# PROTOCOL

## Version: 6

## Date: 17th May 2019

## Sponsor: University Hospitals Dorset NHS Foundation Trust

**Study Title:** **A single-centre, randomised controlled study of Entonox versus midazolam sedation in gastroscopy.**

**Chief Investigator:** **Dr. Simon McLaughlin**

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## TEAM CONTACTS

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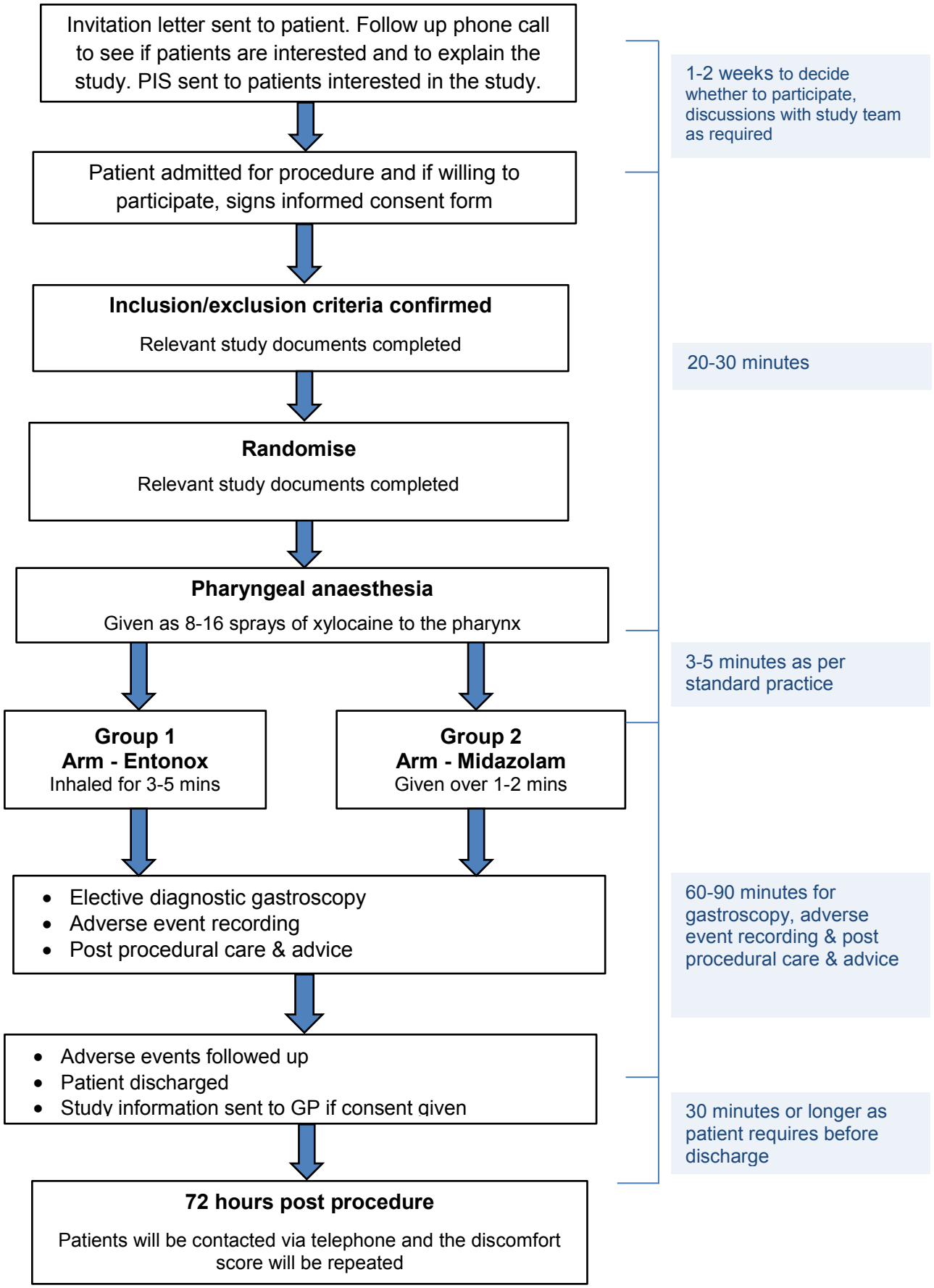
### Clinical Queries

Clinical queries should be directed to Dr Simon McLaughlin in the first instance who will direct the query to the appropriate person.

