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ACCURE-UK 2: the effects of appendix removal on ulcerative colitis

Submission date 12/08/2019	**Recruitment status** No longer recruiting	[X] Prospectively registered [X] Protocol [X] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 03/09/2019	**Overall study status** Completed	
Last Edited 16/04/2025	**Condition category** Digestive System	

Plain English summary of protocol

Background and study aims
Ulcerative colitis (UC) is a form of inflammatory bowel disease. Symptoms of the disease include diarrhoea, abdominal pain and an increase in the need to use the toilet. Patients can go for months with no, or very mild symptoms (remission) and then suffer a flare-up (relapse) where symptoms become much more severe; hospital treatment can become necessary in the worse cases. There is some evidence that the appendix has a role in the regulation of inflammation within the bowel, and that removing the appendix (appendicectomy, also commonly known as appendectomy in Europe/the US) may have a positive impact on how active UC is. Results from a previous study also show that appendicectomy is safe and attractive to patients and their doctors and had better outcomes. However, the study was not designed to be large enough to prove any definite benefit. This study is a larger clinical study to complement a study currently being carried out in The Netherlands using the same design and study procedures. This will allow the researchers to combine their findings with the Dutch group in one large analysis, thereby obtaining a more robust result and in a more timely fashion. The overall aim of the research is to find out whether removing the appendix (appendicectomy) can reduce the chances of a patient experiencing further flare-ups of their Ulcerative Colitis (UC) in the future months.

Who can participate?
Patients aged 18 or over with proven ulcerative colitis who have experienced a flare-up of disease symptoms within the last 12 months, but with currently little or no disease activity (remission)

What does the study involve?
First, patients are checked to see if they are in remission by examining the large bowel with a camera (endoscopy) and/or testing a stool sample (faeces) for signs of inflammation (faecal calprotectin test). If the patient agrees to participate in the study, they are asked to sign a consent form and then asked to complete questionnaires about their quality of life. They are asked to complete the same questionnaires every 3 months for 1 year. The participant is then randomly allocated to either the appendicectomy group or the ‘control’ or comparison group. Those in the appendicectomy group have an operation to remove their appendix, continuing with their usual medication(s). Those in the control group simply continue with their usual medication(s). After this stage, follow-up involves regular reviews to discuss symptoms and

complete further questionnaires. These reviews are scheduled to take place at around 6 weeks (appendicectomy group only for standard post-operative checks), 3, 6, 9 and 12 months after entry to the study and take place in hospital at outpatient clinics. However, the reviews at 3, 6 and 9 months may be done over the telephone. At the end of the trial (12 months) participants are asked to undergo one final camera examination of their bowel. If during the 12 months periods, the participant feels they are developing symptoms of a flare, they are asked to contact the research team at their hospital to arrange an urgent review, and possibly blood tests and a camera examination of the bowel.

What are the possible benefits and risks of participating?
For participants in the control group, there will be no disadvantages from a medical point of view as they will receive standard treatment with medications as they would anyway. Additionally, the reviews planned every 3 months throughout the trial (with the exception of the final 12-month review) can be completed over the phone if visit the outpatient clinics are not always convenient. The only additional burdens are the camera tests at the beginning and end of the study. In addition, the appendicectomy group will have an operation, which is an additional treatment compared to the routine care of patients with UC. Like any surgery there is always the possibility of complications. The researchers have done their best to reduce the chances of these by ensuring that only experienced and specialised colorectal consultant surgeons undertake operations during the trial. All adverse events relating to the operations within the study will be carefully recorded as this is important information to know if this operation is offered more widely to UC patients. For participants in the control group, there is unlikely to be any personal benefit from taking part in the trial, although they will undergo a period of careful disease and medical treatment monitoring. Some patients will draw satisfaction from the knowledge that their involvement, in either group, will help determine if this new proposed treatment has the potential to benefit all patients affected by UC. For the appendicectomy group, if the operation does prove to have an impact on the disease activity in UC, there may be a potential benefit to an individual patient in taking part in terms of reducing the number or severity of disease relapses. This may in turn impact upon the future use of medication, number of hospital admissions and the need for major bowel surgery.

Where is the study run from?
The study will run across the UK including at least 10 hospitals including in Birmingham, Leicester, Cambridge, Sheffield and London.

