

PROMETHEUS in IBD BOOST: What is the impact on recruitment of a brief compared with a standard participant information leaflet? Study within a trial

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Host RCT and SWAT registrations

The brief participant information leaflet intervention will be registered as a sub-study on the MRC SWATs repository.

Host RCT funding period

2017-2022

Host RCT participant recruitment start and end dates

1st June 2019-30th June 2021

Study area

Recruitment

Host RCT name

A randomised controlled trial of supported online self-management for symptoms of fatigue, pain and urgency/incontinence in people with inflammatory bowel disease: the IBD-BOOST trial

Background - The IBD BOOST host RCT

Inflammatory Bowel Disease (IBD) affects 300,000 people in the UK [1], causing unpredictable bouts of gut inflammation, with acute illness, diarrhoea, and pain. In remission, many people with IBD live with fatigue, chronic abdominal pain, and bowel urgency/incontinence [2]. There is no current cure for IBD, which usually starts in childhood or as a young adult. Most previous IBD research has focused on controlling inflammation. However, many people report continuing IBD-related fatigue

(41%), abdominal pain (62%) and difficulty with continence (up to 75%) even when IBD is in remission [2-4]. These symptoms limit peoples' quality of life and ability to work and socialise. Patients feel these symptoms are not taken seriously by health professionals and report that little help is given [3, 5, 6]. However, the James Lind Alliance IBD research priority-setting consensus put fatigue, pain, and continence in the top 10 issues that IBD patients and clinicians want to be addressed by research [7].

The overall aim of the IBD BOOST programme grant is to improve the quality of life for people with IBD by reducing the burden of IBD-related fatigue, abdominal pain, and urgency/incontinence. This involves a pragmatic multi-centre two-arm, parallel group superiority RCT of facilitator-guided online self-management vs. care as usual to manage symptoms of fatigue, abdominal pain, and faecal urgency/incontinence in IBD. A large cross-sectional survey of people with IBD to investigate the inter-relationships of IBD-related symptoms and the proportions wanting support to manage these symptoms will be undertaken prior to the RCT. Survey participants who have symptoms of fatigue, pain or urgency which they want help for, are eligible and have consented to be contacted for further research will be invited to participate in the IBD BOOST RCT. This survey is a strength of this present study as there is the potential to look at recruitment bias. We will have a lot of information on survey responders who express a wish for intervention but who then do not participate in the RCT. Many trials do not collect data on non-participants and so, factors associated with participants can be further explored here.

We propose to undertake a SWAT prioritised by the PROMETHEUS team in IBD BOOST. This SWAT will assess the effectiveness of a shortened Participant Information Leaflet (PIL) compared with a standard length PIL on participant recruitment rates.

Background: the brief participant information leaflet intervention

RCTs delivered via the internet are an increasingly common and acceptable form of generating research evidence [8, 9]. A common method of recruiting participants into internet-delivered RCTs is from registries or databases, where potentially eligible patients are invited to participate in the RCT, and provided with the trial PIL. However, PILs are lengthy and increasingly complex - often about 8 pages long [10]. There is a hypothesis that being asked to read such a large document in one go may act as a deterrent to potential participants becoming involved in the research [11]. In one RCT comparing an electronic interactive information leaflet versus a standard length, Research Ethics Committee (REC) approved, PIL, only 9% of people accessed the detail presented on the standard length REC approved PIL [12]. A shorter PIL may be more appealing to patients initially as it is likely to provide more manageable volume of information, which may encourage more potential participants to contact the trial team and subsequently be recruited into the trial [11].

The latest Cochrane review of recruitment interventions identified two trials that have evaluated a brief PIL compared with a full length PIL [11, 13, 14], and found the brief PIL makes little or no difference to recruitment compared with a full PIL. RD = 0% (95% CI = -2% to 2%); GRADE: moderate. It would be useful to replicate this SWAT in an online setting, where there is evidence people typically read the minimal information provided[15], in order to determine whether a brief or a standard length PIL is more effective in this particular setting. We will also compare retention between the groups, as there is potential for people who have received more information to be more motivated to continue remaining in the trial.

Objective of This SWAT

This SWAT aims to evaluate the effectiveness a shortened PIL compared with a standard length PIL on recruitment and retention rates in the IBD BOOST host RCT.

Inclusion and exclusion criteria

The SWAT will include all patients identified from the previous IBD-BOOST survey as having expressed a desire for an intervention for their symptoms, and so are potentially eligible for the IBD BOOST trial: there are no additional inclusion or exclusion criteria. These survey participants were originally recruited from three sources:

- NHS clinical sites via databases of their IBD patients (unselected patients)
- IBD-BioResource, a national genetics repository (random sample of participants)
- Crohn's & Colitis UK (random sample of membership)

Inclusion criteria for the survey were:

- Aged 18 or over
- Living in the UK
- Diagnosis of any type of inflammatory Bowel Disease

SWAT Intervention and comparator

The SWAT will adopt an RCT design, with potential participants randomised to one of the following interventions which will be provided to patients to access online:

1. A shortened online PIL, with hyperlinks for more detailed information that potential participants can access to read
2. Standard length PIL, will with all required details provided in a single online document

The standard length PIL will be developed by the IBD BOOST team, following National Research Ethics Service (NRES) guidance and will be reviewed by an NHS REC as part of the ethics application for the IBD BOOST RCT. The content of the PIL will include: general information about the purpose of the RCT, how and why the participant might be involved, key trial concepts, such as randomisation, the intervention being tested, and the potential risks and benefits of the intervention, participant's right to withdraw, trial team contact information, confidentiality information, and details on who is funding and monitoring the research. The information will be reviewed by the IBD BOOST patient and public involvement (PPI) and PROMETHEUS PPI panels, and will also be reviewed by the IBD BOOST Trial Steering Committee (TSC). The standard PIL will be approximately 6 A4 pages long, presented in electronic Portable Document Format (PDF) when sent by hyperlink. The accompanying cover email/letter and eligibility checklist will all be on single A4 sized pages.

