) and its key comparators will be included.
Study design	All types of studies will be included, including randomised controlled trials, retrospective studies, observational studies and case reports, studies and series
Language restrictions	None
Search dates	Published data from 1992 (last 20 years) and congress abstracts from 2007 (last 5 years)
Exclusion criteria	
Population	Patients requiring endoscopy, fibrescopy, videoscopy, bronchoscopy for any clinical reason other than difficult, closed or obstructed airway(s) or airway(s) management or tracheotomies, manikin/mannequin studies outside the setting of difficult, closed or obstructed airway(s) or airway(s) management and all laboratory and animal studies will be excluded
Interventions	Any scope, fibrescope/fibreoptic, videoscope, endoscope, bronchoscope or laryngoscope other than aScope (AmbuScope, aScope2) or Olympus, Pentax and Storz
Outcomes	Studies evaluating any outcomes other those described in the inclusion criteria will be excluded
Study design	All types of studies will be included
Language restrictions	None
Search dates	Published data from before 1992 and congress abstracts before 2007

10.2.7 The data abstraction strategy.

All citations were first screened by hand based on the title supplied with each citation. Each citation was screened by two independent reviewers with any discrepancies resolved by a third reviewer. All of the citations that clearly did not meet the eligibility criteria were excluded at this stage.

The abstracts associated with the citations that passed this first screening were then downloaded into a MS Excel database. Again each abstract was screened by two independent reviewers with any discrepancies resolved by a third reviewer. All of the abstracts that did not meet the eligibility criteria were excluded at this stage and reasons for exclusion noted in the database. Full text copies of all the references that were, at this stage, determined to potentially meet all of the eligibility criteria, were then ordered.

Data from the eligible trials were then extracted independently by two reviewers, with any discrepancies resolved by a third reviewer. All data were then included in the relevant tables in Section B of this document.

10.3 Appendix 3: Search strategy for economic evidence (section 8.1.1)

10.3.1 The specific databases searched and the service provider used (for example, Dialog, DataStar, OVID, Silver Platter), including at least:

The following databases were searched in OVID:

- Medline
- Embase
- Medline (R) In-Process
- NHS EED.

10.3.2 The date on which the search was conducted.

June 1st 2012

10.3.3 The date span of the search.

2002 to 2012 (present)

The complete search strategies used, including all the search terms:

1 (airway* or airway*-management or trache* or dilat* or PDT or intubat* or translaryngeal or laryngeal* or tracheal or endotrach* or emergency-resuscitation or foreign-body).mp. [mp=ti, ab, sh, hw, tn, ot, dm, mf, dv, kw, nm, ps, rs, an, ui]

2 (Scope* or fibre* or video* or endoscope* or bronchoscope* or laryngoscope* or sheath*).mp. [mp=ti, ab, sh, hw, tn, ot, dm, mf, dv, kw, nm, ps, rs, an, ui]

3 cost*.mp. [mp=ti, ab, sh, hw, tn, ot, dm, mf, dv, kw, nm, ps, rs, an, ui]

4 1 and 2 and 3

5 limit 4 to yr="2002 -Current"

6 limit 5 to english language

7 remove duplicates from 6

10.3.4 Details of any additional searches (for example, searches of company databases [include a description of each database]).

n/a

10.4 Appendix 4: Resource identification, measurement and valuation (section 9.3.2)

Not applicable

10.5 Appendix 5: Supplementary clinical evidence (section 7.4.1)

Information provided here relates to methodology of studies not included in the submission.

Table 61 Summary of methodology for randomised studies not included in the submission; Saumande2010 (49)

Study name	Saumande2010
Objectives	To evaluate the utility of aScope alone and in combination with the Pentax Airwayscope video-laryngoscope for endoscopic intubation of a difficult airway mannequin
Location	Hopital de Hautepierre
Design	Randomised
Duration of study	Not stated
Sample size	10 anaesthesiologists
Inclusion criteria	Participants had to have performed less than 20 fibrescopies and less than five intubations with the Airwayscope
Exclusion criteria	Not stated
Method of randomisation	Not stated
Method of blinding	N/A
Intervention(s) (n =) and comparator(s) (n =)	aScope vs aScope in combination with Airwayscope. Participants used both the intervention and comparator
Baseline differences	Not stated
Duration of follow-up, lost to follow-up information	Not stated
Statistical tests	Wilcoxon test
Primary outcomes (including scoring methods and timings of	Total time of endotracheal intubation (any endotracheal procedure not completed within 4 minutes was stopped and considered a failure)

assessments)	
Secondary outcomes (including scoring methods and timings of assessments)	• Mouth-glottis time (from passage of the lips to visualisation of vocal cords) • Mouth-carina time • Validated check list score (0–4) (80) • Five-point global rating scale score • Participants' satisfaction was noted on a digital scale (0–10)

Table 62 Summary of methodology for observational studies not included in the submission; Kristensen2010 (46)

