

# A trial to determine if a special liquid diet (exclusive enteral nutrition) before Crohn's disease surgery improves recovery

<b>Submission date</b> 25/07/2023	<b>Recruitment status</b> No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 10/08/2023	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 19/04/2024	<b>Condition category</b> Surgery	<input type="checkbox"/> Individual participant data <input type="checkbox"/> Record updated in last year

## Plain English summary of protocol

### Background and study aims

Crohn's disease is a lifelong inflammatory illness that causes people to have severe stomach pains, chronic diarrhoea, and suffer weight loss. There is no cure. Crohn's disease causes inflammation, ulceration, bleeding and narrowing of the digestive system. People can have periods of good health (remission) and times when symptoms are more active (flare-ups or relapses). Medications can help keep it in remission, however, one-third of people will need surgery to remove/repair part of their diseased gut at some stage.

Previous studies suggest that a special liquid diet might help improve recovery from surgery. This diet is called exclusive enteral nutrition (EEN) because it is the only form of food taken for a period of time. In active Crohn's disease, this special liquid diet can improve symptoms, reduce inflammation and heal the gut better than steroids. EEN is not offered routinely to patients at the moment because we don't have any evidence-based research.

This study aims to find out whether 6 weeks of EEN diet pre-surgery might help participants recover quicker and make the surgery safer with less chance of complications compared to a usual diet pre-surgery.

### Who can participate?

Patients aged 16 years and over from across the UK due to have surgery for Crohn's disease

### What does the study involve?

Participants are randomly allocated to a minimum of 6 weeks of EEN pre-operatively or the usual diet. All patients will undergo surgery and be followed up for 1 year with information about disease activity, medication use, health-related quality of life and health resource usage is obtained. An embedded study will explore patients' and healthcare professionals' views and experiences of all aspects of the study. There is an optional sub-study which involves a more detailed assessment of outcomes related to early/late surgery and dietary aspects in terms of nutrient intake, dietary habits and food-related quality-of-life. The follow-up schedule is designed to collect data only at time points comparable to common clinical practice to reduce patient burden and the need to attend additional hospital appointments.

What are the possible benefits and risks of participating?

If the liquid diet can be shown to improve symptoms, widespread uptake is anticipated.

Participants in both groups will be undergoing elective surgery as part of their standard medical care. The trial intervention is purely nutritional, with the main risk relating to poor tolerance of the EEN. This could mean that some patients in the EEN arm may not meet their nutritional requirements. However, this risk will be mitigated by having close dietitian follow-up and by not mandating a particular type of EEN to be used within the study. Hospitals have more than one type of EEN available. Participants will be allowed to choose from the EEN available at each site until they can find one that they can tolerate. They can also use a variety of EEN supplements to minimise taste fatigue. Participants will be made aware of the risks and benefits during the consent process and written information will be provided in the patient Information Sheet. The participants' GPs will also be informed that their patients are participating in a clinical trial and of the allocated treatment.

Where is the study run from?

Birmingham Clinical Trials Unit based at the University of Birmingham (UK)

When is the study starting and how long is it expected to run for?

May 2022 to April 2026

Who is funding the study?

National Institute for Health and Care Research (NIHR) Health Technology Assessment (HTA) (UK)

Who is the main contact?

[ocean@trials.bham.ac.uk](mailto:ocean@trials.bham.ac.uk)

## Contact information

**Type(s)**

Public

**Contact name**

Miss Pooja Gaddu

**Contact details**

Birmingham Clinical Trials Unit (BCTU)

Public Health Building

University of Birmingham

Edgbaston

Birmingham

United Kingdom

B15 2TT

+44 (0)121 415 9120

[ocean@trials.bham.ac.uk](mailto:ocean@trials.bham.ac.uk)

## Additional identifiers

**Clinical Trials Information System (CTIS)**

Nil known

## **Integrated Research Application System (IRAS)**

325763

### **Protocol serial number**

2.0, IRAS 325763, CPMS 56722

## **Study information**

### **Scientific Title**

Optimisation before Crohn's surgery using exclusive enteral nutrition

### **Acronym**

OCEaN

### **Study objectives**

To determine if pre-operative exclusive enteral nutrition (EEN) is more clinically and cost-effective compared with usual diet in patients undergoing surgery for Crohn's disease (CD).

