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Testing for bile duct stones before gallbladder surgery

Submission date 24/09/2018	**Recruitment status** No longer recruiting	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 02/10/2018	**Overall study status** Ongoing	
Last Edited 13/12/2024	**Condition category** Surgery	

Plain English summary of protocol

Background and study aims
Surgery to remove the gallbladder is required if it contains gallstones that cause problems. About 70,000 operations are performed annually in England. Sometimes, gallstones cause other problems if they pass from the gallbladder into the nearby bile duct (e.g. jaundice/inflammation of the pancreas). If this happens, it is necessary to remove the bile duct stones before or during the gallbladder operation. Because of this, patients requiring gallbladder surgery are assessed for any risk of bile duct stones. If the risk is high, further tests are done to identify if bile duct stones are present. If the risk is moderate or low (although it can be difficult to distinguish between the two), then it is uncertain whether further tests to look for bile duct stones are necessary. As a result, some surgeons choose to perform tests and others don't. A UK-wide research study found that a third of patients undergoing gallbladder surgery were tested, usually before surgery using an MRI scanner. This test, called a Magnetic Resonance Cholangiopancreatography (MRCP), involves a 1-hour visit to hospital and costs the NHS about £365. The MRCP identifies bile duct stones but may delay gallbladder surgery which can lead to increased problems with gallstones whilst waiting. There are other uncertainties about the need for testing using MRCP. Even if the MRCP shows bile duct stones, the stones can pass into the bowel spontaneously; and removing the stones can cause complications. Not having the MRCP avoids these risks, but can lead to bile duct stones being left behind after surgery, which may also cause complications. Research to establish if going straight to gallbladder surgery without testing the bile duct beforehand is needed.
The Sunflower Study will find out whether testing for bile duct stones with MRCP before gallbladder surgery is worthwhile or not in patients with a low or moderate risk of having stones.

Who can participate?
Adults with symptomatic gallstone disease who are scheduled and fit to receive gallbladder surgery, with a low to moderate risk of common bile duct stones

What does the study involve?
Participants in the Sunflower study will be divided into two groups. One group will go straight to surgery (i.e. no additional testing) and the other will receive an MRCP before surgery. The groups will be selected by a process called randomisation to ensure that groups have similar patients in terms of factors such as general health, age and gender. The 'straight to surgery'

group will have twice as many people in as the ‘tested’ group to reduce the number of extra MRCPs performed. Both groups will be followed for 18 months and information about the need for treatment of bile duct stones, complications of surgery and costs collected.

What are the possible benefits and risks of participating?
For participants who receive MRCP, the possible benefit of participating is that this procedure may detect and, if needed, treat problematic bile duct stones. However for participants who do not receive MRCP, the possible benefit is that this allows their gallbladder surgery to go ahead immediately, without the possible disadvantages of testing for bile duct stones.
For participants who receive MRCP, the possible risks of participating is that the procedure may be unnecessary, as bile duct stones often pass safely and spontaneously into the bowel. Additionally, in 10-20% of cases, MRCP may not detec bile duct stones. Additionally, some patients may experience claustrophobia during the scan. For some patients, the scan and endoscope procedure (if required) may lead to a longer wait time for gallbladder surgery, which can lead to problems with gallstones whilst waiting (however, the surgery may not always be delayed by this).
For participants who do not receive MRCP, the possible risk is that any bile duct stones present will not be detected, which could lead to problems after gallbladder surgery (i.e. jaundice, infection, pancreatitis) and therefore require further treatment or readmission to hospital. If bile duct stones are suspected later, a scan and potentially endoscope procedure will be likely needed to remove them.

Where is the study run from?
Leeds Teaching Hospitals NHS Trust and at least 50 hospitals throughout the UK.

