RESEARCH PROTOCOL

FULL TITLE

Clinical Variation in Practice of Cholecystectomy and Surgical Outcomes: a multi-centre, prospective, population-based cohort study

SHORT TITLE

CholeS Study

CHIEF INVESTIGATORS

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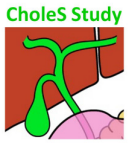

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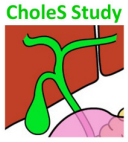
Aneel Bhangu, Anne Gaunt, Emma Hamilton, Marianne Johnstone, Paul Marriott, Pritam Singh, Philip Spreadborough and Andrew Torrance and the following Consultant Surgeons : Derek Alderson, Kay Futaba, Dion Morton, Thomas Pinkney and Sonia Puig.

1.0 PROTOCOL SUMMARY

GENERAL INFORMATION	
Short Title	CholeS Study
Full Title	**Clinical Variation in Practice of Cholecystectomy and Surgical Outcomes: a multi-centre, prospective, population-based cohort study**
Sponsor	University of Birmingham West Midlands Research Collaboration (www.wm**research**.org.uk)
Chief Investigators	Ewen A Griffiths / Ravinder Vohra
Website	www.choles-study.org
Email	Choles-study@uhb.nhs.uk
Co-ordinating Centre	University of Birmingham
STUDY INFORMATION	
Indication	To investigate the variation in practice of cholecystectomies and its effect on surgical outcomes
Design	Observational audit
Primary Outcome	All-cause 30-day readmission rates following following acute, 'delayed' and elective cholecystectomies
Secondary Outcomes	• Variations in practice of pre-operative management and intra-operative technique • Pre-operative (patient demographics, admission type, diagnostic tests) • Peri-operative (surgical approach, conversion rates from laparoscopy to open surgery, complications) • Post-operative (length of stay, complications within 30 days)
STUDY TIMELINES	
Pilot date	04/11/2013 - 11/11/2013
Main study period	01/03/2014 - 01/05/2014
Follow-up duration	30 days
End of Trial Definition	2 months
Data submission	30/06/2014
Data analysis	July/August 2014
Results available	01/09/2014
Paper submission	01/11/2014



2.0 ABSTRACT

Background: Cholecystectomy is one of the most common general surgical operations performed in the UK. Increasing proportions of patients have surgery in the acute setting for biliary colic, cholecystitis and following gallstone pancreatitis. Randomised clinical trials in acute cholecystitis and gallstone pancreatitis suggest early laparoscopic surgery performed in specialist units is safe. Despite this, management still differs between surgeons and centres across the UK. This has been highlighted in a recent commissioning guide produced jointly by the Royal College of Surgeons and the Association of Upper Gastrointestinal Surgeons of Great Britain and Ireland. The impact of these variations on outcomes is unclear.

Aim: To investigate surgical outcomes following acute, 'delayed' and elective cholecystectomies in a population-based cohort.

Audit standard: All-cause 30-day readmission rate should be less than 10% following cholecystectomy (primary outcome measure). Secondary outcome measures are all highlighted variables within the commissioning guide: pre-operative (demographics, admission type, diagnostic tests and planned surgical approach), peri-operative (conversion rates of laparoscopy to open surgery and complications) and post-operative (length of stay and in-hospital morbidity) factors.

Methods: The study will be performed over a two-month period, following a one-week, five centre pilot. The study will be performed using a standardised database at each centre. Inclusion criteria will be all patients presenting for a cholecystectomy in one of the following categories: (1) Acute Cholecystectomy (acute admission with biliary disease through A&E or GP and cholecystectomy performed during that acute admission); (2) Elective Cholecystectomy (planned elective admission for cholecystectomy referred by their GP and added to the routine surgical waiting list from the outpatient department only); and (3) Delayed Cholecystectomy (all other planned cholecystectomies performed on an elective operating list). Variation in practice will be assessed by all-cause 30-day readmission rates, by centre. In

addition, the influence of pre-operative factors and effects on peri- and post-operative measures will be investigated.

Results: These will be presented to investigate 30-day readmissions following acute, 'delayed' and elective cholecystectomies in this population-based cohort.

Discussion: Significant variations in practice between centres may have major impact on clinical outcomes following cholecystectomy. The results can therefore be used to inform commissioning and implement changes within the NHS.

3.0 INTRODUCTION

Cholecystectomy is one of the most commonly performed general surgical procedures in the UK. Approximately 66,000 cholecystectomies were performed during the 2011-12 financial year in England alone [1]. The main indications are biliary colic, cholecystitis (acute and chronic) and gallstone pancreatitis. Historically, such operations were performed by open surgery, although the majority are now performed laparoscopically [2].

In the UK, management still varies widely between surgeons and hospitals [2-4]. Retrospective data from Hospital Episodes Statistics shows that only 12.5% of cholecystectomies are performed as an emergency. Results from this study and a separate retrospective study in Scotland shows that this is more likely to occur in a high volume centre and the proportion of acute cholecystectomies has not increased in line with emergency admissions for gallbladder disease [2, 3]. Both these studies show that the incidence of negative outcomes (re-admissions, re-operations, conversions to an open procedure and mortality) were higher in the 'emergency' group. However, there appeared to be variations between high and low volume centres [2, 3]. This is in contrast to evidence from randomised control trials and meta-analyses which support the role and safety of early or acute laparoscopic cholecystectomy (LC) in biliary colic, cholecystitis and gallstone pancreatitis [5-10]. However, the trial data includes surprisingly small numbers from specialist units in pre-defined cohorts. Taken together, this raises the possibility that such results are not truly generalisable to some non-specialist centres. This has an important impact on patients and the NHS especially as the trial data will be in part used to inform commissioning decisions.

Readmission after surgery is an important measure of quality of care [11]. There may be variations linked to hospital volume and types of surgery. However, there is minimal data on the causes of readmission following cholecystectomy. Small retrospective series report wide variation in readmission rates. Further, a recent commissioning guide produced jointly by the Royal College of Surgeons (RCS)

and the Association of Upper Gastrointestinal Surgeons of Great Britain and Ireland (AUGIS) recommends a readmission rate of less than 10% as a specific audit standard [4].

Several other controversies remain regarding the treatment of this condition. For example, the use of intraoperative cholangiography is known to increase the detection of common bile duct (CBD) injuries which results in improved survival, but it is sporadically performed [12]. Despite level 1 evidence suggesting that peri-operative antibiotics do not prevent wound and intra-abdominal infectious complications, again practice varies [13]. In fact the GallRiks study of 10,927 cholecystectomies suggested that prophylactic antibiotics may increase infectious complications [14].

Within the UK, different practices are adopted [2]. The primary aim of this study is to investigate surgical outcomes following acute, 'delayed' and elective cholecystectomies in a multi-centre, prospective, population-based cohort series to investigate if there are major variations that might in turn influence clinical outcomes.

4.0 RATIONALE OF PROPOSED AUDIT & HYPOTHESIS

Despite randomised control trials supporting acute laparoscopic cholecystectomy (LC) in biliary colic, cholecystitis and gallstone pancreatitis, management still varies widely between hospitals and surgeons. The impact of such variation on surgical outcomes is unclear. The RCS / AUGIS have recently published guidance on several aspects of gallstone disease management which will be used as audit standards.

Our hypothesis is that within the UK and Ireland different practices are being adopted resulting in important differences in surgical outcomes in a non-trial cohort.

5.0 OBJECTIVES

To measure the difference in all-cause 30-day readmission rate following acute, delayed and elective cholecystectomies in a population-based cohort as the recommended audit standard suggests that this should be less than 10% following cholecystectomy (primary aim and primary audit standard) [4].

To measure the differences in other defined surgical outcomes following acute, delayed and elective cholecystectomies (secondary aims) as set within recommended audit standards [4] including:

- Rates of day-case laparoscopic cholecystectomy procedures.
- Rates of open cholecystectomy.
- Rates of bile duct injury.

To test the effect of peri- and post-operative factors on defined surgical outcomes and if acute, delayed and elective cholecystectomies are influenced by preoperative factors (secondary aim).

6.0 DESIGN AND METHODS

Multi-centre, contemporary, prospective, cohort study.

- Any UK or Irish hospital that provides elective or emergency cholecystectomy is eligible to enter patients. A named consultant will act as the local principal investigator (PI) and data collection will be completed by a team of local surgical trainees working at that hospital. It is anticipated that current members of the UK's regional surgical research collaborations will recruit new members to help undertake this study. This study of current practice will be registered and approved by each individual hospital's clinical audit department.

- Patient Eligibility
  - All patients over the age of 18 years who undergo a cholecystectomy can be entered into this cohort study.
  - Patients having cholecystectomy for known gallbladder cancer or as a part of another surgical procedure e.g. Whipple's procedure, bariatric or transplant operations will be excluded.

- Projected numbers
  - Based on cholecystectomy specific Hospital Episode Statistics data from England, 66,000 procedures were coded during the 2011-12 financial year [1]. If there is a uniform distribution of procedures performed between each of the acute care trusts, the 20 centres in the West Midlands alone would perform over 1,500 procedures in 2 months. If all hospitals in UK and Ireland participate, data on nearly 10,000 procedures could be gathered prospectively.

- Study phases
  - Pilot: a one-week pilot across five hospitals was performed in the West Midlands to test the data collection tool from 4th to 10th

November 2013. Adjustments have been made based on these experiences.

- Study phase: the study will be performed across eligible centres from 0800 on the 1st March to 0759 on the 1st May 2014, with the final patient reaching 30-day follow-up on 31st May 2014. A minimum of 20 centres are expected with no maximum. A guide has been produced for local investigators wishing to include their centre (appendix 1).

7.0 OUTCOME MEASURES AND AUDIT STANDARDS

Primary

The definition of the primary endpoint is all-cause 30-day readmission rate following acute, delayed and elective cholecystectomy. This is based on the RCS / AUGIS guidance which states that the audit standard of less than 10% 30-day readmission should be reached by hospitals performing cholecystectomies [4].

Secondary

- Pre-operative
  - Patient demographics
  - Indication for surgery
  - Pre-operative investigations
  - Number of hospital admissions in previous 12 months with biliary symptoms
  - Number of days in hospital prior to cholecystectomy
- Peri-operative
  - Category of operation (elective, acute, delayed)
  - Use of antibiotics
  - Conversion from laparoscopic to open
  - Intraoperative cholangiography
  - Intraoperative complications
  - Drains
  - Length of operation
- Post-operative
  - Day case rate
  - Total length of hospital stay (in days)
  - 30 day all-cause mortality
  - 30 day complications, including bile duct injury and bile leak

All secondary measures are again taken from those identified within a recent commissioning guide produced jointly by the RCS / AUGIS [4].

8.0 DATA COLLECTION

- Variables to be collected (for definitions refer to Section 9):

  Preoperative

  1. Age; Gender; BMI; ASA
  2. Current Admission Date
  3. Operation Date
  4. Timing of Surgery
     a. Elective
     b. Delayed
     c. Acute
  5. Planned day-case
  6. Date decision made to operate
  7. Pre-operative indication
  8. Surgical admissions with biliary symptoms in the previous 12 months
  9. Investigations

  Intra-operative data

  10. Seniority of surgeons
  11. Speciality of responsible consultant surgeon
  12. Use of perioperative antibiotics
  13. Method of operation
  14. Degree of difficulty
  15. Complications
  16. Intraoperative cholangiography
  17. CBD exploration performed
  18. Abdominal drain left at the end
  19. Duration of Surgery

  30-day data

  20. Date of discharge
  21. All-cause 30-day A&E attendance
  22. All-cause 30-day readmission

23. Complications
24. Re-interventions and re-imaging
25. 30-day mortality

- Data collection:
    - Data will be collected in a Microsoft Excel spreadsheet. It is the responsibility of the local investigators to ensure that the data is password protected and held on local trust computer systems as this will include patient identifiers to facilitate 30-day follow-up data.

- Data collection points:
    - 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.
    - Patient identification: Patients should 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.
    - Pre-operative data: This will be completed from information collected from patients' medical records.
    - Operative data: This should be completed either by or with input from the operating surgeon or the assistant.
    - Post-operative data: 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 re-admissions or re-attendances to either 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 post-operative complications.
        - Check for any outpatient attendances within 30 days of surgery

        - Check electronic or paper hospital records or hand-over lists for re-attendances or re-admissions.
        - Check for any A&E re-attendances.
        - Review imaging reports or laboratory results to check for unplanned attendances which may have occurred.
    - Each team should regularly check that all patients are captured during the audit period to ensure consecutive patients are included.
    - Regular checks should be performed to ensure that the data included on the Excel spreadsheet is as complete as possible.

- Validation of a unit's dataset:
    - The supervising consultant(s) will be required to submit the total number of cholecystectomies performed at their Trust between 1st March and 1st May 2014 as reported by the Trust's Coding department to national administrative datasets or from any other local system.
    - Data completeness for all submitted fields should be 95% or greater.
    - For validity, the concordance between the total number of cases submitted to the CholeS study and the numbers submitted to administrative datasets should be 95% or greater. If a Unit's concordance is less than 95%, the local supervising consultant(s) will be asked to investigate and the writing committee will decide if the data from this Unit will be removed from the analysis.

- During the audit period, teams will also need to document the number of patients readmitted with complications from cholecystectomy where the operation **was performed at another hospital**. We do not require any specific details, just the number of patients. This is to address if some patients are readmitted to hospitals other than the one which performed the original operation.

- Data collation:
    - Data will be submitted centrally with all patient identifiers removed.

- Data will be transferred by the secured NHS.net email service (choles-study@uhb.nhs.uk). 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 compared; **but individual surgeons, hospitals or NHS Trusts will not be identified** and will be keep strictly anonymous.
- Hospital related variables: separate variables will be collected through an online questionnaire relating to each hospital's local policies, including the use of laparoscopic cholecystectomy (appendix 2). This will be distributed mid-study.

- Authorship:
  - Preparation of the manuscript for publication will be by performed by a writing committee.
  - Collaborators (maximum 4 per hospital including supervising consultant) contributing to the running of the study and data collection will be eligible to be listed as 'Pubmed' citable authors as part of the CholeS Study group. In return, each collaborating team should participate in the creating of the local system, registering the audit, identifying patients, collecting data and completing 30-day follow-up.
  - The supervising consultant(s) will have to oversee validity (as defined above) by ensuring a complete, accurate dataset is returned.
  - Units who fail to submit data or if a Unit's data is removed will be excluded from the authorship list.
  - If substantially incomplete data is submitted the writing committee may decide to exclude that unit from further analysis.
  - PLEASE RETURN HOSPITAL REGISTRATION FORM (**APPENDIX 3)** TO CHOLES-STUDY@UHB.NHS.UK BY 6 PM 28TH FEBRUARY 2014 AT THE LATEST TO BE INVOLVED.

9.0 DEFINITIONS

The following definitions will be used for this study:

Timing of Surgery

- Acute Cholecystectomy: acute admission with biliary disease through A&E or GP and cholecystectomy performed during that acute admission. This includes patients who have previously been added to an elective waiting list but are admitted acutely and have their procedure performed during that same admission.

- Elective Cholecystectomy: planned elective admission for cholecystectomy referred by their GP and added to the routine surgical waiting list from the outpatient department only*. Patients on an elective waiting list, treated as an emergency should be classed as 'acute' cases.*

- Delayed Cholecystectomy: all other planned cholecystectomies; for example patients who have had one or more admissions with biliary symptoms, but then discharged for a planned procedure on a elective operating list.

Planned Day Case Cholecystectomy

- These are patients who are admitted and planned to be *discharged on the same day as the operation*. The 'true' day case rate will be calculated using the proportion of patients who are actually discharged on the same day as surgery.

Date decision made to operation

- For 'elective' cases this should 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. Please use this date rather than the dates of any subsequent outpatient clinic appointment.

- For ‘acute’ cases this should be the date the decision was made to perform an acute cholecystectomy in that emergency admission. If the patient was previously on an elective waiting list for surgery, please still use the date it was decided to perform the operation as an emergency.

Indications

- Biliary colic: the presence of colicky right upper quadrant pain associated with gallstones or sludge on an USS, but no signs of acute cholecystitis [15].

- Acute cholecystitis: clinical (right upper quadrant pain, with or without fever, WCC > 11 × 109/l.) and ultrasound evidence (thick walled gallbladder (≥ 3mm) and/or pericholecystitis, USS tenderness over the gallbladder, the presence of gallstones of cholecystitis pre-operatively [15].

- Chronic cholecystitis: previous clinical or ultrasound evidence (thick walled gallbladder and/or pericholecystitis, USS tenderness over the gallbladder, the presence of gallstones) of cholecystitis pre-operatively.

- CBD stones: Common bile duct (CBD) stones, as confirmed by pre-operative imaging, that may or may not have been removed preoperatively.

- Gallbladder Polyps: Hyper-echoic lesions on USS imaging which have no acoustic shadowing and do not move with positional changes (and have no features of overt malignancy) [16].

- Dyskinesia: Biliary like abdominal pain, occurring in a normal appearing gallbladder with a functional HIDA scan showing an abnormal gallbladder ejection fraction of less than 40% [17].

- Acalculous (cholecystitis): clinical or ultrasound evidence (thick walled gallbladder and/or pericholecystitis, USS tenderness over the gallbladder, the absence of gallstones) [18].

Investigations

- USS findings: are defined as the findings from the most recent recorded ultrasound scan.

- Gallbladder wall thickness: is defined as normal if it is described as 'normal', 'thin walled' or gallbladder wall thickness is <3 mm. Thick-walled is defined as ≥ 3 mm or described as 'thick walled' [19].
- CBD is defined 'dilated' if greater than 6 mm [20].

Preoperative definitions

- American Society of Anesthesiologists (ASA) physical status classification system is a system for assessing the fitness of patients before surgery [21]. These are:
    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

- Body Mass Index (BMI) is defined as the individual's body mass (in kg) divided by the square of their height (in metres) and will be sub-classified as:
    - Underweight <17.9
    - Normal 18.0 – 24.9
    - Overweight 25.0 – 29.9
    - Moderate Obesity 30.0 – 34.9
    - Severe Obesity 35.0 – 39.9
    - Very severe Obesity >40.0

Method of operation

- Laparoscopic - Multi-port Laparoscopic cholecystectomy performed entirely using laparoscopic ports without any additional open abdominal incision.

- Laparoscopic converted to open – laparoscopic approach converted to an open incision operation, or in which an abdominal incision to assist the procedure was needed.

- Open cholecystectomy – cholecystectomy performed through an upper midline or right subcostal abdominal incision from the start of the procedure.

- SILS - single-incision laparoscopic surgery is a minimally invasive surgical procedure in which the surgeon operates almost exclusively through a single entry point. This can include one extra port.

Intraoperative

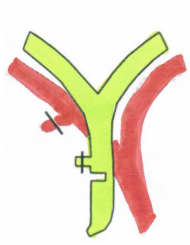
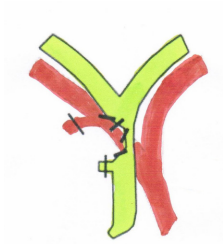
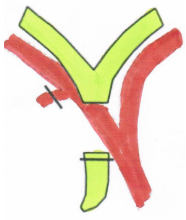
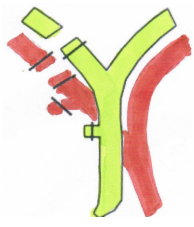
- The grade (<ST6, ST6 or above / staff grade or consultant) of the most senior surgeon scrubbed and whether a consultant surgeon was present during the procedure will be collected.
- Perioperative antibiotics: defined as antibiotics administered at induction
- The Nassar scale of difficulty for cholecystectomy should be used [22]:

	Gallbladder	**Cystic pedicle**	**Adhesions**
Grade I	Floppy, non-adherent	Clear, thin	Simple, to neck and Hartmann's pouch
Grade II	Mucocele Packed with stones	Fat-laden	Simple, up to the body
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	Dense, up to the fundus Involving hepatic flexure or duodenum
Grade IV	Completely obscured Empyema / gangrene Mass	Impossible to clarify	Dense, fibrous, wrapping the GB. Duodenum or hepatic flexure difficult to separate.

- Please see the video links on www.choles-study.org for examples of laparoscopic cholecystectomy operations with different difficulty grades.

- Intraoperative complications
    - Bile spilt – intra-abdominal spillage of bile during the procedure, including when removing the gallbladder from the abdominal cavity.
    - Stones spilt – intra-abdominal spillage of stones during the procedure, including as removing the gallbladder from the abdominal cavity.
    - Bleeding - requiring haemostatic agents (e.g. Surgicel, Fibrillar, etc.), extra clips, suturing or conversion to open procedure.
    - Common bile duct (CBD) injury will be defined as any injury to the main biliary tree and will be classified using the Stewart-Way Classification System (Table 1) [23]:
        - Class 1: defined as incomplete injury to the common bile duct with no loss of duct.
        - Class 2: defined as lateral damage to the common hepatic duct (CHD) with either stricture formation or fistula (bile leak).
        - Class 3: defined as transection of the CBD with excision of a variable portion of the CBD and cystic duct / common duct junction.
        - Class 4: defined as injury to the right hepatic duct with or without injury to the right hepatic artery.

Table 1: Stewart-Way Classification System

Class 1 	Class 2 
Class 3 	Class 4 

- If a CBD injury occurs, record it in the 'intra-operative' section of the proforma, if it was recognised intra-operatively. Delayed presentations of CBD injury, which were missed intra-operatively, should be recorded in the 30 day complication section of the data collection proforma.
- Bowel injury – any iatrogenic injury to the small or large bowel recognised intraoperatively.

- Intraoperative cholangiography:
  - 'Planned' is defined as the decision to perform a cholangiogram before the operation commences; for example due to surgeon preference or to assess for CBD stones.
  - 'Unplanned' are defined as any other reason where a cholangiogram was performed but wasn't anticipated at the start of the operation; for example to assess for unclear anatomy or to assess for potential CBD injury.

- CBD exploration: a procedure during a cholecystectomy to explore the common bile duct (either trans-cystically or via direct choledochotomy) with the indication to remove CBD stones [24].

- Duration of surgery: defined as from skin incision to the end of skin closure

<u>Postoperative</u>

- Readmission is defined as any admission following discharge which requires an overnight stay.
- 30-day post-operative complications – complications occurring within 30 days from the date of surgery including:
  - Bile leak graded as [25]:
    - A – bile leak which requires little or no change in the patients management; resolves with conservative management within 1 week.

- B – bile leak or collection which requires additional diagnostic or interventional procedures; such as ERCP or re-laparoscopy or Grade A bile leak which lasts > 1 week.
- C – bile leak or collection which requires re-laparotomy.

- Wound infection: (1) Purulent drainage from the incision; OR (2) At least two of: pain or tenderness; localised swelling; redness; heat; fever; AND The incision is opened deliberately to manage infection or the clinician diagnoses a surgical site infection; OR (3) Wound organisms AND pus cells from aspirate/ swab.
- Intra-abdominal abscess/collection: (1) A clinical diagnosis of wound infection with dehiscence of any layer below fat/scarpa's fascia; (2) A clinical diagnosis of intra-abdominal collection (fever or abdominal pain) with operative or radiological evidence of a collection.
- Pancreatitis; 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 computed tomography [26].
- CBD stones: the diagnosis of stones in the common bile duct by radiological imaging (ultrasound scan, MRCP, EUS, CT or ERCP) after recent cholecystectomy.
- Delayed presentation of a CBD injury: should be classified as per the Stewart-Way Classification system (as above). Please use the 30-day complication section to indicate whether a delayed presentation of a CBD injury occurred; i.e. one which was not recognised intra-operatively. Only record this in the intra-operative complications section, if the injury was recognised during the surgery.
- ICU/HDU admission: any unplanned episodes, even if unrelated to cholecystectomy.
- Cardiac: all complications (e.g. AF, MI, etc), even if unrelated to cholecystectomy.

- Respiratory: all complications (e.g. infection, PE, etc), even if unrelated to cholecystectomy.
- Urinary: all complications (e.g. UTI, retention, etc), even if unrelated to cholecystectomy.
- Other: Any other undefined complications in the 30 days following surgery (i.e. including DVT, non-specific pain, etc), even if unrelated to cholecystectomy.

- Total length of stay – this will be calculated from date of admission to date of discharge.

- Hospital volume – this will be calculated from the average number of cholecystectomy performed per month in the Hospital.

10.0 STATISTICIAL 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 [27]. Data will be collected and analysed in clinically relevant categories, and the Chi squared tests used to detect differences between groups. Missing data for predictor values will be replaced using the multiple imputation method to create five imputed datasets; all predictor and outcome variables will be entered into the predictive models for imputation.

Binary logistic regression modelling will be used. Multivariable models will be built to produce odds ratios (OR) to account for the impact of predictive variables when assessing outcomes. The OR represents the odds of an adverse event (e.g. all-cause 30-day readmission) occurring in the experimental group (acute cholecystectomy) versus the control groups (delayed and elective cholecystectomy). Different model development will be performed to take into account centre variation and missing data. These models will include:

1. A multilevel model, using the patient at the fixed effect level 1 and the hospital as the random effect level 2 (using the R lmer module).
2. A one level, fixed effect binary logistic regression model using a pooled dataset from 5 multiply imputed datasets. This model will take into account the effect of missing data (using the SPSS multiple imputation MCMC module).

Variable selection will be based upon those which are statistically significant at univariable analysis, and those which are clinically significant but not statistically. Fixed, forced entry will be used to adjust the main outcome measure. The effect of interaction, and sequential removal of non-significant variables will be assessed using changes in Akaike information criterion for multilevel models, and p-values for multiply imputed fixed models.

Finally, risk adjusted funnel plots will be produced to test the performance of individual (anonymised) centres for normal rates.

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12.0 APPENDIX

Appendix 1: How to register this audit

Every hospital has an audit department which should be able to advise on the information required to register the *project.* Please contact them well in advance to ensure all the paper work is correct (we would recommend at least one month prior to the study commencing).

At Trust level:

1. Identify a PI (Primary Investigator) at each trust – this is a Consultant who agrees to support the study.

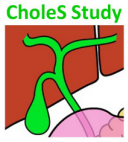
2. Create a team of medical students, FY1-2, CTs and StRs.

3. Contact your hospital's Clinical Audit Department preferably by email
    a. They will provide you with a standard audit form to complete, via email or from the intranet
    b. You can copy and paste from this protocol
    c. Ensure that the audit department know that this is part of a larger project and that you will send anonymised data for central collation via secure nhs.net email addresses

4. Once the form is completed, you may need to ask your supervising consultant to sign it.

5. Form submission
    a. Submit the form and protocol to the Audit Department as soon as possible.

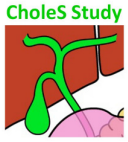
6. Please forward the written approval or email to choles-study@uhb.nhs.uk.



Appendix 2: Assessing Hospital related variables

Provision of emergency surgical services	
Is your centre a:	University hospital/ tertiary centre; District general hospital; Community hospital
How many consultants are on the general surgery on-call rota?	
How many beds does your hospital have?	
Cholecystectomy and biliary services	
Does your hospital provide tertiary HPB services?	Yes / No
Does your hospital provide ERCP service?	Yes / No Availability – weekdays / weekends / out of hours
How many consultant surgeons offer laparoscopic cholecystectomy in your hospital?	
How many consultant surgeons offer acute / emergency laparoscopic cholecystectomy in your hospital?	
How many consultant surgeons offer laparoscopic CBD exploration in your hospital?	
Does your hospital offer dedicated 'hot' gallbladder theatre lists?	Yes / No
What consultant specialities are involved in performing laparoscopic cholecystectomy in your hospital (tick all that apply)	OG, HPB, Colorectal, Breast, Vascular, Endocrine, General, Other
Where are elective laparoscopic cholecystectomies performed in your hospital? (tick all that apply)	Main operating theatre Separate day case unit Onsite treatment centre Offsite treatment centre
Approximately how many cholecystectomies are performed annually in your hospital?	
Does your unit routinely offer day-case laparoscopic cholecystectomy?	Yes / No
During working hours (0800-1800, weekdays), is acute laparoscopic cholecystectomy:	Routinely available; Only available if oncall consultant performs hot gallbladders ; Not available
During weekend days (0800-1800), is acute laparoscopic cholecystectomy:	Routinely available Only available if oncall consultant performs hot gallbladders Not available

An online link for submission of this questionnaire will be provided after the 1st March 2014. Please submit one for each hospital covered in the audit.



Appendix 3: ONE FORM NEEDS TO BE COMPLETED FOR EACH NHS TRUST

PLEASE RETURN TO CHOLES-STUDY@UHB.NHS.UK BY 6 PM 28TH FEBRUARY 2014 AT THE LATEST

CHOLE-S STUDY – REGISTRATION FORM

	Name	Email address
Consultant supervisor		
Trainees		

Name of Hospital Trust……

Hospitals the audit will include are the following

……

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……

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Confirmation of audit approval attached YES / NO

Completion of baseline questionnaire regarding site facilities YES / NO