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None of the investigators have any conflicts of interest.

Confidentiality Statement
This document contains confidential information that must not be disclosed to anyone other than the Sponsor, the Investigator Team, HRA, host organisation, and members of the Research Ethics Committee, unless authorised to do so.

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1. SYNOPSIS

A supraglottic airway device (SAD) is used in the airway management of patients undergoing general anaesthesia. It has two major components, a 'mask' which forms a seal over the glottis with or without the use of an inflatable cuff, and an 'airway tube' which transmits gases during ventilation from the mask to the anaesthetic breathing system. In the years since the introduction of the SADs numerous new devices have been developed. Initially these shared similar characteristics with the first devices and have been named '1st generation' devices. The use of these devices carries a low but recognised risk of complications including aspiration of gastric contents, inadequate laryngeal seal, post-operative sore throat and difficulties with device insertion. In an attempt to address these issues manufacturers have developed '2nd generation' SADs, which are designed to reduce the risk of aspiration and may claim features such as easier insertion, reduced trauma on insertion, superior seal pressures, and integral bite blocks. The LMA® Protector™ is a CE marked new single use SAD developed by Teleflex inc. It is a 2nd generation device which has a number of additional features compared to previous designs, incorporated to improve the safety of the device. We propose a national multi-centre prospective controlled clinical evaluation cohort study, to study the performance of the device and determine its likely place in clinical practice in the UK.

Study Title	Observational study of LMA Protector	
Internal ref. no. / short title	ADEPT 1	
Study Design	Prospective, multi-centre cohort study	
Study Participants	Adult patients undergoing general anaesthesia with a SAD.	
Planned Sample Size	1100 - 2000	
Planned Study Period	2 years	
	Objectives	**Outcome Measures**
Primary	To assess overall performance of the LMA Protector	1)First go insertion success rate, 2)First go successful ventilation rate, 3)Percentage of complication free insertions
Secondary	To assess: 1) Time taken to achieve airway 2) Number of attempts to achieve patent airway 3) Complications during airway insertion 4) Complications during anaesthesia attributed to the airway 5) Complications during device removal 6) Complications after anaesthesia attributed to the airway 7) Quality of ventilation	1) Time to first square capnography waveform 2) Lowest oxygen saturation level 3) Monitor numbers of interventions needed to ensure airway patency 4) Monitor pre-defined complications occurrence during insertion of device, during anaesthesia, and on device removal 5) The quality of ventilation will depend on whether there was: a) adequate chest

		movement, b) tidal volume > 7ml/kg, c) stable SpO2, and d) square capnography trace

2. ABBREVIATIONS

ASA	American Society of Anesthesiologists
ADE	Adverse Device Effect
CI	Chief Investigator
CRF	Case Report Form
GCP	Good Clinical Practice
HRA	Health Research Authority
ICF	Informed Consent Form
LMA	Laryngeal Mark Airway
NHS	National Health Service
NRES	National Research Ethics Service
PACU	Post Anaesthesia Care Unit
PI	Principal Investigator
PIL	Participant/ Patient Information Leaflet
R&D	NHS Trust R&D Department
REC	Research Ethics Committee
SADE	Serious Adverse Device Effect
SOP	Standard Operating Procedure
SAD	Supraglottic Airway Device
TSG	Oxford University Hospitals NHS Foundation Trust/University of Oxford Trials Safety Group.
TV	Tidal Volume
UADE	Unanticipated Adverse Device Effect

3. BACKGROUND AND RATIONALE

Background

A supraglottic airway device (SAD) is used in the airway management of patients undergoing general anaesthesia. It has two major components, a 'mask' which forms a seal over the glottis with or without the use of an inflatable cuff, and an 'airway tube' which transmits gases during ventilation from the mask to the anaesthetic breathing system (1). After the patient is anaesthetised, the device is advanced into the mouth over the tongue into the pharynx, resting in the hypopharynx and covering the supraglottic structures. This enables relative isolation of the trachea from other structures such as the oesophagus. Although the use of

SADs is primarily to enable ventilation during general anaesthesia where endotracheal intubation is deemed unnecessary or inappropriate, they also have an important role in the management of the difficult airway either as a rescue device or as a channel to intubate the trachea via fibre optic intubation (2).

The original SAD, the laryngeal mask airway (LMA), was developed in the UK by Archie Brain and entered widespread use in 1989. Now named the LMA classic (cLMA) it was quickly adopted by the profession and revolutionised anaesthetic practice around the world. In 2010 the Royal College of Anaesthetists (RCoA) carried out the 4th National Audit Project, which analysed major complications of airway management in the UK. At this time, a SAD was in use in more than 50% of all general anaesthetics, the majority using either the cLMA or similar design (3,4).