Study name	Kristensen2010
Objective	To evaluate the utility of aScope for awake intubation of patients with difficult airways
Location	• Copenhagen University Hospital, Rigshospitalet, Denmark • Herlev Hospital, Denmark
Design	Retrospective case study
Duration of study	Not stated
Patient population	Patients with difficult airways
Sample size	N=5 patients
Inclusion criteria	Predicted difficult mask-ventilation or ETT intubation
Exclusion criteria	Not stated
Intervention(s) (n =) and comparator(s) (n =)	aScope (N=5 patients)
Baseline differences	• Patient 1: Male, 59 years, with tumour of the hard palate • Patient 2: Male, 68 years, with oral cancer

	• Patient 3: Male, 60 years, with suspected oropharyngeal cancer • Patient 4: With intra-thoracic goitre severely compressing the trachea • Patient 5: With Mallampati score 3, inter-incisor distance 2.7 cm and inability to prognate
How were participants followed-up (for example, through pro-active follow-up or passively). Duration of follow-up, participants lost to follow-up	Not stated, but one patient underwent a second intubation 3 weeks later
Statistical tests	None performed
Primary outcomes (including scoring methods and timings of assessments)	Intubation success
Secondary outcomes (including scoring methods and timings of assessments)	Not stated

Table 63 Summary of methodology for observational studies not included in the submission; Austin2011 (47)

Study name	Austin2011
Objective	To evaluate aScope for endoscopic monitoring during PDT in ICU
Location	Ninewells Hospital, Dundee, UK
Design	Open-label, non-randomised
Duration of study	Not stated

Patient population	Patients requiring PDT
Sample size	The number of patients included in the study was not reported, but a total five aScopes were used
Inclusion criteria	Patients requiring a bedside PDT in ICU
Exclusion criteria	None stated
Intervention(s) (n =) and comparator(s) (n =)	aScope (see response to 'Sample size' above)
Baseline differences	Not stated
How were participants followed-up (for example, through pro-active follow-up or passively). Duration of follow-up, participants lost to follow-up	Not stated
Statistical tests	Not performed
Primary outcomes (including scoring methods and timings of assessments)	Characteristics, qualities, set-up, handling characteristics and image quality of aScope were compared with standard fibreoptic equipment using a five-point scale: 1=very poor; 2=poor; 3=no difference; 4=improved; 5=much improved
Secondary outcomes (including scoring methods and timings of assessments)	Complications or technical issues related to aScope

Table 64 Summary of methodology for observational studies not included in the submission; Gernoth2010 (48)

Study name	Gernoth2010
Objective	To evaluate aScope for monitoring PDT in long-term ventilated patients in ICU
Location	Neckar-Odenwald-Kliniken gGmbH, Mosbach, Germany
Design	Case study
Duration of study	Not stated
Patient population	Patients requiring PDT
Sample size	N=4 patients
Inclusion criteria	Long-term ventilated patients in ICU who required PDT
Exclusion criteria	None stated
Intervention(s) (n =) and comparator(s) (n =)	aScope (N=4 patients)
Baseline differences	Reasons for long-term ventilation and invasive airway management were urosepsis, chronic obstructive lung disease, recovery from cardiac arrest, and one patient tested positive for methicillin resistant staphylococcus aureus (MRSA)
How were participants followed-up (for example, through pro-active follow-up or passively). Duration of follow-up, participants lost to follow-up	Not stated
Statistical tests	None performed
Primary outcomes (including scoring	• Handling • Quality of view

methods and timings of assessments)	• Whether the maximum operation time of 30 minutes was sufficient to safely perform PDT (however, this time-out feature does not apply to aScope2)
Secondary outcomes (including scoring methods and timings of assessments)	Not stated

10.6 Appendix 6: Supplementary clinical evidence (section 7.5.1)

Information provided here relates to the critical appraisal of studies and how questions were addressed in each study.

Table 65 Critical appraisal of randomised control trials included in the submission; Lenhardt2011 (38, 39)

Study name	**Lenhardt2011**	
Study question	**Response (yes/no/not clear/N/A)**	**How is the question addressed in the study?**
Was randomisation carried out appropriately?	Yes	Patients were randomised to having their tube placed with aScope or use of a preformed stylet. Randomisation was stratified according to whether patients were categorised as predicted difficult airway or having an immobilised cervical spine
Was the concealment of treatment allocation adequate?	N/A	
Were the groups similar at the outset of the study in terms of prognostic factors, for example, severity of disease?	[redacted]	Patients had an American Society of Anaesthesiologist (ASA) physical status of 1–3, and were included in the study if they were considered a difficult airway as determined by measurement of ≥1 common predictive index for difficult intubation
Were the care providers,	Not clear	

participants and outcome assessors blind to treatment allocation? If any of these people were not blinded, what might be the likely impact on the risk of bias (for each outcome)?		
Were there any unexpected imbalances in drop-outs between groups? If so, were they explained or adjusted for?	[redacted]	All patients included in the study were intubated
Is there any evidence to suggest that the authors measured more outcomes than they reported?	Not clear	
Did the analysis include an intention-to-treat analysis? If so, was this appropriate and were appropriate methods used to account for missing data?	N/A	
Adapted from Centre for Reviews and Dissemination (2008) Systematic reviews. CRD's guidance for undertaking reviews in health care. York: Centre for Reviews and Dissemination		

