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STUDY PROTOCOL

Full Title

A multicentre prospective cohort study to investigate the current management of patients undergoing anti-reflux surgery in the United Kingdom: ARROW (Audit & Review of Anti-Reflux Operations & Workup)

The ARROW study team

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Design: Multicentre, prospective audit of current clinical practice.

Abstract

Background

There are a variety of surgical and endoscopic interventions available to treat gastroesophageal reflux disease. There is, however, no consensus on which approach is best.

The aim of this national audit is to describe the current variation in United Kingdom (UK) clinical practice in relation to anti-reflux surgery and to report adherence to available clinical guidelines.

Method

This national audit will be conducted at centres across the UK using the secure online web platform ALEA. The study will comprise two parts: a registration questionnaire and a prospective multi-centre audit of anti-reflux surgery. All participating centres will be required to complete the registration questionnaire comprising details regarding pre-, peri- and post-operative care pathways and whether or not these are standardised within each centre. Following this, a 12-month multi-centre prospective audit will be undertaken to capture data including patient demographics, predominant symptoms, pre-operative investigations, surgery indication, intra-operative details and post-operative outcomes within the first 90 days.

Conclusion

Variation in surgical practice and outcomes after elective surgical intervention are an important quality metric within healthcare. This study will identify and explore variation in the processes and outcomes following anti-reflux surgery within the UK using a collaborative cohort methodology. The results generated by this audit will facilitate local and national quality

improvement initiatives and generate new possibilities for future research in anti-reflux interventions.

Introduction

Gastroesophageal reflux disease (GORD) is a common condition, affecting 10-20% of the Western population[1,2]. In addition to having a detrimental effect on quality of life, GORD is a risk factor for the development of Barrett's metaplasia[3,4] and oesophageal adenocarcinoma[5]. Primary treatments include lifestyle modification and proton pump inhibitors (PPIs) which are generally well tolerated. Some patients continue to have refractory symptoms and others cannot tolerate, or do not wish to take, long-term medication. In these cases anti-reflux surgery (ARS) may be a therapeutic option[6–8]. Current guidelines from the National Institute of Health and Care Excellence (NICE) reflect this, with consideration of laparoscopic fundoplication recommended for patients with a confirmed diagnosis of acid reflux and who are not suitable for long term acid suppression therapy[9].

Despite national guidelines and published evidence from randomised controlled trials (RCTs)[13–15], there is a lack of consensus regarding the most effective ARS technique, and whether procedures should be tailored to a particular patient's symptomology, nature of reflux disease or oesophageal motility. Technical uncertainties in fundoplication (the most common procedure) include the extent of dissection (i.e. hiatal dissection and division of short gastric vessels[14]), wrap formation (i.e. partial, full, anterior or posterior[15–17]), whether gastropexy is required[18,19], and the method of crural repair[20] (including whether this should be undertaken or mesh utilised to reinforce the repair[21]). In addition to fundoplication, other minimally invasive techniques such as LINX™[10], Stretta™[11] and EsophyX™[12] are available, although the precise role of these novel treatments remains to be clearly defined (Appendix 1). There is also anecdotal inconsistency in selection of patients for surgery and in the use of preoperative assessment investigations, despite recommendations from the Association of Upper GI Surgeons (AUGIS)[22], British Society of Gastroenterology (BSG)[23], and the recent International

Consensus Regarding Preoperative Examinations and Clinical Characteristics Assessment to Select Adult Patients for Antireflux Surgery (ICARUS) guidelines[24].

Specific aspects of these guidelines include the need for oesophageal manometry to be performed prior to consideration of anti-reflux surgery which was a strongly endorsed recommendation in the ICARUS and BSG guidelines[23,24]. The primary purpose of oesophageal manometry in the setting of anti-reflux surgery is to identify any major oesophageal motility disorder, gastro-oesophageal outflow obstruction or absence of contractility in order to prevent anti-reflux surgery being performed in patients with a primary motility disorder such as achalasia or diffuse oesophageal spasm[23,24]. Other recommendations include the need for pre-operative oesophagogastroduodenoscopy (OGD) within 12-months of anti-reflux surgery in order to identify the presence of Barrett's oesophagus (and grade dysplasia where present) and assess the size and configuration of any hiatal hernia[24]. These factors can provide important information for operative planning, and although precise timing of OGD prior to anti-reflux surgery has not been specifically studied, a timeframe of having been performed within 12-months of surgery has been selected based on expert opinion[24].

A previous study has highlighted significant variation in England in relation to the provision of ARS, although clinical outcomes were comparable[25]. Variations included the rate of conversion to open procedures, 30-day reintervention or readmission and rates of other adverse events. Unplanned re-admission or re-operation have both been demonstrated as useful quality measures within general surgery, as these issues may be representative of problems relating to the primary procedure itself[26,27]. AUGIS have provided specific recommendations that all units performing ARS should have a rate of conversion to open surgery of under five percent, 30-

day readmission rate of under ten percent, and rate of unplanned return to theatre within 30-days of less than five percent[22].

The aim of this national audit is to describe the current variation in United Kingdom (UK) clinical practice in relation to ARS, to compare adherence to current guidelines and report short-term outcome measures (readmission and re-operation rate). The study will focus on patient selection, pre-operative investigations, operative procedure and techniques, post-operative care and short-term outcomes. This variation will be compared to recommendations from national and international guidelines[22–24].

Rationale of ARROW study and hypothesis

It is known that there is considerable variation in the provision of ARS in England[25]. We aim to undertake a UK wide multicentre study to determine the extent of the variation in practice of anti-reflux surgery. During this analysis, current UK practice will be compared against a number of reported quality standards (Table 1).