When is the study starting and how long is it expected to run for?
May 2019 to April 2024

Who is funding the study?
National Institute for Health Research (NIHR): Efficacy and Mechanism Evaluation (EME) Programme (UK)

Who is the main contact?
Manjinder Kaur, m.kaur@bham.ac.uk

Study website
https://www.birmingham.ac.uk/ACCURE-UK2

Contact information

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
254954

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
CPMS 40580, IRAS 254954

Study information

Scientific Title
An international multicentre randomised controlled trial to assess the effect of Appendectomy on the Clinical Course of ulcerative colitis; UK arm

Acronym
ACCURE-UK 2

Study objectives
Appendicectomy will result in an improved clinical course in UC compared to those undergoing standard care, with an increased chance of maintaining remission and an associated improvement in overall symptoms.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 29/07/2019, East Midlands - Leicester South Research Ethics Committee (The Old Chapel, Royal Standard Place, Nottingham, NG1 6FS, UK; Tel: +44 (0)207 104 8109; +44 (0)207 104 8036; Email: NRESCommittee.EastMidlands-LeicesterSouth@nhs.net), ref: 19/EM/0191

Study design
Multi-centre phase 3 two-arm outcome-assessor blinded prospective randomised controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)

Hospital

Study type(s)
Treatment

Participant information sheet
https://www.birmingham.ac.uk/documents/college-mds/trials/bctu/accure-uk2/accure-uk-2-patient-information-sheet-v5.0-07-dec-21.pdf

Health condition(s) or problem(s) studied
Ulcerative colitis

Interventions
Current intervention as of 27/10/2021:
This UK study will recruit up to 90 UC patients currently in disease remission and randomly allocate them into one of two groups, the appendicectomy group or the control group. Those in the control group take their standard tablet medication as usual. Those in the appendicectomy group also take their usual medication but they also undergo an appendicectomy. All patients will then be followed up for one year with information about disease activity, medication use, health-related quality of life, health resource usage obtained.

Previous intervention:
This UK study will recruit 90 UC patients currently in disease remission and randomly allocate them into one of two groups, the appendicectomy group or the control group. Those in the control group take their standard tablet medication as usual. Those in the appendicectomy group also take their usual medication but they also undergo an appendicectomy. All patients will then be followed up for one year with information about disease activity, medication use, health-related quality of life, health resource usage obtained.

Intervention Type
Procedure/Surgery

Primary outcome measure
Current primary outcome measure as of 27/10/2021:
One-year UC relapse rate (defined both clinically and endoscopically as Mayo score ≥5 with endoscopy subscore of 2 or 3), or in absence of endoscopy based on review by an independent critical event committee of clinical information suggesting relapse such as exacerbation of symptoms and rectal bleeding or FCP>150 (> 4 weeks after surgery) or intensified medical therapy other than 5-ASA therapy.

Previous primary outcome measure:
One-year UC relapse rate (defined both clinically and endoscopically as Mayo score ≥5 with endoscopy subscore of 2 or 3)

Secondary outcome measures
Current secondary outcome measures as of 29/03/2023:

1. Number of relapses per patient at 12 months
2. Time to first relapse (defined as time between randomisation in the control group or laparoscopic appendectomy in the intervention group and, the first day of clinical symptoms of an endoscopically or clinically confirmed relapse)

3. Health-related quality of life and costs measured using (EQ-5D-3L, EORTC-QLQ-C30-QL and IBDQ at 3, 6, 9 and 12 months post-randomisation
4. Disease activity, as measured with the Mayo score at 12 months or relapse (if earlier)
5. Colectomy rate at 12 months
6. Resource usage, including medication usage, diagnostic tests undergone outside of the trial (laboratory work, radiological and endoscopic assessments), inpatient costs and health professional interactions

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Overall study start date
01/05/2019

Completion date
22/04/2024

Eligibility

Key inclusion criteria
Current inclusion criteria as of 29/03/2023:

1. Histologically confirmed Ulcerative Colitis
2. Disease relapse within 12 months prior to randomisation medically treated until remission

3. In clinical remission at time of randomisation with partial Mayo score less than 3 and presumptive endoscopic Mayo subscore of 0 or 1, identified by either:
3.1. Colonoscopy (within 3 months) examining the full length of the colon and rectum
3.2. Sigmoidoscopy (within 3 months) examining the last part of the colon (sigmoid and rectum) with faecal calprotectin less than 150 ug/g (within 3 months)
3.3 FCP less than 150 µg/g (within 3 months) with a personal history of raised FCP levels (>500 µg /g) during a previous disease flare-up at any stage
4. Aged 18 or over
5. Patient able and willing to give written informed consent