Table 66 Critical appraisal of randomised control trials included in the submission; Piepho2010 (53)

Study name	**Piepho2010**	
Study question	**Response (yes/no/not clear/N/A)**	**How is the question addressed in the study?**
Was randomisation carried out appropriately?	Yes	The order of participation in the scenarios, and order in which the devices were used, were randomised

Was the concealment of treatment allocation adequate?	N/A	
Were the groups similar at the outset of the study in terms of prognostic factors, for example, severity of disease?	Yes	Only one type of manikin was used in the study
Were the care providers, participants and outcome assessors blind to treatment allocation? If any of these people were not blinded, what might be the likely impact on the risk of bias (for each outcome)?	Not clear	
Were there any unexpected imbalances in drop-outs between groups? If so, were they explained or adjusted for?	N/A	
Is there any evidence to suggest that the authors measured more outcomes than they reported?	No	
Did the analysis include an intention-to-treat analysis? If so, was this appropriate and were appropriate methods used to account for missing data?	N/A	
Adapted from Centre for Reviews and Dissemination (2008) Systematic reviews. CRD's guidance for undertaking reviews in health care. York: Centre for Reviews and Dissemination		

Table 67 Critical appraisal of randomised control trials included in the submission; Vijayakumar2011 (52)

Study name	**Vijayakumar2011**	
Study question	**Response (yes/no/not clear/N/A)**	**How is the question addressed in the study?**
Was randomisation carried out appropriately?	Yes	Each participant was asked to complete a task on the manikin with both the aScope and Olympus reusable fibrescope in a computer-generated order
Was the concealment of treatment allocation adequate?	N/A	
Were the groups similar at the outset of the study in terms of prognostic factors, for example, severity of disease?	Yes	Only one type of manikin was used in the study
Were the care providers, participants and outcome assessors blind to treatment allocation? If any of these people were not blinded, what might be the likely impact on the risk of bias (for each outcome)?	Not clear	
Were there any unexpected imbalances in drop-outs between groups? If so, were they explained or adjusted for?	N/A	
Is there any evidence to suggest that the authors measured more outcomes than they reported?	No	
Did the analysis include an intention-to-treat analysis? If so,	N/A	

was this appropriate and were appropriate methods used to account for missing data?		
Adapted from Centre for Reviews and Dissemination (2008) Systematic reviews. CRD's guidance for undertaking reviews in health care. York: Centre for Reviews and Dissemination		

Table 68 Critical appraisal of randomised control trials included in the submission; Scutt2011 (51)

Study name	**Scutt2011**	
Study question	**Response (yes/no/not clear/N/A)**	**How is the question addressed in the study?**
Was randomisation carried out appropriately?	Yes	The order of fibrescope, manikin and route of intubation were randomised
Was the concealment of treatment allocation adequate?	N/A	
Were the groups similar at the outset of the study in terms of prognostic factors, for example, severity of disease?	Yes	Three different types of manikins were used
Were the care providers, participants and outcome assessors blind to treatment allocation? If any of these people were not blinded, what might be the likely impact on the risk of bias (for each outcome)?	Not clear	
Were there any unexpected imbalances in drop-outs between	N/A	

groups? If so, were they explained or adjusted for?		
Is there any evidence to suggest that the authors measured more outcomes than they reported?	No	
Did the analysis include an intention-to-treat analysis? If so, was this appropriate and were appropriate methods used to account for missing data?	N/A	
Adapted from Centre for Reviews and Dissemination (2008) Systematic reviews. CRD's guidance for undertaking reviews in health care. York: Centre for Reviews and Dissemination		

Table 69 Critical appraisal of randomised control trials included in the submission; Kumar2011 (50)

Study name	**Kumar2011**	
Study question	**Response (yes/no/not clear/N/A)**	**How is the question addressed in the study?**
Was randomisation carried out appropriately?	Not clear	
Was the concealment of treatment allocation adequate?	N/A	
Were the groups similar at the outset of the study in terms of prognostic factors, for example, severity of disease?	Yes	Only one type of manikin was used in the study
Were the care providers, participants and outcome	Not clear	

assessors blind to treatment allocation? If any of these people were not blinded, what might be the likely impact on the risk of bias (for each outcome)?		
Were there any unexpected imbalances in drop-outs between groups? If so, were they explained or adjusted for?	N/A	
Is there any evidence to suggest that the authors measured more outcomes than they reported?	No	
Did the analysis include an intention-to-treat analysis? If so, was this appropriate and were appropriate methods used to account for missing data?	N/A	
Adapted from Centre for Reviews and Dissemination (2008) Systematic reviews. CRD's guidance for undertaking reviews in health care. York: Centre for Reviews and Dissemination		