### SAE Reporting

| | | |
|---|---|---|
| **Safety Reporting** | ResearchOffice@rbch.nhs.uk | 01202 962378 |

**Figure 1: STUDY PROCESS FLOW DIAGRAM**



## SUMMARY

This study aims to determine whether Entonox (gas and air) is at least as good as intravenous midazolam in providing analgesia and sedation during gastroscopy. Entonox is used as an adjunct in lower gastrointestinal procedures but is not routinely used in gastroscopy, and there is only one similar published study to date, which was performed in children. The main advantage of Entonox over midazolam is the quick recovery time following withdrawal of the agent, which enables patients to return to independent normal life. We would like to be able to offer Entonox to patients as an option for sedation during gastroscopy, this study is being conducted to determine if it is a safe and feasible option.

## INTRODUCTION

Gastroscopy is an uncomfortable but usually a short diagnostic procedure. At present the options for patients are to have the procedure with intravenous sedation (with or without local-pharyngeal anaesthesia) or local-pharyngeal anaesthesia without any sedation. General anaesthetic may be offered in exceptional circumstances. The aims are for patients to have a pain-free procedure with minimal side effects, no complications and a choice of options to suit individual preference. Conscious sedation using benzodiazepines reduces anxiety and promotes amnesia but has some hangover effects, which, according to national guidelines, mean patients are deemed unsafe to drive or work for 24 hours after the procedure and require both a responsible adult to accompany them home and to stay with them for 12 hours[1]. Local anaesthesia of the pharynx has no anxiolytic effect, is acceptable to some patients and has the advantage of lasting for around 1 hour with no psychomotor effects. To have an option that combines the advantages of both these routinely used modalities would be ideal for many patients.

Entonox is a 50:50 mix of nitrous oxide and oxygen and has long been used in a variety of settings as a short-term analgesic with sedative and amnesic properties. It has an induction time of 2-5 minutes with a duration of effect of 3-5 minutes after withdrawal[2,3]. Side effects are minimal but may include nausea, vomiting, headache, dizziness and paraesthesia[2]. It is without long-lasting psychomotor effects that typically affect the ability to drive[3,4,5]. Entonox is already used in many endoscopy units during lower gastrointestinal endoscopy, often as an adjunct to intravenous sedation and analgesia and has been found to be beneficial[5,6,7,8]. The advantages of Entonox over traditional sedation with midazolam are that patients are deemed fit to drive 30 minutes after their procedure (British Society of Gastroenterologists guidance 2011). In addition, they do not require a responsible adult to accompany them home and can return to work the same day. This has obvious benefits especially for those who are self-employed. The benefit to the NHS as a result of this reduced recovery time may have a positive impact on departmental throughput.

In a Cochrane review (2011) of nitrous oxide with conventional intravenous analgesia during colonoscopy, nitrous oxide is comparable in efficacy and safer, with a shorter recovery period[9]. Its use in flexible bronchoscopy has also been studied and, in combination with local anaesthesia, found to be a good alternative to general anaesthesia[10,11].

To the best of our knowledge the use of Entonox during gastroscopy has been examined in only one published study to date in paediatric patients. Michaud et al (1998) studied 37 participants, 30 of whom underwent gastroscopy using Entonox either before or both before and during the procedure. The authors found that Entonox provided safe and effective analgesia without heavy sedation and allowed adequate patient relaxation and efficient endoscopy with quick recovery times of 3-5 minutes[2]. However this study did not compare Entonox to conventional methods of sedation and analgesia.