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Previous participant inclusion criteria as of 27/10/2021:

1. Histologically confirmed Ulcerative Colitis
2. Disease relapse within 12 months of randomisation medically treated until remission
3. In clinical remission at time of randomisation with partial Mayo score less than 3 and presumptive endoscopic Mayo subscore of 0 or 1, identified by either:
3.1. Colonoscopy (within 3 months) examining the full length of the colon and rectum
3.2. Sigmoidoscopy (within 3 months) examining the last part of the colon (sigmoid and rectum) with faecal calprotectin less than 150 ug/g
3.3 FCP less than 150 µg/g (within 3 months) with a personal history of raised FCP levels (>500 µg /g) during a previous disease flare-up at any stage
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Previous participant inclusion criteria:

1. Histologically confirmed Ulcerative Colitis
2. Disease relapse within 12 months of randomisation medically treated until remission
3. In clinical remission at time of randomisation with partial Mayo score less than 3 and presumptive endoscopic Mayo subscore of 0 or 1, identified by endoscopy (within 3 months). The endoscopy will be either:
3.1. Colonoscopy examining the full length of the colon and rectum
3.2. Sigmoidoscopy examining the last part of the colon (sigmoid and rectum) with faecal calprotectin less than 150 ug/g
4. Aged 18 or over
5. Patient able and willing to give written informed consent

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex

Both

Target number of participants
Planned Sample Size: 272

Total final enrolment
201

Key exclusion criteria
Current participant exclusion criteria as of 27/10/2021:
1. Previous appendicectomy or other major abdominal surgery precluding safe laparoscopic appendicectomy
2. Any suspicion of Crohn's disease
3. Disease recently treated with biologicals (within 3 months of randomisation)
4. Patients with significant comorbidity (e.g. unstable heart failure, liver or kidney failure, major lung co-morbidity)

Previous participant exclusion criteria:
1. Previous appendicectomy or other major abdominal surgery precluding safe laparoscopic appendicectomy
2. Any suspicion of Crohn's disease
3. Disease recently treated with biologicals (within 3 months of randomisation)
4. Severe disease ever treated with biologicals and stopped due to secondary non-response
5. Toxic megacolon or severe ongoing active colitis at time of randomisation
6. Patients with significant comorbidity (e.g. unstable heart failure, liver or kidney failure, major lung co-morbidity)

Date of first enrolment
03/09/2019

Date of final enrolment
01/09/2022

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Queen Elizabeth Hospital Birmingham
University Hospitals Birmingham NHS Foundation Trust
Mindelsohn Way
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B15 2WB

Study participating centre
Queen Elizabeth Hospital Birmingham
University Hospitals Birmingham NHS Foundation Trust
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Study participating centre
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Study participating centre
St Marks Hospital
London North West University Healthcare NHS Trust
Watford Road
Harrow
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HA1 3UJ

Study participating centre
Addenbrooke's Hospital
Cambridge University Hospitals NHS Foundation Trust
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CB2 0QQ

Study participating centre
Northern General Hospital
Sheffield Teaching Hospitals NHS Foundation Trust
Herries Road
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United Kingdom
S5 7AU

Study participating centre
Medway Maritime Hosptial
Medway NHS Foundation Trust
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ME7 5NY

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Queen's Medical Centre
Nottingham University Hospitals NHS Trust
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NG7 2UH

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G51 4TF

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East Sussex Healthcare NHS Trust
The Ridge
St Leonards-on-Sea
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TN37 7RD

Study participating centre
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Wolverhampton Road
Wolverhampton
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WV10 0QP

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Sponsor type
University/education

ROR
https://ror.org/03angcq70

Funder(s)

Funder type
Government

Funder Name
NIHR Evaluation, Trials and Studies Co-ordinating Centre (NETSCC); Grant Codes: 16/61/35

Results and Publications

Publication and dissemination plan
The protocol is available on the ACCURE-UK 2 website (https://www.birmingham.ac.uk/ACCURE-UK2). The findings will be published in international medical journals, publicised on the trial website and presented at relevant conferences.

Intention to publish date
30/11/2024

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from Dr Laura Magill (e.l.magill@bham.ac.uk). Access to available anonymised data may be granted following review.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol (other)	5.0	07/12/2021	29/03/2023	No	No
HRA research summary			28/06/2023	No	No
Statistical Analysis Plan		26/03/2024	27/03/2024	No	No
Results article		11/04/2025	16/04/2025	Yes	No