In the years since the introduction of the cLMA numerous new SADs have been developed. Initially these shared similar characteristics with the cLMA and have been named '1st generation' devices. The use of these devices carries a low but recognised risk of complications including aspiration of gastric contents, inadequate laryngeal seal, post-operative sore throat and difficulties with device insertion (3). In an attempt to address these issues manufacturers have developed '2nd generation' SADs, which are designed to reduce the risk of aspiration and may claim features such as easier insertion, reduced trauma on insertion, superior seal pressures, and integral bite blocks (5,6). These improvements have led to true advancement in the field (7-10) and have led to calls from experts for 2nd generation device use to become a standard of care (11).

In 2011 the Difficult Airway Society (DAS), in response to concerns from the anaesthetic community that devices used in airway management were being introduced into clinical practice with minimal trial based evidence of their benefit, formed the ADEPT (Airway Device Evaluation Project Team) working group. The group made a number of recommendations on the evaluation of airway equipment prior to purchase, published in *Anaesthesia* in 2011 (12). These were subsequently adopted by DAS as guidance to its members involved in the procurement of airway equipment. The ADEPT guidance identifies that, although such devices may be sold under the Medical Devices Directive with little evidence of efficacy and safety, they should not be bought and used unless there is a minimum standard of evidence available proving such. The minimum acceptable level of evidence according to ADEPT guidance is 3b, i.e. a single case-control or historical case-control study, with more robust evidence preferred if feasible and practical. The guidance is clear that it does not consider RCT (1b) or systematic review (1a) to be necessary for airway device evaluation where more pragmatic and less resource intensive study designs may be adequate (12).

Rationale

The LMA® Protector™ is a new single use SAD developed by Teleflex inc. It is a 2nd generation device which has a number of additional features compared to previous designs, incorporated to improve the safety of the device (13). These features are:

- Allows access to and functional separation of respiratory and digestive tracts
- Two drainage channels enabling either direct suction at the upper oesophageal sphincter or the passage of a gastric tube
- Integrated bite block

- A fixation system preventing proximal displacement
- An elongated cuff enhancing the seal at the distal end of the mask at the upper oesophageal sphincter, designed to potentially reduce risk of aspiration
- An integrated cuff pressure indicator enabling continuous monitoring of cuff pressure and optimisation (Cuff Pilot™ Technology)
- Enables passage of tracheal tubes up size 7.5mm internal diameter

The device is an evolution on the design of previous 2nd generation SADs developed by Intavent Orthofix and now owned by Teleflex which are in everyday use around the world - LMA® ProSeal™, the LMA® Supreme™, and the Guardian CPV ™ airways, all with good evidence of safety and efficacy (7-10).

The LMA® Protector™ is CE marked, produced in a number of sizes, and has been marketed for clinical use since mid-2016, without any design changes until now, and there is as yet only limited trial data on its use beyond pilot studies (14). Given the enhanced design of the LMA® Protector™ there are clear potential advantages to its use, and trial data is required to determine its safety and efficacy. In order to fulfil the ADEPT guidance minimum standard of evidence the device must be further evaluated before it may be safely recommended for purchase by hospital trusts in the UK. We propose a national multi-centre prospective controlled clinical evaluation cohort study, as sufficient to delineate the performance of the device and determine its likely place in clinical practice in the UK (or similar) rather than presupposing we will "recommend it". The LMA® Protector™ is not used in standard care in any of the hospital trusts involved in the study.

Study outline and research questions
We will conduct a prospective multi-centre cohort study to evaluate the performance of the device. The main research questions pertain to the device performance, focusing on quality of the airway, ease of insertion, quality of ventilation, and incidence of complications.

Participants
All patients aged above 18, ASA grade 1 to 3, presenting for elective surgical procedures and requiring and suitable for a supraglottic airway device will be invited to take part in the study. Exclusion criteria are: a) patient refusal, b) below 18 years of age, c) requiring intubation, d) risk factors for aspiration, e) ASA 4 and above, f) mouth opening of less than 2.5cm and deemed to require awake intubation.

Potiential risks
The potential risks and burdens are the same compared to using other airway devices during anaesthesia. We will minimise them by ensuring adequate training in the use of the device is used, by recruiting investigators who are anaesthetists with experience of using similar airway devices more than 200 times.

