Protocol for a multicentre, prospective, population-based cohort study of variation in practice of cholecystectomy and surgical outcomes (The CholeS study)

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ABSTRACT

Introduction: Cholecystectomy is one of the most common general surgical operations performed. Despite level one evidence supporting the role of cholecystectomy in the management of specific gallbladder diseases, practice varies between surgeons and hospitals. It is unknown whether these variations account for the differences in surgical outcomes seen in population-level retrospective data sets. This study aims to investigate surgical outcomes following acute, elective and delayed cholecystectomies in a multicentre, contemporary, prospective, population-based cohort.

Methods and analysis: UK and Irish hospitals performing cholecystectomies will be recruited utilising trainee-led research collaboratives. Two months of consecutive, adult patient data will be included. The primary outcome measure of all-cause 30-day readmission rate will be used in this study. Thirty-day complication rates, bile leak rate, common bile duct injury, conversion to open surgery, duration of surgery and length of stay will be measured as secondary outcomes. Prospective data on over 8000 procedures is anticipated. Individual hospitals will be surveyed to determine local policies and service provision. Variations in outcomes will be investigated using regression modelling to adjust for confounders.

Ethics and dissemination: Research ethics approval is not required for this study and has been confirmed by the online National Research Ethics Service (NRES) decision tool. This novel study will investigate how hospital-level surgical provision can affect patient outcomes, using a cross-sectional methodology. The results are essential to inform commissioning groups and implement changes within the National Health Service (NHS). Dissemination of the study protocol is primarily through the trainee-led research collaboratives and the Association of Upper Gastrointestinal Surgeons (AUGIS). Individual centres will have access to their own results and the collective results of the study will be published in peer-reviewed journals and presented at relevant surgical conferences.

INTRODUCTION

Cholecystectomy is one of the most commonly performed general surgical procedures in the UK. Approximately 66 000 cholecystectomies were performed during the 2011–2012 financial year in England alone. The pathway for these patients can be divided into three distinct groups: (1) acute admission with biliary disease and the cholecystectomy performed during that acute admission (acute group); (2) planned elective admission with biliary disease and the cholecystectomy performed during that planned elective admission (elective group); and (3) all other planned cholecystectomies performed on an elective operating list for a cholecystectomy referred by their family doctor and added to the routine surgical waiting list from the outpatient department (delayed group). This is shown in figure 1.

The management of GB disease and whether patients have acute, elective or delayed operations varies widely between surgeons and hospitals. Level one evidence...
supports the role and safety of early or acute laparoscopic cholecystectomy in biliary colic, cholecystitis and gallstone pancreatitis. Population-level data from Hospital Episodes Statistics (HES) and a retrospective study from Scotland, both suggest however, that early or acute operations may be associated with poor surgical outcomes. These studies also suggest that differences in outcomes may be linked to hospital size and volume.

Different surgical outcomes are commonly used to measure quality of healthcare, such as readmissions, reoperations and mortality. In particular, reducing hospital readmissions following surgery can lower hospital costs and improve patient satisfaction. The causes of readmission after cholecystectomy have been poorly studied, but are likely to vary by hospital size, case volume and whether patients have acute, elective or delayed operations performed.

Taken together, this raises the possibility that trial evidence of common surgical procedures is not generalisable to population level, non-trial cohorts. Furthermore, differences in patient outcomes may be linked to hospital service provision. These factors both have an important impact on patients and the National Health Service (NHS), especially as trial data is in part used to inform commissioning decisions. It is not clear currently, why such variations occur in the NHS, or what the impact of these variations is on surgical outcomes.

METHODS AND ANALYSIS

Primary aim
To measure the difference in all-cause 30-day readmissions following acute, delayed and elective cholecystectomies in a contemporary, population-based cohort.

Hypothesis
The 30-day readmission rate, following risk adjustment, should be equivalent in patients following elective cholecystectomies compared with acute and delayed procedures.

Study design
We plan to undertake a multicentre, contemporary, prospective, cohort audit which will be conducted through trainee-led research collaboratives as described previously.

