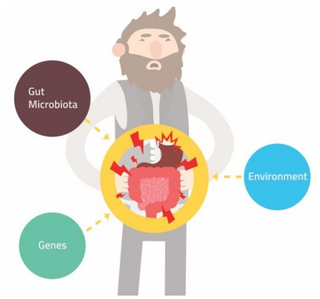

PREdiCCt

The PRognostic effect of Environmental factors in Crohn's and Colitis

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INTRODUCTION

Inflammatory bowel disease (IBD) is a chronic intestinal disorder which often confers a lifetime of unpleasant, intrusive and potentially dangerous burden of intestinal inflammation. It is hypothesised that the interplay between our genetic makeup, environment and gut microbiota influence disease onset as well as disease course. Currently it is very hard to predict which IBD patients in remission will flare and when. **The focus of the PREdiCCt study is towards understanding how diet, lifestyle and the gut microbiota influence flare and recovery in IBD.**

DISEASE FLARES IN IBD

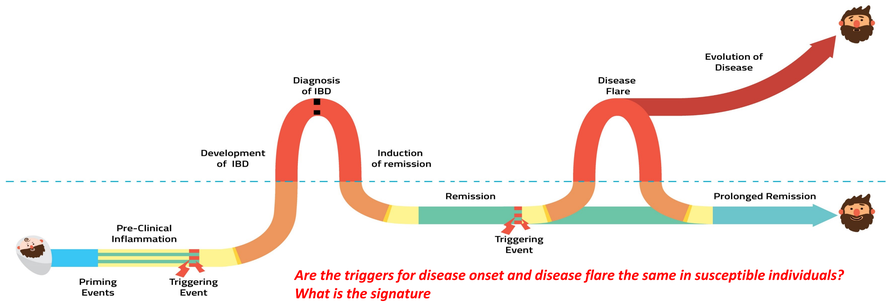
How often do disease flares occur in IBD?

What causes disease flare in IBD?

Can we predict who will flare?

What can people with IBD do to prevent flares?
"what should I eat doctors?"

Can we work out what factors are associated with prolonged (deep) remission?



Are the triggers for disease onset and disease flare the same in susceptible individuals? What is the signature

STUDY DESIGN

The study is a **prospective UK wide, multi-centre**, observational cohort study involving **3100 patients with IBD in clinical remission** followed up for **24 months**.

STUDY OBJECTIVES

Primary Objective: To determine which aspects of **a) baseline habitual diet, b) the environment, c) genetic variation** and **d) the gut microbiota**, predict disease flare in Crohn's disease and /or ulcerative colitis. The primary objectives are to test associations with:

1. Total animal protein intake (red meat, dairy, poultry, fish)
2. Dietary fibre
3. N-6 PUFAs
4. Dietary emulsifiers (lecithin)
5. Total bacterial gene count in stool

Secondary Objectives: To build predictive models of IBD prognosis and natural history utilising multi-level clinical, environmental, microbial & genetic data.

OUTCOME MEASURES

Primary outcome: :
1. Clinical flare (See Box 1)

Secondary outcomes
1. Hard clinical flare (See Box 1)
2. Total number of clinical flares and hard flares in the 24 month follow-up

BOX 2. Inclusion & Exclusion Criteria

1. Inclusion Criteria
Confirmed Crohn's disease or ulcerative colitis or IBDU (Lennard-Jones/Porto criteria).
Clinical remission (see Box 1)
>6 months since diagnosis with Crohn's disease, ulcerative colitis or IBDU
>2 months since any change in therapy for Crohn's disease, ulcerative colitis or IBDU
Aged six years or over at study entry
Written informed consent obtained from patient or parent / guardian

2. Exclusion Criteria
Patient unwilling to take part in all aspects of the study
Unable to obtain written informed consent
Systemic corticosteroids (oral or intravenous) or surgery within the last two months
Thiopurines / methotrexate / biologic therapy started in the preceding two months

STUDY POPULATION AND RECRUITMENT

3100 participants, consisting of 1550 patients with **Crohn's disease** and 1550 with **ulcerative colitis** and /or **IBDU** (see Box 2). Approximately 30 adult and paediatric IBD sites across the UK are being established as PREdiCCt centres.