4. OBJECTIVES AND OUTCOME MEASURES

Objectives	Outcome Measures	Timepoint(s) of evaluation of this outcome

		measure (if applicable)
Primary Objective To assess the performance of the LMA Protector	1) First go insertion success rate, 2) First go successful ventilation rate, 3) Percentage of complication free insertions	At time of anaesthesia
Secondary Objectives To assess: 1) Time taken to achieve airway 2) Number of attempts to achieve patent airway 3) Complications during airway insertion 4) Complications during anaesthesia attributed to the airway 5) Complications during device removal 6) Complications after anaesthesia attributed to the airway 7) Quality of ventilation	1) Time to first square capnography waveform 2) Lowest oxygen saturation level 3) Monitor numbers of interventions needed to ensure airway patency 4) Monitor pre-defined complications occurrence during insertion of device, during anaesthesia, and on device removal 5) The quality of ventilation will depend on whether there was: a) adequate chest movement, b) tidal volume > 7ml/kg, c) stable SpO2, and d) square capnography trace	At time of anaesthesia and post-operatively

5. STUDY DESIGN

This is a prospective, multi-centred cohort observational study, where all suitable participants will have the LMA Protector used. The centres involved will be: Oxford University Hospitals NHS Foundation Trust, Northampton General Hospital, Royal Berkshire Hospital, Royal United Hospital, and University Hospital of Wales. The participants will be involved in the study for maximum 48 hours starting from approach for consent on the morning of surgery, while they are in the pre-operative area, until the second interview (either in person if participant is an inpatient, or via telephone if participant had been discharged). Data will be collected while the anaesthetic is being conducted apart from the information regarding the complications of the device removal and postoperatively. The order of events will be: a) consent, b) general anaesthetic as per standard care but using LMA protector, c) brief interview by clinician following operation in hospital at first available opportunity, d) another interview 24 to 48 hours later with the same questions either in hospital or at home by telephone.

Data that will be collected will be: a) investigator name, b) number of previous insertions of the device by the investigator, c) patient age, d) patient gender, e) weight, f) height, g) ASA class, h) operation, i) anaesthetic drugs and dosages, j) anaesthetic technique, k) mode of ventilation, l) if further muscle relaxant used. Moreover, we will collect:

1) Airway assessment including Malampatti classification
2) The number of attempts at the insertion will be recorded

3) Volume of air in cuff to achieve intracuff pressure of 60cmH_2O
4) Airway leak pressure
5) The ease of insertion
6) The lowest oxygen saturation recording
7) The quality of ventilation
8) The quality of the airway during maintenance
9) The ease of hands free anaesthesia
10) The overall usefulness of the device in the patient
11) The overall performance of the device
12) The time to first square capnography trace
13) Positive or negative bubble test
14) Airway manipulations to establish airway
15) Complications on insertion, during use, and on removal of the device
16) Post-operative oropharyngeal sequelae

The data will be collected from the anaesthetic record. Data c, d, e, f will be collected from the electronic notes.
All data will be recorded in the CRF/data collection form.

6. PARTICIPANT IDENTIFICATION

6.1. Study Participants

Inclusion Criteria

- Adult participants who are having a general anaesthetic.
- Participant is willing and able to give informed consent for participation in the study.
- Male or Female, aged 18 years or above.
- ASA 1 – 3 category patients
- Elective operations
- Urgent operations
- Patients suitable for an SAD based on patient and operation factors.

6.2. Exclusion Criteria

The participant may not enter the study if ANY of the following apply:

- Refusal of consent
- Age less than 18 years
- Require intubation for the operation
- Risk of regurgitation
- ASA 4 and above
- Mouth opening less than 2.5cm
- Require awake intubation

7. STUDY PROCEDURES

7.1. Recruitment

Potential participants will be identified on the morning of surgery during the preoperative anaesthetic visit. The investigator will be a member of the of the direct care team, i.e. the anaesthetist for the case. The investigator will examine whether the potential participant fulfils any of the inclusion criteria and none of the exclusion criteria apply to them. The

participant information leaflet will be given to the patient, the investigator will answer any questions the patient might have, and at least one hour will be given to the patient, which the study team feels this is an acceptable amount of time to ensure they have not been rushed into taking a decision. They will be asked to sign the consent form, of which the participant will keep a copy, another copy will be placed in the study file, and the original will be placed in the patient's note.

7.2. Screening and Eligibility Assessment

On the morning of surgery, the investigator will examine their operating list and decide if the operations are suitable for the LMA Protector. The investigator will be a member of the of the direct care team, i.e. the anaesthetist for the case.