Table 70 Critical appraisal of randomised control trials included in the submission; R-PS-7-2009/Kristensen (41)

Study name	**R-PS-7-2009/Kristensen**	
Study question	**Response (yes/no/not clear/N/A)**	**How is the question addressed in the study?**
Was randomisation carried out appropriately?	[redacted]	[redacted]

		[redacted]
Was the concealment of treatment allocation adequate?	[redacted]	
Were the groups similar at the outset of the study in terms of prognostic factors, for example, severity of disease?	[redacted]	[redacted]
Were the care providers, participants and outcome assessors blind to treatment allocation? If any of these people were not blinded, what might be the likely impact on the risk of bias (for each outcome)?	[redacted]	
Were there any unexpected imbalances in drop-outs between groups? If so, were they explained or adjusted for?	[redacted]	
Is there any evidence to suggest that the authors measured more outcomes than they reported?	[redacted]	
Did the analysis include an intention-to-treat analysis? If so, was this appropriate and were appropriate methods used to account for missing data?	[redacted]	[redacted]
Adapted from Centre for Reviews and Dissemination (2008) Systematic reviews. CRD's guidance for undertaking reviews in health care. York: Centre for Reviews and Dissemination		

Table 71 Critical appraisal of randomised studies not included in the submission; Saumande2010 (49)

Study name	**Saumande2010**	
Study question	**Response (yes/no/not clear/N/A)**	**How is the question addressed in the study?**
Was randomisation carried out appropriately?	Yes	After theoretical training, participants attempted, in a randomised sequence, endoscopic intubation with either aScope alone or in combination with Airwayscope
Was the concealment of treatment allocation adequate?	N/A	
Were the groups similar at the outset of the study in terms of prognostic factors, for example, severity of disease?	Yes	Only one type of manikin was used in the study
Were the care providers, participants and outcome assessors blind to treatment allocation? If any of these people were not blinded, what might be the likely impact on the risk of bias (for each outcome)?	Not clear	
Were there any unexpected imbalances in drop-outs between groups? If so, were they explained or adjusted for?	N/A	
Is there any evidence to suggest that the authors measured more outcomes than they reported?	No	
Did the analysis include an	N/A	

intention-to-treat analysis? If so, was this appropriate and were appropriate methods used to account for missing data?		
Adapted from Centre for Reviews and Dissemination (2008) Systematic reviews. CRD's guidance for undertaking reviews in health care. York: Centre for Reviews and Dissemination		

Table 72 Critical appraisal of observational studies included in the submission; Piepho2010 (53)

Study name	**Piepho2010**	
Study question	**Response yes/no/not clear/N/A)**	**How is the question addressed in the study?**
Was the cohort recruited in an acceptable way?	Yes	Patients with either unanticipated or anticipated difficult airway who required tracheal intubation in the operating room. Written consent was retrospectively obtained from each patient
Was the exposure accurately measured to minimise bias?	N/A	
Was the outcome accurately measured to minimise bias?	N/A	
Have the authors identified all important confounding factors?	Not clear	
Have the authors taken account of the confounding factors in the design and/or analysis?	N/A	
Was the follow-up of patients complete?	N/A	
How precise (for example, in terms	N/A	

of confidence interval and p values) are the results?		
Adapted from Critical Appraisal Skills Programme (CASP): Making sense of evidence 12 questions to help you make sense of a cohort study		

Table 73 Critical appraisal of observational studies included in the submission; Pujol2010 (54)

Study name	**Pujol2010**	
Study question	**Response** **yes/no/not clear/N/A)**	**How is the question addressed in the study?**
Was the cohort recruited in an acceptable way?	Yes	Following approval from the Ethics and Research Committee of the Hospital Clinic, 10 adult patients with predicted difficult intubation were recruited for the case study. The procedure was explained during the pre-operative visit and all patients gave their consent for general anaesthesia and awake fibreoptic intubation
Was the exposure accurately measured to minimise bias?	N/A	
Was the outcome accurately measured to minimise bias?	Yes	After completion of the procedure, aScope was evaluated for ease of use using a three-point scale, image quality was assessed using a four-point scale, and the presence of fogging was noted and the distribution of local anaesthetic over the cords and trachea was assessed
Have the authors identified all important confounding factors?	Not clear	
Have the authors taken account of the confounding factors in the design and/or analysis?	N/A	
Was the follow-up of patients	N/A	

complete?		
How precise (for example, in terms of confidence interval and p values) are the results?	N/A	
Adapted from Critical Appraisal Skills Programme (CASP): Making sense of evidence 12 questions to help you make sense of a cohort study		

