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

Submission date 25/07/2023	**Recruitment status** No longer recruiting	[X] Prospectively registered [ ] Protocol [ ] Statistical analysis plan [ ] Results [ ] Individual participant data [ ] Record updated in last year
Registration date 10/08/2023	**Overall study status** Ongoing	
Last Edited 19/04/2024	**Condition category** Surgery	

Plain English Summary

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

Study website
https://www.birmingham.ac.uk/ocean

Contact information

Type(s)
Public

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
325763

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
2.0, IRAS 325763, CPMS 56722

Study information

Scientific Title
Optimisation before Crohn's surgery using exclusive enteral nutrition

Acronym
OCEaN

Study hypothesis
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

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format

Condition
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 measure
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

Secondary outcome measures
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.

Overall study start date
01/05/2022

Overall study end date
01/04/2026

Eligibility

Participant inclusion criteria
1. Any patient undergoing planned surgery for small bowel and/or colonic CD (primary or repeat surgery)
2. Age ≥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

Age group
Adult

Lower age limit
16 Years

Upper age limit
99 Years

Sex
Both

Target number of participants
618

Participant 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

Recruitment start date
11/04/2024

Recruitment end date
31/01/2025

Locations

Countries of recruitment
England

Northern Ireland

Scotland

United Kingdom

Wales

Study participating centre
Dorset County Hospital
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Study participating centre
Barts Health NHS Trust
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PL6 8DH

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Organisation
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Sponsor type
University/education

Website
http://www.birmingham.ac.uk/index.aspx

ROR
https://ror.org/03angcq70

Funder(s)

Funder type
Government

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
On completion of the trial, the data will be analysed, and a Final Study Report prepared. Results of this trial will be submitted for publication in a peer reviewed journal and the findings of the trial will be made public. This manuscript will be prepared by the CI and members of the TMG and submitted to the whole TMG in a timely fashion and in advance of being submitted for publication to allow time for review.
Outputs from this trial will be published under a corporate authorship group. Each publication will include a detailed description of the exact contributions of each person, following accepted guidelines for collaborative authorship models.
Any secondary publications and presentations prepared by investigators must be reviewed and approved the TMG. Manuscripts should be submitted to the TMG in a timely fashion and in advance of being submitted for publication, to allow time for review and resolution of any outstanding issues. In all publications, authors must acknowledge that the trial was performed with the support of NIHR, University Hospitals Birmingham and the University of Birmingham (the Sponsor) and Birmingham Clinical Trials Unit. Intellectual property rights will be addressed in the OCEaN Clinical Trial Site Agreement between Sponsor and site.
Participants can request the published trial results from their PI once available.

Intention to publish date
01/10/2026

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

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			20/09/2023	No	No