

Eating behaviour in Crohn's disease

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Short title: Eating behaviour in Crohn's disease

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STUDY PERSONNEL AND CONTACT DETAILS

Sponsor:

Contact name

University of Nottingham
Ms Angela Shone
Head of Research Governance
Research and Graduate Services
King's Meadow Campus
Lenton Lane
Nottingham
NG7 2NR

Chief investigator:

Dr Gordon William Moran
Clinical Associate Professor of Gastroenterology
NIHR Nottingham Digestive Diseases Biomedical
Research Unit
D1405, West Block, D Floor, Queen's Medical
Centre, Nottingham University Hospitals, NG7 2UH
Phone: 0115 (82) 30461
Fax: 0115 (82) 31409
Email: gordon.moran@nottingham.ac.uk

Co-investigators:

Dr Graham Finlayson
Associate Professor Institute of Psychological
Sciences
Institute of Psychological Sciences
University of Leeds
Telephone +44(0)113 343 7601
Work Email g.s.finlayson@leeds.ac.uk

Dr Richard Anthony Wardle
Rotational Foundation Year 1 Doctor
Royal Derby Hospital
Uttoxeter New Rd
Derby
DE22 3NE
Telephone 01332 340131
Work Email richardwardle@nhs.net

Study Statistician:

Alyshah Abdul Sultan
Division of Epidemiology and Public Health
City Hospital Campus, University of Nottingham
Room B126 Clinical Science Building 2
Hucknall Road, Nottingham
NG5 1PB
Work Email:
alyshah_abdul_sultan@nottingham.ac.uk

Study Coordinating Centre:

NIHR Nottingham Digestive Disease Centre
Biomedical Research Unit, E Floor, West Block,
Queen's Medical Centre, Nottingham University
Hospitals, NG7 2UH

SYNOPSIS

Title	Eating behaviour in Crohn's disease
Short title	Eating behaviour in Crohn's disease
Chief Investigator	Dr Gordon Moran
Objectives	<p>The primary objective is to quantify food intake in Crohn's disease (CD) patients with active disease and compare it to healthy volunteers. Measures of food intake will be repeated in these patients when in remission.</p> <p>The secondary objectives of this study is to quantify changes in appetite and eating behaviour in patients with active CD and compare these to those in HV and inactive CD as measured by the appetite-related questionnaires</p>
Study Configuration	Qualitative questionnaire based study
Setting	A tertiary setting
Sample size estimate	Due to the exploratory nature of this study and lack of previous data, we feel the sample size suggested is achievable and will be sufficient to provide robust statistics and 95% confidence intervals. This work will provide pilot data to further power downstream work.
Number of participants	<p>Crohns: n = 60</p> <p>Healthy volunteers: n = 60</p> <p>Participants will be age-, gender- and BMI-matched.</p>
Eligibility criteria	<p><u>Patients:</u></p> <p>We will study a cohort of CD patients (aged 16-75yrs) with active disease as defined by:</p> <ul style="list-style-type: none"> • CD activity index (CDAI) of 220-450 or, • faecal calprotectin of >250μg/g and • one of the following: ileocolonoscopy, CT or MR enterography showing active inflammatory uncomplicated disease of the ileum (B1L1 or B1L3 phenotype). • Stable doses of immunosuppressive agents or anti-TNF agents will be permitted. • Body mass index (BMI) of 18-30. <p><u>Healthy Volunteers Controls</u></p> <ul style="list-style-type: none"> • Aged 16-75yrs old (age, weight and sex-matched).
Description of interventions	<p><u>CD and Healthy volunteer (HV) control group</u></p> <ol style="list-style-type: none"> 1. Measure of food intake through three telephone-administered 24-h dietary recalls

	2. Eating behaviour traits will be measured through self-reported measures: Three Factor Eating Questionnaire (TFEQ) Restraint, Disinhibition and Hunger subscales; the Binge Eating Scale; the Power of Food Scale; the Dutch eating behaviour questionnaire and the Control of Eating Questionnaire
Duration of study	Study Duration: 24 months Each participant will be in the study for 1 week. (Participants restudied back when in remission will be within the study for a maximum of 12 months of initial recruitment).
Methods of analysis	Differences in food intake (measured as mean total 24 hr kcal intake) and eating behaviour traits between the three groups (active CD, inactive CD and HV) will be carried out with an analysis of variance with a post-hoc <i>Bonferroni</i> correction. To identify potential mechanistic links between mean food intake and eating behaviour, these data will be correlated to measures of disease activity (CRP and faecal calprotectin). Data will be presented as mean. P<0.05 will be considered as significant.