Table 74 Critical appraisal of observational studies included in the submission; Vincent2011 (42)

Study name	**Vincent2011**	
Study question	**Response** **yes/no/not clear/N/A)**	**How is the question addressed in the study?**
Was the cohort recruited in an acceptable way?	Yes	Adult patients with anticipated difficult airway requiring elective ENT and maxillofacial surgeries were recruited, and their airway was assessed by modified Mallampati score, mouth opening, neck movement and jaw protrusion before making a decision on awake fibreoptic intubation
Was the exposure accurately measured to minimise bias?	N/A	
Was the outcome accurately measured to minimise bias?	Yes	A standardised VRS was used to assess the performance of the device
Have the authors identified all important confounding factors?	Not clear	
Have the authors taken account of the confounding factors in the design and/or analysis?	N/A	
Was the follow-up of patients complete?	N/A	

How precise (for example, in terms of confidence interval and p values) are the results?	N/A	
Adapted from Critical Appraisal Skills Programme (CASP): Making sense of evidence 12 questions to help you make sense of a cohort study		

Table 75 Critical appraisal of observational studies included in the submission; Perbet2011 (55)

Study name	**Perbet2011**	
Study question	**Response** **yes/no/not clear/N/A)**	**How is the question addressed in the study?**
Was the cohort recruited in an acceptable way?	Yes	Patients requiring a bedside PDT were recruited for the case series
Was the exposure accurately measured to minimise bias?	N/A	
Was the outcome accurately measured to minimise bias?	Yes	Conditions of procedure were evaluated using a four-point scale
Have the authors identified all important confounding factors?	Not clear	
Have the authors taken account of the confounding factors in the design and/or analysis?	N/A	
Was the follow-up of patients complete?	N/A	
How precise (for example, in terms of confidence interval and p values) are the results?	N/A	

Adapted from Critical Appraisal Skills Programme (CASP): Making sense of evidence 12 questions to help you make sense of a cohort study

Table 76 Critical appraisal of observational studies included in the submission; Jamadarkhana2011 (43)

Study name	**Jamadarkhana2011**	
Study question	**Response** **yes/no/not clear/N/A)**	**How is the question addressed in the study?**
Was the cohort recruited in an acceptable way?	Yes	Patients who underwent PDT on the Adult General and Neurosurgical ICUs were enrolled in this study, and ethics committee approval was questioned but not required, and informed assent was obtained from next of kin
Was the exposure accurately measured to minimise bias?	N/A	
Was the outcome accurately measured to minimise bias?	Yes	Quality of images was assessed using a scale of 1–10 (1=poor view, 10=best view)
Have the authors identified all important confounding factors?	Not clear	
Have the authors taken account of the confounding factors in the design and/or analysis?	N/A	
Was the follow-up of patients complete?	N/A	
How precise (for example, in terms of confidence interval and p values) are the results?	N/A	
Adapted from Critical Appraisal Skills Programme (CASP): Making sense of evidence 12 questions to help you make sense of a cohort study		

Table 77 Critical appraisal of observational studies not included in the submission; Kristensen2010 (46)

Study name	**Kristensen2010**	
Study question	**Response** **yes/no/not clear/N/A)**	**How is the question addressed in the study?**
Was the cohort recruited in an acceptable way?	Yes	Patients included in the case study were selected following departmental procedure, i.e., intubated awake if a difficult airway was predicted
Was the exposure accurately measured to minimise bias?	N/A	
Was the outcome accurately measured to minimise bias?	N/A	
Have the authors identified all important confounding factors?	Not clear	
Have the authors taken account of the confounding factors in the design and/or analysis?	N/A	
Was the follow-up of patients complete?	N/A	
How precise (for example, in terms of confidence interval and p values) are the results?	N/A	
Adapted from Critical Appraisal Skills Programme (CASP): Making sense of evidence 12 questions to help you make sense of a cohort study		

Table 78 Critical appraisal of observational studies not included in the submission; Austin2011 (47)

Study name	**Austin2011**	
Study question	**Response** **yes/no/not clear/N/A)**	**How is the question addressed in the study?**
Was the cohort recruited in an acceptable way?	Not clear	
Was the exposure accurately measured to minimise bias?	N/A	
Was the outcome accurately measured to minimise bias?	Yes	An evaluation form devised and set-up, handling characteristics and image quality were compared with a standard fibreoptic equipment using a five-point scale
Have the authors identified all important confounding factors?	Not clear	
Have the authors taken account of the confounding factors in the design and/or analysis?	N/A	
Was the follow-up of patients complete?	N/A	
How precise (for example, in terms of confidence interval and p values) are the results?	N/A	
Adapted from Critical Appraisal Skills Programme (CASP): Making sense of evidence 12 questions to help you make sense of a cohort study		

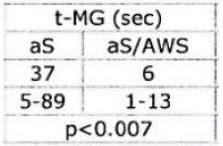
Table 79 Critical appraisal of observational studies not included in the submission; Gernoth2010 (48)

