ALiCE
Audit of LaparoscopIc CBD Exploration

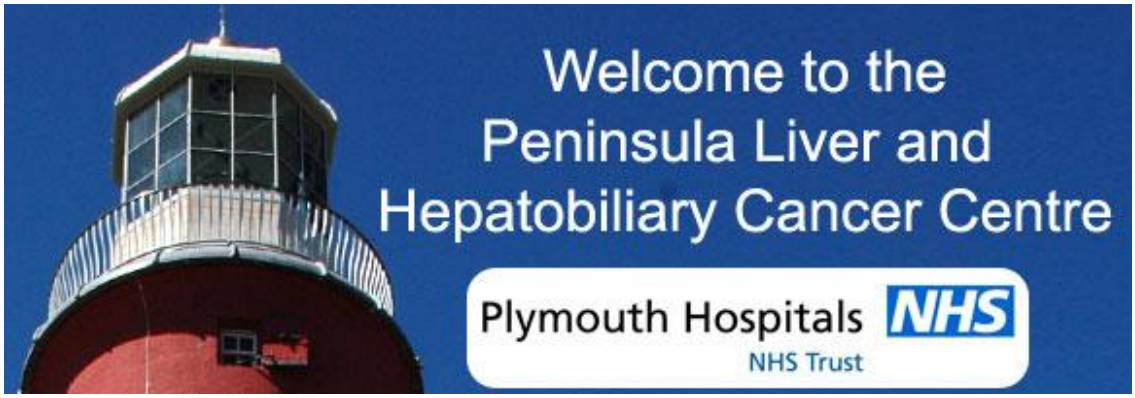
UNIVERSITY OF PLYMOUTH

ALiCE Study

Audit of Laparoscopic Common Bile Duct Exploration

UK, Multi-centre, Prospective, Population-based Cohort Study

Variation in clinical practice of Laparoscopic Common Bile Duct Exploration and Surgical Outcomes



RESEARCH PROTOCOL

Full Title

Audit practice of Laparoscopic Common Bile Duct Exploration

A UK, Multi-centre, Prospective, Population-based study
Variation in the clinical practice of Laparoscopic Common Bile Duct Exploration and Surgical Outcomes

Short Title

ALiCE Study –**A**udit of **L**aparoscop**i**c **C**BD **E**xploration

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Background

Patients with symptomatic gallstones within the gallbladder are recommended to undergo laparoscopic cholecystectomy (LC) for treatment and prevention of further complications. However, 10-15% of patients undergoing LC have concurrent common bile duct stones (choledocholithiasis-CBDS)[1]. Traditionally, these patients would undergo endoscopic retrograde cholangiopancreatography (ERCP) prior to LC. Laparoscopic common bile duct exploration (LCBDE) has emerged in the last decade as an alternative to ERCP and has the advantage that it can be performed at the time of LC, as a single combined procedure.

Randomised controlled trials comparing the single-stage procedure (LC with simultaneous LCBDE) with the two-stage procedure (pre-operative ERCP+ LC or LC + post-operative ERCP) have demonstrated equivalent outcomes in terms of mortality, success rates, complications and recurrence. However, the single-stage procedure results in shorter hospital length of stay and reduced costs. Additionally, it results in fewer procedures.[2-4]

A meta-analysis including 13 RCTs comparing single stage with the two-stage procedure has demonstrated a higher stone clearance rate, lower conversion to other procedure, perioperative complications, stone retention, stone recurrence, total procedure time, length of stay and total cost in preference of LCBDE, while mortality was similar[5]. Despite the emerging superiority of LCBDE over ERCP, LCBDE is not routinely performed in most centres in the UK. Possible factors underlying this could be due to the long-established existence of an ERCP service within these centres, non-availability of theatre space and time, lack of training in LCBDE and lack of equipment that is essential for intra-operative imaging and bile duct exploration. Only a few centres, in the UK, have published their experience of bile duct exploration. However, in comparison with the number of patients estimated to present with choledocholithiasis to these centres, the numbers included in these series are relatively low. Furthermore, a published report of trends in the management of bile duct stones in the USA from 1998 to 2013 has demonstrated a decline in the practice of LCBDE, with evidence ERCP is the favoured strategy[6]. It is unclear whether this practice has changed recently in the UK and USA.