ABBREVIATIONS

AE	Adverse Event
ANOVA	Analysis of Variance
ASL	Arterial Spin Labelling
BOLD	Blood-oxygen level-dependant
CD	Crohn's Disease
CI	Chief Investigator overall
CNS	Central Nervous System
CRF	Case Report Form
DAP	Data Analysis Plan
DMC	Data Monitoring Committee
EC	Enterendoocrine Cells
GCP	Good Clinical Practice
GM	Grey Matter
HV	Healthy Volunteer
IBD	Inflammatory Bowel Disease
ICF	Informed Consent Form
NDDBRU	Nottingham Digestive Diseases Biomedical Research Unit
NHS	National Health Service
P/GIS	Parent / Guardian Information Sheet
PI	Principal Investigator at a local centre
PIS	Participant Information Sheet
REC	Research Ethics Committee
R&D	Research and Development department
RFX	Random effects group analysis
ROI	Region of Interest
SAE	Serious Adverse Event

SPMMRC	Sir Peter Mansfield Magnetic Resonance Centre
SPM	Statistical Parametric Mapping
TMG	Trial Management Group
TSC	Trial Steering Committee
UoN	University of NottinghaM
VAS	Visual analogue scores
VBM	Voxel-based Morphometry

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STUDY BACKGROUND INFORMATION AND RATIONALE

Crohn's disease (CD) patients can present with a variety of luminal and extra-luminal symptoms but nutritional abnormalities are a very common but poorly studied¹ problem in this disease². Apart from disease burden and repeated surgery, reduced appetite³ and associated symptoms such as nausea undoubtedly contribute, with a major impact on quality of life.

Appetite and satiation, the processes by which a meal is terminated, involve complex interactions of homeostatic and hedonic factors. While the hypothalamus is central in the homeostatic control of food intake, other neural circuits integrate environmental and emotional cues to constitute the hedonic drive of appetite regulation. The homeostatic control of food intake is governed by the enteroendocrine-gut brain axis. Enteroendocrine cells (EC) play a pivotal role in orchestrating physiological functions in the gastrointestinal (GI) tract. Sensing the nutrient content of the lumen, they secrete multiple peptides and amines that control gut secretory and motor functions. Gut hormones act on vagal afferents in the GI tract, directly relaying to key central nervous system (CNS) nuclei that interface within the hypothalamus and other cortical areas to regulate food intake. CD patients with active small bowel inflammation show significant up-regulation of EC cells with an increase in ileal expression of chromogranin A^{4,5}, glucagon-like peptide-1 (GLP-1)⁴, key transcription factors in the stem cell to EC differentiation pathway⁴, plasma polypeptide YY (PYY)³, cholecystokinin (CCK)⁶ levels and a reduction in the key enzyme dipeptidyl peptidase-4 expression⁷. This increase in plasma peptide levels is associated with the symptoms of nausea and anorexia, with both symptoms, and tissue and plasma EC-peptide expression decreasing to normality in remission³.

An increase in EC expression at the tissue and plasma level might affect appetite regulation through an increase in CNS signalling.

Fatty-acids infused in the gut, lead to a CCK-dependent increase in CNS activity in areas related to homeostatic control of feeding such as the brainstem, the pons, hypothalamus, cerebellum and the motor cortical areas⁸. Glucose has been shown to decrease the response in the upper hypothalamus⁹, possibly via a GLP-1-mediated pathway¹⁰. Ghrelin and PYY have known homeostatic CNS signalling properties but play a hedonic role in the control of food intake¹¹. In effect, the increase in plasma PYY and GLP-1 seen after Roux-en-Y gastric bypass surgery in obese subjects or after parenteral administration¹² is associated with a lower activation in brain-hedonic food responses and a healthier eating behaviour¹³. In CD, we expect a subdued reward value of food, but postulate that this would be aversive, and inappropriately impairing appetite and food intake.