Setting
This study can take place in any UK or Irish hospital performing acute, elective or delayed cholecystectomies. Each centre will contribute 2 months of consecutive patient data.

Participants
Inclusion criteria: All patients over the age of 18 years who are undergoing a cholecystectomy can be entered into this audit.

Exclusion criteria: Patients having a cholecystectomy for known GB cancer, or as part of another surgical procedure for example, Whipple’s procedure, bariatric, anti-reflux or transplant operations, will be excluded.

Outcome measures
The primary outcome measure is all-cause 30-day readmission rate, which is defined as any admission following discharge which requires an overnight stay. This standard and definition is based on the Royal College of Surgeons (RCS) and the Association of Upper Gastrointestinal Surgeons (AUGIS) of Great Britain and Ireland guidance.
which states that the audit standard of less than 10% 30-day readmission rate should be reached by hospitals performing cholecystectomies. Secondary outcome measures are listed in Table 1.

### Data collection

Data will be collected in a standardised Microsoft Excel spreadsheet. It will be the responsibility of the local investigators to ensure that the data is password protected and held on local trust computer systems. Each trust/hospital site will need to identify locations where laparoscopic cholecystectomy are performed (main theatre, day-case unit, treatment centre) to ensure full capture of cases during the audit period. Patients will be identified on a daily basis from the elective operating lists and by on-call teams, at handovers, from on-call lists and from emergency theatre booking lists and logbooks. Operative data should be completed either by or with input from the operating surgeon or the assistant. All patients will be followed for 30 days following their operation. The hospital’s electronic or paper records should be checked by the team to identify any readmissions or reattendances to the hospital’s emergency department, surgical assessment unit or wards. Local arrangements may include:

- Reviewing the patient or patient’s notes during admission to identify inpatient complications.
- Check the discharge summary or letter to check for any postoperative complications.
- Check for any outpatient attendances within 30 days of surgery.

### Data validation and management

Following data collection, only data sets with ≥95% data completeness will be accepted for pooled national analysis. The consultant surgeon principle investigator (PI) at selected sites will identify an independent assessor to validate all data points, with a target of ≥98% accuracy. Overall, at least 5% of the data set will be independently validated. In addition, the independent assessor will be asked to examine operating theatre logbooks and trust data systems, to ensure case ascertainment. If the concordance between the total number of cases submitted to the trial management group is <95%, the hospital’s data will be removed from the analysis.

A standardised Microsoft Excel spreadsheet (Excel 2007; Microsoft, Redmond, Washington, USA) with preset fields will be used to collect the data. Data protection regulations at each centre will be complied with. Patient identifiable data will not be transmitted to the trial management group. Data will be submitted centrally via a secure NHS email address with all patient identifiers removed. Patient anonymised data will be then be analysed and reported by the writing committee. Outcome data specific to each individual surgeon who participates will not be collected. Anonymised hospital data will be
Table 2 Data fields