Table 1: Details of audit standards utilised for the purposes of the current study.

Source	Measure	Evidence	Expectation
British Society of Gastroenterology (BSG) Guidelines[23] ICARUS Guidelines[24]	Oesophageal manometry is mandatory in the work-up of patients for anti-reflux surgery	Documentation in patient care record	100%
ICARUS Guidelines[24]	In patients with non-erosive GORD Reflux monitoring is mandatory in the work-up of patients for anti-reflux surgery	Documentation in patient care record	100%
ICARUS Guidelines[24]	Endoscopy is mandatory in the work-up of patients for anti-reflux surgery and has to be carried out in the last year prior to anti-reflux surgery	Documentation in patient care record	100%
The Provision Of Services For Upper Gastrointestinal Surgery Association of Upper GI Surgeons (AUGIS)[22]	Patients undergoing anti-reflux surgery should have this procedure completed laparoscopically (Unit level:<5% open conversion rate)	Documentation in patient care record	95%
The Provision Of Services For Upper Gastrointestinal Surgery AUGIS[22]	Patients undergoing anti-reflux surgery should not have an unplanned readmission (Unit level <10% readmission rate at 30 days postoperatively)	Documentation in patient care record	90% (unit level)
The Provision Of Services For Upper Gastrointestinal Surgery AUGIS[22]	Patients undergoing anti-reflux surgery should not have an unplanned reoperation (Unit level <5% reoperation rate at 30 days postoperatively)	Documentation in patient care record	95%

Although other recommendations are available within each of these clinical guidelines, these audit standards have been specifically chosen pragmatically as each can be objectively measured as part of the current audit and were strongly endorsed by the reporting guidelines as listed above[22–24]. Other recommendations within these guidelines were not selected for measurement within the present audit as they may have related to patient selection (and therefore not possible to capture data from those patients not selected for ARS based on the current methodology), or were considered to be potentially subjective and therefore difficult to define as a specific audit standard. Full details of all standards reported within these guidelines are provided in Appendix 2 alongside details of the rationale for excluding those which were not included as specific audit standards for the current study.

Study group

The study has been devised following a research development meeting held under the oversight of Royal College of Surgeons and AUGIS into unmet research need in upper gastrointestinal (UGI) Surgery. The study group has been formed of UGI surgeons and trainees who have expressed interest in this project and is operating under the umbrella of AUGIS.

Study approach

The study will comprise two parts: a registration questionnaire and a prospective multi-centre audit of laparoscopic anti-reflux surgery.

All participating centres will be required to complete the registration questionnaire (Appendix 3), comprising specific details about pre-, peri- and post-operative care pathways and whether or not these are standardised within each centre. Following this, a 12-month multicentre prospective audit will be undertaken.

Local registration with institution audit department / Caldicott guardian

Each centre will be responsible for registering the ARROW study with their local audit department and Caldicott guardian. Research ethics approval is not required for this study and this has been confirmed by the use of the online National Research Ethics Service (NRES) decision tool (http://www.hra-decisiontools.org.uk/research/, accessed 13/12/2019, Appendix 4). Inclusion in this study will not have any effect upon an individual patient's clinical pathway. Once ARROW has been registered with a local audit department, confirmation of this should be submitted to the ARROW steering committee by email to arrowsurgerystudy@gmail.com.

Eligible patients

All patients aged 18 and over, undergoing primary or revisional ARS (and/or para-oesophageal hernia repair for reflux symptoms) of any type will be eligible for inclusion. As well as fundoplication, patients undergoing LINX™, Stretta™ or EsophyX™ for reflux symptoms will be eligible for inclusion. Patients undergoing gastric bypass surgery following a primary referral for management of reflux symptoms will also be eligible for inclusion. Those referred initially as part of a weight-management pathway will be excluded, as will individuals undergoing conversion to gastric bypass for reflux following previous bariatric surgery. Patients undergoing ARS as part of treatment of a non-reflux related upper gastrointestinal condition (such as during treatment for achalasia or upper gastrointestinal cancer) will be excluded. Patients undergoing para-oesophageal hernia repair for non-reflux related symptoms will also be excluded.

Patients will be identified from theatre scheduling systems, multi-disciplinary team meetings and co-ordination with the lead upper gastrointestinal (UGI) surgeon in each centre.

Eligible centres and surgeons

All centres and surgeons undertaking ARS will be eligible to take part. There will be no restrictions on volume of practice. Centres within the National Health Service and private healthcare sector will be eligible for inclusion. Eligible centres will be identified through the National Research Collaborative network, individual surgical trainee research collaboratives (which encompass hospitals from most areas of the UK) and AUGIS. Regions without collaboratives will be identified and specific trainees targeted in order to ensure coverage from all areas of the UK.

Previous studies estimated that 2,400 anti-reflux procedures are completed in England per year[25]. We hope to capture a minimum of 25% of procedures over a 12-month period (with the additional benefit of collecting data from centres in the rest of the United Kingdom not included in previous Hospital Episode Statistics databases). We anticipate a minimum of 600 procedures to be recorded in this dataset. The number of cases recorded will not be capped.

Each centre will have a nominated lead surgeon who will be assisted by other team members to undertake patient identification, collection of a full dataset and entry into the study registry. Prior to publication, each lead surgeon will be responsible for collating a list of contributors from their site.