In the LCBDE, the common bile duct (CBD) is accessed either through the cystic duct (trans-cystic approach, TC-LCBDE) or directly through an incision on the bile duct (trans choledochal approach, TD-LCBDE). The TC-LCBDE approach has a lower complication profile (almost similar to LC) compared to the TD approach. However, the practical success of a trans-cystic approach is dependent on several variables, and these include cystic duct (CD) diameter, the length, location and angle of CD insertion into the CBD, stone size, and stone location. In the trans-choledochal approach, CBD is explored through a choledochotomy incision, and stones are removed with the help of retrieval baskets. Following CBD clearance, the choledochotomy is closed with or without a biliary stent or a T-Tube, and an abdominal drain. However, TD-LCBDE is only recommended in a sufficiently dilated CBD to avoid the risk of biliary stricture.

The major complication from TD-LCBDE is bile leak, usually from the choledochotomy site and occurring in up to 17% of patients in some studies[2]. In some patients, this is self-limiting, while in others, it can result in biliary peritonitis requiring further surgery. In some patients, bile leak can be persistent, requiring ERCP and sphincteromy+/- stent insertion. As outcomes have only been published from a few high-volume centres[7,8] the rate of bile leak and other complications from low volume units is unknown. Additionally, the impact of different approaches to LCBDE and methods of duct closure on bile leak is unknown. There is also a paucity of data on the number of hospitals performing LCBDE and the use of T-tube/biliary stent following bile duct exploration. The insertion of a trans-ampullary biliary stent at the time of LCBDE has been shown to reduce the bile leak rate by 50% in one small non-

randomised study[9], though no further studies, randomised or otherwise, have sought to verify this finding.

There is high variability amongst surgeons' opinions and techniques regarding LCBDE. The variations include patient selection, indications for LCBDE, the necessity of pre-operative bile duct imaging versus intraoperative imaging, exploration with a choledochoscope versus radiologically guided exploration, type of choledochotomy (longitudinal versus transverse incision), primary biliary closure vs T-tube use, method of choledochotomy closure, and use of abdominal drains following choledochotomy. Thus, the outcomes following LCBDE, including complications, length of stay, and re-intervention rates are not known on a national scale. To date, this variability between surgeons and surgical departments has not been quantified, and no attempt has been made to find associations between these variables and outcomes.

Aim

This audit aims to find out the current practice of LCBDE in the UK, evaluate the outcomes of LCBDE and to identify the risk factors for complications associated with LCBDE.

Currently, there are no studies that have examined the LCBDE rate and overall complications associated with LCBDE in the UK. There are also no studies which have examined the variations in the practice of LCBDE and their impact on complication rates. Evaluation of LCBDE in the UK will provide us with the necessary data regarding variability in practice, outcomes, and complications associated with LCBDE. It will also help us to understand the possible reasons for low uptake of LCBDE, and to plan future research studies with a particular focus on reducing post-operative complications.

This study will prospectively collect data on all LCBDEs performed in the UK. Data collected will include demographics, pre-operative blood results and imaging, intra-operative techniques and events and postoperative data including bile leak rates, and other complications. This will be explained in detail in the Data Collection section of the protocol.

Outcomes

Primary outcomes:

- Overall 30-day morbidity (all post-operative complications graded using Clavien-Dindo Classification)

Secondary outcomes:

- Duration of surgery, intra-operative and post-operative complications, length of stay, stone clearance rate, 30 and 90-day all-cause mortality.

Patient Selection

Inclusion Criteria

- Patients undergoing Laparoscopic Common Bile Duct Exploration (LCBDE) for choledocholithiasis between 01/11/2020 and 31/04/2021

*(*including patients requiring LCBDE after failed ERCP)*

Exclusion Criteria

Any patient:

- <16 years old
- Undergoing common bile duct exploration for reasons other than choledocholithiasis (stent removal etc.)
- Undergoing planned open common bile duct exploration

Methods

Register Audit/Service Evaluation

- Each Local Team will register the study as Audit/Service Evaluation with each trust.
- Please see **Appendix 2** and **Appendix 4** for more details.

Case identification

Patients to be identified prospectively by the Local Teams.
Please use all available resources to identify the patients prospectively:

- Booking coordinators
- Surgical secretaries
- Theatre Information Teams
- Daily operating lists
- Emergency operating lists and coordinators

Case identification period

- **6 months (Nov 2020-Apr 2021)**

Data Collection and Entry

- Data will be collected by Local Data Collection teams in each trust in **RedCap** (https://www.project-redcap.org/). No patient identifiable information will be entered onto **RedCap**. Data Collection teams will hold a reference log on a trust computer which will have the only link between the **RedCap ID** and the patient's **Hospital number**. This will stay with the local teams and will not be transferred to main site investigators (Plymouth). This will only be used for audit purposes or for data corruption/validation issues.