To the best of our knowledge there are no published data on the use of Entonox for gastroscopy in adults.

## AIMS

### Primary Aim

To establish whether Entonox and pharyngeal anaesthesia could provide levels of patient comfort equal to that of midazolam sedation and pharyngeal anaesthesia when performing gastroscopy.

### Secondary Aim

To establish whether completion rates of gastroscopy using Entonox and pharyngeal anaesthesia are equal to those performed with midazolam when performing gastroscopy.

## METHODS

### Population

Adult participants attending for diagnostic gastroscopy who are suitable for sedation will be approached to enroll in this study. We aim to recruit 200 participants.

**Inclusion criteria**

- Male/female aged 18 years or over
- Confirmed clinical requirement to undergo diagnostic gastroscopy
- Suitable for sedation
- Able to provide informed consent

**Exclusion criteria**

- History of severe chronic respiratory or significant cardiac disease
- Requirement for longer procedure eg Barrett's surveillance
- Previous known adverse reaction to Entonox or Midazolam
- Patients who are pregnant or breastfeeding
- Entonox use in the previous 4 days
- Any of the following known contra-indications to Entonox (Entonox should not be used in any condition where gas is entrapped in a part of the body where its expansion may be dangerous, such as air lodged in an artery or artificial traumatic or spontaneous pneumothorax), Specifically:
    - Pneumothorax in the past 3 months
    - Air embolism in the past 2 months
    - Sub aqua diving activity within the last 2 weeks
    - Air encephalography in the past 2 weeks
    - Severe bullous emphysema
    - Myringoplasty in the past 2 weeks
    - Gross abdominal distension eg. Pseudobstruction.
    - Severe injuries to the face and jaw in the past 2 months
    - Severe head injuries in the past 2 months
    - Eye surgery requiring injections of gas to be used in the past 2 months

**Recruitment**

Patients will be recruited in a number of ways. The method of recruitment will depend on the capacity of the research and endoscopy staff.

Patients who are awaiting a diagnostic gastroscopy will be sent a letter of invitation asking them if they want to take part in the study. The following week, after the invitation letter has been sent, the research nurse will telephone the patient and an opportunity will be given to the patient to discuss the study in more detail and see if they may be interested in taking part. From a practical point of view, at times it may be easier if we group all the research participants onto one list. If we plan to do this then patients will be approached prior to them receiving a date for their procedure.

We will also display posters in the waiting room and research staff may approach patients in the waiting area. If patients express an interest in the study on the day of their procedure we will ensure that they have had sufficient time to read through the information sheet and consent form, that the study has been explained to them and that they have had the opportunity to ask any questions before signing the consent form.

**Randomisation**

Randomisation will be achieved by opening the next numbered sealed envelope stored in the study site file in the research office. They are a sequence of opaque envelopes containing a group number (either group 1 or group 2) and associated treatment allocation (either midazolam sedation combined with pharyngeal anaesthesia or Entonox combined with pharyngeal anaesthesia).

**Informed Consent**

Patients will be consented on the day that they come in for their procedure. A research nurse or GCP trained endoscopist/endoscopy nurse trained in consent who has been delegated the task, will explain the procedure to them and go through the information sheet and consent form. They will ask the patient if they have any questions and ensure that any questions are answered to the patient's satisfaction prior to signing the informed consent form. The patient and then the health care professional gaining consent will sign and date the consent form. A copy of the signed consent form will be given to the patient to retain. In addition to signing a study consent form, the patient will also sign the hospital endoscopy consent form which is the normal procedure run by the endoscopy department.

**Eligibility**

Eligibility for the study will be determined by any suitably trained health care professional deemed competent by the CI and who has been delegated this task. This could be an

endoscopy or research nurse experienced in the use of Entonox for endoscopy, medical or nursing endoscopist experienced in the use of Entonox for endoscopy, who holds a current GCP certificate. Clinical Trial Assistants cannot assess eligibility for this study.

**Study Procedures**

All participants will arrive having fasted for 4 hours before the procedure in order to visualize the upper gastrointestinal tract as per the endoscopy unit standard protocol. The standard process of admission to the department will take place, including clinical observations of pulse rate, blood pressure and oxygen saturation. The consent forms will be completed as described above and the patient will then be randomised to either the Entonox or Midazolam arm (standard of care).

Once the participant is in the endoscopy room they will then receive pharyngeal anaesthesia, given as 8-16 sprays of xylocaine to the pharynx; 3 minutes will be given to allow the pharynx to become anaesthetized.

Participants randomized to receive Entonox will be given the 50:50 nitrous oxide:oxygen mix via a mouthpiece with a demand valve system, once in position for the procedure. Inhalations will be given for 3-5 minutes (or until the participant feels adequately sedated) measured using a stopwatch. Oxygen will be given at 2 litres per minute via nasal cannulae during the procedure, (standard care for sedated procedures). The endoscopist will then proceed to intubate the cricopharynx and perform the procedure in the standard manner.

Participants randomized to receive midazolam will have an intravenous cannula sited and, following the administration of xylocaine throat spray as above, will be put into the left lateral position. They will then be given up to 5mg midazolam as appropriate to achieve conscious sedation as for standard protocol in endoscopy.

All participants will be monitored throughout the procedure in both study groups, with continuous oxygen saturation and pulse rate monitored via finger probe, as per standard departmental protocol.

**Post- procedure care**

Participants who have received Entonox will be recovered in the seated recovery area or in the recovery area of the Endoscopy Unit depending on the time taken to meet discharge criteria of full responsiveness, stable vital signs and ability to walk unaided. The Endoscopy nursing staff are fully trained in safe discharge of patients. We anticipate that this will only require a maximum of 10 minutes, based on our previous experience with its use in lower

GI procedures and product literature. Participants are allowed to drive 30 minutes after discharge, according to British Society of Gastroenterology guidance. Post-procedure safety and contact information will be given on discharge.

Participants who have received midazolam will be recovered in the recovery area and then discharged from the department by the endoscopy nursing staff with standard information regarding safe time to eat and drink following the procedure.

The comfort score as assessed by the nurse, will be completed during the routine procedure write up. One attending nurse will use the modified Global Rating Scale scoring system (the system used by all endoscopy departments to comply with JAG recommended data recording) to assess the patient's perceived comfort during the procedure. This comfort score will be recorded on the endoscopy departments HICCS database and on the study proforma and the scoring system is shown below.

Modified Global Rating Scale Comfort score

0 – Not Specified/entered.
1 – Extreme discomfort frequently during procedure.
2 – Significant discomfort, experienced several times during procedure.
3 – More than two episodes of discomfort, adequately tolerated.
4 –One or two episodes of mild discomfort, well tolerated.
5 – None – resting comfortably throughout.

Following the procedure, when the patient is in the recovery area, all patients will be asked to score their discomfort/pain on a scale of 1 to 5 similar to the Global Rating Scale system. In addition they will be asked to score their comfort on a 100mm visual analogue scale, detailed below.