### **Ethics approval required**

Ethics approval required

### **Ethics approval(s)**

approved 11/07/2023, London City & East REC (Research Ethics Committee Centre, 2nd Floor, 2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 (0)207 1048171; cityandeast.rec@hra.nhs.uk), ref: 23/LO/0513

### **Study design**

Multi-centre two-arm parallel-group open-label pragmatic randomized controlled trial with a mixed methods internal pilot

### **Primary study design**

Interventional

### **Study type(s)**

Treatment

### **Health condition(s) or problem(s) studied**

Planned surgery for small bowel and/or colonic Crohn's disease (primary or repeat surgery)

### **Interventions**

The intervention is a minimum of 6 weeks of EEN pre-operatively. The control group is the usual diet.

Following randomisation into the trial, participants will be reviewed by the local dietitian, and their feed will be prescribed. The type of EEN formula prescribed to each participant will be decided by dietitian preference and/or local availability. If participants cannot tolerate the first feed prescribed, an alternate EEN formula can be used, or participants can use a variety of EEN feeds to reduce taste fatigue. Feeds may be concentrated to reduce the volume of feeds consumed. If tolerance remains poor, nasogastric feeding can be offered.

The start date of EEN will be agreed between the dietitian and the participant. An online support tool (FutureLearn Ltd), developed with the patient panel and Crohn's and Colitis UK, will provide information, peer support and assistance to participants randomised to EEN, which will also help facilitate adherence to an EEN diet. The OCEaN trial team have developed some EEN diet patient support sheets to help support patients on the liquid diet, as well as standardise the delivery of the EEN across the sites as much as possible. EEN is often started by the hospital dietitian and then continued by either the hospital or provision is transferred to the community dietitians and/or the GP. This pathway is likely to vary between sites, and so will be directed by local practice and local resources.

## **Intervention Type**

Supplement

## **Primary outcome(s)**

Dual primary outcomes at 6 weeks post-surgery:

1. Crohn's Life Impact Questionnaire (CLIQ; a CD-specific patient reported outcome assessing QoL)

2. Post-surgery complications using the Comprehensive Complication Index (CCI)

If we demonstrate benefit for EEN on either of the primary outcomes this establishes effectiveness

## **Key secondary outcome(s)**

Patient reported:

1. QoL over time using the CLIQ which will be collected post-surgery, fortnightly until 12 weeks post-surgery and then monthly up to 24 weeks post-surgery

2. Post-surgery recovery using the Surgical Quality of Recovery-15 (QoR-15) on day 3 post-surgery (or pre-discharge if discharged before day 3). The QoR-15 is a short form version of the QoR-40 and consists of 15 items each with a numerical rating score of 0-10. The total score therefore ranges from 0 to 150, with higher scores indicating better quality of recovery.

Clinical:

3. Length of post-operative hospital stay (measured in nights in hospital)

4. Length of bowel resected (in centimetres measured along anti-mesenteric border) at time of surgery before being put in formalin

5. Number of anastomoses formed at surgery as documented in the operation notes or from discussion with the operating surgeon

6. Number of participants requiring stoma formation either at index operation or within 30 days of surgery due to re-operation

7. Number of participants who develop an anastomotic leak (either radiological concern or confirmed at reoperation) within 30 days of surgery

8. Number of participants re-admitted within 30 days of date of discharge

9. Number of participants requiring re-operation within 30 days of surgery

10. Number of participants who develop enterocutaneous fistulae within 90 days of surgery. This is defined as any new fistula tract from any point in the gastrointestinal tract opening on to skin at any site from day of surgery to 90 days later. Enterocutaneous fistula diagnosis can be confirmed following clinical assessment. Radiological confirmation is not required.

11. Number of participants who develop clinical recurrence of their CD at 24 and 52 weeks post-surgery as assessed by the Crohn's Disease Activity Index (CDAI)

12. Number of participants who develop endoscopic disease recurrence assessed endoscopically on colonoscopy performed between 24 and 52 weeks post-surgery as part of standard of care. (66, 67) Modified Rutgeert's score should be used to grade the severity of recurrence. (67) If

endoscopy is not performed but patient has cross sectional imaging (e.g. Magnetic resonance imaging (MRI), Computerised Tomography (CT) or ultrasound) as part of standard of care (routine assessments), the presence or absence of disease recurrence on imaging can be used as an alternative.

13. Number of participants on steroids at baseline who were able to wean off steroids prior to surgery. Steroid usage and dosage (including prednisolone (oral/rectal), Budesonide (oral/rectal), Hydrocortisone (intravenous/oral)) will be recorded at baseline and on day of surgery to determine change in use or dose. Inhaled or topical steroid use is not relevant to this trial.