If the patients do not meet any exclusion criteria then they will be asked whether they wanted to participate in the study, the PIL will be given to them and they will be given at least one hour to make up their mind. The investigator will then approach the patient again, answer any remaining questions and obtain informed consent.

7.3. Informed Consent

Informed consent will be taken by the anaesthetist investigator when they see the participant prior to the surgery. The participant must personally sign and date the latest approved version of the Informed Consent form before any study specific procedures are performed.

Written and verbal versions of the Participant Information and Informed Consent will be presented to the participants detailing no less than: the exact nature of the study; what it will involve for the participant; the implications and constraints of the protocol and any risks involved in taking part. It will be clearly stated that the participant is free to withdraw from the study at any time for any reason without prejudice to future care, without affecting their legal rights, and with no obligation to give the reason for withdrawal.

The participant will be allowed an hour to consider the information, and the opportunity to question the Investigator, or other independent parties to decide whether they will participate in the study. Written Informed Consent will then be obtained by means of participant dated signature and dated signature of the person who presented and obtained the Informed Consent. The person who obtained the consent must be suitably qualified and experienced, and have been authorised to do so by the Chief/Principal Investigator. A copy of the signed Informed Consent will be given to the participant. The original signed form will be retained at the study site.

7.4. Randomisation, blinding and code-breaking

Participants will not be randomised in this study. We are evaluating the performance of the LMA Protector airway device and thus if the participant signs the consent form the device will be used for their anaesthetic.

7.5. Assessments during Anaesthesia

The following measurements will be noted:

1. Assessment of the airway including Malampatti classification
2. The number of attempts at the insertion
3. Volume of air in cuff to achieve intracuff pressure of 60cmH_2O
4. Airway leak pressure
5. The ease of insertion
6. The time to first square capnography trace
7. Positive or negative bubble test

8. Lowest recorded oxygen saturation reading
9. Airway manipulations to establish airway
10. Complications during insertion
11. Complications intraoperatively
12. Complications during removal
13. Complications postoperatively

In addition to the above measurements the following aspects of the use of the device will be scored:

1) The quality of ventilation
2) The quality of the airway during maintenance
3) The ease of hands free anaesthesia
4) The overall usefulness of the device in the patient
5) The overall performance of the device

Lastly the investigators will note any complications during insertion, use and on removal of the device. Additionally, the participants will be asked about any post-operative oropharyngeal sequelae.

7.6. Subsequent Visits

First visit

During the first visit by the anaesthetist to the participant, at the anaesthetist's earliest opportunity, either in the recovery area or on the ward, the participants will be asked about the following complications, which will be graded as none, mild, moderate or severe).

1) Vomiting
2) Lip or tongue swelling
3) Hearing changes
4) Ear pain
5) Sore throat
6) Pain on swallowing
7) Jaw pain
8) Neck or mouth ache
9) Pain on speaking
10) Numbness of the tongue

Second visit (or telephone consultation)

During the second visit 24-48 hours post-operatively on the ward or via telephone the participants will be asked about the following complications, which will be graded as none, mild, moderate or severe).

1) Vomiting
2) Lip or tongue swelling
3) Hearing changes
4) Ear pain
5) Sore throat
6) Pain on swallowing
7) Jaw pain
8) Neck or mouth ache
9) Pain on speaking
10) Numbness of the tongue

7.7. Discontinuation/Withdrawal of Participants from Study

Each participant has the right to withdraw from the study at any time. In addition, the Investigator may discontinue a participant from the study at any time if the Investigator considers it necessary for any reason including:

- Ineligibility (either arising during the study or retrospectively having been overlooked at screening)
- Significant protocol deviation
- Significant non-compliance with treatment regimen or study requirements
- Withdrawal of Consent
- Loss to follow up

The reason for withdrawal will be recorded in the CRF.
If the device cannot be inserted after 3 unsuccessful attempts to insert it, the study will be stopped, an alternative airway device will be used and the failure noted on the CRF. Participants who have been withdrawn will not be replaced. If a patient is withdrawn their research data will not be used in final analysis.

7.8. Definition of End of Study

The end of the study is following the final interview of the last patient (which could be on the ward or by telephone).

8. INTERVENTIONS

8.1. Interventions during anaesthesia

Nothing listed below deviates from normal clinical practice for any similar SAD device, or for almost any type of anaesthetic:

Preoperative assessment:
During the preoperative visit, patient information leaflet will be given to the patients meeting the eligibility criteria.
Wherever possible, suitable patients will be identified in the preoperative assessment clinic and the information leaflet given. They will be given adequate time to read this information and any queries will be answered before being asked to sign a consent form. A detailed airway assessment will be performed by one of the investigators and documented on the study proforma.