We hypothesize that in CD and small bowel inflammation we will observe a change in eating behaviour with loss of hedonic drives and food reward responses and an accentuated homeostatic response.

STUDY OBJECTIVES AND PURPOSE

PURPOSE

The overall purpose of the study is to quantify food intake in patients with active Crohn's disease and compare it to when they are in remission and to healthy age, BMI and gender-matched healthy cohort of volunteers. We will quantify eating behaviour traits in the same patient cohort when in active disease and repeat when in remission. These data will be compared to that of healthy volunteers.

PRIMARY OBJECTIVE

The primary objective is to quantify food intake in patients with active CD and compare this to HV.

SECONDARY OBJECTIVES

The secondary objectives of this study are to a) quantify food intake in patients with active CD and compare that when in inactive disease. b) quantify changes in appetite and eating behaviour in patients with active CD and compare these to those in HV and inactive CD as measured by the appetite-related questionnaires

STUDY DESIGN

STUDY CONFIGURATION

This is an open label study design.

Primary endpoint

The primary endpoints for this study will be food intake as measured by three telephone-administered 24-h dietary recalls.

Secondary endpoint

The secondary endpoints for this study will be a) eating behaviour traits as measured through self-reported measures: Three Factor Eating Questionnaire (TFEQ) Restraint, Disinhibition and Hunger subscales; the Binge Eating Scale; the Power of Food Scale; the Dutch eating behaviour questionnaire; and the Control of Eating Questionnaire.

Safety endpoints

None of the endpoints in this study are safety endpoints.

Stopping rules and discontinuation

These studies deal with patients with active CD. We are planning a set of studies to be carried out when they experience an active disease flare as measured by a set of inclusion criteria. Usually such patients at this point are symptomatic due to their inflammatory disease. An increase or change in their anti-inflammatory treatment will be postponed till after the investigative research studies will be have been completed.

To minimise any patient risk:

- a) We aim to complete all studies within a 1 week period
- b) Patients will be allowed to exit the study at any point
- c) They will have an IBD helpline accessible to them at all times.

Clinical discretion will be exercised at all times. If a patient is deemed too sick to be recruited or too sick to continue the study once recruited: we will institute the appropriate medical treatment immediately and they will be promptly excluded from their study.

RANDOMIZATION AND BLINDING

There is randomisation or blinding needed for this study.

Maintenance of randomisation codes and procedures for breaking code

N/A

STUDY MANAGEMENT

The Chief Investigator has overall responsibility for the study and shall oversee all study management.

The data custodian will be the Chief Investigator.

DURATION OF THE STUDY AND PARTICIPANT INVOLVEMENT

Study Duration: The study will last for 24 months

Participant Duration: Healthy volunteer participants will be included in this study for 1 week. CD participants will be included in the study until they are re-assessed in remission. A time limit of 12 months will be given.

End of the Study

This will be the last visit of the last study participant or the receipt of the last questionnaire from the last participant whichever is the later.

SELECTION AND WITHDRAWAL OF PARTICIPANTS

Recruitment

The CI is a specialist in Inflammatory Bowel disease and also an associate professor of gastroenterology at the University of Nottingham and Nottingham University Hospital which is a tertiary-level care academic institution covering a population of approximately 1 million people for secondary-level care and 4.5 million people for tertiary-level care. Collectively we manage approximately 4000 IBD patients.

Participants shall be recruited from two sources:

1. CD patients from clinic.

Members of the study team will be primarily recruiting patients with active Crohn's disease from clinical practice. These participants can have a screening visit to give written consent in clinic. If they are unable to consent in clinic, they will be invited back to the Nottingham Digestive Diseases Biomedical Research Unit (NDDBRU) at University of Nottingham for a screening visit to give written consent. This will be done primarily by the CI and his colleagues. Potential Participants will be identified through their medical records and at their standard clinic appointments. There is an existing collaborative network with the endoscopy, radiology and paediatric departments to enhance recruitment. Moreover there are 5 IBD nurses who are existing members of the research team that are key in identifying possible study recruits.