14. Safety assessed through adverse event and serious adverse event reporting

15. Number of participants whose planned surgery did not proceed due to clinical improvement. If planned surgery is cancelled by the local team because clinical improvement deems it no longer necessary, these participants will continue to follow the trial protocol (e.g., follow-up assessments etc.)

16. Number of participants who required expedited or emergency surgery. This refers to participants whose elective/planned CD surgery date is brought forward due to clinical deterioration.

Economic outcomes:

17. The EuroQoL-5D-5 Level (EQ-5D-5L) questionnaire and an incremental cost-utility analysis will determine the cost per quality-adjusted life year (QALY) gained over the 52 weeks post-surgery. The EQ-5D-5L will be collected pre-operatively, and then at 6 weeks post-operatively, and then also at 24 and 52 weeks post operatively.

Qualitative outcomes:

18. Interviews will be undertaken with participants randomised to both trial groups, and also with staff involved in the trial. This research aims to provide in-depth qualitative data concerning the acceptability and experience of EEN as a pre-surgical intervention.

Exploratory outcomes:

19. Change in the Harvey-Bradshaw Index (HBI) and CLIQ between baseline and pre-operatively to determine if EEN improves HBI and CLIQ.

20. To determine if baseline microbiome compositional and metabolomic signatures, and changes after 6-weeks of EEN, can predict primary and secondary trial outcomes including post-surgical complications and likelihood of disease recurrence at follow-up. The samples are being collected as part of the main trial in order to measure faecal calprotectin. Further analysis will be performed and funded separately by UoG.

COAST sub-study outcomes:

21. COAST will analyse the subset of participants who are having surgery for terminal ileal CD to determine the impact of surgical timing on QoL and cost.

Microbiome analysis outcomes:

22. As an exploratory trial outcome, we will study if baseline microbiome compositional and metabolomic signatures, and changes after 6-weeks of EEN, can predict primary and secondary trial outcomes including post-surgical complications and likelihood of disease recurrence at follow-up.

**Completion date**

01/04/2026

## Eligibility

**Key inclusion criteria**

1. Any patient undergoing planned surgery for small bowel and/or colonic CD (primary or repeat surgery)
2. Age  $\geq$ 16 years
3. Willingness to go on EEN for the duration of the intervention period (minimum of 6 weeks)
4. Capacity to give consent

**Participant type(s)**

Patient

**Healthy volunteers allowed**

No

**Age group**

Adult

**Lower age limit**

16 years

**Upper age limit**

99 years

**Sex**

All

**Key exclusion criteria**

1. Surgery for peri-anal CD, ulcerative colitis, or inflammatory bowel disease unclassified (IBDU)
2. Patients who require parenteral nutrition in the 6 weeks prior to surgery
3. Inability to comply with the trial schedule and follow up

**Date of first enrolment**

11/04/2024

**Date of final enrolment**

31/01/2025

**Locations****Countries of recruitment**

United Kingdom

England

Northern Ireland

Scotland

Wales

**Study participating centre**

**Dorset County Hospital**

Williams Avenue  
DORCHESTER  
United Kingdom  
DT1 2JY

**Study participating centre**

**Barts Health NHS Trust**

The Royal London Hospital  
80 Newark Street  
London  
United Kingdom  
E1 2ES

**Study participating centre**

**County Durham and Darlington NHS Foundation Trust**

Darlington Memorial Hospital  
Hollyhurst Road  
Darlington  
United Kingdom  
DL3 6HX

**Study participating centre**

**Imperial College Healthcare NHS Trust**

The Bays  
St Marys Hospital  
South Wharf Road  
London  
United Kingdom  
W2 1BL

**Study participating centre**

**North Tees and Hartlepool NHS Foundation Trust**

University Hospital of Hartlepool  
Holdforth Road  
Hartlepool  
United Kingdom  
TS24 9AH

**Study participating centre**

**University College London Hospitals NHS Foundation Trust**  
250 Euston Road  
London  
United Kingdom  
NW1 2PG

**Study participating centre**  
**Liverpool University Hospitals NHS Foundation Trust**  
Prescot Street  
Liverpool  
United Kingdom  
L7 8XP

**Study participating centre**  
**Maidstone and Turnbridge Wells NHS Trust**  
Hermitage Lane  
Maidstone  
United Kingdom  
ME16 9QQ