- Data Collection points:

A. **PRE-OPERATIVE DATA**:
   - Patient demographics (age, BMI, ASA etc.)
   - Indication for LCBDE
   - CBD diameter (mention the diameter if it is available)
   - Type and number of pre-operative investigations
   - Details of pre-op imaging (US, MRCP, CT, EUS etc.)
   - Co-morbidities
   - Number of days in the hospital prior to LCBDE

B. PERI-OPERATIVE DATA:
   - Category of operation (acute or elective)
   - Use of antibiotics
   - Use of Intra-operative cholangiogram (IOC)/Intra-operative ultrasound (IOUS)
   - Approach to LCBDE: trans-cystic, trans-choledochal
   - Choledochotomy incision type (longitudinal, transverse, T-shape)

- Method of closure (interrupted, continuous)
- Type of suture material used for the closure of choledochotomy (monofilament/braided, absorbable/non-absorbable)
- Biliary (common bile duct) stent/T-tube Y/N
- Surgical drain Y/N
- Conversion from laparoscopic to open (the reason for conversion)
- Duration of operation
- Intra-operative complications (bleeding, CBD injury etc.)

C. POST-OPERATIVE DATA:

- The total length of hospital stay (LOS) in days
- Post-op length of stay in days
- 30-day morbidity
- 90-day mortality
- Details of all post-operative complications
- Retained stone rate
- Post-op ERCP rates
- Readmission rate within 30- days
- Reasons for readmission

Data collation

- Data will be collated in RedCap by the main site investigators (Plymouth)
- Outcome data specific to each surgeon will not be collected.
- **We will analyse anonymised hospital data; Individual surgeons, hospitals or NHS Trusts will not be identified and will be kept strictly anonymous.**

Data analysis

- We require 95% completed data for each patient. It is the responsibility of the lead consultant to check. This is also a requirement for authorship.

- Data analysis: Continuous variables will be summarised with means and standard deviations. Frequencies, percentages, and graphs will be used for categorical variables. Univariate and multivariate analyses will be evaluated using appropriate statistical techniques. As a hypothesis-generating, exploratory investigation, no hypothesis testing will be undertaken and comparisons of the outcomes of interest made through summary measures, with uncertainty expressed through the presentation of 95% confidence intervals.

Project Timeline

REGISTRATION OF AUDIT/SERVICE EVALUATION LOCALLY	Aug 2020 - Sep 2020
DATA COLLECTION WINDOW	Nov 2020 – Apr 2021
DATA ANALYSIS	Apr 2021 – June 2021
MANUSCRIPT WRITING AND PUBLICATION	July 2021 – onwards

Study Structure

Study Management Group

The Management Group will be responsible for the overall study and designing the protocol. They will also be responsible for data analysis and dissemination, including the write-up.

Data Collection Teams:

Each team should comprise of one of each of the staff categories listed below:

Lead Consultant (PI)

- A local Consultant Surgeon in either HPB or OG Surgery. Their responsibilities:
  - Named consultant for the local audit registration process
  - Permanent point of contact for the audit
  - Supporting the local teams with the data collection and mediating any issues with data supply departments (audit departments, coding teams etc.)
  - PI will also be responsible for the security of the data collection spreadsheet. The data collection sheet will have to be held for two years after completion of data collection.
  - Responsibility of the data collection accuracy and completeness (>95%)

Lead Trainee

- Should be a Surgical Speciality/Core Trainee or a Trust Doctor. Their responsibilities:
  - Recruit and manage the other members of the data collection team
  - Ensure data collection completeness and robustness
  - Register the audit locally in keeping with local procedures
  - It is expected for the lead trainee to remain in the trust at least six months after commencement of the audit. If they rotate to another trust, they have the option to remain Lead or transfer the responsibility to another trainee.