2. CD patients and HV via the study flyer and social media.

Our study flyer with relevant contact details, will be placed throughout Nottingham University Hospitals and University of Nottingham campuses, in local press, in

departmental Facebook and Twitter posts and in any departmental mailing/ emailing lists to people who have agreed to be contacted with such information.

After making contact with the study team, prospective participants will be offered the invitation letter along with the patient information sheet. If agreeable to take part in the study they will be invited to the NDDBRU for a screening visit to obtain written consent by the study team.

It will be explained to all participants that entry into the trial is entirely voluntary and that their treatment and care (in the case of CD patients) will not be affected by their decision. It will also be explained that they can withdraw at any time but attempts will be made to avoid this occurrence. In the event of their withdrawal it will be explained that their data collected so far cannot be erased and we will seek consent to use the data in the final analyses where appropriate.

Eligibility criteria

Please see below:

Inclusion criteria

We will study a cohort of CD patients with active disease as defined by:

1. Age 16-75 years
2. CD activity index (CDAI) of 220-450 or,
3. faecal calprotectin of >250 μ g/g and
4. one of the following: ileocolonoscopy, CT or MR enterography showing active inflammatory uncomplicated disease of the ileum (B1L1 or B1L3 phenotype).
5. Stable doses of immunosuppressive agents or anti-TNF agents will be permitted.
6. Body mass index (BMI) of 18-30.

For HV participants, inclusion criteria's 1 and 6 apply.

Exclusion criteria

1. Present or recent (within 12 weeks) corticosteroid usage
2. Malignant disease
3. BMI <18 or >30.
4. Significant cardiovascular or respiratory disease
5. Diabetes mellitus
6. Current Infection
7. Neurological or cognitive impairment; significant physical disability
8. Significant hepatic disease or renal failure
9. Abnormal blood results other than those explained by CD including bleeding diatheses (apart from in the case of HV where all unexplained blood results are an exclusion criteria)
10. Subjects currently participating in (or in the last three months) any other research project
11. pregnancy or breastfeeding or
12. Severe CD where a delay in a change in medical treatment for 1 weeks would not be clinically advisable

For HV participants, all exclusion criteria apply with the exception of criteria no.12

Expected duration of participant participation

Healthy volunteer participants will be included in this study for 1 week. CD participants will be included in the study until they are re-assessed in remission. A time limit of 1 year will be given.

Participant Withdrawal

Participants may be withdrawn from the trial either at their own request or at the discretion of the Investigator (in case deemed too unwell from their CD). The participants will be made aware that this will not affect their future care. Participants will be made aware (via the information sheet and consent form) that should they withdraw the data collected to date cannot be erased and may still be used in the final analysis.

Informed consent

All participants will provide written informed consent. The Informed Consent Form will be signed and dated by the participant before they enter the trial. The Investigator will explain the details of the trial and provide a Participant Information Sheet, ensuring that the participant has sufficient time to consider participating or not. There will be at least 24 hours between provision of the information sheet and consent. The Investigator will answer any questions that the participant has concerning study participation.

All participants will have a good command of the English Language and have capacity to consent. Any participant who loses capacity after giving consent or withdraws consent will be withdrawn from the study. Identifiable data or tissue already collected with consent would be retained and used in the study. No further data or tissue would be collected or any other research procedures carried out on or in relation to the participant. No prisoners will be approached for this study.

Informed consent will be collected from each participant before they undergo any interventions (including physical examination and history taking) related to the study. One copy of this will be kept by the participant, one will be kept by the Investigator, and a third will be retained in the patient's hospital records. Only two records will be kept for healthy volunteers, one by the participant and the other by the investigator as none will be retained in their hospital records. Should there be any subsequent amendment to the final protocol, which might affect a participant's participation in the trial, continuing consent will be obtained using an amended Consent form which will be signed by the participant.