Induction of anaesthesia:
On arrival in the anaesthetic room patients will be monitored with pulse oximetry, electrocardiography and invasive or non-invasive blood pressure measurements. After intravenous access is secured and the pre-surgical checklist completed, all patients will be pre-oxygenated using a facemask to achieve end tidal oxygen concentration of at least 80%. A 'sniffing' position of the head and neck and a 20 degree head-up bed tilt will be used for pre-oxygenation. General anaesthesia will be induced intravenously. After induction of anaesthesia, facemask ventilation will be commenced and anaesthesia maintained with an inhalational anaesthetic agent in oxygen or with total intravenous anaesthesia. The volatile agent's (anesthetic gases) concentration of 1 MAC adjusted for the patient's age will be achieved and maintained. This is normal process of anaesthesia applicable for all patients irrespective of participation in the study.

Supraglottic airway device (SAD) insertion:
Once deep plane of anaesthesia is confirmed, with the absence of movement to jaw thrust stimulation the SAD (LMA protector) will be inserted. The size of the device will be based on the manufacturer's recommendations for the body weight. The breathing system will be connected to the device. Ventilation of the lungs will be then confirmed by observing adequate bilateral chest inflation and square end-tidal capnogram wave with positive pressure ventilation. Adequate ventilation will be recorded if three tests are passed: 1) adequate chest movement, 2) an expired tidal volume of at least 7 ml/kg and 3) stable oxygenation. Time would continue until LMA® ProtectorTM inserted successfully. If it is not possible to insert the device or ventilate through it, two more attempts at placement of the device will be allowed. If placement has failed after two further attempts, the study will be abandoned and the other device will be used. If this fails on first attempt a different LMA or tracheal tube will be used as appropriate.

Maintenance of anaesthesia and recovery
At the end of operation, anaesthetic agents will be discontinued while the device is left in place. The device will be removed after the patient has regained consciousness, and has responded to verbal command to open the mouth. Any complications that occur during the use of the device will be recorded.

Postoperative assessment
Postoperatively in recovery or on the ward, we will visit each patient and determine whether the following airway complications are present after surgery: sore throat (constant pain, independent of swallowing), dysphagia (difficulty in, or pain provoked by, swallowing), sore jaw, dysphonia (difficulty in, or pain on, speaking), numbness of the tongue or the oropharynx, ear pain, neck or mouth ache, hearing changes. Each complication will be graded as none, mild, moderate or severe. The same questions will be asked 24-48 hours later.
The main interventions refer to the insertion of the airway device into the patient to obtain a airway and allow the conduct of the anaesthetic and therefore the surgery. However, if there are problems with the device and the airway obtained is suboptimal then the below interventions are allowed (which will be noted in the data collection form):

1) Neck extension – move patient's neck upward
2) Neck flexion – move patient's neck downward
3) Chin lift - manoeuvre to open the airway
4) Jaw thrust – manoeuvre to open the airway
5) Reposition of the device

8.2. Maintenanace and storage of the device

The devices are single use. They will be stored in the anaesthetic store rooms in the operating theatre suites at the John Radcliffe, Churchill, West Wing, Women's Centre, and Nuffield Orthopaedic theatres.

9. SAFETY REPORTING

9.1. Definitions

9.1.1 Adverse Event (AE):

An AE or adverse event is:
Any untoward medical occurrence in a patient or other clinical investigation participant taking part in a trial of a medical device, which does not necessarily have to have a causal relationship with the device under investigation.
An AE can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom or disease temporally associated with the use of the device, whether or not considered related to the device.

9.1.2: Adverse Device Effect (ADE)

All untoward and unintended responses to the medical device.
The phrase "responses to a medical device" means that a causal relationship between the device under investigation and an AE is at least a reasonable possibility, i.e., the relationship cannot be ruled out.
All cases judged by either the reporting medically qualified professional or the sponsor as having a reasonable suspected causal relationship to the device qualifies as a device effect.
This also includes any event resulting from insufficiencies or inadequacies in the instruction for use or deployment of the device and includes any event that is a result of a user error.