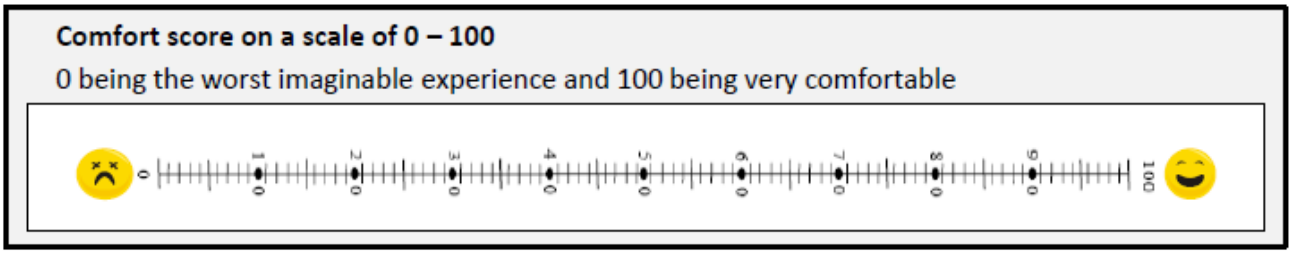



***Figure 2. Visual analogue scale patients complete after the procedure.***

If there are any concerns about a participant's fitness for discharge the endoscopist, or suitable other clinician, will be asked to review the participant and formulate a plan, as is standard practice in the Endoscopy department.

All patients will be given contact information for members of the research team and asked to contact them immediately if they experience any problems, even if they appear to be unrelated to the procedure.

The research team will review the discharge summary/nursing and medical records from endoscopy team to identify any adverse events that could have occurred following administration of midazolam or Entonox.

After 72 hours post procedure the patient will be contacted by the research team by telephone to repeat their comfort level score and check if they have experience any adverse events from either medication.

## STUDY DRUG SUPPLY

### Storage

Cylinders of Entonox are used and stored in the Endoscopy Unit on a continuous basis, in conditions recommended by the manufacturers. A cylinder clearly labeled for 'clinical trial use only' will be stored in the medical gasses unit at Royal Bournemouth Hospital as per the Medical Gases Operational Policy.

### Accountability

The endoscopy staff and research team will be accountable for the correct storage of Entonox cylinders and for recording the drug batch numbers for the Entonox supply which is delivered to each patient.

The supply of midazolam will come from the endoscopy department stock drugs, which pharmacy will supply in accordance with standard practice.

The midazolam and Entonox are both used routinely in the endoscopy department and are prescribed within the HICCS system and recorded as administered in the HICCS system and in the endoscopy care plan. In order to emulate clinical practice this same process will be followed.

### Dispensing

The Entonox will be dispensed in the endoscopy room where the procedure takes place. The batch number of the Entonox cylinder used will be recorded for each participant. As Entonox is self-administered the nurse or doctor who has observed the patient administering the Entonox will document the time that the Entonox was used for in the research notes.

The midazolam will be dispensed in the endoscopy room with the endoscopy team present. The batch number of the midazolam will be recorded for each participant and the amount of midazolam given will be recorded as per standard practice.

**Returns**

Any excess Entonox will be returned to the supplying company, BoC Healthcare and recorded on a study specific returns log. Should a problem be found with the Entonox supply, the batch will be withdrawn from use and returned to BoC Healthcare. Such an event will be documented as an adverse event and the Sponsor will be informed along with the ethics committee and regulatory authority if required.

There will be no midazolam returns as ward stock is being used.

## CONCURRENT MEDICATION/TREATMENT

All participants enrolling in this study will receive pharyngeal throat spray (unless they decline). This and the midazolam will be supplied via the Royal Bournemouth Hospital Pharmacy department and managed by the Trust's Pharmacy department according to Trust standard operating procedures for medication management and standard endoscopy practice.

Other medications normally taken by the participant will be recorded on admission as per standard protocol on individual case report forms.

**Cautions:**

Entonox has an additive effect on centrally acting drug such as opiates and benzodiazepines.

## STUDY DURATION

| | |
|---|---|
| Recruitment: | 0-8 years |
| Data analysis: | 3 months |
| Total duration: | 8 years |
| End of study: | Last patient, last visit. |

## ASSESSMENT OF EFFICACY

All data collected will be analysed for any evidence that Entonox is not an efficacious form of sedation in gastroscopy. Data will be reviewed by the investigators to ensure participant safety is a priority.

Participants will be asked about any adverse effects experienced. These will be documented and reported in accordance with regulatory requirements and Trust policy. The sponsor will be informed of all adverse events.

## ADVERSE EVENTS

### Definitions

**Adverse Event (AE):** any untoward medical occurrence in a patient or clinical study subject.

Patients will be closely monitored for adverse events from the point of joining the study (consent) until they leave the endoscopy department. Between this point and 72hrs post procedure only serious adverse events will be identified and recorded by the research team contacting the patient at 72 hours.

As the patient is receiving Midazolam or Entonox for sedation and pain relief then the following events are expected and therefore will not be recorded as adverse events:

- Mild sedation
- Euphoria
- Dizziness
- Headache
- Dry mouth
- Tiredness
- Nausea
- Vomiting
- Paraesthesia

*Over* sedation requiring reversal agents ie flumazenil for midazolam should be recorded as an AE.

**Serious Adverse Event (SAE):** any untoward and unexpected medical occurrence or affect that:

- **Results in death**

- **Is life-threatening** – *refers to an event in which the subject 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*
- **Requires hospitalisation, or prolongation of existing inpatients' hospitalisation**
- **Results in persistent or significant disability or incapacity**
- **Is a congenital anomaly or birth defect**

Medical judgement should be exercised in deciding whether an AE is serious in other situations. Important AEs that are not immediately life-threatening or do not result in death or hospitalisation but may jeopardise the subject or may require intervention to prevent one of the other outcomes listed in the definition above, should also be considered serious.

**Common** side effects of Entonox are:

Euphoria, nausea, headache, dizziness, dry mouth, tiredness and paraesthesia.

**Uncommon** side effects of Entonox are:

Usually due to frequent or prolonged usage and include raised intercranial pressure, bowel distension, middle ear damage, rupture of eardrums, respiratory depression, inactivation of Vitamin B12/folate leading to neurological toxicity and megaloblastic anaemia/agranulocytosis.

**Rare** side effects of Entonox are:

High dose oxygen may increase risks of amiodarone induced adult respiratory distress syndrome, bleomycin pulmonary toxicity, paraquat pulmonary toxicity.

Entonox will also diffuse rapidly into air-containing body cavities, which can result in a temporary increase in either pressure and/or volume depending upon distensibility. This can result in significant morbidity and even death.

If any serious uncommon or rare adverse events occur the study will be suspended until the event is fully assessed by the Chief Investigator, Sponsor, Medicines and Healthcare Regulatory Agency (MHRA) and Research Ethics Committee (REC) as per the reporting procedure below.

**Causality**

Investigators will be required to record their opinion as to whether the SAE as defined above was related to the study medication. It is accepted that a causality assessment is not always available at the time of the initial report (see reporting procedure below), however, this opinion should be provided as soon as possible to ensure regulatory reporting timelines are met.

**Expectedness**

The Sponsor team will assess the SAE for expectedness. A limited number of specifically delegated reviewers on behalf of the Sponsor will assess the expectedness of reported events. When assessing expectedness, reviewers should refer to the following reference safety information documentation:

| Study drug | Document used as Reference Safety Information | Relevant section |
|---|---|---|
| Entonox | Current Summary of Product Characteristics (held by BOC) | 4.8 |
| Midazolam | Current Summary of Product Characteristics (held by ADVANZ Pharma) | 4.8 |

**Reporting procedure**

All adverse events should be reported. Depending on the nature of the event the reporting procedures below should be followed. Any questions concerning adverse event reporting should be directed to the Chief Investigator in the first instance. All project team members will be GCP trained.

All such events, whether expected or not, should be recorded in the CRF, a member of the research team will:

- review all documentation (e.g. hospital notes, laboratory and diagnostic reports) relevant to the event
- record the event and relevant comments in the subject's medical notes/endoscopy report on HICCS (or source data where this is not the medical notes)
- record the event in detail on a case record form to allow analysis at a later stage.