When is the study starting and how long is it expected to run for?
January 2018 to November 2025

Who is funding the study?
National Institute for Health Research (NIHR) Health Technology Assessment Programme (UK)

Who is the main contact?
Stephen Palmer
sunflower-study@bristol.ac.uk

Study website
https://sunflowerstudy.blogs.bristol.ac.uk/

Contact information

Type(s)
Public

Contact name
Mr Stephen Palmer

Contact details
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BS8 1NU
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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
16/142/04

Study information

Scientific Title
The Sunflower Study: A randomised controlled trial to establish the clinical and cost effectiveness of expectant management versus pre-operative imaging with MRCP in patients with symptomatic gallstones undergoing laparoscopic cholecystectomy at low or moderate risk of common bile duct stones

Acronym
The Sunflower Study

Study objectives
We will test the hypothesis that expectant management is non-inferior to magnetic resonance pancreaticogram (MRCP) with respect to hospitalisation for treatment for a complication of gallstones up to 18 months after randomisation.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 10/12/2018, Yorkshire & The Humber – South Yorkshire Ethics Committee (NHSBT Newcastle Blood Donor Centre, Holland Drive, Newcastle upon Tyne, NE2 4NQ; Tel: +44 (0)207 1048091; Email: nrescommittee.yorkandhumber-southyorks@nhs.net), ref: 18/YH/0358

Study design
Interventional multi-centre pragmatic randomized controlled trial with an internal pilot phase (Phase
I) and a quintet recruitment intervention (QRI)

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Diagnostic

Participant information sheet
See study outputs table

Health condition(s) or problem(s) studied
Symptomatic gallbladder disease, requiring gallbladder surgery

Interventions
Participants will be randomly allocated in a 1:2 ratio to receive either a reoperative magnetic resonance pancreaticogram (magentic resonance cholangiopancreatography - MRCP) or no MRCP (expectant management) using an online system.
In the MRCP arm, participants will undergo an MRCP prior to their gallbladder surgery. An MRCP takes on average 20-30 minutes. In the expectant management arm, participants will proceed directly to surgery without undergoing an MRCP. The follow up will be the same in both groups – a 20% sample will be asked to complete questionnaires at 3, 6, 12 and 18 months post randomisation.

Intervention Type
Other

Primary outcome measure
Current primary outcome measure:
Any of the following:
1. Any hospital admission within 18 months of randomisation for treatment of complications of gallstones whether in the CBD or gallbladder
2. Complications during the admission for LC for the treatment for gallstones or any readmission for complications of the LC leading to a hospital stay of >2 days. Complications will include, but not be limited to:
2.1. Return to theatre post LC for any cause
2.2. Percutaneous radiological drainage
2.3. ERCP for non-diagnostic reasons (e.g. for a bile leak). It does not include a diagnostic ERCP performed following an MRCP where CBD stones were identified.
3. Complications during any ERCP for the treatment for gallstones. Complications will include:
3.1. Blood transfusion post ERCP
3.2. Percutaneous radiological drainage
3.3. Treatment of a perforation occurring during ERCP
3.4. Acute pancreatitis
3.5. Other complications leading to a hospital stay of >2 days
This will be acquired from routine data sources, such as HES data from NHS Digital in England. The HES data will be reviewed and specific OPCS-4 and ICD-10 codes will be searched for. These codes identify specific diagnoses, procedures, etc which will form the primary outcome measure. This will be measured in the 18 months following randomisation.

Previous primary outcome measure:
Any of the following:
1. Any hospital admission within 18 months of randomisation for treatment of complications of gallstones whether in the CBD or gallbladder
2. Complications during the admission for LC for the treatment for gallstones or readmission for complications of the LC. Complications comprise:
2.1. Return to theatre post LC for any cause
2.2. Percutaneous radiological drainage
2.3. ERC
3. Complications during the index admission for ERCP for the treatment for gallstones (i.e. an ERCP performed following an MRCP where CBD stones were identified). Complications comprise:
3.1. Blood transfusion post ERCP
3.2. Percutaneous radiological drainage
3.3. Further ERCP
3.4. Treatment of a perforation occurring during ERCP
3.5. Acute pancreatitis
3.6. Respiratory complications leading to extended hospital stay of > 2 days
3.7. Cardiac complications leading to extended hospital stay of > 2 days
3.8. Infective complications leading to extended hospital stay of > 2 days
3.9. Other complications leading to extended hospital stay of > 2 days (detail to be recorded).
This will be acquired from routine data sources, such as HES data from NHS Digital in England. The HES data will be reviewed and specific OPCS-4 and ICD-10 codes will be searched for. These codes identify specific diagnoses, procedures, etc which will form the primary outcome measure. This will be measured in the 18 months following randomisation.

Secondary outcome measures
1. Health-related quality of life, assessed using the EQ-5D-5L questionnaire at time of randomisation, admission for LC and 3, 6, 12 and 18 months after randomisation (participants will not be asked to complete the admission for LC questionnaire if they have completed their baseline questionnaire within the previous two days)
2. Items in the LC core outcome set, which is due to be published at the end of 2018
3. NHS resource use to 18 months post randomisation, taken from routine data sources such as HES data from NHS Digital in England

Overall study start date
01/01/2018

Completion date
30/11/2025

Eligibility

Key inclusion criteria
Current inclusion criteria as of 15/01/2020:
1. Aged 18 years or older
2. Symptomatic gallbladder disease, confirmed by trans-abdominal ultrasound scan (USS) or computed tomography (CT) scan, including, for example:
2.1. Biliary colic
2.2. Cholecystitis
2.3. Mild and severe gallstone pancreatitis
2.4. Gallbladder polyps

2.5. Gallbladder dyskinesia, etc
3. Scheduled and fit for laparoscopic cholecystectomy (LC) as an elective or urgent procedure
4. Low or moderate risk of common bile duct (CBD) stones, including all of the following:
4.1. CBD diameter ≤8 mm on USS
4.2. Bilirubin ≤ 50umol/l
4.3. Alanine transferase less than three times the upper limit of normal (≤3 x ULN) and/or alkaline phosphatase ≤3 x ULN
If a patient does not meet the definition of low or moderate risk of CBD stones solely because both alanine transferase and alkaline phosphatase are > 3 x ULN, if repeat blood tests are carried out and at least one of the second or subsequent test results is within range (i.e. ≤ 3 x ULN) the patient may be recruited at that time.
If a patient does not meet the definition of low or moderate risk of CBD stones solely because bilirubin > 50umol/l, if repeat blood tests are carried out and at least one of the second or subsequent test results is within range the patient may be recruited at that time.
If CBD cannot be seen on USS or CT scan, the patient may be recruited as long as all the other inclusion criteria are met and there is no intrahepatic duct dilatation reported.

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2.1. Biliary colic
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2.3. Mild and severe pancreatitis
2.4. Gallbladder polyps
2.5. Gallbladder dyskinesia
3. Scheduled and fit for laparascopic cholecystectomy (LC) as an elective or urgent procedure
4. Low or moderate risk of common bile duct (CBD) stones, including all of the following:
4.1. CBD diameter ≤8 mm on USS
4.2. Bilirubin ≤ 50umol/l
4.3. Alanine transferase less than twice the upper limit of normal (≤2 x ULN) and/or alkaline phosphatase ≤2 x ULN.
If a patient does not meet the definition of low or moderate risk of CBD stones solely because both alanine transferase and alkaline phosphatase are > 2 x ULN, if repeat blood tests are carried out and at least one of the second or subsequent test results is within range (i.e. ≤ 2 x ULN) the patient may be recruited at that time.
If a patient does not meet the definition of low or moderate risk of CBD stones solely because bilirubin > 50umol/l, if repeat blood tests are carried out and at least one of the second or subsequent test results is within range the patient may be recruited at that time.
If CBD cannot be seen on USS or CT scan, the patient may be recruited as long as all the other inclusion criteria are met and there is no intrahepatic duct dilatation reported.

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
7,457

Total final enrolment
7471

Key exclusion criteria
Current exclusion criteria as of 15/01/2020:
1. Unable to undergo MRCP
2. Evidence of empyema or perforated gallbladder requiring urgent intervention
3. Previous gastric bypass
4. Previous MRCP or endoscopic ultrasound (EUS) within last 3 months
5. Any previous ERCP
6. Haemolytic disease
7. Pregnancy
8. Unwilling to participate in follow up
9. Unable to provide written informed consent
10. Prisoner

Previous exclusion criteria:
1. Unable to undergo MRCP
2. Evidence of empyema or perforated gallbladder requiring urgent intervention
3. Previous duodenal bypass
4. Previous MRCP within last 3 months
5. Haemolytic disease
6. Pregnancy
7. Unwilling to participate in follow up
8. Unable to provide written informed consent
9. Prisoner

Date of first enrolment
01/12/2018

Date of final enrolment
30/08/2024

Locations

Countries of recruitment
England

Northern Ireland

Scotland

United Kingdom

Wales

Study participating centre
Leeds Teaching Hospitals NHS Trust
United Kingdom
LS1 3EX

Study participating centre
Calderdale and Huddersfield NHS Foundation Trust
Huddersfield Royal Infirmary
Acre Street
Lindley
Huddersfield
United Kingdom
HD3 3EA

Study participating centre
Nottingham University Hospitals NHS Trust
Queens Medical Centre Campus
Derby Road
Nottingham
United Kingdom
NG7 2UH

Study participating centre
Worcestershire Acute Hospitals NHS Trust
Worcestershire Royal Hospital
Worcester
United Kingdom
WR5 1DD

Study participating centre
North Bristol NHS Trust
Southmead Hospital
Bristol
United Kingdom
BS10 5NB

Study participating centre

University Hospitals Bristol NHS Foundation Trust
Marlborough Street
Bristol
United Kingdom
BS2 8HW

Study participating centre
Surrey and Sussex Healthcare NHS Trust
East Surrey Hospital
Canada Avenue
Redhill
United Kingdom
RH1 5RH

Study participating centre
Countess of Chester Hospital NHS Foundation Trust
Countess of Chester Hospital
Liverpool Road
Chester
United Kingdom
CH2 1UL

Study participating centre
Buckinghamshire Healthcare NHS Trust
Stoke Mandeville Hospital
Mandeville Road
Aylesbury
United Kingdom
HP21 8AL

Study participating centre
Northumbria Healthcare NHS Foundation Trust
North Tyneside General Hospital
Rake Lane
North Shields
United Kingdom
NE29 8NH

Study participating centre
University Hospitals Plymouth NHS Trust
Derriford Hospital

Plymouth
United Kingdom
PL6 8DH

Study participating centre
Northern Devon Healthcare NHS Trust
North Devon District Hospital
Raleigh Park
Barnstaple
United Kingdom
EX31 4JB

Study participating centre
Guy's and St Thomas' NHS Foundation Trust
St Thomas' Hospital
Westminster Bridge Road
London
United Kingdom
SE1 7EH

Study participating centre
Sherwood Forest Hospitals NHS Foundation Trust
Kings Mill Hospital
Mansfield Road
Sutton In Ashfield
United Kingdom
NG17 4JL

Study participating centre
Great Western Hospitals NHS Foundation Trust
Great Western Hospital
Marlborough Road
Swindon
United Kingdom
SN3 6BB

Study participating centre
Sheffield Teaching Hospital NHS Foundation Trust
Northern General Hospital

Sheffield
United Kingdom
S5 7AU

Study participating centre
Basildon and Thurrock University Hospitals NHS Foundation Trust
Basildon University Hospital
Nethermayne
Basildon
United Kingdom
SS16 5NL

Study participating centre
University Hospital of Derby and Burton NHS Foundation Trust
Queen's Hospital
Belvedere Road
Burton-on-Trent
United Kingdom
DE13 0RB

Study participating centre
Gloucestershire Hospitals NHS Foundation Trust
Gloucester Royal Hospital
Great Western Road
Gloucester
United Kingdom
GL1 3NN

Study participating centre
Bradford Teaching Hospitals NHS Foundation Trust
Bradford Royal Infirmary
Duckworth Lane
Bradford
United Kingdom
BD9 6RJ

Study participating centre
County Durham and Darlington NHS Foundation Trust
University Hospital of North Durham
North Road
Durham

United Kingdom
DH1 5TW

Study participating centre
The Royal Bournemouth and Christchurch Hospitals NHS Foundation Trust
Royal Bournemouth Hospital
Castle Lane East
Bournemouth
United Kingdom
BH7 7DW

Study participating centre
Royal Free NHS Trust
Pond St
London
United Kingdom
NW3 2QG

Study participating centre
Royal Devon and Exeter Foundation Trust Hospital
Barrack Road
Exeter
United Kingdom
EX2 5DW

Study participating centre
Hereford County Hospital
Hereford
United Kingdom
HR1 2ER

Study participating centre
Royal Bolton Hospital
Minerva Road
Bolton
United Kingdom
BL4 0JR

Study participating centre

Royal Blackburn Hospital
Haslingden Road
Blackburn
United Kingdom
BB2 3HH

Study participating centre
Tameside General Hospital
Fountain Street
Ashton Under Lyne
United Kingdom
OL6 9RW

Study participating centre
The Whittington Hospital
Magdala Avenue
London
United Kingdom
N19 5NF

Study participating centre
Royal Derby Hospital
Uttoxeter Rd
Derby
United Kingdom
DE22 3NE

Study participating centre
Musgrove Park Hospital
Taunton
United Kingdom
TA1 5DA

Study participating centre
Worthing Hospital
Lyndhurst Road
Worthing
United Kingdom
BN11 2DH

Study participating centre
Royal Albert and Edward Infirmary
Wigan Lane
Wigan
United Kingdom
WN1 2NN

Study participating centre
Weston General Hospital
Grange Road
Uphill
Weston-Super-Mare
United Kingdom
BS22 4TQ

Study participating centre
Royal Lancaster Infirmary
Ashton Road
Lancaster
United Kingdom
LA1 4RP

Study participating centre
St Mary's Hospital
Parkhurst Road
Newport
United Kingdom
PO30 5TG

Study participating centre
University Hospitals Coventry and Warwickshire
Clifford Bridge Road
Coventry
United Kingdom
CV2 2DX

Study participating centre
Forth Valley Royal Hospital
Stirling Road
Larbert

United Kingdom
FK5 4WR

Study participating centre
University Hospital of North Tees
Stockton-on-Tees
United Kingdom
TS19 8PE

Study participating centre
Southend University Hospital NHS Foundation Trust
Westcliff on Sea
United Kingdom
SS0 0RY

Study participating centre
Sunderland Royal Hospital
Kayll Road
Sunderland
United Kingdom
SR4 7TP

Study participating centre
Royal United Hospitals Bath NHS Foundation Trust
Combe Park
Bath
United Kingdom
BA1 3NG

Study participating centre
Aneurin Bevan University Health Board
Royal Gwent Hospital
Cardiff Road
Newport
United Kingdom
NP20 2UB

Study participating centre

St George’s Hospital NHS Foundation Trust
Ground Floor
Jenner Wing
Cranmer Terrace
London
United Kingdom
SW17 0RE

Study participating centre
Milton Keynes University Hospital
Standing Way
Eaglestone
Milton Keynes
United Kingdom
MK6 5LD

Study participating centre
University Hospitals Birmingham NHS Foundation Trust
Birmingham
United Kingdom
B15 2TH

Study participating centre
University Hospital Southampton NHS Foundation Trust
Southampton General Hospital
Southampton
United Kingdom
SO16 6YD

Study participating centre
Doncaster Royal Infirmary
Armthorpe Road
Doncaster
United Kingdom
DN2 5LT

Study participating centre
Freeman Hospital
Newcastle Upon Tyne
United Kingdom
NE7 7DN

Study participating centre
Northampton General Hospital
Cliftonville
Northampton
United Kingdom
NN5 1BD

Study participating centre
Belfast Health and Social Care Trust
Trust Headquarters, A Floor
Belfast City Hospital
51 Lisburn Road
Belfast
United Kingdom
BT9 7AB

Study participating centre
York and Scarborough Teaching Hospitals NHS Foundation Trust
Wiggington Road
York
United Kingdom
YO31 8HE