Study name	Gernoth2010	
Study question	**Response** **yes/no/not clear/N/A)**	**How is the question addressed in the study?**
Was the cohort recruited in an acceptable way?	Yes	Patients, in whom PDT was planned, were consented to be recruited to the study by their legally appointed guardians
Was the exposure accurately measured to minimise bias?	N/A	
Was the outcome accurately measured to minimise bias?	Not clear	
Have the authors identified all important confounding factors?	Not clear	
Have the authors taken account of the confounding factors in the design and/or analysis?	N/A	
Was the follow-up of patients complete?	N/A	
How precise (for example, in terms of confidence interval and p values) are the results?	N/A	
Adapted from Critical Appraisal Skills Programme (CASP): Making sense of evidence 12 questions to help you make sense of a cohort study		

10.7 Appendix 7: Supplementary clinical evidence (section 7.6.1)

Information provided here relates to outcomes of studies not included in the submission.

Table 80 Outcomes from published and unpublished studies not included in the submission; Saumande2010 (49)

Study name		**Saumande2010**
Size of study groups	**Treatment**	aScope
	Control	aScope in combination with Airwayscope
Study duration	**Time unit**	N/A
Type of analysis	**Intention-to-treat/per protocol**	N/A
Outcome	**Name**	Primary outcome: Total time of endoscopic intubation
	Unit	Seconds
Effect size	**Value**	Median total intubation time (range) was 140 (70–265) seconds with aScope alone (aS) and 69 (48–81) seconds with aScope in combination with Airwayscope (aS/AWS)
	95% CI	N/A
Statistical test	**Type**	Wilcoxon test
	p value	<0.007
Other outcome	**Name**	Secondary outcome: Mouth-glottis time (t-MG)
	Unit	Seconds
Effect size	**Value**	Mouth-glottis time (t-MG) was significantly shorter with aScope in combination with Airwayscope (aS/AWS) than aScope alone (aS) (see below)  t-MG (sec) aS | aS/AWS 37 | 6 5-89 | 1-13 p<0.007 all values as median, minimum and maximum
	95% CI	N/A

<table>
<tr><td rowspan="2">Statistical test</td><td>Type</td><td>Wilcoxon test</td></tr>
<tr><td>p value</td><td><0.007</td></tr>
<tr><td rowspan="2">Other outcome</td><td>Name</td><td>Secondary outcome: Mouth-carina time (t-MC)</td></tr>
<tr><td>Unit</td><td>Seconds</td></tr>
<tr><td rowspan="2">Effect size</td><td>Value</td><td>Mouth-carina time (t-MC) was significantly shorter with aScope in combination with Airwayscope (aS/AWS) than aScope alone (aS) (see below)
<table><tr><td colspan="2">t-MC (sec)</td></tr><tr><td>aS</td><td>aS/AWS</td></tr><tr><td>110</td><td>15</td></tr><tr><td>43-214</td><td>10-30</td></tr><tr><td colspan="2">p<0.005</td></tr></table>all values as median, minimum and maximum</td></tr>
<tr><td>95% CI</td><td>N/A</td></tr>
<tr><td rowspan="2">Statistical test</td><td>Type</td><td>Wilcoxon test</td></tr>
<tr><td>p value</td><td><0.005</td></tr>
<tr><td rowspan="2">Other outcome</td><td>Name</td><td>Checklist (0–4)</td></tr>
<tr><td>Unit</td><td>Number</td></tr>
<tr><td rowspan="2">Effect size</td><td>Value</td><td>Participants rated aScope in combination with Airwayscope (aS/AWS) significantly higher than aScope alone (aS) (see below)
<table><tr><td colspan="2">checklist (0-4)</td></tr><tr><td>aS</td><td>aS/AWS</td></tr><tr><td>1.9</td><td>3.3</td></tr><tr><td>0-4</td><td>2-4</td></tr><tr><td colspan="2">p<0.026</td></tr></table>all values as median, minimum and maximum</td></tr>
<tr><td>95% CI</td><td>N/A</td></tr>
<tr><td rowspan="2">Statistical test</td><td>Type</td><td>Wilcoxon test</td></tr>
<tr><td>p value</td><td><0.026</td></tr>
<tr><td>Other</td><td>Name</td><td>Global rating scale (five-point)</td></tr>
</table>

outcome	**Unit**	Number
Effect size	**Value**	Participants rated aScope in combination with Airwayscope (aS/AWS) significantly higher than aScope alone (aS) (see below) global rating scale score aS: 3 (1-5) vs aS/AWS: 4.5 (4-5) p<0.011 all values as median, minimum and maximum
	95% CI	N/A
Statistical test	**Type**	Wilcoxon test
	p value	<0.011
Other outcome	**Name**	Participants' satisfaction
	Unit	Digital scale (0–10)
Effect size	**Value**	Participants' satisfaction (range) was 6.2 (5–9) with aScope alone and 8.5 (8–9) with aScope in combination with Airwayscope
	95% CI	N/A
Statistical test	**Type**	Wilcoxon test
	p value	<0.002
Comments		All 10 endoscopic intubations assisted by Airwayscope were successfully completed at the first attempt. When performed with aScope alone, five of 10 endoscopic intubations required more than one attempt: four were then completed within the allotted 4 minutes and one ran out of time

