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What is the best treatment for patients after treatment for bile duct stones?

Submission date
01/04/2025

Recruitment status
Recruiting

Registration date
29/04/2025

Overall study status
Ongoing

Last Edited
30/06/2025

Condition category
Digestive System

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol
Background and study aims
This study aims to improve treatment for patients after gallstones (common bile duct stones). We want to find out if patients benefit from having their gallbladder removed after gallstone treatment.
Gallstones are solid deposits that form in the gallbladder. When these stones move into the bile duct, they can cause pain and lead to complications, often needing urgent medical treatment. Each year, around 20,000 endoscopic retrograde cholangiopancreatography (ERCP) procedures are performed in England to remove these stones. After ERCP, patients are usually advised to talk to a surgeon about the possible removal of their gallbladder to prevent future complications from gallstones. Although the National Institute for Health and Care Excellence (NICE) recommends this surgery, practice varies a lot, and nearly half of patients who are eligible for surgery don't have an operation. This inconsistency means that around half of the patients could either be under- or over-treated. We need more evidence to confirm which approach is best for patients.

Who can participate?
Adult patients aged 18 years and over who have recently had bile duct stones cleared from their bile duct and are considered fit for surgery.

What does the study involve?
Participants will be randomly assigned to one of two groups. Half of the participants will be in the surgery group and have an operation to remove their gallbladder. The other half will be in the expectant management group, who will not have a scheduled operation to remove their gallbladder. Instead, they will be monitored by their healthcare team (with no intention of undergoing gallbladder-removal surgery).
All participants will be followed up for 2 years from when they enter the study. Clinical data will be collected about participants when they enter the study and then at 3, 6, 12 and 24 months afterwards.
Participants will be asked to complete a set of quality of life questionnaires when they enter the study and then every three months for 2 years. In between the 3-monthly questionnaires, participants will also be asked to complete a short questionnaire each month about their pain. Some study data will be collected from Hospital Episode Statistics, a standard NHS registry.

For randomly selected participants, copies of their scans and reports from the procedure they had done to remove their bile duct gallstones prior to study entry will be collected by the study team for central review purposes.
Interviews will take place with some of the patients who were approached for the ROSIER study, to find out why they chose to take part in the study or not. Interviews will also be carried out with participating hospital staff to find out their views about the study and the study processes.

What are the possible benefits and risks of participating?
We don't know if participants will personally benefit from taking part in this research, but it is possible. As the research involves treatments that participants could get in standard care, we don't anticipate there being any extra risk to participants from taking part in the study.
For participants who have gallbladder-removal surgery during their participation in the study, the operation would be performed as per local routine care. Therefore, the risks of undergoing this procedure would be the same both inside and outside of the study.

Where is the study run from?
The study is being run from the Clinical Trials Research Unit at the University of Leeds in the UK.

When is the study starting and how long is it expected to run for?
June 2024 to September 2030

Who is funding the study?
The study is funded by the National Institute for Health and Care Research (NIHR) (UK)

Who is the main contact?
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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
333432

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
CPMS 58170, Grant Code: NIHR159585

Study information

Scientific Title
The ROSIER trial: requirement for surgical intervention after endoscopic retrograde cholangiopancreatography

Acronym
ROSIER

Study objectives
Following endoscopic retrograde cholangiopancreatography (ERCP), treatment with expectant management (managed with the intention of not undergoing cholecystectomy) is non-inferior to laparoscopic cholecystectomy in patients with common bile duct stones.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 13/03/2025, London - Bloomsbury Research Ethics Committee (Health Research Authority, 2 Redman Place, Stratford, London, E20 1JQ, UK; +44 (0)207 104 8384, +44 (0)207 104 8256, +44 (0)207 104 8276; bloomsbury.rec@hra.nhs.uk), ref: 25/LO/0110

Study design
Randomized; Interventional; Design type: Treatment, Surgery, Active Monitoring

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Common bile duct stones

Interventions
ROSIER is an IDEAL stage 3, multicentre, pragmatic, unblinded, two-arm individually randomised controlled non-inferiority trial with an embedded group-sequential interim analysis to evaluate the effectiveness and cost-effectiveness of expectant management (EM) compared with laparoscopic cholecystectomy after endoscopic retrograde cholangiopancreatography (ERCP) for clearance of gallstones from the common bile duct. Expectant management means monitoring patients with the intention of not having surgery. Laparoscopic cholecystectomy is a keyhole operation to remove the gallbladder. Both treatment options are available to patients in routine NHS care.

A 12-month internal pilot phase will assess recruitment feasibility and an integrated qualitative sub-study will assess: a) factors influencing trial participation, including willingness to randomise and be randomised b) experiences of the study interventions and process, c) factors likely to influence wider implementation of study findings.