9.1.3 Serious Adverse Event (SAE):

SAE is an adverse event that

- Led to death
- Led to fetal distress, fetal death or congenital abnormality or birth defect.
- Led to serious deterioration in the health of the subject that
    - Resulted in a life-threatening illness or injury
      NOTE: The term "life-threatening" in the definition of "serious" refers to an event in which the participant was at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe.
    - Resulted in a permanent impairment of a body structure or a body function
    - Required in-patient hospitalisation or prolongation of existing hospitalisation
    - Resulted in medical or surgical intervention to prevent permanent impairment to a body structure or a body function
    - Other important medical events*
      *Other events that may not result in death, are not life threatening, or do not require hospitalisation, may be considered a serious adverse event when, based upon appropriate medical judgement, the event may jeopardise the patient and may require medical or surgical intervention to prevent one of the outcomes listed above

To ensure no confusion or misunderstanding of the difference between the terms "serious" and "severe", which are not synonymous, the following note of clarification is provided:
The term "severe" is often used to describe the intensity (severity) of a specific event (as in mild, moderate, or severe myocardial infarction); the event itself, however, may be of relatively minor medical significance (such as severe headache). This is not the same as "serious," which is based on patient/event outcome or action criteria usually associated with events that pose a threat to a participant's life or functioning. Seriousness (not severity) serves as a guide for defining regulatory reporting obligations.

9.1.4 Serious Adverse Device Effects (SADE):

A serious adverse device effect (SADE) is any untoward medical occurrence seen in a patient that can be attributed wholly or partly to the device which resulted in any of the characteristics or led to a characteristics of a Serious adverse event.
SADE is also any event that may have led to these consequences if suitable action had not been taken or intervention had not been made or if circumstances has been less opportune.
All cases judged by either the reporting medically qualified professional or the sponsor.

9.1.5 Unanticipated Adverse Device Effect (UADE):
Any serious adverse device effect on health or safety or any life-threatening problem or death caused by, or associated with a device, if that effect, problem, or death was not previously identified in nature, severity or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that related to the rights, safety or welfare of the subject.

9.2. Reporting of AE

All AE's occurring during the study observed by the investigator or reported by the participant, whether or not attributed to the device under investigation will be recorded on the CRF as specified in the protocol. All ADE's will be recorded in the CRF.
The following information will be recorded: description, date of onset and end date, severity, assessment of relatedness to device, other suspect drug or device and action taken. Follow-up information should be provided as necessary.
The relationship of AEs to the device will be assessed by a medically qualified investigator or the sponsor/manufacturer and will be followed up until resolution or the event is considered stable.
All ADE that result in a participant's withdrawal from the study or are present at the end of the study, should be followed up until a satisfactory resolution occurs.
Where relevant, any pregnancy occurring during the clinical study and the outcome of the pregnancy, should be recorded and followed up for congenital abnormality or birth defect.

9.3. Reporting Procedures for All SAEs/ SADEs/ UADEs

All SAE/SADE/UADEs need to be reported to the sponsor/legal representative and manufacture and OUH R&D **within one working day** of the investigator team becoming aware of them.
Reports of related and unexpected SAEs should be submitted to ethics within 15 days of the Chief Investigator becoming aware of the event, using the SAE report form for non-CTIMPs published on the NRES website.
All reporting to ORH R&D should be by email to ouhsae.reports@ouh.nhs.uk giving as much information about the incident as possible, and should be signed by the PI or Co-investigator.
The ORH SADE reporting form should be used for ORH sponsored studies.

The ORH R&D Department will undertake an initial review of the information and ensure it is reviewed by the ORH/University of Oxford Trial Safety Group Medical Monitor. Events will be followed up until resolution, any appropriate further information will be sent by the research team in a timely manner.
Reporting to the MHRA will be done in liaison with the Chief Investigator and the Manufacturer.

The Manufacturer has a legal obligation to report all events that need to be reported to the Nominated Competent Authority immediately (without any unjustifiable delay) after a link is established between the event and the device, but no more than:

- 2 days following the awareness of the event for Serious Public Health Threat.
- 10 days following awareness of the event for Death or unanticipated serious deterioration in health.
- 30 days following the awareness of the event for all other event meeting the SAE criteria.

9.4. Annual Reports

In addition to the above reporting the Chief Investigator will submit once a year, throughout the trial, or on request a progress/safety report to the REC and R&D.

10. STATISTICS AND ANALYSIS

10.1. Description of Statistical Methods

The data in this single arm study will be described by descriptive statistics only, using binomial confidence where necessary.

10.2. The Number of Participants

We will recruit 1100 - 2000 patients with an interim analysis at 1100 patients.