STUDY REGIMEN

We will study a cohort of CD patients (n=60) with active disease as defined by a CD activity index (CDAI) of 220-450, faecal calprotectin of >250 μ g/g and one of the following: ileocolonoscopy, CT or MR enterography showing active inflammatory uncomplicated disease of the ileum (B1L1 or B1L3 phenotype)¹⁴. This information will be obtained from patient's hospital notes and online medical records. Due to the exploratory nature of the studies, number of recruits is based on previous literature^{8, 15, 16} by our group. Stable doses of immunosuppressive agents (12 weeks), or anti-TNF agents (16 weeks) will be permitted. A similar subset of age, weight and sex-matched healthy volunteers will be recruited. A hospital anxiety and depression scale questionnaire and a health questionnaire will be completed by each study participant.

Patient demographics: Data on disease phenotype¹⁴, age, gender, weight, body mass index, pharmacological, surgical and smoking history will be collected.

1. **Eating behaviour constructs:** Eating behaviour traits will be measured through self-reported measures: Three Factor Eating Questionnaire (TFEQ) Restraint, Disinhibition

and Hunger subscales¹⁷; the Binge Eating Scale¹⁸; the Power of Food Scale¹⁹, the Dutch eating behaviour questionnaire²⁰. Additionally, the Control of Eating Questionnaire will be used to assess perceptions of food cravings and control over meal intake during the previous 7-days²¹. These questionnaires will be filled in by the participants at home.

2. **Dietary intake:** Routine energy intake will be measured using three telephone-administered 24-h dietary recalls (Automated Multi-Pass Method)²².

Compliance

There will be no compliance issues with this study. If we have an incomplete participant data set it will be removed from the study, but we have the right (as indicated on the consent form) to use the data we have.

Criteria for terminating the study

The participant's involvement in the study will only be terminated if a) in the case of all study participants, the participant wishes to do so or in b) CD participants, if the patient or caring clinician feels that the patients is too unwell to carry on with the study.

ANALYSES

Methods

Data will be analysed by Dr Richard Wardle under the supervision of Dr Gordon Moran (CI for this study) in collaboration with Dr Graham Finlayson (University of Leeds). Differences in food intake (measured as mean total 24 hr kcal intake) and eating behaviour traits and states between the three groups (active CD, inactive CD and HV) will be carried out with an analysis of variance with a *post-hoc Bonferroni* correction. To identify potential mechanistic links between mean food intake and eating behaviour, these data will be correlated to measures of disease activity (CRP and faecal calprotectin). Data will be presented as mean. P<0.05 will be considered as significant. Spearman or Pearson test will be used.)

Sample size and justification

Due to the exploratory nature of this study and lack of previous data, we feel the sample size suggested is achievable and will be sufficient to provide robust statistics and 95% confidence intervals. This work will provide pilot data to further power downstream work.

Assessment of efficacy

The primary and secondary endpoints for this study were listed earlier in the study design section. For the appropriate statistical analysis please consult the METHODS section of ANALYSES.

Procedures for missing, unused and spurious data

Participants with missing data will be excluded from the final analysis.

Definition of populations analysed

Primary and secondary outcomes will be assessed on both the full analysis set and the per protocol set.

The Chief Investigator will assess and classify violations of eligibility criteria and other deviations from protocol. Major protocol deviations (violations) from protocol will lead to exclusion of a participant from the per protocol set.

ADVERSE EVENTS

The occurrence of an adverse event as a result of participation within this study is not expected and no adverse event data will be collected.

ETHICAL AND REGULATORY ASPECTS

ETHICS COMMITTEE AND REGULATORY APPROVALS

The trial will not be initiated before the protocol, informed consent forms and participant and GP information sheets have received approval / favourable opinion from the Research Ethics Committee (REC), and the respective National Health Service (NHS) Research & Development (R&D) department. Should a protocol amendment be made that requires REC approval, the changes in the protocol will not be instituted until the amendment and revised informed consent forms and participant information sheets (if appropriate) have been reviewed and received approval / favourable opinion from the REC and R&D departments. A protocol amendment intended to eliminate an apparent immediate hazard to participants may be implemented immediately providing that the REC are notified as soon as possible and an approval is requested. Minor protocol amendments only for logistical or administrative changes may be implemented immediately; and the REC will be informed.

The trial will be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki, 1996; the principles of Good Clinical Practice, and the Department of Health Research Governance Framework for Health and Social care, 2005.