Trial population:
The main trial will recruit 1318 adult participants, aged ≥ 18 years who have undergone ERCP, sphincterotomy and duct clearance for common bile duct stones who are fit to undergo surgery. Participants must be able and willing to give written informed consent and be able and willing to comply with the terms of the protocol, including completion of quality of life questionnaires.

Site eligibility:
The trial will open in approximately 33 NHS research sites across the UK.
To be eligible to participate in the trial, research sites must meet the following criteria:
1. Be a secondary or tertiary care centre offering laparoscopic cholecystectomy
2. Offer ERCP
3. Have the anticipated capacity to recruit approximately 1-2 participants per month

Participant identification and consent (main trial):
Patients who have undergone ERCP, sphincterotomy and duct clearance for common bile duct stones will be screened for eligibility at participating research sites. Patients will be approached

for possible recruitment into the trial following completion of ERCP for duct clearance and once they are considered fit for surgery. Suitability for inclusion in the trial will be assessed according to the trial eligibility criteria and patients will be provided with verbal and written details.

A verbal explanation of the trial along with the approved Participant Information Sheet (PIS), will be provided by a suitably qualified member of the healthcare team for the patient to consider. The PIS will provide detailed information about the rationale, design and personal implications of the study. A PIS Supplementary Information Document, containing additional information about the trial, will also be provided to the participant. Reading the Supplementary Information Sheet is optional for patients and they do not need to read this document in order to consent to the ROSIER trial, if they do not wish to do so.

Following information provision, patients will be given the opportunity to discuss the trial with their family and medically qualified members of the healthcare team before they are asked whether they would be willing to take part in the trial. Patients will be given as long as they need to consider participation in the trial, ideally this will be at least 24 hours. The right of the patient to refuse consent without giving reasons will be respected.

Patients who wish to participate will be invited to provide written informed consent including explicit consent for the transfer of a copy of their signed consent form to the CTRU. Following consent patients will be formally assessed for eligibility. Informed consent may only be obtained by the Principal Investigator (PI) or an appropriate, delegated, healthcare professional. The healthcare professional must have knowledge of the trial interventions and have received training in the principles of GCP and the Declaration of Helsinki 1996. The healthcare professional must be fully trained in the trial according to the ethically approved protocol and be authorised and approved by the PI to take informed consent as documented in the trial Authorised Personnel Log.

Randomisation:
Participants will be randomised on an equal basis, using a computer-generated minimisation algorithm incorporating a random element, to undergo either expectant management or laparoscopic cholecystectomy.
Randomisation will be based on a minimisation algorithm with random component, ensuring that treatment groups will be balanced for the following minimisation factors:
• Cholangitis prior to ERCP (yes, no)
• Obstructive jaundice without sepsis prior to ERCP (yes, no)
• Pancreatitis prior to ERCP (yes, no)
• Biliary pain or colic prior to ERCP (yes, no)
• Cholecystitis prior to ERCP (yes, no)
• Randomising site

Pre-operative investigations (only applicable to patients who undergo laparoscopic cholecystectomy):
For participants who have laparoscopic cholecystectomy (LC), pre-operative investigations and preparation will be as per institutional protocol. This applies to all participants who undergo LC during their participation in the trial, whether they were randomised to the LC arm and have surgery, or they were randomised to expectant management but undergo LC.

Interventions:

Laparascopic cholecystectomy:
For participants undergoing laparoscopic cholecystectomy, the operation should be performed

as per institutional protocol, and by whichever surgeon would ordinarily carry out the procedure according to the local standard of care. LC may be performed using a laparoscopic or robotic approach. This applies to all participants who undergo LC during their participation in the trial, whether they were randomised to the LC arm and have surgery, or they were randomised to expectant management but undergo LC.

Expectant management:
EM participants will be managed with the intention of not undergoing cholecystectomy. EM will be at the discretion of the surgical team and according to local practice. During follow-up, if there is a clinical change, and it is clinically appropriate, surgery may occur as part of this treatment. If an EM patient requires LC for a clinically valid reason, for example, severe biliary pain, this will be compliant with the randomised treatment allocation. The participant will continue to be followed up until 24 months post-randomisation.

Post-operative care (only applicable to participants who undergo laparoscopic cholecystectomy):
For participants undergoing LC, post-operative care will be as per institutional protocol. This applies to all participants who undergo LC during their participation in the trial, whether they were randomised to the LC arm and have surgery, or they were randomised to expectant management but undergo LC. All participants (regardless of trial arm) will be followed up for trial purposes for 24 months post-randomisation.

Trial follow-up:
Clinical assessments: All participants will undergo a clinical review for trial purposes at 3, 6, 12 and 24 months post-randomisation. The trial follow-up assessments can be done via telephone if the participant is not due to be seen in clinic as part of local standard care at these timepoints, and will likely take around 15 minutes. Data collected at the clinical follow-ups will include (but will not be limited to):
• Assessment details
• Adverse events and severity
• Need for further biliary intervention
Any further clinical assessments/visits will be according to local standard clinical practice.