The brief PIL will consist of a single online screen (approximately ½-1 page of A4 text, with hyperlinks to further detailed information if the potential participant clicks on a link. It will provide a succinct and concise summary of the IBD BOOST RCT. The information will be reviewed by the IBD BOOST and PROMETHEUS PPI panels and will also be reviewed by the IBD BOOST TSC. As with the full PIL, this will be reviewed by an NHS REC as part of the ethics application for the IBD BOOST RCT. The cover email/ letter will explain that the brief PIL provides a summary of the research in order for potential participants to decide if they might be interested in participating, and that they can access the included hyperlink for more details should they wish to read them before responding to the invitation.

Outcome Measures

Primary outcome:

1. The primary outcome is the effectiveness of the brief PIL compared with the standard PIL. This is defined as the recruitment rate, being the proportions of participants in each intervention group that are randomised into the IBD BOOST RCT.

Secondary outcomes:

1. The proportion of patients in each group who express an interest in participating in IBD BOOST
2. How many participants in the shortened PIL arm accessed the full PIL information
3. Number of follow up queries received prior to randomisation by the study team
4. Retention rates of participants at 6 and 12 months

Statistical methods

Randomisation

The type of information leaflet each potential participant will be sent will be determined by random allocation. Potential participants will be randomised in a 1:1 ratio, stratified by their entrance pathway (i.e whether they participated in the checklist and algorithm study following the IBD survey or a direct entry route, see appendix 1: Flow Chart). Block randomisation with random varying block sizes will be used, with the block sizes will be specified by a statistician and not shared with other researchers.

The allocation lists will be generated by a randomisation system and shared and accessed only with staff sending the invitations. Participants are sent invitation on a link via email. Invitations sent by the research team are automatically recorded by the system. For quality assurance we will check a 10% sample of invitations after every 50 randomisations.

Patients will not know that they are part of a trial testing a recruitment intervention so will be blind to the SWAT hypothesis as is the case with MRC funded Prometheus studies.

Sample size calculation

The sample size calculation for the IBD BOOST RCT has been outlined in the main trial protocol and the target sample size is 680 participants randomised.

As is usual with a SWAT, we did not undertake a formal power calculation to determine the sample size (19), since the sample size is constrained by the number of patients being approached in the IBD BOOST host RCT. The sample size will therefore be the total number of patients invited into the IBD BOOST host trial. Based on response rates achieved in the survey, we estimate we will need to invite 846 people who have symptoms and want help for them in order to recruit 680 to the trial, representing a recruitment rate of about 80%. This would provide 95% power to identify an 8.8% difference between the groups in recruitment rate.

Statistical analysis

All analyses will be conducted by intention to treat. The participants will be analysed according to the group they were randomised to, irrespective of which PIL was received. A two-sided p value of <0.05 will be taken to indicate a statistically significant result.

The numbers and percentages within each group will be reported for categorical outcomes; means (with SD) within each group will be reported for continuous outcomes. Proportion of patients approached who are subsequently randomised will be compared using logistic regression adjusting

for entrance pathway and reported as an adjusted odds ratio with 95% confidence interval. Secondary outcomes of proportions will be analysed in the same way. Secondary outcomes of continuous measures will be analysed using linear regression adjusting for entrance pathway and reported as an adjusted difference in means odds with 95% confidence interval.

Anonymised data from this SWAT will ultimately be combined in a meta-analysis with data from similar host RCTs participating in PROMETHEUS, in accordance with the PROMETHEUS data sharing agreement.

Project timetable

Date	Action
December 2018	Peer review of IBD SWAT proposal
January 2019	Documentation for the SWAT agreed & signed off
January 2019	Submission to REC of application
May 2019	Recruitment to the SWAT begins
June 2021	Recruitment to the SWAT ends
March 2022	Data cleaning and submission of data by QMUL PCTU
March 2022	Collation of results and analysis, begin write up of trial level paper

Level of funding required

We estimate the proposed SWAT will cost £4,962 (100% of directly incurred costs).

£962 for 5.5 days of staff time at King's College London time to support set-up

£1,000 for QMUL PCTU statistician's time

£2,500 for additional randomisation and database development at QMUL PCTU etc.

£500 to support adaptations to recruitment procedure at PCTU QMUL.

Expertise of team

Our team comprises experienced applied health researchers with methodological expertise covering all the methods used in the programme, in collaboration with a clinical trials unit experienced in complex interventions in the NHS, who will also provide statistical and health economics expertise to both the trial and the embedded SwaT. Between us we have substantial current research grants for trials evaluating complex behavioural interventions, self-help interventions and internet delivered self-management including in IBD research.

Professor Christine Norton, KCL is the Chief Investigator of the IBD BOOST programme grant and an experienced trialist.

Professor Rona Moss-Morris, KCL is lead for the RCT

Dr Clare Relton, QMUL is expert advisor on the SWAT

Sally Kerry QMUL is the senior statistician for the RCT

Zohra Zenasni, QMUL is the statistician for the RCT

Professor Ailsa Hart, St Mark's Hospital is clinical lead for IBD-BOOST

Jonathan Syred, KCL is the Programme Manager for IBD-BOOST programme

Ann Thomson, QMUL is the senior Trials Manager for the RCT

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