**Study participating centre**  
**The Newcastle upon Tyne Hospitals NHS Foundation Trust**  
Freeman Road  
Newcastle upon Tyne  
United Kingdom  
NE7 7DN

**Study participating centre**  
**Lewisham and Greenwich NHS Trust**  
Lewisham High Street  
LONDON  
United Kingdom  
SE13 6LH

**Study participating centre**  
**Royal Cornwall Hospitals NHS Trust**  
Royal Cornwall Hospital  
Treliske  
Truro  
United Kingdom  
TR1 3LJ

**Study participating centre**  
**Dartford and Gravesham NHS Trust**  
Darenth Wood Road  
DARTFORD  
United Kingdom  
DA2 8DA

**Study participating centre**  
**Croydon Health Services NHS Trust**  
530 London Road  
Thornton Heath  
United Kingdom  
CR7 7YE

**Study participating centre**  
**St Marks Bowel Cancer Screening Centre**  
Watford Road  
Harrow  
United Kingdom  
HA1 3UJ

**Study participating centre**  
**King's College Hospital NHS Foundation Trust**  
Denmark Hill  
LONDON  
United Kingdom  
SE5 9RS

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

**Study participating centre**  
**Manchester University NHS Foundation Trust**  
Cobbett House

Oxford Road  
Manchester  
United Kingdom  
M13 9WL

**Study participating centre**  
**Leeds Teaching Hospitals NHS Trust**  
Beckett Street  
LEEDS  
United Kingdom  
LS9 7TF

**Study participating centre**  
**University Hospitals Plymouth NHS Trust**  
Derriford Road  
PLYMOUTH  
United Kingdom  
PL6 8DH

**Study participating centre**  
**The Royal Wolverhampton NHS Trust**  
New Cross Hospital  
Wolverhampton Road  
Heath Town  
Wolverhampton  
United Kingdom  
WV10 0QP

**Study participating centre**  
**The Dudley Group NHS Foundation Trust**  
Pensnett Road  
Dudley  
United Kingdom  
DY1 2HQ

**Study participating centre**  
**Nottingham University Hospitals NHS Trust**  
Queens Medical Centre  
Derby Road

NOTTINGHAM  
United Kingdom  
NG7 2UH

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

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

**Study participating centre**  
**NHS Greater Glasgow and Clyde**  
J B Russell House  
Gartnavel Royal Hospital  
1055 Great Western Road Glasgow  
Glasgow  
United Kingdom  
G12 0XH

**Study participating centre**  
**University Hospital Southampton NHS Foundation Trust**  
Tremona Road  
Southampton  
United Kingdom  
SO16 6YD

**Study participating centre**  
**Cambridge University Hospitals NHS Foundation Trust**  
Hills Road  
Cambridge  
United Kingdom  
CB2 0QQ

**Study participating centre**

**University Hospitals Birmingham NHS Foundation Trust**

Queen Elizabeth Hospital

Mindelsohn Way

Edgbaston

Birmingham

United Kingdom

B15 2GW

**Study participating centre**

**University Hospitals of Leicester NHS Trust**

Infirmery Square

Leicester

United Kingdom

LE1 5WW

**Study participating centre**

**London North West University Healthcare NHS Trust**

Northwick Park Hospital

Watford Road

Harrow

United Kingdom

HA1 3UJ

**Study participating centre**

**Northern Care Alliance NHS Foundation Trust**

Stott Lane

Manchester

United Kingdom

M6 8HD

**Study participating centre**

**Medway NHS Foundation Trust**

Windmill Road

Gillingham

United Kingdom

ME7 5NY

# Sponsor information

## Organisation

University of Birmingham

## ROR

<https://ror.org/03angcq70>

# Funder(s)

## Funder type

Government

## Funder Name

Health Technology Assessment Programme

## Alternative Name(s)

NIHR Health Technology Assessment Programme, Health Technology Assessment (HTA), HTA

## Funding Body Type

Government organisation

## Funding Body Subtype

National government

## Location

United Kingdom

# Results and Publications

## Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study will be available upon request from the BCTU Data Sharing Committee.  
[ocean@trials.bham.ac.uk](mailto:ocean@trials.bham.ac.uk)

## IPD sharing plan summary

Available on request

## Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">HRA research summary</a>			20/09/2023	No	No
<a href="#">Study website</a>	Study website	11/11/2025	11/11/2025	No	Yes