Foundation doctor or medical student

- A foundation doctor or medical student is encouraged to be recruited in the team.
  - They can help with data collection and data entry under the supervision of the Lead trainee.
- One person per team, 2 in specialist units

Appendix 1: Audit Standards

- *"Patients with abnormal liver function tests (with or without dilated bile ducts) on ultrasound but without frank jaundice or cholangitis, have <15% risk of CBD stones and may proceed to LC without additional pre-operative imaging. Per-operative on- table cholangiography followed by laparoscopic bile duct exploration or post-operative ERCP is a more cost-effective and safe approach."* (AUGIS/RCSEng Commissioning guide 2016)

- *"Patients with symptomatic CBD stones should undergo CBD stone extraction by ERCP or surgical bile duct exploration (laparoscopic or open). A single-stage LC & LBDE offers improved resource utilisation, reduced costs and lower length of stay compared to a two-stage ERCP and LC strategy. Patients with asymptomatic gallstones in the bile ducts should also be considered for stone extraction."* (AUGIS/RCSEng Commissioning guide 2016)

- *"It is recommended that, in patients undergoing laparoscopic cholecystectomy, transcystic or transductal laparoscopic bile duct exploration (LBDE) is an appropriate technique for CBDS removal. There is no evidence of a difference in efficacy, mortality or morbidity when LBDE is compared with perioperative ERCP, although LBDE is associated with a shorter hospital stay. It is recommended that the two approaches are considered equally valid treatment options."* (BSG Updated guideline on the management of common bile duct stones)

- *"It is suggested that training of surgeons in LBDE is to be encouraged in order to decrease the number of interventions required to manage CBDS."* (BSG Updated guideline on the management of common bile duct stones)

- *"People with symptomatic or asymptomatic common bile duct stones are offered bile duct clearance and laparoscopic cholecystectomy"* (NICE Guideline 188 - 2014 with surveillance evidence 2018)

- *"People with symptomatic or asymptomatic common bile duct stones have bile duct clearance either:*
    - *surgically at the time of laparoscopic cholecystectomy or*
    - *with endoscopic retrograde cholangiopancreatography (ERCP) before or at the time of laparoscopic cholecystectomy. "*

  (NICE Guideline 188 - 2014 with surveillance evidence 2018)

Appendix 2: Audit /Service Evaluation Registration Toolkit

STEPS for participating in the ALICE Study

1. Complete the online form to express an interest in participating in the study (https://alice-study.org)

2. Select a "Lead Consultant or PI" and a "Lead Trainee" and email this to the Study Management Group at lcbdestudy@gmail.com who will connect you to anyone else in your trust who has expressed interest. This will allow you to build you data collection team.

3. Register ALICE as an audit or service evaluation with your trust. Follow local protocol and paperwork. Appendix 4 is the HRA Decision tool (http://www.hra-decisiontools.org.uk/research/) which classes ALiCE Study as an audit or service evaluation and not research. If you encounter difficulty, please contact the ALICE Study email, and we will try to assist you.

4. Once registered, please forward the confirmation email to the Study Management Group at lcbdestudy@gmail.com who will send you all the relevant paperwork for the study, including the Data Collection Spreadsheet.

Appendix 3: Data Collection - RedCap

- Each trust will register the audit locally. Once registered please email the Audit Approval ID to lcbdestudy@gmail.com.

- Once confirmed, a **RedCap login** will be set-up for the Data Collection Team. Please be aware each member of the team will have their own login details.

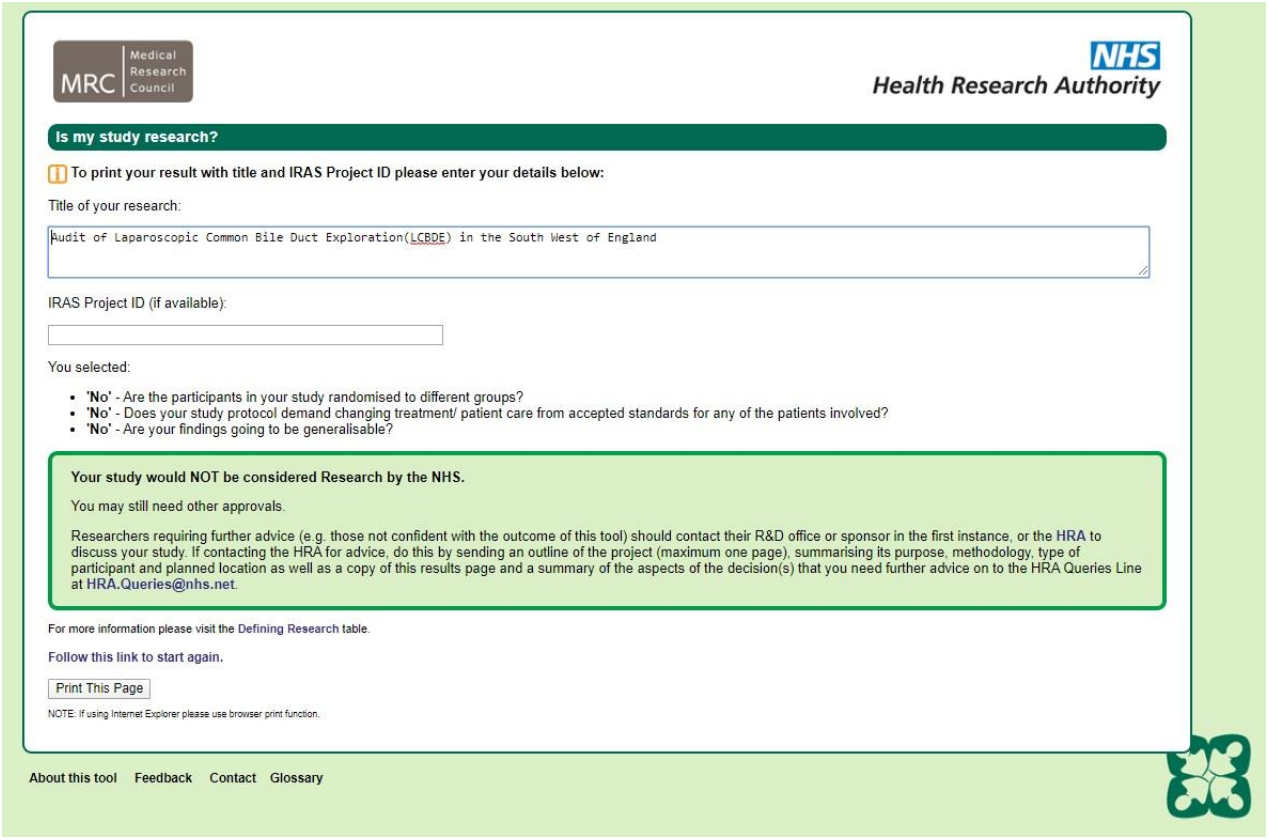
- Percentage of data completion for each patient is 95%. This is a requirement for authorship and publication.

- Each Local Team will hold a **Reference File**. This will be an Excel file, stored on a local trust computer. This file will contain the only link between the RedCap ID generated for each patient and the patient's Hospital Number. This file WILL NOT be transferred to the main site investigators (Plymouth). The Reference File will only be used for audit, data corruption or data validation issues.

- All the information entered onto **RedCap** will be fully **ANONYMOUS**. No patient identifiable information will be entered onto **RedCap**.

- At the end of data collection, the data entered must be validated by the Lead Consultant in each trust. Only validated data will be considered for analysis and publication.

Appendix 4: Health Research Authority Decision Making Tool



MRC Medical Research Council

NHS Health Research Authority

Is my study research?

To print your result with title and IRAS Project ID please enter your details below:

Title of your research:

Audit of Laparoscopic Common Bile Duct Exploration(LCBDE) in the South West of England

IRAS Project ID (if available):

You selected:

- **'No'** - Are the participants in your study randomised to different groups?
- **'No'** - Does your study protocol demand changing treatment/ patient care from accepted standards for any of the patients involved?
- **'No'** - Are your findings going to be generalisable?

Your study would NOT be considered Research by the NHS.

You may still need other approvals.

Researchers requiring further advice (e.g. those not confident with the outcome of this tool) should contact their R&D office or sponsor in the first instance, or the HRA to discuss your study. If contacting the HRA for advice, do this by sending an outline of the project (maximum one page), summarising its purpose, methodology, type of participant and planned location as well as a copy of this results page and a summary of the aspects of the decision(s) that you need further advice on to the HRA Queries Line at HRA.Queries@nhs.net.

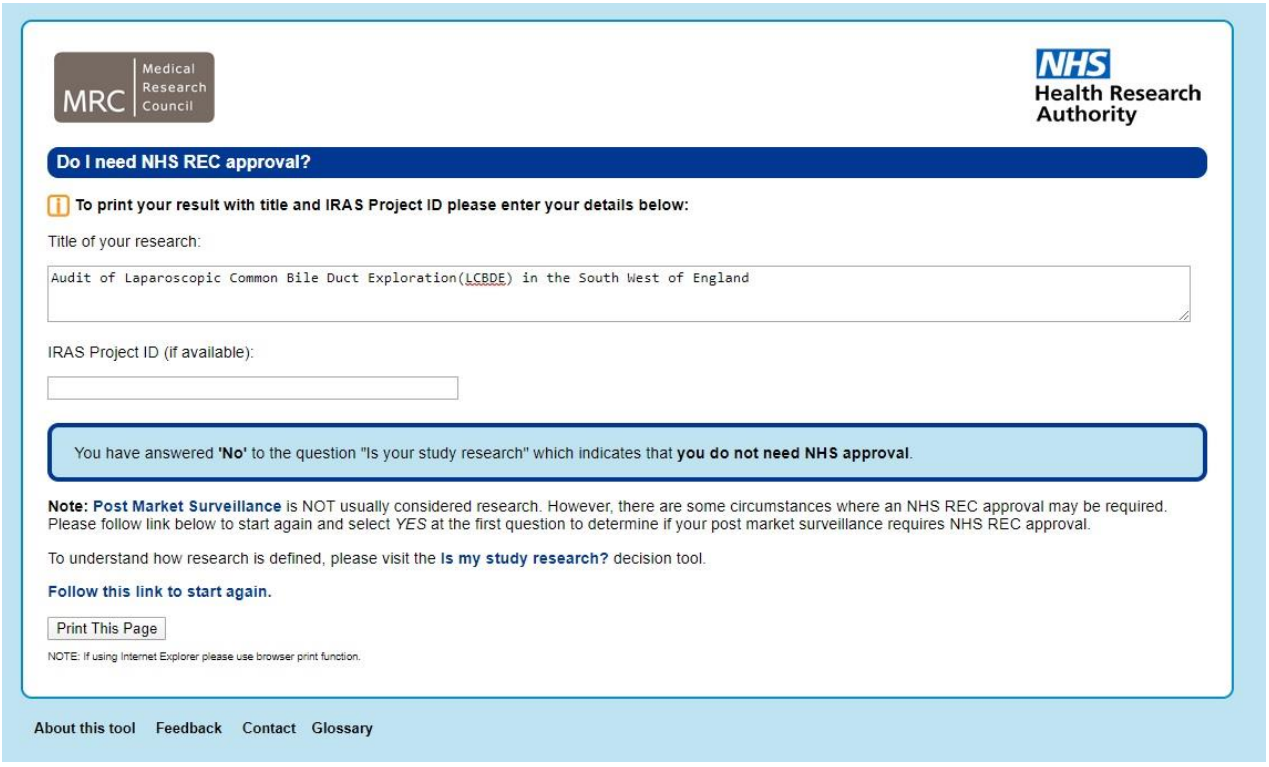
For more information please visit the Defining Research table.

Follow this link to start again.

Print This Page

NOTE: If using Internet Explorer please use browser print function.

About this tool Feedback Contact Glossary



MRC Medical Research Council

NHS Health Research Authority

Do I need NHS REC approval?

To print your result with title and IRAS Project ID please enter your details below:

Title of your research:

Audit of Laparoscopic Common Bile Duct Exploration(LCBDE) in the South West of England

IRAS Project ID (if available):

You have answered **'No'** to the question "Is your study research" which indicates that **you do not need NHS approval**.

Note: Post Market Surveillance is NOT usually considered research. However, there are some circumstances where an NHS REC approval may be required. Please follow link below to start again and select *YES* at the first question to determine if your post market surveillance requires NHS REC approval.

To understand how research is defined, please visit the **Is my study research?** decision tool.

Follow this link to start again.

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Appendix 5: Authorship

- A writing committee will write the manuscripts for publication.

- Collaborators (max 4 per hospital including Lead Consultant/PI will be eligible for citable authors part of the ALiCE Study Group). We would be using a corporate authorship model (https://bit.ly/2NIRzbS). This ensures that everyone is listed by name and PubMed citable link. (example: "ALiCE Study Group collaborators, see appendix X for full list").

- Lead Consultant/PI will oversee the validity of dataset, ensuring a complete (>95%) and the accurate dataset is returned.

- Units who fail to submit their data or the data is removed from analysis due to validity issues will be excluded from authorship list.

References

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