The sample size is based on the paper:
Pandit JJ. If it hasn't failed, does it work? On 'the worst we can expect' from observational trial results, with reference to airway management devices. Anaesthesia. 2012 Jun;67(6):578-83.
That explains how binomial confidence intervals can be used in observational airway research of this type.
The conclusions were:

- Investigators in observational studies should state what they regard as 'success' or 'failure' of using the device in question. Where the main endpoint is a continuous variable, researchers should define a justifiable threshold so that it can also be described as a caterogical (binomial) endpoint,
- For all results, the upper limit of the 95% confidence interval (CI) should be quoted,
- For airway devices such as SADs, a 95% CI upper limit failure rate > 2.5% ('the worst we can expect') in the chosen endpoint should generally lead to a conclusion that the device is poor or unsuitable for clinical use, compared with established devices,
- In planning an observational trial, the minimum sample size should be calculated to yield (99% CI) for at least one failure of the device, which generally means that sample sizes should exceed 250,
- Observational studies with < 250 patients are unlikely to provide useful evidence in favour of a device's clinical acceptability, although they may provide useful information suggestive of its lack of acceptability.

We followed all of these conclusions and our expected 1100 recruited patients are a lot more than the 250 expected to show a 2.5% failure rate with 95% CI.

10.3. Analysis of Outcome Measures

The study will recruit up to 2000 patients, with an interim analysis at 1100 looking at the device failure rate. This is an observational study only. If we apply binomial confidence intervals according to the reference cited, and assume a 'failure rate' of clinical importance as 5%, we find an upper limit 95% CI of 6.54% with 1000 patients. For 2000 patients this upper limit is 6.05%. Thus, the gain of precision in studying up to 2000 patients may be very marginal if this is what an interim analysis at 1100 patients shows. We will however, continue the study if the 'failure rate' is >10% as then the precision in estimate benefit of studying 2000 patients is greater.

The data in this single arm study will be described by descriptive statistics only, using binomial confidence where necessary.

11. DATA MANAGEMENT

11.1. Access to Data

Direct access will be granted to authorised representatives from the Sponsor and host institution for monitoring and/or audit of the study to ensure compliance with regulations.

11.2. Data Recording and Record Keeping

Data will be collected prospectively on data collection sheets completed by the anaesthetist / investigator during anaesthesia. Each site will manage their own data set and the data will be pooled at the end of the recruitment phase across all sites. Data will be sent from sites to the lead study team only at the end of the data collection.
Consent form and initial data collection forms will be filed in the master folder and kept locked in the dedicated research locker in the department.
Each site will assign a study ID for each participant and a record of these IDs will be kept in the site file. Only anonymised data will be sent from each trust to the main study team. No personal data will be sent to the coordinating centre.

Management of data at sites

At each participating site participants will be assigned a trial ID at the moment of enrolment. The log of trial IDs and patient data will be kept in the site file in a locked cupboard in the anaesthetic department in each site. It will be separate to the CRF. The PI at each site will have access to this log.
The trial ID will be noted on the CRF and the consent form.
Data will be recorded by hand on the CRF by the investigator and later will be transcribed on a study database / excel spreadsheet kept on the Trust servers. The CRF will be identifiable by study ID only.
The hard copies of the consent forms and CRF will be kept locally, but separately, in the anaesthetic departments in secure locked filling cabinets.
Electronic data will be kept on a password protected database/excel spreadsheet stored on NHS servers on the hospital intranet of each site (this means it is backed up).
Telephone numbers will be accessed from hospital records with the consent of the participant. If the investigator chooses to record the telephone number of patient, this will be recorded on a separate electronic file, not on the enrolment log, and the file will be destroyed within three months of the study ending. The PI on each site will have access to the research files. Personal data be kept for 3 months and study data be kept for 5 years.

The only data that will be shared with the lead study team will be the data spreadsheet that will only have study IDs and no identifiable data. It will be sent electronically and the password will be sent separately to the spreadsheet.
Data from the research sites will be shared with the lead sire only by using secure NHS email accounts.

Management of data by lead study team
The lead study team will receive the anonymised data spreadsheet, on which information will be recorded with study ID only.
All the information will be collated and stored, anonymously, entered onto a central database on OUH trust servers, with each participant identifiable by the study ID.
Study the data be kept for 5 years.

12. QUALITY ASSURANCE PROCEDURES

The study may be monitored, or audited in accordance with the current approved protocol, GCP, relevant regulations and standard operating procedures.

13. ETHICAL AND REGULATORY CONSIDERATIONS

13.1. Declaration of Helsinki
The Investigator will ensure that this study is conducted in accordance with the principles of the Declaration of Helsinki.

13.2. Guidelines for Good Clinical Practice
The Investigator will ensure that this study is conducted in accordance with relevant regulations and with Good Clinical Practice.

