MRC START in [*host trial name*]: What are the effects of a re-written and re-designed Participant Information Sheet? A randomised controlled trial

[Protocol Version x.x]

[DATE]

1. Background

In the UK, the NIHR vision sees 'more patients and health professionals participating in health research'[1]. Fundamental to health research is the testing of interventions through RCTs. Achieving high participation in RCTs has traditionally been difficult. Published data show that a minority of RCTs recruit successfully [2,3]. Recruitment problems reduce the total recruited sample (limiting internal validity), and the proportion of eligible participants who are recruited (limiting external validity).

Clearly, there is a need to develop and test interventions to improve recruitment, and one method is to 'nest' trials of recruitment interventions in ongoing randomised trials. Given the consensus among the research community concerning the challenge of recruitment, it is surprising that nested trials of recruitment interventions are so rare. Two recent reviews identified only 14 nested studies in real trials[4] and 27 overall [5]. Recruitment for science is not underpinned by a science of recruitment.

The MRC START study is designed to develop the conceptual, methodological and logistical framework for nested studies, and to assess their feasibility. At the completion of MRC START, we will have rigorously tested two potential interventions for adoption in to routine practice (improved PIS, and a multimedia decision aid), and provided the framework to make delivery of nested recruitment RCTs a routine activity. This will assist the rapid development of recruitment to meet policy goals [12]. [*Host trial]* is acting as a host trial to test an MRC START recruitment intervention. This protocol details the work that will be undertaken for MRC START in [*Host trial].*

2. The intervention – Participant information sheets

Research has reported patients' rather patchy understanding at the end of a trial, such as one in five participants not knowing the name of the medicine being tested [6] and similar proportions not knowing that they could withdraw at any time [7]. These findings are confirmed by a systematic review of consent in cancer trials [8] in which aspects such as treatment risks and benefits and the right to withdraw consent, were found to be not well understood. The review concluded that "patients do not appear to be adequately informed" (p.304). A lack of participant knowledge might result from the difficulty in understanding complex information, such as randomisation [9], or because of the way the Participant Information Sheet (PIS) is written. The level of literacy required to understand a study PIS is often higher than that found within the general population [10], and poor information provision may particularly affect older or less educated patients [11].

One promising approach to improving the quality of the written information provided is to develop the PIS through User Testing. In this process people in the target group for the trial read the PIS and are then asked to find and show an understanding of key information contained in the sheet. Any identified problems are rectified by the use of clear writing and by changing the way the PIS is laid out and designed. Further User Testing then tests whether the changes have led to improvements to the way the PIS performs. Three small, recent studies suggest that a combination of re-writing, design and testing results in a PIS that works much better to inform potential trial participants and which they prefer [13, 14, 15]. These studies have involved hypothetical settings, with participants being asked to imagine themselves being recruited to a trial, and what remains unknown is the effect of such changes to the PIS in actual trials. In particular, does an improved PIS impact on either of the quality of informed consent and the rate of recruitment?

3. Study details

The [*Host trial name*] study – [*brief description of trial]* - plans to use a [*describe approach to recruitment*] in recruiting patients. Potential participants will [*describe approach to patients]*. The NRES-approved PIS is *x* pages in length [*any further info on PIS]* .

A revised PIS will be developed through User Testing. The content of the original PIS will be retained but it will be re-written and re-designed based on the outcomes of the User Testing process. It would be useful to know if the revised PIS impacts on rate of recruitment and the

quality of informed consent, in comparison with the original PIS. A nested randomised controlled trial would be the best approach to evaluate its effects.

4. Research Objectives

4.1 To establish if the number of patients recruited in to [*Host trial name*] is improved by the use of a participant information sheet developed through User Testing, compared to routine participant information sheet.

4.2 To explore whether user testing of the PIS improves retention in [*Host trial]*

4.3 *[To establish if the quality of informed consent given by those patients who consent to be included in the trial is affected by the type of participant information sheet they initially receive]* – delete as appropriate.

4.4 [*To explore whether the reasons patients give for consenting or declining to participate in the [Host trial name] are affected by the type of participant information sheet they receive]* – delete as appropriate

5. Method

5.1 Design

The proposed study will use a *[design of host trial]* design. Patients who are to be offered participation in the trial will be randomly allocated to one of two interventions:

a) sent the original [*host trial*] participant information sheet (see Appendix 1);
b) sent the user tested participant information sheet (see Appendix 2).

5.2 Inclusion / exclusion criteria

The recruitment trial will include all patients identified as potentially eligible for the [*Host trial*] study: there are no additional inclusion or exclusion criteria.

5.3 Recruitment and Randomisation

Potential participants in the [*Host trial*] study will be identified by [*describe process of identifying potential participants*]. All potentially eligible patients will [*describe process for contacting patients and the point at which the PIS will be introduced*]. The type of PIS included in each pack will be determined by random allocation using a method which is robust and ensures concealment of allocation, such as a computerised randomisation programme where feasible, conducted by someone independent from those undertaking recruitment.

[*describe any specific aspects of randomisation process*].
[*Specify what data will be recorded by the host research team and how*]. .