Data collection

Details of the data collection form are provided in Appendix 5. Data will be collected in the following categories:

- Demographic details
- Referral details
- Predominant symptoms
- Pre-operative investigations
- Indications for surgery
- Intra-operative details
- Post-operative details
- Details of any readmission
- Post-operative patient outcomes at last follow up point

Data management

ARROW will use ALEA Clinical (www.aleaclinical.eu) to host electronic records. Collaborators will be granted online access to the survey section of the study and on completion of the survey and evidence that they have registered ARROW with their local audit department they will be provided access to the prospective patient entry section. Collaborators will be asked to complete electronic Case Report Forms (eCRFs) for each patient in a timely manner using source documents from each individual case.

Data will be collected and retained in accordance with local laws and regulations, for example the General Data Protection Regulation (2018) in the UK. The Lead Surgeon at each site is responsible for ensuring the accuracy, completeness, and timeliness of the data. Any study documents will be retained in a secure central location at the University of Southampton during and after the study has finished. During the study, all data will be reported in pseudo-anonymised form and identified by the assigned participant number. Individual sites will only have access on ALEA to data collected via their specific site, including that which links a

participant to their assigned participant number. The administrative centre (University of Southampton) will have access via ALEA to all data except that which links a participant to their assigned participant number, from all investigation sites. Ultimate responsibility for security and safety of data submitted to ALEA rests with the Professor Tim Underwood and the University of Southampton Clinical Informatics Research Unit.

Only the Lead Surgeon at each site and authorised personnel should enter or change data in the electronic Case Report Forms (eCRFs) in ALEA. An audit trail will be incorporated into the eCRFs whereby any changes to the data originally entered will be documented. A table of all changes including the original value, new value, field, relevant visit details, individual responsible for changes and why the changes were made, will be stored in a table in the study database. Further details regarding data collection and storage via the ALEA online platform are provided in Appendix 6.

Quality of the data entered into the eCRF data fields will be controlled by limiting free text fields, drop down options and predefined data formats. Range checks for chosen fields will automatically appear where data points are outside of a pre-specified range. Verification and explanation for unexplained data point will be required and will subsequently appear in a query log for the study team to check.

Data validation

Data completeness from individual centres for all study fields should be 95% or greater. If data completeness is less than 95% then the local study team will be required to investigate. Failure to do so will be considered by the steering committee, and data from that centre may not be

included in the final analysis. Individual units will be asked to nominate an independent data validator as part of the study team who will review 10% of submitting patient files and 25% of data points within these submissions. The overall responsibility for data completeness and accuracy will rest with the lead Consultant for that institution.

Data analysis

Results will be prepared in accordance with the guidelines as set by the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) statement for observational studies[28]. Data will be collated and analysed in clinically relevant categories, and chi-square tests used, where appropriate, to detect differences in proportions between groups. Procedures performed for missing data, if identified, will include multiple imputation.

Results will be analysed to compare adherence to the established audit standards as detailed in Table 1.

An initial pilot data collection period will occur at five UK hospitals (Musgrove Park, North Bristol, University Hospital Bristol, Southampton, and Brighton) prior to commencement of the study in order to test the feasibility of the collection of proposed data points using the ALEA eCRF. Sites will be required to pre- register for the audit and obtain local study approval as per institution policy prior to commencement of the study.

Proposed Study Timeline

Data collection and analysis will be completed along the following timeline:

- 1st February 2020 to 29th February 2020 – Pilot study period within five United Kingdom centres.
- 1st April 2020 to 31st March 2021 – Main study data collection period.

- 29th June 2021 – Main study 90-day follow up ends.
- 2nd Sept 2021 – Central data submission anticipated to be complete.
- 30th Dec 2021 – Anticipated that independent data validation completed.
- 28th March 2022 – Initial data analysis anticipated to be complete.

Discussion

Variation in surgical practice and outcomes after elective surgical intervention are an important quality metric within healthcare. This study will identify and explore variation in process and outcome after anti-reflux surgery within the United Kingdom using a collaborative cohort methodology. The results generated by this audit will facilitate local and national quality improvement initiatives and generate new possibilities for future research in anti-reflux interventions.

Dissemination of results

This study will follow the previously reported approach for dissemination amongst surgical research collaboratives. Local teams will retain access to their own data to facilitate local quality improvement. The full dataset will be reported at national and international scientific congresses and will contribute to peer-reviewed publications and national quality improvement initiatives.

Authorship

Manuscript preparation following data analysis will be undertaken by a writing committee. All members of the ARROW protocol writing group, steering committee, lead surgeons and team members for individual centres will be Pubmed citable collaborators as part of the ARROW study group. Units who fail to submit data, or whose data is incomplete (as outlined above)

will be excluded from the authorship list. Prior to publication, each lead surgeon will be responsible for collating a list of authors from their site.

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APPENDIX 1

Novel interventions for GORD and their mechanism of action

Novel Interventions for GORD

LINX	Magnetic Sphincter Augmentation	Ethicon, Somerville, NJ, USA
Stretta	Radio-frequency stimulation of Lower Oesophageal Sphincter	Restech, Houston, TX, USA
EsophyX	Transoral/Endoscopic Incisionless Fundoplication	EndoGastricSolutions, Redmond, WA, USA
IM RefluxStop	Implant to augment angle of His	Implantica, Baar, Switzerland

APPENDIX 2

Details of clinical recommendations considered for inclusion as audit standards and reasons for exclusion where applicable.

Audit Standard	Included as audit measure	Reason for exclusion
ICARUS Guidelines[24]		
ARS can be considered for patients with typical symptoms of heartburn, with a good response to PPI.	No	Measures of patient selection for ARS not being collected as part of ARROW.
Patients with functional heartburn and patients with eosinophilic oesophagitis are poor candidates for ARS.	No	Measures of patient selection for ARS not being collected as part of ARROW.
Patients with morbid obesity and patients with substance abuse are not excluded from ARS.	No	Measures of patient selection for ARS not being collected as part of ARROW.
Endoscopy (during the last year) is mandatory prior to referral for ARS.	Yes	N/A
Patients with GORD symptoms and a hiatal hernia, Barrett's oesophagus or erosive oesophagitis grade B or higher at endoscopy are good candidates for ARS.	No	Measures of patient selection for ARS not being collected as part of ARROW.
Patients without erosive oesophagitis are not excluded from ARS.	No	Measures of patient selection for ARS not being collected as part of ARROW.
There is no need to obtain routine biopsies of the distal oesophagus in patients considered for ARS.	No	Not possible to develop audit standard to measure adherence against.
A barium X-ray should be obtained in patients with a suspicion of a hiatal hernia or short oesophagus when considered for ARS.	No	Potential subjective interpretation of guidelines would make measurement of audit standard potentially inaccurate.
Patients with GORD symptoms and a hiatal hernia on X-ray are good candidates for ARS.	No	Measures of patient selection for ARS not being collected as part of ARROW.
Patients with GORD symptoms and a para-oesophageal hernia on X-ray are good candidates for ARS in addition to para-oesophageal hernia repair.	No	Measures of patient selection for ARS not being collected as part of ARROW.
A short oesophagus on barium X-ray does not preclude the patient from ARS.	No	Measures of patient selection for ARS not being collected as part of ARROW.
Oesophageal manometry and oesophageal pH monitoring (±impedance) are mandatory prior to	Yes	N/A

referral for ARS (pH monitoring only mandatory in patients with non-erosive reflux diseas).		
Patients with normal pH-monitoring off PPI are poor candidates for ARS.	No	Measures of patient selection for ARS not being collected as part of ARROW.
Response to baclofen does not enhance patient eligibility to ARS.	No	Measures of patient selection for ARS not being collected as part of ARROW.
There is no need to asses gastric emptying rate in patients considered for ARS.	No	Not possible to develop audit standard to measure adherence against.
British Society of Gastroenterology (BSG) Guidelines[23]		
Any staff member performing manometry or reflux monitoring should either be fully trained or accredited by the AGIP in this procedure or supervised by a fully trained and accredited practitioner.	No	Oesophageal physiology quality measures beyond the scope of ARROW study.
All patients undergoing manometry for the investigation of dysphagia should undergo at least one form of adjunctive testing (eg: larger volumes of water, solid/viscous swallows or a test meal).	No	Oesophageal physiology quality measures beyond the scope of ARROW study.
All patients undergoing manometry to investigate dysphagia should have previously undergone endoscopy and mucosal biopsy.	No	Only patients with reflux symptoms (rather than dysphagia alone) included and performance of endoscopy prior to ARS captured separately.
All patients undergoing reflux monitoring should have manometry to guide probe placement	No	Oesophageal physiology quality measures beyond the scope of ARROW study.
All patients undergoing ARS should have manometry to exclude major oesophageal motility disorders.	Yes	N/A
All impedance recordings should be manually edited to ensure accurate reflux symptom association	No	Oesophageal physiology quality measures beyond the scope of ARROW study.
All patients should have at least two methods of symptom association assessed (eg: SAP and SI).	No	Oesophageal physiology quality measures beyond the scope of ARROW study.
All patients should undergo reflux monitoring prior to ARS.	No	Included for patients with non-erosive reflux disease as per ICARUS guidelines.

The Provision Of Services For Upper Gastrointestinal Surgery Association of Upper GI Surgeons (AUGIS)[22]		
Unit rate of conversion to open surgery during ARS of <5%	Yes	N/A
Unit readmission rate following ARS of <10% within 30 days of surgery	Yes	N/A
Unit re-operation rate at 30 days following ARS of <5%	Yes	N/A
Laparoscopic ARS minimum activity per surgeon of >5 per annum	No.	Important to gain accurate clinical representation of current United Kingdom practice in this audit which units will voluntarily participate in. Therefore necessary to also include any potential low-volume clinical centres for ARS.

APPENDIX 3

Surgeon Survey

Registration

Name of surgeon:

Email address:

Please enter all hospitals the surgeon works for and select the main one:

- Hospital name …
- County …
- Main one: ☐

Surgeon Survey

Date completed …

Please select job role:

- Consultant ☐
- Associate Specialist ☐

Year first appointed as a consultant/associate specialist:

Primary practice:

- Benign upper GI ☐
- Bariatric ☐
- OG resectional ☐
- HPB resectional ☐
- General Surgery ☐
- Colorectal ☐

Please estimate how many anti-reflux surgery cases you perform per year:

- NHS …
- Private …

Which preoperative investigations would you consider **compulsory** for anti-reflux surgery:

Tick all that apply

- OGD ☐
- Upper GI contrast study ☐
- CT ☐
- 24-hour pH monitoring ☐
- Wireless pH monitoring (BRAVO) ☐
- 24-hour impedance monitoring ☐
- High resolution manometry ☐
- Standard resolution manometry ☐
- Other ☐

Where is your oesophageal physiology testing (including pH monitoring, manometry and impedance) performed?

- NHS laboratory situated within your Trust ☐
- NHS laboratory at another hospital Trust ☐
- External laboratory ☐
- Not sure ☐

Which of the following procedures might you undertake for GORD?

- Fundoplication: ☐
- LINX: ☐
- Stretta: ☐
- EsophyX: ☐
- Roux-en-Y gastric bypass ☐
- RefluxStop™ ☐
- Other: (please name) ☐

Which of the following procedures might you perform when doing a fundoplication?

- Nissen posterior 360º ☐
- Toupet posterior 270º ☐
- Toupet posterior 180º ☐
- Dor anterior 180º ☐
- Watson anterior 120º ☐
- Partial anterior 90º ☐
- Collis: ☐
- Other ☐

Do you tailor the type of wrap performed for each individual?

- Yes, based on manometry findings ☐
- Yes, based on clinical symptoms ☐
- Never ☐

Which procedures might you perform as an intended day-case?

- Fundoplication: ☐
- LINX: ☐
- Stretta: ☐
- EsophyX: ☐
- Roux-en-Y gastric bypass ☐
- None performed as intended day case procedure: ☐
- Other: (please name) ☐

What criteria do you apply for same-day discharge following anti-reflux surgery (other than standard requirements for day-case surgery)?

- Tolerance of solid oral intake ☐
- Tolerance of liquid oral intake ☐
- Proximity of patient residence from hospital ☐
- Surgery completed by a specific time ☐
- Other (please give details): _____

Do you divide the short-gastric vessels?

- Routinely ☐
- Selectively ☐
- Never ☐

Do you perform an anterior cruroplasty?

- Routinely ☐
- Selectively ☐
- Never ☐

Do you perform a posterior cruroplasty?

- Routinely ☐
- Selectively ☐
- Never ☐

Do you perform a Collis oesophageal lengthening procedure?

- Routinely ☐
- Selectively ☐
- Never ☐

Do you repair over a bougie or orogastric tube?

- Routinely ☐
- Selectively ☐
- Never ☐

Do you maintain a prospective database of your anti-reflux surgery practice?

- Yes ☐
- No ☐

Do you record severity/symptom or quality of life scores pre-operatively?

- Routinely ☐
- Selectively ☐
- Never ☐

Do you record severity/symptom or quality of life scores post-operatively?

- Routinely ☐
- Selectively ☐
- Never ☐

Post-Op workup: Do you carry out a routine post-operative assessment of the wrap with:

OGD

- Yes ☐
- No ☐

Upper GI contrast study

- Yes ☐
- No ☐

Do you believe that anti-reflux surgery (other than gastric bypass for reflux disease) is effective for patients with obesity?

- Yes ☐
- No ☐

Do you believe that increasing patient BMI potentially influences the likelihood of a successful outcome with anti-reflux surgery (other than gastric bypass for reflux disease)?

- Yes ☐
- No ☐

What is the upper limit of a patient's BMI that you would perform anti-reflux surgery (other than gastric bypass for reflux disease)?

- <25 ☐
- <30 ☐
- <32 ☐
- <35 ☐
- <40 ☐
- <45 ☐
- <50 ☐
- No limit ☐
- Alternative criteria used ☐

Do you request patients with obesity complete a pre-operative liver shrinkage diet prior to surgery?

- Yes ☐
- No ☐
- Selectively ☐

If yes do you use specific clinical or BMI criteria for advising patients to complete this?

- Do not utilise ☐
- BMI>32 ☐
- BMI>35 ☐
- BMI>40 ☐
- BMI>45 ☐
- BMI>50 ☐
- Central pattern obesity ☐
- Clinical examination of abdominal wall stiffness in RUQ ☐
- Alternative criteria used ☐
- No specific criteria ☐

Do you discharge patients home with an anti-emetic?

- Yes ☐
- No ☐
- Selectively ☐

Do you discharge patients home with opioid analgesia?

- Yes ☐
- No ☐
- Selectively ☐

Are you the lead surgeon for the Arrow Audit at any institution?

- Yes ☐
- No ☐

(if Yes opens Institutional survey)

Institutional survey

Estimated number of cases of anti-reflux surgery performed annually at your institution …

Number of surgeons completing anti-reflux surgery at your institution: …

Is oesophago-gastric resectional surgery performed at your institution?

- Yes ☐
- No ☐

Is bariatric surgery performed at your institution?

- Yes ☐
- No ☐

Does your institution have set funding criteria for anti-reflux procedures? If so, please describe or supply a copy of funding criteria?

- Yes ☐
- No ☐
- Details: _____

Is your institution required to apply to the local Clinical Commissioning Group for funding of anti-reflux surgery on an individual patient basis?

- Yes ☐
- No ☐

Preop workup: Which of the following does your institution have access to for the investigation of reflux:

- OGD ☐
- Upper GI contrast study ☐
- CT ☐
- 24-hour pH monitoring ☐
- Wireless pH monitoring (eg. BRAVO™) ☐
- 24-hour impedance monitoring ☐
- High resolution oesophageal manometry ☐
- Standard resolution oesophageal manometry ☐

Where is your oesophageal physiology testing (including pH monitoring, manometry and impedance) performed?

- NHS laboratory situated within your Trust ☐
- NHS laboratory at another hospital Trust ☐
- External laboratory ☐
- Not sure ☐

Does your institution maintain a prospective database of anti-reflux surgery practice?

- Yes ☐
- No ☐

Does your institution have access to a benign UGI MDT to discuss patients prior to anti-reflux surgery?

- Routinely ☐
- Selectively ☐
- Only prior to revision surgery ☐
- Never ☐

If your institution holds a benign UGI MDT is this held:

- Locally ☐
- Regionally (in person) ☐
- Regionally (via tele-link) ☐

If your institution holds a benign MDT who are your core members?

- UGI Surgeons ☐
- Gastroenterologists ☐
- Radiologist ☐
- Physiologist ☐
- UGI Nurse Specialist ☐
- Other (details below) ☐
- Details of other team members: _____

Does your institution give a standardised pre-operative information sheet/booklet to patients?

- Yes ☐
- No ☐

Does your institution have a standardised advice sheet for post-operative diet?

- Yes ☐
- No ☐

Do all surgeons in your institution follow the same post-operative diet protocol?

- Yes ☐
- No ☐

What routine clinical follow up does your institution perform?

- In-person clinic appointment (doctor) ☐
- In-person clinic appointment (nurse) ☐
- Telephone clinic (doctor) ☐
- Telephone clinic (nurse) ☐
- None ☐

APPENDIX 4

APPENDIX 5

Case Report Form (CRF)
[Completed via online portal through ALEA]

1. Registration

Patient Initials: _____

Date of birth: _ _/_ _/_ _ _ _

2. Patient History

2.1 Demographics

Sex: Male ☐
Female ☐

ASA: I ☐
II ☐
III ☐
IV ☐
V ☐

Height: _____ metres

Weight: ____ Kg

OR

BMI (derived): _____

Previous Thoracic Surgery: Yes ☐
No ☐
Unknown ☐

If Yes Thoracoscopic ☐
Open ☐
Both ☐

Previous abdominal surgery: Yes ☐
No ☐
Unknown ☐

If yes: Laparoscopic ☐
Open ☐
Both ☐
Unknown ☐

Any Co-morbidities: Yes ☐
No ☐
Unknown ☐

If yes:
Charlson comorbidity index:

Acute myocardial infarction	☐
Cancer	☐
Cerebral vascular accident	☐
Congestive heart failure	☐
Connective tissue disorder	☐
Dementia	☐
Diabetes	☐
Diabetes complications	☐
HIV	☐
Liver disease	☐
Metastatic cancer	☐
Paraplegia	☐
Peptic ulcer	☐
Peripheral vascular disease	☐
Pulmonary disease	☐
Renal disease	☐
Severe liver disease	☐

Total score: ____

Smoking status:

Current smoker	☐
Ex-smoker	☐
Never smoked	☐
Unknown	☐

Vaping status:

Current vaper	☐
Ex- vaper	☐
Never vaped	☐
Unknown	☐

2.2 Referrals

Date of referral:

Source of referral:
- GP/Primary care ☐
- Gastroenterology ☐
- ENT ☐
- Respiratory ☐
- Transplant ☐
- Other hospital specialist ☐
- Unknown ☐

If not primary care:
Was this referral from:
- The same hospital ☐
- Another hospital ☐

Duration of symptoms at referral:
- 0 - 6 months ☐
- 6 - 12 months ☐
- 1 - 2 years ☐
- 2 - 5 years ☐
- > 5 years ☐
- > 10 years ☐

Current use of PPI:
- Yes (continuous) ☐
- Yes (intermittent) ☐
- No ☐
- Unknown ☐

Current use of H_2 Antagonist (eg Ranitidine):
- Yes (continuous) ☐
- Yes (intermittent) ☐
- No ☐
- Unknown ☐

2.3 Symptoms

Heartburn

Daytime heartburn:
- Yes ☐
- No ☐
- Unknown ☐

Nocturnal heartburn:
- Yes ☐
- No ☐
- Unknown ☐

Positional heartburn: Yes ☐ No ☐ Unknown ☐

Documented as responsive to PPI:
Yes ☐ No ☐ Unknown ☐

Regurgitation

Daytime regurgitation: Yes ☐ No ☐ Unknown ☐

Nocturnal regurgitation: Yes ☐ No ☐ Unknown ☐

Positional regurgitation: Yes ☐ No ☐ Unknown ☐

Other Symptoms

Epigastric/chest pain: Yes ☐ No ☐ Unknown ☐

Sleep disturbance: Yes ☐ No ☐ Unknown ☐

Dysphagia: Yes ☐ No ☐ Unknown ☐

Chronic cough: Yes ☐ No ☐ Unknown ☐

Chronic laryngitis: Yes ☐ No ☐ Unknown ☐

Dental erosions: Yes ☐ No ☐ Unknown ☐

Any Patient Reported Outcome Measures used:

No ☐
GERDQ ☐
GSFQ ☐
Other – please specify

2.4 Workup

OGD performed: Yes ☐ No ☐ Unknown ☐

Date of most recent OGD: …

OGD findings:

Barrett's Oesophagus: Yes ☐ No ☐ Unknown ☐

Oesophagitis: No ☐ Yes - Grade A ☐ Yes - Grade B ☐ Yes - Grade C ☐ Yes - Grade D ☐ Yes - Grade Unknown ☐ Unknown ☐

Stricture: Yes ☐ No ☐ Unknown ☐

Hiatus Hernia: Yes ☐ No ☐

Hiatus Hernia Size: Small<2cm ☐ Medium 2-5cm ☐ Large >5cm ☐ >50% intrathoracic Stomach ☐ Total intrathoracic Stomach ☐

24h pH monitoring performed: Yes ☐
No ☐
Incomplete ☐

Total time pH <4 ….hrs ….mins or ….%
Symptom Correlation Index ….% or value 0-1
Symptom Association Probability ….% or value 0-1

DeMeester Score ….

Impedance monitoring performed Yes ☐
No ☐
Incomplete ☐

Impedance results:
Acid reflux ☐
Weak-acid reflux ☐
Non-acidic reflux ☐

Manometry performed: Yes ☐
No ☐
Incomplete ☐

If yes: High resolution ☐
Standard resolution ☐

Peristalsis:

Normal ☐

Weak ☐

Absent ☐

Lower Oesophageal Sphincter Pressure: …
Integrated Relaxation Pressure IRP: …

Contrast swallow performed: Yes ☐
No ☐

CT performed: Yes (oral contrast) ☐
Yes (no contrast) ☐
No ☐

Hiatus Hernia Size: Small<2cm ☐
Medium 2-5cm ☐
Large >5cm ☐
>50% intrathoracic Stomach ☐
Total intrathoracic Stomach ☐

Other intra-abdominal organs within hiatus hernia
None ☐
Colon ☐
Pancreas ☐
Spleen ☐
Other ☐

Other investigation performed: [Details] _____

3. Surgery

3.1 – Revisional surgery

Is this a revisional procedure?

Yes ☐
No ☐

If Yes:
How long ago was the primary procedure?

< 6 months ☐
6-12 months ☐
1-5 years ☐
>5 years ☐
>10 years ☐

What was the primary procedure?

Fundoplication ☐
LINX ☐
EsophyX ☐
Stretta ☐
Gastric bypass ☐
Other – please specify

Has this patient had previous revisions?

Yes ☐
No ☐

Indication for this revision:

Recurrence of symptoms ☐
Dysphagia ☐

3.2 Primary Indication for Surgery

What is the primary indication for surgery? (Tick one only)

- Symptoms not sufficiently controlled by PPI ☐
- Not compliant with PPI ☐
- Side effects with PPI ☐
- Symptoms adequately controlled but patient prefers surgical management: ☐
- Intra-oesophageal complications of GORD ☐
- Lung transplant patient ☐
- Non-oesophageal symptoms/complications of GORD ☐
  - Info: Chronic cough, dental erosions, aspiration pneumonia etc.
- Other: [Details] _____

3.3 Surgery

Date of operation: _ _/_ _/_ _ _ _

Grade of primary surgeon:
- ST3-6 ☐
- ST7-8 ☐
- Staff Grade ☐
- Associate Specialist ☐
- Post CCT Fellow ☐
- Consultant ☐

Was the procedure a training case:
- Yes(in part) ☐
- Yes(in full) ☐
- No ☐
- Unknown ☐

Was the operation as part of an unplanned admission:
- Yes ☐
- No ☐
- Unknown ☐

Procedure performed:
- Fundoplication ☐
- LINX ☐
- EsophyX ☐
- Stretta ☐
- Gastric bypass ☐
- Other – please specify

Was the planned procedure performed:
- Yes ☐
- No ☐
- Unknown ☐

If No: Procedure planned:
- Fundoplication ☐
- LINX ☐
- EsoPhyx ☐
- Stretta ☐
- Gastric bypass ☐
- Other – please specify

Was the procedure planned as a day case:
- Yes ☐
- No ☐
- Unknown ☐

Procedure Specific Details

Procedure Duration:	<1hr	☐
	1-2hrs	☐
	2-3hrs	☐
	3-4hrs	☐
	>4hrs	☐

Fundoplication intra-operative details [Additional drop-down menu]

Approach:	Open	☐
	Laparoscopic	☐
	Robotic	☐
	Endoscopic	☐
	Lap converted to open	☐
	Robotic converted to lap	☐
	Robotic converted to open	☐
	Endo converted to lap	☐
	Endo converted to open	☐
Posterior cruroplasty:	Yes	☐
	No	☐
Anterior cruroplasty:	Yes	☐
	No	☐
Suture material:	Absorbable	☐
	Non-absorbable	☐
Sizing of repair:	Bougie/OG tube	☐
	Visual	☐
Mesh used:	No	☐
	Biologic	☐
	Synthetic – non-absorbable	☐
	Synthetic – absorbable	☐
	Composite – synthetic	☐
	Composite – synthetic + biological	☐

If mesh used:

Mesh fixation:	Absorbable sutures	☐
	Non-absorbable sutures	☐
	Metal tacks	☐
	Non-metal tacks – absorbable	☐
	Non-metal tacks – non-absorbable	☐

Hepatic vagal fibres preserved:	Yes	☐
	No	☐
Anterior vagus preserved:	Yes	☐
	No	☐
Posterior vagus preserved:	Yes	☐
	No	☐
Division of short gastrics:	Yes	☐
	No	☐
Wrap anterior/posterior:	Anterior	☐
	Posterior	☐
Wrap 180/270/360:	90	☐
	120	☐
	180	☐
	270	☐
	360	☐
Oesophageal stitch:	Yes	☐
	No	☐
Diaphragmatic stitch:	Yes	☐
	No	☐
Collis (oesophageal lengthening procedure):	Yes	☐
	No	☐
Other modifications: [Details]	…	

Roux-en-Y Gastric Bypass:

Alimentary limb length	…
Biliary limb length	…

LINX intra-operative details [Additional drop-down menu]

LINX Size:	10	☐
	11	☐
	12	☐
	13	☐
	14	☐
	15	☐
	16	☐
	17	☐
	18	☐

All Procedures:

Intraoperative complications:	Yes	☐
	No	☐
Pneumothorax (requiring drain):	Yes	☐
	No	☐
Major visceral injury:	No	☐
	Oesophagus	☐
	Stomach	☐
	Spleen	☐
	Liver	☐
	Colon	☐
	Small Bowel	☐
	Heart/ Pericardium	☐
	Other	…
Major vascular injury:	No	☐
	Aorta	☐
	Inferior Vena Cava	☐
	Other	…
Estimated blood loss:		
	Minimal	☐
	100-500ml	☐
	500-1000ml	☐
	1-2l	☐
	>2l	☐

3.3 Post-Operative

Date of discharge:	…	
Delayed discharge?	Yes	☐
	No	☐
If yes: Reason:	Dysphagia	☐
	Inadequate oral intake	☐
	Vomiting	☐
	Pain	☐
	Pneumonia	☐
	Pneumothorax	☐
	Urinary retention	☐
	Social	☐
	Other – please specify	

Investigations:

- None ☐
- Laparoscopy ☐
- Contrast swallow ☐
- CT ☐
- OGD ☐
- CXR ☐
- Other – please specify

(able to select multiple options)

Interventions:

- None ☐
- Antibiotics ☐
- Chest drain ☐
- Return to theatre ☐
  - If ticked – please specify ….
    - Date of operation …
- Pneumatic dilatation ☐
- Other – please specify

(able to select multiple options)

Complications?

- Yes ☐
- No ☐

If yes: Number of Complications (per Clavien Dindo):
(on index admission)

- Grade 1 …
- Grade 2 …
- Grade 3a …
- Grade 3b …
- Grade 4a …
- Grade 4b …
- Grade 5 …

Readmission within 90 days? (Including admission for day case procedure/investigation)

- No ☐
- Yes ☐

If yes:

Date of readmission …

Date of discharge from readmission …

Reason:

- Dysphagia ☐
- Inadequate oral intake ☐
- Vomiting ☐
- Pain ☐
- Pneumonia ☐
- Pneumothorax ☐
- Urinary retention ☐
- Social ☐
- Other – please specify

Investigations:

- None ☐
- Laparoscopy ☐
- Contrast swallow ☐
- CT ☐
- OGD ☐
- CXR ☐
- Other – please specify

(able to select multiple options)

Interventions:

- None ☐
- Antibiotics ☐
- Chest drain ☐
- Return to theatre ☐
  - If ticked – please specify ….
    - Date of operation …
- Pneumatic dilatation ☐
- Other – please specify

(able to select multiple options)

Complications?

- Yes ☐
- No ☐

If yes:

Number of Complications (per Clavien Dindo):
(on index admission)

- Grade 1 …
- Grade 2 …
- Grade 3a …
- Grade 3b …
- Grade 4a …
- Grade 4b …
- Grade 5 …

4. Outcomes

Follow-up within 90 days of operation:

Routine Outpatient-Doctor	☐
Routine Outpatient-Nurse	☐
Unplanned re-presentation	☐
Telephone - Doctor	☐
Telephone - Nurse	☐
No follow-up planned	☐
Did not attend follow-up	☐

If followed up:

Date of first follow-up: _ _/_ _/_ _ _ _

Discharged after first follow-up:

Yes	☐
No	☐

Any Patient Reported Outcome Measures used:

No	☐
GERDQ	☐
GSFQ	☐
Other – please specify	

Resolution of symptoms?

Yes	☐
No	☐
Partial	☐

Ongoing PPI used:

Yes	☐
No	☐

APPENDIX 6

Data storage technical details

ALEA eCRF is an electronic Case Report Forms service for the data collection in clinical trials. It provides a comprehensive, user friendly forms service which can be used with a standard browser running on any computer connected to the internet. The system has been validated and has been certified by registered auditors to be in compliance with regulation, such as the FDA's CFR 21 Part 11.

ALEA consists of a study design (SD) component and a data management (DM) component. During setup and maintenance of the study, the SD component is used to create or modify the design of the study. The DM component exists on a test/development, acceptance and production instance. The test/development instance provides an environment to test the setup and modifications for the CIRU (Clinical Informatics Research Unit) programmers while the acceptance instance is used by the client for user acceptance testing. The production instance is used once the study is live. These environments are physically isolated, and do not share data and accounts.

SD and the test/development environment of data management are hosted in Amsterdam. The acceptance and production environments of DM are hosted in Den Bosch. This location is a secured, ISO 27001 certified data centre operated by InterConnect BV in Den Bosch, the Netherlands. FormsVisions' Quality Assurance includes formal disaster management procedures for management of issues related to the operational environment. Measurements include failover, local data recovery, and site recovery. Each physical server is equipped with RAID5 disk redundancy, redundant power supply and redundant network connectivity. The server facilities in Den Bosch include both hot standby and cold standby servers. Hot standby

servers (DBSHV3 and DBSSQL2) allow for near-instant failover to a running server in case of physical server failure. In case of logical server failure, cold standby servers (DBSHV4, DBSHV5) provide local data recovery in case the site is operational. In case of site failure, the disaster recovery procedure provides transfer of all operational services to our hosting facilities in Amsterdam.

APPENDIX 7

Definitions

Gastro-Oesophageal Reflux Disease	A condition which develops when the reflux of stomach contents causes troublesome symptoms and/or complications[1].
Heartburn	A burning sensation in the retrosternal area (behind the breastbone) [1].
Regurgitation	The perception of flow of refluxed gastric content into the mouth or hypopharynx[1].
Typical Reflux Syndrome	Heartburn and regurgitation are the characteristic symptoms of the typical reflux syndrome[1].
Nonerosive Reflux disease	The presence of troublesome reflux-associated symptoms and the absence of mucosal breaks at endoscopy[1].
Reflux Oesophagitis	Defined endoscopically by visible breaks of the distal esophageal mucosa[1].
Reflux Stricture	A persistent luminal narrowing of the esophagus caused by GORD[1].
Dysphagia	A perceived impairment of the passage of food from the mouth into the stomach[1].
Lower Oesophageal Sphincter	A specialized thickened region of the circular muscle layer of the distal oesophagus

1. Vakil, N; van Zanten, S; Kahrilas, P; Dent, J; Jones R. The Montreal Definition and Classification of Gastroesophageal Reflux Disease: A Global Evidence-Based ConsensusCMEThe Montreal Definition and Classification of GERD. Am J Gastroenterol. 2006 (101):1900–20.