| Field                                | Options (definitions)                                                                                                                                 |
|--------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------|
| Age                                  | In years                                                                                                                                              |
| Gender                               | Male, female                                                                                                                                           |
| Body mass index                      | Individual’s body mass will be subclassified as:                                                                                                      |
|                                      | ▶ Underweight (<17.9 kg/m²)                                                                                                                                |
|                                      | ▶ Normal (18.0–24.9 kg/m²)                                                                                                                                |
|                                      | ▶ Overweight (25.0–29.9 kg/m²)                                                                                                                               |
|                                      | ▶ Moderate obesity (30.0–34.9 kg/m²)                                                                                                                          |
|                                      | ▶ Severe obesity (35.0–39.9 kg/m²)                                                                                                                             |
|                                      | ▶ Very severe obesity (>40.0 kg/m²)                                                                                                                             |
| ASA score                            | Classifies as:                                                                                                                                        |
|                                      | 1. A normal healthy patient                                                                                                                                   |
|                                      | 2. A patient with mild systemic disease                                                                                                                       |
|                                      | 3. A patient with severe systemic disease                                                                                                                 |
|                                      | 4. A patient with severe systemic disease that is a constant threat to life                                                                               |
|                                      | 5. A moribund patient who is not expected to survive without the operation                                                                               |
| Admission date                       | Day/month/year                                                                                                                                               |
| Operation date                       | Day/month/year                                                                                                                                               |
| Timing of surgery                    | Classified as: acute; elective or delayed elective                                                                                                          |
| Planned day-case                     | Yes (defined as patients who are planned to be admitted and discharged on the same day as the operation)                                                           |
| Date decision made to operate       | For ‘elective’ cases this will be the date the patient was seen in the outpatient clinic. For ‘delayed’ cases this is the date the patient was last discharged from hospital with biliary disease. For ‘acute’ cases this should be the date the decision was made to perform an acute cholecystectomy in that emergency admission |
| Preoperative indication              | *Biliary colic* (the presence of colicky right upper quadrant pain associated with gallstones or sludge on an USS, but no signs of acute cholecystitis)           |
|                                      | *Acute or chronic cholecystitis* current or previous clinical or ultrasound evidence of cholecystitis (thick-walled GB and/or pericholecystitis, USS tenderness over the GB, the presence of gallstones) |
|                                      | *Gallstone pancreatitis* (pancreatitis secondary to gallstones. Should be diagnosed using the Atlanta guidelines which state the diagnosis of acute pancreatitis requires two of the following three features: (1) abdominal pain consistent with acute pancreatitis (acute onset of a persistent, severe, epigastric pain often radiating to the back); (2) serum lipase activity (or amylase activity) at least three times greater than the upper limit of normal; and (3) characteristic findings of acute pancreatitis on contrast-enhanced CT)18 |
|                                      | *CBD stones* (as confirmed by preoperative imaging, that may or may not have been removed preoperatively)                                                  |
|                                      | *GB polyps* (hyperechoic lesions on USS imaging which have no acoustic shadowing and do not move with positional changes (and have no features of overt malignancy)) |
|                                      | *Dyskinesia* (biliary-like abdominal pain, occurring in a normal appearing GB with a functional HIDA scan showing an abnormal GB ejection fraction of less than 40%) |
|                                      | *Acalculous cholecystitis* (clinical or ultrasound evidence (thick-walled GB and/or pericholecystitis, USS tenderness over the GB, the absence of gallstones)) |
| Surgical admissions with biliary symptoms in the previous 12 months | Number of surgical admissions with biliary symptoms in the previous 12 months: 0, 1, 2, 3, 4, 5, >6                                                                 |
compared; individual surgeons, hospitals or NHS Trusts will not be identified. The required anonymous data fields are shown in Table 2. Individual centres will be surveyed at the end of the audit period to determine local policies and service provision (Table 3). Anonymous patient-level data will be linked to the results of the hospital service survey to allow detailed analysis of these variables and patient outcome.

### Anticipated recruitment

On the basis of cholecystectomy-specific HES data from England, 66 000 procedures were coded during the 2011–2012 financial year. If there is a uniform distribution of procedures performed between each of the acute care trusts and all hospitals in the UK and Ireland participate, data on 11 000 procedures could be potentially gathered prospectively. Minimum expected recruitment would be approximately 1500 procedures from 20 centres from the West Midlands.

### Study timeline

Data collection and analysis will be performed using the following timelines:

- 4 November 2013–11 December 2013—Pilot study period.
- 1 March 2014–1 May 2014—Main study data collection period.
- 1 June 2014—Main study 30-day follow-up period ends.