INFORMED CONSENT AND PARTICIPANT INFORMATION

The process for obtaining participant informed consent will be in accordance with the REC guidance, and Good Clinical Practice (GCP) and any other regulatory requirements that might be introduced. The investigator or their nominee and the participant shall both sign and date the Informed Consent Form before the person can participate in the study.

The participant will receive a copy of the signed and dated forms and the original will be retained in the Trial Master File. A second copy will be filed in the participant's medical notes and a signed and dated note made in the notes that informed consent was obtained for the trial.

The decision regarding participation in the study is entirely voluntary. The investigator or their nominee shall emphasize to them that consent regarding study participation may be withdrawn at any time without penalty or affecting the quality or quantity of their future medical care, or loss of benefits to which the participant is otherwise entitled. No trial-specific interventions will be done before informed consent has been obtained.

The investigator will inform the participant of any relevant information that becomes available during the course of the study, and will discuss with them, whether they wish to continue with the study. If applicable they will be asked to sign revised consent forms.

If the Informed Consent Form is amended during the study, the investigator shall follow all applicable regulatory requirements pertaining to approval of the amended Informed Consent Form by the REC and use of the amended form (including for ongoing participants).

RECORDS

Case Report Forms

Each participant will be assigned a study identity code number, allocated at randomisation, for use on CRFs other study documents and the electronic database. The documents and database will also use their initials (of first and last names separated by a hyphen or a middle name initial when available) and date of birth (dd/mm/yy).

CRFs will be treated as confidential documents and held securely in accordance with regulations. The investigator will make a separate confidential record of the participant's name, date of birth, local hospital number or NHS number, and Participant Study Number (the Study Recruitment Log), to permit identification of all participants enrolled in the study, in accordance with regulatory requirements and for follow-up as required.

CRFs shall be restricted to those personnel approved by the Chief or local Principal Investigator and recorded on the 'Study Delegation Log.'

All paper forms shall be filled in using black ballpoint pen. Errors shall be lined out but not obliterated by using correction fluid and the correction inserted, initialled and dated.

The Chief or local Principal Investigator shall sign a declaration ensuring accuracy of data recorded in the CRF.

Source documents

Source documents shall be filed at the investigator's site and may include but are not limited to, consent forms, current medical records, laboratory results and records. A CRF may also completely serve as its own source data. Only study staff as listed on the Delegation Log shall have access to trial documentation other than the regulatory requirements listed below.

Direct access to source data / documents

The CRF and all source documents, including progress notes and copies of laboratory and medical test results shall made be available at all times for review by the Chief Investigator, Sponsor's designee and inspection by relevant regulatory authorities.

DATA PROTECTION

All study staff and investigators will endeavour to protect the rights of the trial's participants to privacy and informed consent, and will adhere to the Data Protection Act, 1998. The CRF will only collect the minimum required information for the purposes of the trial. CRFs will be held securely, in a locked room, or locked cupboard or cabinet. Access to the information will be limited to the study staff and investigators and relevant regulatory authorities (see above). Computer held data including the study database will be held securely and password protected. All data will be stored on a secure dedicated web server. Access will be restricted by user identifiers and passwords (encrypted using a one way encryption method).

Information about the study in the participant's medical records / hospital notes will be treated confidentially in the same way as all other confidential medical information.

Electronic data will be backed up every 24 hours to both local and remote media in encrypted format.

QUALITY ASSURANCE & AUDIT

INSURANCE AND INDEMNITY

Insurance and indemnity for study participants and study staff is covered within the NHS Indemnity Arrangements for clinical negligence claims in the NHS, issued under cover of HSG (96)48. There are no special compensation arrangements, but study participants may have recourse through the NHS complaints procedures.

The University of Nottingham as research Sponsor indemnifies its staff, research participants and research protocols with both public liability insurance and clinical trials insurance. These policies include provision for indemnity in the event of a successful litigious claim for proven non-negligent harm.

STUDY CONDUCT

Study conduct may be subject to systems audit of the Study Master File for inclusion of essential documents; permissions to conduct the study; Study Delegation Log; CVs of study staff and training received; local document control procedures; consent procedures and recruitment logs; adherence to procedures defined in the protocol (e.g. inclusion / exclusion criteria, correct randomisation, timeliness of visits); adverse event recording and reporting; accountability of study materials and equipment calibration logs.

