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The ADDapt diet in reducing Crohn's disease inflammation

Submission date 29/07/2019	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 29/07/2019	**Overall study status** Completed	
Last Edited 17/10/2024	**Condition category** Digestive System	

Plain English summary of protocol

Background and study aims

Crohn’s disease (CD) results in chronic intestinal inflammation, is of increasing incidence both in the developed and developing world and has a marked impact on patient quality of life. The prevalence of CD is 10.6 per 100,000 people in the UK and represents a significant annual financial burden of around €16.7 million in Europe.

A wide range of nutrients and food components have been investigated for their role in the pathogenesis and course of CD. A common theme suggests that CD risk is associated with a “Western diet”, including high fat, high sugar and processed foods. However, intervention studies that exclude specific aspects of the diet such as sugar or that compare low and high fat diets have failed to show effectiveness in practice. Observational human and experimental animal studies suggest that certain food additives used extensively by the food industry play a role in the pathogenesis and natural history of CD. However, to date no evidence exists for the effectiveness of a diet low in these food additives in CD.

Therefore, the aim of this study is to investigate the effects of a diet low in certain food additives compared to a normal UK diet on CD activity, health-related quality of life, gut bacteria, gut permeability, gut inflammation and dietary intake, in patients with mildly active, stable CD. We will recruit patients with mildly active CD and will randomise them to receive either the diet low in the food additives of interest, or the diet representative of a normal UK diet. Patients will follow the diet for 8 weeks and will attend study visits at the start and end of the trial, at which points questionnaires will be completed and samples will be collected.

Who can participate?

Adults aged 16 years or older (updated 03/02/2022, previously: aged 18 years or older) with mildly active Crohn's disease.

What does the study involve?

Patients will be asked to follow a set diet for 8-weeks, during which time they will attend clinic visits to gather information on food intake, general health, and to provide samples for analysis.

What are the possible benefits and risks of participating?

The results of this study may help to answer scientific questions about whether reducing specific food ingredients improves intestinal inflammation in patients with active Crohn’s disease, and

whether there is any beneficial effect on the gut bacteria. The ADDapt diet can be challenging to follow because certain pre-prepared and convenience foods are excluded. There are still plenty of convenience foods, pre-prepared foods and ready-meals that are suitable, and these can still be eaten provided you check their suitability with the dietitian. The ADDapt diet is nutritionally balanced and your dietitian will be able to help answer any questions you have whilst you are on the diet. If you are preparing food for other people, it is safe for them to eat the same meals as you.

Where is the study run from?
King's College, London

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

Who is funding the study?
1. Leona M. and Harry B. Helmsley Charitable Trust
2. National Institute for Health Research (NIHR), UK

Who is the main contact?
Dr Aaron Bancil
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Contact information

Type(s)
Scientific

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Dr Aaron Bancil

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
NCT04046913

Secondary identifying numbers
CPMS 41991

Study information

Scientific Title
The ADDapt diet in reducing Crohn's disease inflammation

Acronym
ADDapt

Study objectives
There is a difference in the proportion of patients achieving at least a 70 point reduction in the Crohn's Disease Activity Index (CDAI) between baseline and end of the trial, between the two diet groups.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 15/07/2019, East of Scotland Research Ethics Service (EoSRES) (Tayside medical Science Centre, Residency Block Level 3. George Pirie Way, Ninewells Hospital and Medical School, Dundee, DD1 9SY; +441382383878; eosres.tayside@nhs.net), ref: 19/ES/0049

Study design
Randomized; Interventional; Design type: Treatment, Dietary

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Quality of life

Participant information sheet
Not available in web format, please use the contact details to request a patient information sheet

Health condition(s) or problem(s) studied
Crohn's disease

Interventions
Current intervention as of 03/02/2022:
This will be an 8-week randomised double-blind, placebo-controlled trial in 154 patients with mildly active, stable Crohn's disease. Patients will be recruited from five London inflammatory

bowel disease (IBD) centres.
These will be Guy's and St Thomas' NHS Foundation Trust, Barts Health NHS Trust, St Marks Hospital, University College Hospital NHS Foundation Trust and Royal Free Hospital NHS Foundation Trust. Further trusts have been added recently.

In this trial, all patients will follow a low food additive background diet. Patients will be randomised to either the low food additive diet or control diet (mimicking a habitual UK diet) group, in a 1:1 ratio. Block randomisation will be stratified according to Crohn's Disease location (ileal, ileo-colonic, colonic) and whether the patient opts for sigmoidoscopy or not. The randomisation schedule will be constructed using an online program by a researcher not involved in trial planning or recruitment. The researcher randomising participants and measuring trial outcomes will not be aware of diet allocation.

In addition to following the background low food additive diet, patients in the diet groups will receive the following foods:
Low food additive diet (intervention) group:
- Additive-free trial foods formulated specifically for this project, to be eaten in specific portions every day during the trial.
Control group:
- A supply of food additive-containing trial foods formulated specifically for this project.

Trial procedures:

Screening:
Trial investigators will attend gastroenterology clinics at each of the five recruitment sites each week. Gastroenterologists, IBD nurses and IBD pharmacists will refer potentially suitable and willing patients for screening. Patients will be given a participant information sheet (PIS) and offered their hospital's leaflet on sigmoidosopies and will be screened against inclusion and exclusion criteria. Patients will be given at least 24 hours to consider the study and ask questions prior to consent.
Suitable patients wishing to take part will be allowed to consent to the trial on the day of screening if this is more convenient for them than attending a separate consent visit. Otherwise, patients will attend the hospital clinic or the metabolic research unit at King's College London to provide consent.
After consent, eligible patients will be instructed by an experienced research dietitian to complete a 7-day food and symptom diary, which will be used to assess disease activity and dietary intake.

Baseline visit:
Patients meeting all of the inclusion criteria and none of the exclusion criteria and having consented will attend a baseline visit at either the hospital clinic or the metabolic research unit at King's College London (whichever is most convenient for the patient) following an overnight fast. The following procedures will be undertaken:
• Demographic characteristics
• Patient-completed questionnaires
• A whole stool sample will be collected within 2 hours of the visit
• A baseline urine sample will be collected for intestinal permeability
• Blood samples will be collected
• Participants opting into the sigmoidoscopy sub study (n=77) will undergo an unprepared flexible sigmoidoscopy
• All participants will be provided with thorough instruction on the low food additive diet by an experienced specialist dietitian.

Patients will be randomized to either the low food additive diet or control diet and will receive a supply of the foods described above.

Monitoring and safety: Patients will be given contact details for the study investigators and will be telephoned once a week to monitor progress with the intervention, compliance to the low food additive diet and consumption of the trial foods. Furthermore, any reported adverse events will be recorded at these contacts, and investigators will address any concerns that patients may have regarding any aspects of the trial.
Compliance: Compliance with the experimental diet allocation and the trial foods will be monitored and encouraged at the weekly telephone contacts.
Follow-up visit: After the 8-week trial, participants will return for an end of trial visit after an overnight fast. Participants will complete a food and symptom diary, identical to that completed during screening, for 7 days prior to this visit. At this visit, the following will take place:
• The Crohn's Disease Activity Index (CDAI) score will be calculated
• Stool, urine and blood samples will be collected using the methods described in the baseline visit. Flexible, unprepared sigmoidoscopies will be performed as described in the baseline visit

Long-term follow-up:
Following completion of the 8-week trial, patients will have the option of continuing to follow the experimental diet for an additional 16 weeks. At monthly intervals during this period, a telephone visit will be conducted, to investigate diet compliance and acceptability and to provide patient support.
At the end of trial visit (following the 8-week trial), patients will be provided with a blank 7-day food and symptom diary and will be instructed to complete it for the 7 days prior to a long-term visit, which will take place after a total of 24 weeks

At the long-term visit, the following procedures will take place:
• CDAI score will be calculated
• Patient-completed questionnaires
• A whole stool sample and blood samples will be collected using the methods described above.
Following completion of the trial (or withdrawal), patients will be instructed to return to their normal diet and will be provided with written general dietary guidance for Crohn's disease (Crohn’s and Colitis UK).

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Previous intervention:
This will be an 8-week randomised double-blind, placebo-controlled trial in 154 patients with mildly active, stable Crohn's disease. Patients will be recruited from five London inflammatory bowel disease (IBD) centres.
These will be Guy's and St Thomas' NHS Foundation Trust, Barts Health NHS Trust, St Marks Hospital, University College Hospital NHS Foundation Trust and Royal Free Hospital NHS Foundation Trust.

In this trial, all patients will follow a low food additive background diet. Patients will be randomised to either the low food additive diet or control diet (mimicking a habitual UK diet) group, in a 1:1 ratio. Block randomisation will be stratified according to Crohn’s Disease location (ileal, ileo-colonic, colonic) and whether the patient opts for sigmoidoscopy or not. The randomisation schedule will be constructed using an online program by a researcher not involved in trial planning or recruitment. The researcher randomising participants and measuring trial outcomes will not be aware of diet allocation.

In addition to following the background low food additive diet, patients in the diet groups will receive the following foods:
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Suitable patients wishing to take part will be allowed to consent to the trial on the day of screening if this is more convenient for them than attending a separate consent visit. Otherwise, patients will attend the hospital clinic or the metabolic research unit at King's College London to provide consent.
After consent, eligible patients will be instructed by an experienced research dietitian to complete a 7-day food and symptom diary, which will be used to assess disease activity and dietary intake.

Baseline visit:
Patients meeting all of the inclusion criteria and none of the exclusion criteria and having consented will attend a baseline visit at either the hospital clinic or the metabolic research unit at King's College London (whichever is most convenient for the patient) following an overnight fast. The following procedures will be undertaken:
• Demographic characteristics
• Patient-completed questionnaires
• A whole stool sample will be collected within 2 hours of the visit
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• Participants opting into the sigmoidoscopy sub study (n=77) will undergo an unprepared flexible sigmoidoscopy
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Compliance: Compliance with the experimental diet allocation and the trial foods will be monitored and encouraged at the weekly telephone contacts.
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Following completion of the 8-week trial, patients will have the option of continuing to follow the experimental diet for an additional 16 weeks. At monthly intervals during this period, a telephone visit will be conducted, to investigate diet compliance and acceptability and to provide patient support.
At the end of trial visit (following the 8-week trial), patients will be provided with a blank 7-day food and symptom diary and will be instructed to complete it for the 7 days prior to a long-term visit, which will take place after a total of 24 weeks

At the long-term visit, the following procedures will take place:
• CDAI score will be calculated
• Patient-completed questionnaires
• A whole stool sample and blood samples will be collected using the methods described above.
Following completion of the trial (or withdrawal), patients will be instructed to return to their normal diet and will be provided with written general dietary guidance for Crohn's disease (Crohn's and Colitis UK).

Intervention Type
Other

Primary outcome measure
Reduction in the Crohn's Disease Activity Index (CDAI) between baseline and end of trial (8-weeks)

Secondary outcome measures
1. Crohn's disease activity as measured using the Crohn's Disease Activity Index (CDAI) at baseline, week 8 and week 26
2. Gastrointestinal inflammation as measured using faecal calprotectin at baseline, week 8 and week 26
3. Systemic inflammation as measured using CRP concentration at baseline, week 8 and week 26
4. Perceived disease control as measured by the IBD-control questionnaire at baseline, week 8 and week 26
5. Health related quality of life as measured by the Inflammatory Bowel Disease Questionnaire (IBD-Q) at baseline, week 8 and week 26.
6. Dietary intake as measured by 7-day food diaries at baseline, week 8 and week 26
7. Dietary compliance and acceptability as measured by acceptability questionnaire and food-related Quality of Life questionnaire at baseline, week 8 and week 26
8. Gastrointestinal permeability as measured by urine analysis at baseline and week 8
9. Gastrointestinal microbiota as measured by faecal microbiota composition and mucosal microbiota composition at baseline and week 8 (in a subset of participants)
10. Mucosal immune gene expression as measured on immune cells from rectal biopsies at baseline and week 8 (in a subset of participants)

Overall study start date
01/01/2019

Completion date

31/12/2024

Eligibility

Key inclusion criteria
Current participant inclusion criteria as of 03/02/2022:
1. Adults aged ≥16 years
2. Crohn's disease diagnosis (defined by standard clinical, histological and radiological criteria) of at least 6 months
3. Mildly active disease as defined by:
3.1 Defined by physician assessment that no change in medication is required
3.2 Faecal calprotectin >150 µg/g
3.3 CDAI between 150-250
3.4 Current body weight of ≥50 kg
3.5 Individuals able to give informed consent and willingness to participate

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Previous participant inclusion criteria:
1. Adults aged > = 18 years
2. Crohn's disease diagnosis (defined by standard clinical, histological and radiological criteria) of at least 6 months
3. Mildly active disease as defined by:
3.1 Defined by physician assessment that no change in medication is required
3.2 Faecal calprotectin > 150 µg/g
3.3 CDAI between 150-250
3.4 Current body weight of > = 50 kg
3.5 Individuals able to give informed consent and willingness to participate

Participant type(s)
Patient

Age group
Adult

Lower age limit
16 Years

Sex
Both

Target number of participants
Planned Sample Size: 154; UK Sample Size: 154

Total final enrolment
154

Key exclusion criteria
1. Changes in dose to azathioprine, 6-mercaptopurine, methotrexate or anti-TNF-α agents or other biologics during the preceding 8 weeks, oral 5-ASA during the preceding four weeks.

Currently receiving oral prednisolone/budesonide or discontinued within the last 4 weeks, unless they are on a stable dose of 10 mg/day or less prednisolone (3 mg or less budesonide) for at least 4 weeks with the intention to continue this long term.
2. Used rectal 5-ASA or rectal steroids in the preceding 4 weeks
3. Previous extensive bowel resection, defined as having had > 2 intestinal resections, a sub-total colectomy or documented short bowel syndrome
4. Poorly controlled bile acid malabsorption
5. Current stoma
6. Recent use of the following treatments: antibiotics, probiotics, prebiotic or fibre supplements in the preceding four weeks, NSAIDs during the preceding week
7. Full bowel preparation for a diagnostic procedure in preceding 4 weeks
8. Comorbidities including sepsis/fever, diabetes or coeliac disease, or other concomitant serious comorbidity e.g. significant psychiatric, hepatic, renal, endocrine, respiratory, neurological or cardiovascular disease
9. Exclusive enteral nutrition in the past 8 weeks
10. Assessed as at nutritional risk, as defined by any of the following:
10.1 BMI < = 18.5 kg/m2
10.2 Previous or current eating disorder
10.3 Currently receiving prescribed oral nutritional supplements
11. Following a restrictive diet (e.g. multiple restrictions due to numerous self-reported allergies) as judged by the dietitian
12. Reported pregnancy or lactation

Date of first enrolment
12/08/2019

Date of final enrolment
29/02/2024

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Guy's Hospital
Guy's & St Thomas' NHS Foundation Trust
Great Maze Pond
London
United Kingdom
SE1 9RT

Study participating centre
Northwick Park Hospital
Watford Road

Harrow
United Kingdom
HA1 3UJ

Study participating centre
University College London Hospitals NHS Foundation Trust
235 Euston Road
London
United Kingdom
NW1 2BU

Study participating centre
Royal Free Hospital
Pond Street
London
United Kingdom
NW3 2QG

Study participating centre
The Royal London Hospital
Whitechapel Road
Whitechapel
London
United Kingdom
E1 1BB

Study participating centre
Chelsea and Westminster Hospital NHS Foundation Trust
Chelsea & Westminster Hospital
369 Fulham Road
London
United Kingdom
SW10 9NH

Study participating centre
Addenbrookes
Addenbrookes Hospital
Hills Road
Cambridge
United Kingdom
CB2 0QQ

Study participating centre
Pennine Acute Hospitals NHS Trust
Trust Headquarters
North Manchester General Hospital
Delaunays Road, Crumpsall
Manchester
United Kingdom
M8 5RB

Study participating centre
County Durham and Darlington NHS Foundation Trust
Darlington Memorial Hospital
Hollyhurst Road
Darlington
United Kingdom
DL3 6HX

Study participating centre
University Hospital Bristol
Bristol Royal Infirmary
Marlborough Street
Bristol
United Kingdom
BS2 8HW

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

Study participating centre
United Leeds Teaching Hospital NHS Trust
Trust Hq
Leeds General Infirmary
Great George St
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United Kingdom
LS1 3EX

Study participating centre
NHS Lothian
Crewe Rd S
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United Kingdom
EH4 2XU

Study participating centre
East Sussex Healthcare NHS Trust
The Ridge
St Leonards-on-Sea
United Kingdom
TN37 7RD

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

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

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

Study participating centre
Imperial College Healthcare NHS Trust
St Mary's Hospital
Praed Street
London
United Kingdom
W2 1NY

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

Sponsor information

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Sponsor type
University/education

ROR
https://ror.org/0220mzb33

Funder(s)

Funder type
Charity

Funder Name
Leona M. and Harry B. Helmsley Charitable Trust

Alternative Name(s)
Helmsley Charitable Trust, The Leona M. and Harry B. Helmsley Charitable Trust, Leona M. & Harry B. Helmsley Charitable Trust, The Helmsley Charitable Trust

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United States of America

Funder Name
National Institute for Health 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

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal

Intention to publish date
28/02/2025

Individual participant data (IPD) sharing plan
The current data sharing plans for this study are unknown and will be 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?
HRA research summary			28/06/2023	No	No