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**Table 2**

| Field                          | Options (definitions)                                                                 |
|-------------------------------|---------------------------------------------------------------------------------------|
| Seniority of surgeons         | ▶ <Specialty trainee (ST6)                                                             |
|                               | ▶ ST6 or above or staff grade                                                         |
|                               | ▶ Consultant                                                                          |
| Perioperative antibiotics     | ▶ Yes/no                                                                               |
| Method of operation           | ▶ Laparoscopic                                                                         |
|                               | ▶ Laparoscopic converted to open                                                       |
|                               | ▶ Open cholecystectomy                                                                 |
|                               | ▶ SILS                                                                                |
| Degree of difficulty          | **Grade I** Floppy, non-adherent gallbladder. Clear, thin cystic pedicle. Simple      |
|                               | adhesions to neck and Hartmann’s pouch only                                           |
|                               | **Grade II** Mucocele; packed with stones gallbladder. Fat-laden cystic pedicle.      |
|                               | Simple adhesions, up to the body of gallbladder                                        |
|                               | **Grade III** Deep fossa; acute cholecystitis; contracted, fibrous Hartmann’s pouch    |
|                               | adherent to CBD or with stone impaction. Abnormal anatomy; cystic duct short, dilated |
|                               | or obscured.                                                                         |
|                               | **Grade IV** Completely obscured gallbladder; empyema/gangrene                         |
|                               | Or mass. Impossible to clarify cystic pedicle. Dense, fibrous adhesions wrapping the  |
|                               | GB. Duodenum or hepatic flexure difficult to separate                                  |
| Intraoperative complications  | ▶ Bile split (intra-abdominal spillage of bile during the procedure, including        |
|                               | when removing the GB from the abdominal cavity)                                       |
|                               | ▶ Stones split (intra-abdominal spillage of stones during the procedure,               |
|                               | including as removing the GB from the abdominal cavity)                               |
|                               | ▶ Bleeding (requiring haemostatic agents (eg, Surgicel, Fibrillar, etc), extra clips,  |
|                               | suturing or conversion to open procedure)                                             |
|                               | ▶ CBD injury (will be defined as any injury to the main biliary tree and will be       |
|                               | classified using the Steward-Way Classification System (1, 2, 3, 4))                   |
| Intraoperative cholangiography| ▶ Planned (defined as the decision to perform a cholangiogram before the operation   |
|                               | starts; eg, due to surgeon preference or to assess for CBD stones)                     |
|                               | ▶ Unplanned (defined as any other reason where a cholangiogram was performed but was  |
|                               | not anticipated at the start of the operation; eg, to assess for unclear anatomy or   |
|                               | to assess for potential CBD injury)                                                   |
| CBD exploration               | Yes/no                                                                                 |
| Abdominal drain               | Yes/no                                                                                 |
| Date of discharge             | Day/month/year                                                                         |
| All-cause 30-day A&E attendance| Yes/no                                                                                 |
| All 30-day reinterventions and | Yes/no                                                                                 |
| reimaging                     | 30-day mortality                                                                       |

A&E, accident and emergency department; ASA, American Society of Anesthesiologist; CBD, common bile duct; GB, gallbladder; HIDA, hepatobiliary iminodiacetic acid; SILS, single-incision laparoscopic surgery; USS, ultrasound scan.
Statistical analysis
The report of this study will be prepared in accordance to guidelines set by the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) statement for observational studies.\textsuperscript{14} Data will be collected and analysed in clinically relevant categories, and $\chi^2$ tests used to detect differences between groups. Missing data will be analysed and multiple imputation used if required.

Binary logistic regression modelling will be used to adjust the influence of timing of surgery for key confounding variables. Data will be adjusted for patient (age, gender, American Society of Anesthesiologist (ASA) score and body mass index), disease (indication, ultrasound scan findings, the need of other imaging and endoscopic retrograde cholangiopancreatography (ERCP)), surgeon (consultant present, specialty and number of surgeons performing cholecystectomy) and hospital (number of hospital beds, university hospital, tertiary hepatopancreato-biliary services, acute admissions, ERCP services and ‘Hot’ GB lists) factors. Multivariate models will be built to produce ORs to account for the impact of predictive variables when assessing outcomes. The OR represents the odds of all-cause 30-day readmission occurring, comparing the experimental groups (acute and delayed) versus the reference group (elective). A second model will compare acute cholecystectomy against a reference of delayed cholecystectomy. Variable selection including hospital-level data will be based on those which are statistically significant at univariate analysis, and those which are clinically significant, but not statistically. Depending on data requirements, models will be developed using fixed-entry binary logistic regression, multilevel modelling and multiply imputed data sets, to compare outputs based on statistical technique.

The main strength of this project is the multicentre, prospective, contemporary methodology with independent validation of the data. This will give high quality, validated data on cholecystectomy provision and outcome throughout the UK and Ireland from a wide range of hospital types.

Limitations include the inability to assess postoperative visits to the general practitioner. In addition, a minority of patients will re-present to other hospitals with complications following surgery. However, during the audit

| Table 3 Hospital-level variables | Option (definition) |
|---------------------------------|---------------------|
| Field                           | Option (definition) |
| Location                        | England; Scotland; Wales; Northern Ireland; Republic of Ireland |
| University hospital             | Yes/no |
| Total number of beds            | <100; 100–500; 500–1000; >1000 |
| Tertiary HPB services           | Yes/no |
| ERCP services                   | Yes/no |
| Acute admissions                | Number |
| Number of consultant surgeons on the general surgery on-call rota | Oesophagogastric |
| Consultant specialties involved in performing cholecystectomies | Hepatobiliary |
| Colorectal                      | General |
| Vascular                        | Transplant |
| Endocrine                       | Other |
| Does your hospital offer dedicated ‘hot’ gallbladder theatre lists | MRCP |
| Performing an intraoperative cholangiography | Endoscopic USS |
| Additional hospital services available | Functional scans |
| CBD, common bile duct; ERCP, endoscopic retrograde cholangiopancreatography; HPB, hepatopancreato-biliary; MRCP, MR cholangiopancreatography; USS, ultrasound scan.
period, teams will also document the absolute number of patients readmitted with complications from cholecystectomy performed at other hospitals. Our study uses the standard 30 day follow-up period as this is the international standard and allows comparison with other studies. However, complications which may occur after 30 days, such as retained common bile duct stones or late biliary strictures will not be reported. In the acute group, it may not be possible to fully elucidate whether the decision to operate was due to hospital policies, surgeon preference or patient-related factors. However, we will collect data on patient, disease, surgeon and hospital factors to assess which is associated with acute cholecystectomy.

**DISCUSSION**

Variations in outcomes following common surgical procedures such as cholecystectomy are a concern for the NHS. This paper describes the protocol for a novel study to investigate how hospital-level surgical provision can affect patient outcomes using cross-sectional methodology. The results of this audit are essential to inform commissioning groups and implement changes within the NHS. Furthermore, the development of consultant PIs across the UK enables a network of new investigators who can be approached to collaborate on further studies.

**ETHICS AND DISSEMINATION**

The proposed study will not affect clinical care and compares an outcome to a defined audit standard. 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/). This has been further supported by written confirmation and advice from the Research and Development Director at University Hospitals Birmingham NHS Foundation Trust, UK. The study will be registered as a clinical audit or service evaluation at each participating hospital. Patient consent is not deemed necessary and inclusion in the study will not incur any risk to individual patients.

The generic collaborative methodology underlying protocol dissemination and collaborator recruitment has been described previously. The protocol will be disseminated primarily through the trainee-led research collaboratives (http://www.asit.org/resources/collaboratives), and members of the Association of Surgeons in Training (ASIT; http://www.asit.org), AUGIS (http://www.augis.org) and the SchoolofSurgery.org (http://www.schoolofurgery.org). A consultant surgeon PI will be designated at each hospital to facilitate coordination of the study. The protocol document and data collection tools will be made available online (http://www.choles-study.org). Individual centres will have access to their own results and the collective results of the study will be published in peer-reviewed journals and presented at relevant surgical conferences. These results can then be used to inform commissioning and implement changes within the NHS.

**Contributors** RSV and EAG contributed in the conception, design, writing and editing of the protocol. AB, MJ, PM, PS, DGM and DA contributed in the design and writing of the protocol. AB and RSV participated in the statistical analysis. EAG is the guarantor. All authors read and approved the final manuscript.

**Competing interests** None.

**Ethics approval** NRES and Research and Development Director at University Hospitals Birmingham NHS Foundation Trust, UK.

**Provenance and peer review** Not commissioned; externally peer reviewed.

**Data sharing statement** It is the intention of the study group, that once the study is completed, and the research articles stemming from the study have been published, that any remaining data that is fully anonymised and not sensitive, be made open access.

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*BMJ Open* 2015 5:
doi: 10.1136/bmjopen-2014-006399

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