STUDY PROCEDURES AND DATA COLLECTION

A custom online PREdiCCt web-portal has been created to allow for timely accurate electronic data collection. At recruitment patients are provided with a unique log-in and instructions on how to then complete and upload environmental data.

Phenotyping and Standard Labs: At their baseline visit, all patients have **blood** sent as part of routine clinical care (incl vitamin D). Detailed **phenotyping** forms are completed online by the local study team. This includes date of diagnosis, disease location and behaviour, current and prior drug therapy, surgical interventions, family history, and smoking status. The database produces a one page PDF **summary of the clinical phenotyping** generated for use by the local clinical team.

BOX 1. Study definitions
Clinical remission: Patients answering "yes" to the question "*Do you think your disease has been well controlled in the past 1 month?* "

Deep remission: Clinical remission in addition have:
Crohn's Disease: HBI <4 (adults) or wPCDAI <12.5 (children)
Ulcerative colitis: Mayo score <2 (adults) or PCUAI <10 (children)

In addition to:
•CRP <5mg/L AND faecal calprotectin <200mcg/g

Clinical flare: Patient answering "no" to the question "*Do you think your disease has been well controlled in the past 1 month?*"

Hard clinical flare: Clinical flare plus commencement of any new medication; altered dosing of existing medication for the treatment of IBD flare, with an increase in CRP (>5mg/L) and / or faecal calprotectin (>200mcg/g).

Environmental, Lifestyle and Dietary Data Collection: This consists of a detailed environmental and lifestyle questionnaire which participants complete at home within 14 days of the index visit. This includes a validated electronic version of the Scottish Collaborative Group Food Frequency Questionnaire (FFQ) and a **4-day weighed food diary**. Other validated questionnaires collect data on **quality of life** (SF-12, IBD QoL, CUCQ-8), **emotions & mood** (HADS, PHQ15), stressful **life events** (Holmes and Rahe Top20), global **physical activity** (GPAQv2), **sleep** (Pittsburgh index), **drug compliance** (MMASv8) and foreign **travel**.

DNA & Gut Microbiota: Salivary and stool collection packs are issued and samples returned from patient's home by post. Host and genomic microbial DNA are extracted at WTCRF in Edinburgh. Coded genomic and microbial DNA samples are sent to the Sanger Institute for whole-genome and metagenomic sequencing.
Faecal Calprotectin and Short chain fatty acids (SCFAs): are measured on stool samples (Clinical biochemistry, WGH)

Follow-up: All recruited patients are followed-up remotely for the duration of the study (**24 months follow-up**). Patients are asked to log into the web-portal every month to record their therapy, complete a symptom score (using the **validated IBD-Control dataset**) . The first question establishes whether or not they have had a clinical flare (by answering "*yes*" or "*no*" to "*Has your disease been well controlled over the past 1 month*"). Through the portal patients are asked to report any relevant investigations (imaging or endoscopy), hospitalisations or significant intercurrent illness, and document any environmental exposures (including over-the-counter drugs, infections, travel, major life events). Patients receive automatic reminders to log-in by email and SMS message. At 12 and 24 months the portal issues patients with a more detailed questionnaire.

At **flare** patients return further stool samples for microbiome and faecal calprotectin analysis. Patients remain in follow-up in order to capture multiple flares during the study.

WHO IS ORGANISING THE PREdiCCt STUDY

The PREdiCCt study is coordinated by the University of Edinburgh and NHS Lothian and has contributions from gastroenterologists & research scientists across the UK. It is funded by Cure Crohn's & Colitis, Crohn's and Colitis in Childhood, NHS Lothian and the Chief Scientist Office. Project management conducted by the Edinburgh Clinical Trials Unit (@ECTU). If you would like to invest to help PREdiCCt expand please contact the Chief Investigator Charlie.lees@ed.ac.uk (@Charlie_lees).
The **PREdiCCt trial steering committee** is chaired by Professor Jon Rhodes, with Dan Gaya, Paul Henderson and patient representatives.
The **analytical committee** is chaired by Professor Chris Weir, with Richard Parker, Carl Anderson, Luke Jostins, Nick Kennedy & Georgina Hold

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For more Information on the study or how to participate as a PREdiCCt centre please contact us via email or social media