Table 81 Outcomes from published and unpublished studies not included in the submission; Kristensen2010 (46)

Study name		**Kristensen2010**
Size of study	**Treatment**	aScope (N=5 patients with difficult airways)

groups	**Control**	N/A
Study duration	**Time unit**	N/A
Type of analysis	**Intention-to-treat/per protocol**	N/A
Outcome	**Name**	Clinical performance
	Unit	Participants' opinion
Effect size	**Value**	N/A
	95% CI	N/A
Statistical test	**Type**	N/A
	p value	N/A
Other outcome	**Name**	N/A
	Unit	N/A
Effect size	**Value**	N/A
	95% CI	N/A
Statistical test	**Type**	N/A
	p value	N/A
Comments		All five patients were intubated successfully with aScope. Patient 1 was intubated orally with an 8.0 mm internal diameter ETT over the insertion cord of aScope, via a Berman airway; Patient 2 was intubated orally awake with a 7.0 mm internal diameter ETT over the aScope; Patient 3 was intubated orally with 6.0 internal diameter ETT over the aScope; Patient 4 was intubated awake with the aScope, allowing the tip of the tube to be positioned distally to the tracheal compression; Patient 5 was intubated orally awake (6.0 mm internal diameter ETT) with the aScope by a first-year resident

Table 82 Outcomes from published and unpublished studies not included in the submission; Austin2011 (47)

Study name		**Austin2011**
Size of study groups	**Treatment**	aScope (N=5 patients requiring PDT)
	Control	N/A
Study duration	**Time unit**	N/A
Type of analysis	**Intention-to-treat/per protocol**	N/A
Outcome	**Name**	N/A
	Unit	N/A
Effect size	**Value**	N/A
	95% CI	N/A
Statistical test	**Type**	N/A
	p value	N/A
Other outcome	**Name**	N/A
	Unit	N/A
Effect size	**Value**	N/A
	95% CI	N/A

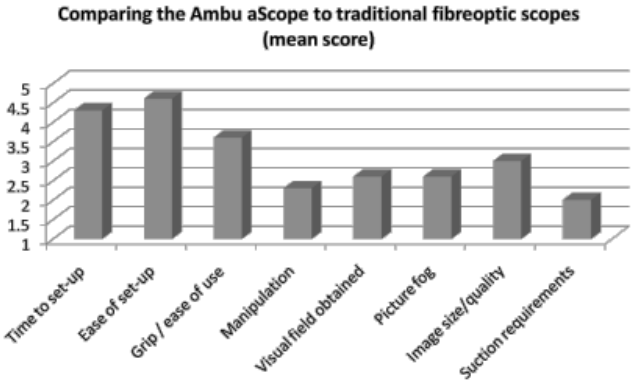
Statistical test	**Type**	N/A
	p value	N/A
Comments		• A total of five aScopes were evaluated and all elective procedures were completed successfully • Mean duration of use was 21 minutes • No complications were directly attributed to aScope • Compared with traditional fibreoptic scopes, aScope was rated higher for the time to set-up, ease of set-up, grip/ease of use, but lower for the ability to manipulate the tip and picture fog; picture quality and size rated as no different (see below)  Criteria were evaluated on a five point scale: 1 = very poor 2 = poor 3 = no difference 4 = improved 5 = much improved

Table 83 Outcomes from published and unpublished studies not included in the submission; Gernoth2010 (48)

Study name		**Gernoth2010**
Size of study groups	**Treatment**	aScope (N=4 patients requiring PDT)
	Control	N/A
Study duration	**Time unit**	N/A
Type of analysis	**Intention-to-treat/per protocol**	N/A
Outcome	**Name**	N/A
	Unit	N/A
Effect size	**Value**	N/A
	95% CI	N/A
Statistical test	**Type**	N/A
	p value	N/A
Other outcome	**Name**	N/A
	Unit	N/A
Effect size	**Value**	N/A
	95% CI	N/A
Statistical test	**Type**	N/A
	p value	N/A
Comments		• Handling and positioning of the aScope through the orally placed tubes (internal diameter 7–8 mm) was easy, and a good view that enabled identification of relevant structures was obtained in all patients within 30 seconds • In all patients, PDT was accomplished smoothly, and a good endoscopic view was obtained for monitoring, puncturing of the trachea, guide wire insertion, dilatation and positioning of the tracheostomy

	tube • Total mean endoscopy time was 18 minutes

11 Related procedures for evidence submission

11.1 Cost models

An electronic executable version of the cost model should be submitted to NICE with the full submission.