The Chief Investigator will keep the Sponsor, REC and Regulatory Authority informed of any relevant significant findings. At the conclusion of the study all adverse event/reactions, recorded during the study will be reviewed and subsequent conclusions included in the final study report.

If it becomes apparent during monitoring of the study that there are multiple minor adverse events relating to the study drug then a discussion with the study team, sponsor and ethics committee will be mandatory and the study may have to be stopped prematurely.

## Serious Adverse Events (SAE)

Immediately (within a maximum of 24 hours) after a member of the research team becoming aware of a serious adverse event the sponsor must be notified, by emailing the completed SAE/SUSAR reporting form (provided by the Sponsor) to Research.Office@rbch.nhs.uk. The initial report will include as much information as is available at the time.

After the initial report the Investigator will actively follow up the subject. The Investigator (or delegated person) will provide follow-up information when new information is available or as requested by the Sponsor team. The Sponsor team, in collaboration with the Chief Investigator, are responsible for informing the regulatory bodies as required. SAE's will be followed up until the SAE has resolved or a decision for no further follow up has been taken by the Sponsor team.

Suspected Unexpected Serious Adverse Reactions (SUSARs) will be reported to the MHRA in line with The Medicines for Human Use (Clinical Trials) Regulations 2004.

The reporting period for SAE's for this study is 72 hours from dose administration. This means that any events that occur within 72 hours of study drug administration, will be reporting according to the Sponsor's standard operating procedures.

## PATIENT WITHDRAWAL/VIOLATIONS

Participants will be advised that they may withdraw their consent to participate in the study at any time.

If it is not possible for the patient to tolerate the procedure with the allocated treatment, then alternative sedation, as per standard of care, will be given to the patient by the Endoscopist. If this occurs, it will be recorded as an incomplete procedure and the reason documented. All other data points will continue to be collected including the post procedure follow up.

If the patient wishes to withdraw consent from the study then it will be discussed with the patient if they are happy for the data to continue to be used. The patient's wishes will be followed and the conversation will be clearly documented in the patient's medical/research notes and in a file note.

## DATA RECORDING

### Data Collection

Data will be collected on the proforma and entered onto the electronic case report form (eCRF). The following will be recorded.

- Time of the administration of entonox or midazolam
- Time the procedure was completed
- Time from procedure end to discharge from the unit
- Total amount of midazolam given and time it was given.
- Questions about the patients experience, comfort scale and discomfort questionnaire.
- If the procedure could not be completed and the reasons for this
- Any adverse events experienced
- Contact patient over the phone within 72 hours post procedure to repeat their comfort level score.
- Concomitant medications related to adverse events

## OUTCOME MEASURES

### Primary outcome measure

The primary endpoint of percentage of patients with a score of 4 or 5 on the 5-point comfort scale, as measured by the patient, will be compared between the midazolam and entonox groups, per protocol.

The results will be analysed per-protocol; (defined as the data from any patient who received study medication).

### Secondary outcome measures

- Percentage of patients with a score of 4 or 5 on the 5-point comfort scale, as measured by the endoscopy nurse, will be compared between the midazolam and Entonox groups, per protocol.
- Percentage of procedures completed, per protocol.

- Comparison of procedure time, defined as start time to end time in the per protocol population, between the two groups.
- Comparison of procedure start time to discharge time in the per protocol population between the two groups.
- Number of patients with adverse events.
- Comparison of VAS scores between the two groups (per protocol).
- The number of people who moved from a score of 4/5 on the modified GRS to <3 at 72 hours post-procedure.

## SOURCE DATA/DOCUMENTS/CONFIDENTIALITY

The participants' electronic and paper medical records will be used for the purposes of recording source data for the procedure. All research related data will be collected through a proforma and the standard gastroscopy care plan. The required data will then be transcribed into the electronic Case Report Form. Paper copies of the study data will also be kept in a file and transferred onto a secure NHS electronic patient record (EVOLVE). The Data Protection Act (2018), Caldicott Principles and GDPR (2016) will be adhered to at all times.

## STATISTICAL CONSIDERATIONS

This sample size will provide 100 participants allocated to receive Entonox plus anaesthetic throat spray, and 100 participants to receive midazolam plus anaesthetic throat spray. This will provide the power to detect a 6% difference between the two forms of sedation using the Comfort Score Scale. If recruitment is more difficult than anticipated, then 150 patients will enable a power detection of 7%.

This sample size was decided upon based on a published study comparing entonox with midazolam and pethidine in colonoscopy which had a sample of 137 patients, and acceptable comfort score in 97% of patients who receive midazolam and throat spray in our department. The sample size was calculated as a non-inferiority study with power to detect a 6% difference between the two methods of sedation.

The primary endpoint of percentage of patients with a score of 4 or 5 on the 5-point comfort scale will be compared between the midazolam and entonox groups using the chi-squared test or the Fisher's exact test if the numbers in some categories are small. A 1-sided 95% confidence interval for the difference in percentage with scores 4 or 5 between the treatment groups will be calculated. The visual analogue scale will be summarised using means and standard deviations and a 95% confidence interval for the difference between

the treatment groups calculated. The t-test will be used to compare mean scores on the visual analogue scale between the treatment groups. If the distributions of the visual analogue scale are skewed, medians and interquartile ranges will be used and the treatment groups compared using the Mann-Whitney test.

## ETHICAL CONSIDERATIONS

The ethical risks in this study are minimal. The use of pharyngeal anaesthesia and midazolam is as for routine care and although Entonox is widely used in various settings including as an adjunct in lower GI endoscopy, it may not meet the expectations of participants in terms of sedation. Major side effects are not reported.

The Chief Investigator has obtained approvals from the Research Ethics Committee and NHS R&D department. The study will be conducted in accordance with the recommendations for physicians involved in research on human subjects adopted by the 18th World Medical Assembly, Helsinki 1964 and later revisions.

## SAFETY MEASURES

Standards of safety and quality will be monitored using the modified Global Rating Scale as for all endoscopic procedures. The outcome of each participant in this study will be reviewed by the CI/co-investigator within 2 working days of recruitment to identify any safety concerns. Any complications which arise during or after the procedure will be managed according to the clinical judgement of the endoscopist and hospital policy, e.g. if a patient's oxygen saturations drop to less than 92%, then the procedure may be abandoned as clinically appropriate. They will be recorded as adverse events and related concomitant medications recorded appropriately.

## QUALITY ASSURANCE/QUALITY CONTROL

This study will adhere to the principles outlined in the UK Policy Framework for Health and Social Care Research (2017). It will be conducted in compliance with the protocol, the Data Protection Act and other regulatory requirements as appropriate.

The study will be monitored and audited in accordance with ICH GCP requirements by the Sponsor. Compliance with the protocol by investigators and participants will be scrutinized and reported. The study will be monitored by the Sponsor at regular intervals throughout.

## END OF STUDY

At the end of the study the Chief Investigator will submit an end of study report to the Sponsor, MHRA and REC. The study will be archived in accordance with Trust policy.

## PUBLICATION POLICY

The Chief Investigator will retain ownership of all data arising from this trial. The intention is to publish this research in a specialist peer reviewed scientific journal on completion of the study. The results may also be presented at scientific meetings and/or used for other academic research purposes. The Investigators will be involved in reviewing drafts of the manuscripts, abstracts, press releases and any other publications arising from the study. They will retain final editorial control.

All data collected will be anonymised.

## SPONSOR

University Hospitals Dorset NHS Foundation Trust is the Sponsor for this research study. For further information regarding the Sponsorship of this study please contact the R&D Office at:

Rm501, 5th Floor
Royal London House
Christchurch Road
Bournemouth
BH1 3LT
01202 962376

## FUNDING

The study will be funded by University Hospitals Dorset NHS Foundation Trust. The study will be managed and conducted by the study team and the Sponsor.

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