STUDY DATA

Monitoring of study data shall include confirmation of informed consent; source data verification; data storage and data transfer procedures; local quality control checks and procedures, back-up and disaster recovery of any local databases and validation of data manipulation. The Chief Investigator, or where required, a nominated designee of the Sponsor, shall carry out monitoring of study data as an ongoing activity.

Entries on CRFs will be verified by inspection against the source data. A sample of CRFs (10% or as per the study risk assessment) will be checked on a regular basis for verification of all entries made. In addition the subsequent capture of the data on the study database will be checked. Where corrections are required these will carry a full audit trail and justification.

Study data and evidence of monitoring and systems audits will be made available for inspection by REC as required.

RECORD RETENTION AND ARCHIVING

In compliance with the ICH/GCP guidelines, regulations and in accordance with the University of Nottingham Research Code of Conduct and Research Ethics, the Chief or local Principal Investigator will maintain all records and documents regarding the conduct of the study. These will be retained for at least 7 years or for longer if required. If the responsible investigator is no longer able to maintain the study records, a second person will be nominated to take over this responsibility.

The study Master File and trial documents held by the Chief Investigator on behalf of the Sponsor shall be finally archived at secure archive facilities at the University of Nottingham. This archive shall include all trial databases and associated meta-data encryption codes.

DISCONTINUATION OF THE STUDY BY THE SPONSOR

The Sponsor reserves the right to discontinue this study at any time for failure to meet expected enrolment goals, for safety or any other administrative reasons. The Sponsor shall take advice as appropriate in making this decision.

STATEMENT OF CONFIDENTIALITY

Individual participant medical information obtained as a result of this study are considered confidential and disclosure to third parties is prohibited with the exceptions noted above.

Participant confidentiality will be further ensured by utilising identification code numbers to correspond to treatment data in the computer files.

Such medical information may be given to the participant's medical team and all appropriate medical personnel responsible for the participant's welfare. If information is disclosed during the study that could pose a risk of harm to the participant or others, the researcher will discuss this with the Chief Investigator and where appropriate report accordingly.

Data generated as a result of this trial will be available for inspection on request by the participating physicians, the University of Nottingham representatives, the REC, local R&D Departments and the regulatory authorities.

PUBLICATION AND DISSEMINATION POLICY

The study results will be presented at national and international conferences when data analyses will be finalised (within 12 months of finishing study). Our data will be published in international reports and peer reviewed journals within 12-24 months. Data will be anonymised and participants will be unidentifiable.

USER AND PUBLIC INVOLVEMENT

We have involved the patients and public at multiple levels.

1. Design of the Research:

We have set up an IBD patient panel during the design phase of the study. We have discussed with them the importance of the research question put forward and been reassured by a positive response from the panel. Separately, we asked a subgroup of the patient advisory group to review the patient-related study documentation and we constructively used their feedback into our methodology.

2. Undertaking the research:

We will try to involve patient relatives, spouses and carers as healthy volunteers. This is part of the feedback from our IBD patient panel group. This will be very useful for patient support.

3. Dissemination of findings:

We have been invited to disseminate our findings at the Crohn's and Colitis UK Nottinghamshire group meetings.

The NDDBRU is in the process of developing the role of a "Study Mentor". This role will be filled by a participant in previous clinical trials who will be trained to act as an advisor to study participants independently of the research team. Their role will be to act as a point of information about the clinical trials process, rather than as a source of clinical advice.

We hope to appoint to this role in 2014. When the post is filled, participants will be made aware of this independent source of advice and information.

STUDY FINANCES

Funding source

Funding secured by internal moneys from the PI.

Participant stipends and payments

Participants will be donated £15 at the end of their assessment (completing questionnaires and complying with the three telephone-administered 24-h dietary recalls). CD participants re-assessed in remission will be donated this inconvenience allowance again.

SIGNATURE PAGES

Signatories to Protocol:

Chief Investigator: (name) _____

Signature: _____

Date: _____

REFERENCES

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