NICE accepts executable cost models using standard software – that is, Excel, TreeAge Pro, R or WinBUGs. If you plan to submit a model in a non-standard package, NICE should be informed in advance. NICE, in association with the External Assessment Centre, will investigate whether the requested software is acceptable, and establish if you need to provide NICE and the External Assessment Centre with temporary licences for the non-standard software for the duration of the assessment. NICE reserves the right to reject cost models in non-standard software. A fully executable electronic copy of the model must be submitted to NICE with full access to the programming code. Care should be taken to ensure that the submitted versions of the model programme and the written content of the evidence submission match.

NICE may distribute the executable version of the cost model to a consultee if they request it. If a request is received, NICE will release the model as long as it does not contain information that was designated confidential by the model owner, or the confidential material can be redacted by the model owner without producing severe limitations on the functionality of the model. The consultee will be advised that the model is protected by intellectual property rights, and can be used only for the purposes of commenting on the model's reliability and informing comments on the medical technology consultation document.

Sponsors must ensure that all relevant material pertinent to the decision problem has been disclosed to NICE at the time of submission. NICE may request additional information not submitted in the original submission of evidence. Any other information will be accepted at NICE's discretion.

When making a full submission, sponsors should check that:

- an electronic copy of the submission has been given to NICE with all confidential information highlighted and underlined
- a copy of the instructions for use, regulatory documentation and quality systems certificate have been submitted

- an executable electronic copy of the cost model has been submitted
- the checklist of confidential information provided by NICE has been completed and submitted.

- A PDF version of all studies (or other appropriate format for unpublished data, for example, a structured abstract) included in the submission have been submitted

11.2 Disclosure of information

To ensure that the assessment process is as transparent as possible, NICE considers it highly desirable that evidence pivotal to the Medical Technologies Advisory Committee's decisions should be publicly available at the point of issuing the medical technology consultation document and medical technology guidance.

Under exceptional circumstances, unpublished evidence is accepted under agreement of confidentiality. Such evidence includes 'commercial in confidence' information and data that are awaiting publication ('academic in confidence').

When data are 'commercial in confidence' or 'academic in confidence', it is the sponsor's responsibility to highlight such data clearly, and to provide reasons why they are confidential and the timescale within which they will remain confidential. The checklist of confidential information should be completed: if it is not provided, NICE will assume that there is no confidential information in the submission. It is the responsibility of the manufacturer or sponsor to ensure that the confidential information checklist is kept up to date.

It is the responsibility of the sponsor to ensure that any confidential information in their evidence submission is clearly underlined and highlighted correctly. NICE is assured that information marked 'academic in confidence' can be presented and discussed during the public part of the Medical Technologies Advisory Committee meeting. NICE is confident that such public presentation does not affect the subsequent publication of the information, which is the prerequisite allowing for the marking of information as 'academic in confidence'.

Please therefore underline all confidential information, and highlight information that is submitted under 'commercial in confidence' in blue and information submitted under 'academic in confidence' in yellow.

NICE will ask sponsors to reconsider restrictions on the release of data if there appears to be no obvious reason for the restrictions, or if such restrictions would

make it difficult or impossible for NICE to show the evidential basis for its guidance. Information that has been put into the public domain, anywhere in the world, cannot be marked as confidential.

Confidential information submitted will be made available for review by the External Assessment Centre and the Medical Technologies Advisory Committee. NICE will at all times seek to protect the confidentiality of the information submitted, but nothing will restrict the disclosure of information by NICE that is required by law (including in particular, but without limitation, the Freedom of Information Act 2000).

The Freedom of Information Act 2000, which came into force on 1 January 2005, enables any person to obtain information from public authorities such as NICE. The Act obliges NICE to respond to requests about the recorded information it holds, and it gives people a right of access to that information. This obligation extends to submissions made to NICE. Information that is designated as 'commercial in confidence' may be exempt under the Act. On receipt of a request for information, the NICE secretariat will make every effort to contact the designated company representative to confirm the status of any information previously deemed 'commercial in confidence' before making any decision on disclosure.

11.3 Equality

NICE is committed to promoting equality and eliminating unlawful discrimination, including paying particular attention to groups protected by equalities legislation. The scoping process is designed to identify groups who are relevant to the evaluation of the technology, and to reflect the diversity of the population. NICE consults on whether there are any issues relevant to equalities within the scope of the evaluation, or if there is information that could be included in the evidence presented to the Medical Technologies Advisory Committee to enable them to take account of equalities issues when developing guidance.

Evidence submitters are asked to consider whether the chosen decision problem could be impacted by NICE's responsibility in this respect, including when considering subgroups and access to recommendations that use a clinical or biological criterion.

For further information, please see the NICE website (www.nice.org.uk/aboutnice/howwework/NICEEqualityScheme.jsp).