13.3. Approvals
The protocol, informed consent form, participant information sheet and any proposed advertising material will be submitted to an appropriate Research Ethics Committee (REC), and HRA for written approval.
The Investigator will submit and, where necessary, obtain approval from the above parties for all substantial amendments to the original approved documents.

13.4. Reporting
The CI shall submit once a year throughout the study, or on request, an Annual Progress report to the REC Committee, HRA (where required) host organisation and Sponsor. In addition, an End of Study notification and final report will be submitted to the same parties.

13.5. Participant Confidentiality
No participant identifiable data will be published.
The study staff will ensure that the participants' anonymity is maintained. The participants will be identified only by a participant ID number on all study documents and any electronic database, with the exception of the CRF, where participant initials may be added. All documents will be stored securely and only accessible by study staff and authorised personnel. The study will comply with the Data Protection Act, which requires data to be anonymised as soon as it is practical to do so.

13.6. Expenses and Benefits

No payment will be made to participants.

13.7. Other Ethical Considerations

There are no other ethical issues involved in this study.

14. FINANCE AND INSURANCE

14.1. Funding

The study is funded to the requested sum of £56,400, £20,000 of which would be paid immediately for consumables and the rest to be held as a contingency if needed, and there is no time limit although DAS reserves the right to withdraw the funds from January 2022.
Costs of devices are covered by a grant from the Difficult Airway Society (DAS) to the University of Oxford for the sum of £15,400. The rest of the grant money is for a PhD through DAS and has no bearing with the funds available for the study. We are awaiting an invoice from DAS that soon should be raised and we will (via the university) pay this sum over to them, soon after which the devices will arrive.

Each research site will obtain the devices directly from the central store area. The orders will be placed with the company Teleflex, and on the orders will be specified which site to send the devices to. Once the order is placed the company will ship them as required.

Each researcher is a consultant with an NHS contract. This consists of Direct Care Programmed Activities (DCC) and Supporting Professional Activity (SPA). The latter is, within the contract, up to 10 hours per week, and is assigned to activities including research and quality improvement. If a consultant does not deliver on these goals or use that paid time for these activities s/he is in breach of contract. Moreover, if they seek or take additional payment for these activities then they are being paid twice for the same work which is illegal. Moreover, the use of SPA time (up to 10 hours/wk) in any given year is specified at Appraisal which is a mandatory and directional meeting to assign goals for the coming year. Therefore, this project is explicitly factored in to the fully funded development goals.

A study coordinator will be put in place covered by funding from the Difficult Airway society.

14.2. Insurance

NHS bodies are legally liable for the negligent acts and omissions of their employees. If you are harmed whilst taking part in a clinical research study as a result of negligence on the part of a member of the study team this liability cover would apply.
Non-negligent harm is not covered by the NHS indemnity scheme. The Oxford University Hospitals NHS Foundation Trust, therefore, cannot agree in advance to pay compensation in these circumstances.
In exceptional circumstances an ex-gratia payment may be offered.

15. PUBLICATION POLICY

The Investigators will be involved in reviewing drafts of the manuscripts, abstracts, press releases and any other publications arising from the study. Authors will acknowledge that

the study was funded by DAS. Authorship will be determined in accordance with the ICMJE guidelines and other contributors will be acknowledged.

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17. APPENDIX A: STUDY FLOW CHART
SCHEDULE OF OBSERVATIONS

SAD insertion time (from picking up device until upstroke of 1st square wave capnography trace)
SAD insertion attempts
Cuff volume to achieve 60cmH_2O cuff pressure
Leak pressure: pressure at which audible leak starts or airway pressure plateaus, with fresh gas flow set at 5L/ min
Score following parameters using 11-point NRS **(0 – very difficult / inadequate, 10 – very easy / excellent)** Ease of insertion Adequacy of ventilation Hands free anaesthesia or overall usefulness of device
Note airway manipulations to maintain airway: Additional Neck extension Neck flexion Chin lift Additional Jaw thrust
Note following complications during device insertion / airway maintenance / removal of device: Failure to establish airway Loss of adequate airway Soft tissue damage Dental damage Regurgitation Aspiration Laryngospasm Stridor Coughing Gagging Hiccough Desaturation
After surgery note following events: Vomiting Lip or tongue swelling Hearing changes Ear pain Sore throat Dysphagia Sore jaw Dysphonia Numbness of tongue / oropharynx Pain on speaking Neck or mouth ache

18. APPENDIX C: AMENDMENT HISTORY

Amendment No.	Protocol Version No.	Date issued	Author(s) of changes	Details of Changes made

List details of all protocol amendments here whenever a new version of the protocol is produced. This is not necessary prior to initial REC submission.