Participant-completed questionnaires (3-monthly):
Participants will complete a number of questionnaires designed to capture health-related quality of life and the costs involved with each treatment. All participants will complete the health-related quality of life questionnaire packs at baseline and then 3-monthly up to and including 24 months post-randomisation. Each questionnaire pack will consist of three validated questionnaires and a Health and Social Care Resource Use questionnaire, and will take approximately 30 minutes to complete. The baseline questionnaires will be administered to the participants by the local site research team and completed on paper. The baseline questionnaires should be completed after informed consent but prior to randomisation, or at least before the participant is informed of their randomisation result.

The follow-up questionnaires will be administered directly to participants by the ROSIER CTRU trial team by SMS, email or post (depending on the participant's QoL completion preferences). If participants choose to complete their follow-up questionnaires in paper format via post, a freepost envelope will be provided so that they can return their completed questionnaire pack to the CTRU. Should a completed questionnaire not be received at the CTRU by the required time-point, the CTRU will send one reminder to the participant either by post, SMS or email (depending on the participant’s questionnaire-completion preferences).

Monthly pain questionnaire:
Participants will be asked to complete a short pain questionnaire, consisting of the two bodily pain domain questions of the SF36 survey, on a monthly basis in between the 3-monthly questionnaire packs throughout the 24-month follow-up period. The monthly pain questionnaire will ideally be completed by participants via SMS to minimise research burden, but participants will also have the option of completing this via email or on paper (via diary card), if they'd prefer. For paper completers, the diary card on which they can record their monthly pain responses for the next two months will be sent out alongside the 3-monthly questionnaire packs. Participants will then be able to return their completed diary card for the previous two months with their next 3-monthly pack. Pre-paid addressed envelopes will be provided for the return of the paper QoL questionnaires to CTRU.

ERCP Central Review:
As part of the trial eligibility criteria, all participants must have undergone ERCP (as per local standard practice) prior to being recruited to the ROSIER trial. ERCP details will be collected for all participants on the trial electronic case report forms. To validate the ERCP dataset, 10% of randomly selected occlusion cholangiogram images (taken during ERCP) and reports will be collected by the CTRU for central review.

Hospital Episode Statistics (HES) Data Collection:
Hospital admission data:
Details of hospital admissions for biliary events, complications or treatment within 24 months of randomisation will be obtained from HES data. The CTRU trial team will submit a data access request to HES to obtain this data so there is no input required from sites.

Readmissions (longer-term follow-up data):
It is planned that late readmissions for biliary events, complications and treatment within 10 years post-randomisation will be derived from HES data. A separate ethics application and protocol will be submitted for this planned element of the research at an appropriate timepoint in the future. However, consent to collect the longer-term follow-up HES data will be obtained from trial participants from the outset as part of the main trial consent process - this is covered in the ROSIER Participant Information Sheet and Informed Consent Form.

Qualitative sub-study:
The qualitative sub-study incorporates mixed qualitative methods including interviews with patients and health professionals and audio-recording of recruitment conversations. Data collection and analysis will commence during study set-up and will focus on the internal pilot. The approach will be flexible and respond to project needs at the different stages of the trial. A summary of the activities in the sub-study is given below:

Site survey:
All participating sites will be asked to describe their current organisation of care for patients with bile duct stones (e.g. number of surgeons involved; number of procedures annually), including expectant management and perioperative LC management, and including any written information for patients. This will inform the purposive sample.

Interviews with patients declining trial participation (during internal pilot only):
During the internal pilot phase, patients (n = 10-12) who are approached for the ROSIER trial but decline to participate will be invited to take part in a single qualitative interview, which is anticipated to take around 45 minutes.

Interviews with trial consenters (throughout the trial):
Throughout the trial, a subset of participants who consent to take part in the ROSIER trial will be invited to take part in a qualitative interview (n = 24-28). Research site staff will invite all participants to consent to contact as part of the informed consent process for the main trial. Some patients may be asked to do a second interview to follow their experience over time. No patient will be asked to do more than two interviews. Each interview is anticipated to take approximately 45 minutes. To better understand patients' experience over time we will invite patients to contribute photos that communicate their experience of treatment or symptoms of bile duct stones (photo-elicitation). This will be optional. An amendment will be submitted for the materials relating to this element of the research prior to photos being requested from participants.

Interviews with patients (both main trial consenters and decliners) will take place via telephone or video chat (e.g., via Microsoft Teams or Zoom). With permission from participants, the interviews will be audio-recorded, using digital encrypted recorders, or via the secure digital platform for interviews conducted virtually.