Study participating centre
Queen Elizabeth Hospital Gateshead
Queen Elizabeth Avenue
Gateshead
United Kingdom
NE9 6SX

Study participating centre
St Mary's Hospital
London
United Kingdom
W2 1NY

Study participating centre

Princess of Wales Hospital
Coity Road
Bridgend
Bridgend County Borough
United Kingdom
CF31 1RQ

Study participating centre
Hull University Teaching Hospitals NHS Trust
Castle Hill Hospital
Castle Road
Cottingham
United Kingdom
HU16 5JQ

Study participating centre
Ipswich Hospital
Heath Road
Ipswich
United Kingdom
IP4 5PD

Study participating centre
Shrewsbury & Telford Hospital NHS Trust
Mytton Oak Road
Shrewsbury
United Kingdom
SY3 8XQ

Sponsor information

Organisation
Leeds Teaching Hospitals NHS Trust

Sponsor details
Leeds General Infirmary
Great George Street
Leeds
England
United Kingdom
LS1 3EX

Sponsor type
Hospital/treatment centre

ROR
https://ror.org/00v4dac24

Funder(s)

Funder type
Not defined

Funder Name
Health Technology Assessment Programme

Alternative Name(s)
NIHR Health Technology Assessment Programme, HTA

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
The data from this study will be used to produce outputs including publications in peer-reviewed academic journals, and presentations at national and international conferences. A simplified version of the findings will also be disseminated as newsletters to patients, in accordance with advice from the PPI group about how best to do this effectively.
A report to the funding body (HTA) will be sent to the NIHR in May 2024, and will provide a summary of the work undertaken during the life of the study. The target journals for the main study paper and other related publications (e.g. health economics, qualitative) have not been identified, but these will be Open Access and should be completed by early 2025. These will communicate the results of the primary and secondary outcomes of the study. The main study paper should be published in Summer 2024. A summary for stakeholders will be provided in late 2024, and will be aimed both externally (e.g. general public/patients, media, commissioners) and internally (e.g. participating Trust stuff, operational staff). All outputs will be reviewed by the Chief Investigator and other collaborators, as necessary.
Findings will be shared with the Association of Upper Gastrointestinal Surgeons of Great Britain and Ireland (AUGIS) and the Great Britain and Ireland Hepato Pancreato Biliary Association (GBIHPBA). The Chief Investigator and co-applicants have close links with these groups who are

already aware and supportive of the study and awaiting its results. The study team intend to make presentations to both of them. Presentations will be given at national and international conferences relevant to gallbladder surgery e.g. The International Hepatopancreatobiliary Association and other sister Societies (e.g. European and African Hepatopancreatobiliary Association and the American Hepatopancreatobiliary Association). We expect that the results of the study will be used by NHS England to formulate a commissioning policy and will inform national and international guidelines.

Intention to publish date
30/11/2026

Individual participant data (IPD) sharing plan
Data requests would be sent to the study manager via sunflower-study@bristol.ac.uk. The full de-identified dataset would be available and will be held indefinitely. Access would be dependent on provision of an ethically approval study protocol and could cover numerous analysis types. The mechanism of data sharing would be determined at the time. Consent from participants will be obtained for data sharing. Data will be de-identified. Ethical approval for a new project would need to be in place.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol file	version v4.0	18/08/2020	23/09/2020	No	No
Protocol article		29/06/2021	13/08/2021	Yes	No
Protocol file	version 5.0	08/09/2021	27/10/2021	No	No
Participant information sheet	version 7.0	11/07/2022	29/07/2022	No	Yes
HRA research summary			28/06/2023	No	No
Protocol file	version 7.0	07/09/2023	17/10/2023	No	No
Protocol file	13/12/2024: The sunflower-study contact stated that based on funder recommendations protocol v8.0 had been withdrawn and the withdrawal has been confirmed by the HRA/REC, which fully withdrew the amendment to introduce version 8.0. Protocol v7.0, dated 07/09/2023 is in use. version 8.0	10/10/2024	20/11/2024	No	No