5.4 Intervention

The original participant information sheet for the [*Host trial*] study (see Appendix 1) was written in accordance with NRES guidance. It is presented as [*describe existing PIS*]. It was approved by an NHS REC as part of the application to conduct the [*Host trial*] study.

The revised participant information sheet will contain the same content as the original version but will differ in the way that the information is laid out, written and presented. It will be developed through User Testing with members of the public selected to reflect the target patients for the PIS, who will read and then be asked to find and show an understanding of key facts contained in the PIS. The testing will be undertaken in several rounds: the first round testing the original PIS; then several rounds with different iterations of the revised PIS until we were confident that the PIS could perform well to inform potential trial participants.

5.5 Outcome measures

The primary outcome will be the number of patients recruited to [*Host trial name].* We will keep a record of all patients who were identified as potential participants and which intervention group they were in.

Secondary outcomes will be: *[Secondary outcomes relate to different trial settings and studies which choose to include additional measures]*

- *The proportion of recruited patients who are retained to the end of the end of [host study name] or the number remaining in the study six months prior to the end of the MRC START programme*
- *the proportion of patients in each intervention group who* agree to participate in *[Host trial] (where this differs from the number actually recruited, due to eg exclusion criteria); - delete as appropriate*
- *[the proportion of patients who decline to participate, who endorse the 'not understanding enough about the study' as a reason (see Appendix 5), according to each intervention group]* – delete as appropriate;

- *Quality of Informed Consent data (specify measure?) (see Appendix 6), among patients who consent to take part, according to each intervention group]* - delete as appropriate.

***5.6 Qualitative study* – delete as appropriate**

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6. Statistical considerations

6.1 Sample size

START is powered to detect a significant improvement in recruitment rate, defined as an increase in response of 10%. 400 patients per arm are required to provide 80% power to detect a 10% difference (alpha 0.05). Involvement in START has therefore been restricted to RCTs that will appraoch at least this many patients (note this is the number approached, not the number randomised: the former will often be many times higher than the latter).

[*Host trial*] is powered on recruiting *XXX* participants. Based on ??? it is predicted that *XXX* invitation letters will be sent, of which around *XX% (XXX)* will respond positively [*further details of sample size if available*].

6.2 Analysis

Anonymised data from [*host trial]* will be sent to the MRC START team in accordance with the MRC START data sharing agreement (see Appendix 3).
The proportion of participants who return consent forms will be calculated for the two intervention groups (original and revised PIS). The difference between the two proportions will be calculated along with the corresponding 95% confidence interval.
Results from this trial will ultimately be combined in a meta-analysis with response rate data from other host trials participating in the MRC START programme

7. Ethical issues

NRES approval will be sought to conduct the [*Host trial*] study, using the recruitment method described above.

Patients will not have the opportunity to give informed consent to enter into the nested recruitment study. This has been approved by NRES Committee Yorkshire and the Humber –

South Yorkshire (REC Reference 11/YH/0271) on the basis that the nested study is not withholding information – just changing the way it is presented.
[Participants in the focus group study will be posted a study invitation letter, participant information sheet and consent form (Appendices 7- 9) specifically for this aspect.] – delete as appropriate

The nested study (MRC START in [Host trial]) will be registered by the *[host trial]* as a sub-study on *[details of host trail registration]*

8. Financial and Insurance Issues

The user testing for the nested trial is funded as part of MRC START which is sponsored by the University of Manchester. It forms a sub-study to the [*Host trial name*] study, which is sponsored by [*name of host trial sponsor*]. Normal NHS indemnity procedures will apply.

9. Project Timetable

Date	**Action**
	Documentation for the nested study agreed & signed off
	User Testing of original PIS and development and testing of revised PIS
	Submission to REC of application for substantive amendment
	Recruitment to the nested trial begins
	Conduct focus groups with participants in the qualitative study – delete as appropriate
	Interim analysis of nested trial data
	Recruitment to the nested trial ends
	Data cleaning and submission of data set to MRC START team
	Collation of results and analysis, begin write up of trial level paper

10. Dissemination of research

The results of this nested sub-study will be published in a peer-reviewed journal to further improve evidence base regarding effective recruitment strategies in trials. This publication will

be led by the [*Host trial*] team. In addition the data will be included in a meta analysis of all studies recruited to the MRC START programme led by the MRC START team. Dissemination of research findings will be conducted in line with the MRC START authorship arrangements (see appendix 4).

11. References

[1] Department of Health. Best Research for Best Health - a new national health research strategy. London. Department of Health, 2006.

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[15] Knapp P, Raynor DK, Silcock J, Parkinson B. Can user testing of a clinical trial patient information sheet make it fit-for-purpose? – a randomised controlled trial. *BMC Medicine* (in press).

Appendices

Core study

1. Original *[Host trial]* Participant Information Sheet
2. Revised *[Host trial]* Participant Information Sheet
3. MRC START Data Sharing Agreement
4. MRC START Authorship Arrangements

Additional elements

5. *[Host trial] 'Decline form' – delete as appropriate*
6. *Quality of Informed Consent (QuIC) data – delete as appropriate*
7. *Focus group study invitation letter – delete as appropriate*
8. *Focus group study participant information sheet – delete as appropriate*
9. *Focus group study consent form – delete as appropriate*