Interviews with healthcare professionals (throughout the trial):
Interviews with healthcare professionals involved in recruitment to ROSIER or in delivering the trial interventions(n = 24-30) will take place throughout the trial and are anticipated to take around 45 minutes each time. Most of the healthcare professional interviews will be done via telephone/virtual video conferencing platform (Microsoft Teams or Zoom), although some may be done face to face (for example, to coincide with a site observation). With permission from participants, the interviews will be audio-recorded, using digital encrypted recorders, or via the secure digital platform for interviews conducted virtually.

GP focus groups:
Two focus groups with GPs will be undertaken to understand primary care perspectives of the trial arms. Topic guides will be developed based on the initial findings from the ROSIER hospital health professional/patient interviews and will be submitted, with the relevant recruitment and consent materials, as an amendment.

Audio recording of recruitment conversations:
Sites taking part in the internal pilot will be asked to record their recruitment conversations with potential participants. A purposive sample of sites during the main trial (e.g. those struggling to recruit) will also be recruited (n= approximately 150 recordings in total across all sites - approximately 10 per site).

Observation of ROSIER meetings (e.g. Site Initiation Visits and investigator meetings):
It is planned that qualitative researchers will attend ROSIER meetings such as Site Initiation Visits and investigator meetings and make notes of points raised. During the internal pilot, site set-up meetings will be conducted to map trial and clinical pathways.

Analysis will incorporate rapid qualitative analysis (during internal pilot); pen portrait and thematic analysis approaches and will be informed by Normalisation Process Theory.

Timetable for research:
There will be a 30-month recruitment period and all participants will be followed up until 24 months post-randomisation. The qualitative sub-study will run throughout the trial.

One-sided superiority testing will be performed at two stages: in an interim analysis and at the full sample size of 1318 participants, prior to the non-inferiority analysis. The interim superiority

analysis is estimated to require 530 participants with complete data – i.e., 664 (332 per arm) participants, assuming 20% attrition. Should superiority be demonstrated at either of these two stages the trial will close.

The end of the trial is defined as the last participant's last data item within the 24-month follow-up period.

Intervention Type
Procedure/Surgery

Primary outcome(s)
Patient-reported pain, defined by the area under the curve (AUC) of the SF-36 bodily pain domain within 24 months of randomisation. This will be assessed monthly over the 24-month post-randomisation period.

Key secondary outcome(s))
1. Overall patient wellbeing measured using the condition-specific Otago Gallstones Condition Specific Questionnaire (CSQ) every 3 months up to 24 months post-randomisation
2. SF-36 physical functioning, physical role limitations, general health perceptions, energy /vitality, social functioning, emotional, and mental health domains, assessed every 3 months for up to 24 months post-randomisation
3. Adverse events occurring within 24 months post-randomisation
4. Subsequent disease or intervention-related surgeries occurring within 24 months post-randomisation
5. Number and timing of readmissions (for biliary events, complications and treatment) occurring within 24 months of randomisation, derived from Hospital Episode Statistics (HES) data
6. Cost-utility as measured by the EQ-5D-5L and health care resource use questionnaires assessed every 3 months up to 24 months post-randomisation
7. All-cause mortality within 24 months post-randomisation

Exploratory outcome measure:
Identifying potential risk factors that may predict the need for laparoscopic cholecystectomy within 24 months of randomisation to expectant management. Potential risk factors that may be explored will include, but are not necessarily limited to, age, sex, BMI, cholangitis, obstructive jaundice without sepsis, pancreatitis, biliary pain or colic, cholecystitis, previous abdominal surgery, bile duct related factors (stone size, number of stones, duct size, obstruction in Hartmann’s pouch), and gallbladder wall thickness on ultrasound. Full details of risk factors to be explored will be detailed a priori in the statistical analysis plan.

Completion date
30/09/2030

Eligibility

Key inclusion criteria
1. Aged >=18 years
2. Undergone ERCP, sphincterotomy and duct clearance for common bile duct stones
3. Fit for and willing to undergo laparoscopic or robotic cholecystectomy
4. Able and willing to provide written informed consent
5. Able and willing to comply with the terms of the protocol, including completion of QoL questionnaires

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Pregnancy or planned pregnancy
2. Evidence of empyema or perforated gallbladder requiring urgent intervention
3. Cholecystostomy insertion
4. Undergone previous cholecystectomy

Date of first enrolment
27/06/2025

Date of final enrolment
31/08/2027

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Leeds Teaching Hospitals NHS Trust
St. James's University Hospital
Beckett Street
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LS9 7TF

Study participating centre
University of Leeds
Woodhouse Lane
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LS2 9JT

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Sponsor information

Organisation
University of Leeds

ROR
https://ror.org/024mrxd33

Funder(s)

Funder type
Government

Funder Name
National Institute for Health and Care Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The data-sharing plans for the current study are unknown and will be made available at a later date

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes