

MRC START in STOP-ACEi:
What are the effects of a multimedia resource on recruitment?
A nested, randomised controlled trial

[Protocol Version 1.0]
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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, 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].

The STOP-ACEi 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 the STOP-ACEi study.

2. The intervention – Multimedia resource (MMI)

At present most patient information about trial participation is given in written form, but this does not necessarily represent the best way to communicate with patients about taking part in a trial. Multimedia interventions may offer a useful strategy to improve communication about trial participation and so facilitate greater trial accrual and retention rates. The diverse methods of information delivery possible via multimedia platforms provide alternative channels for health communication, in particular the Internet provides an opportunity for self-directed and tailored learning (Antoniou et al., 2011, Shneerson et al., 2012). However the impact of multimedia information on patient identified barriers and motivators to clinical trial participation has not been rigorously explored.

The MRC START team has developed a multimedia resource in conjunction with www.healthtalkonline.org (the award winning website of the DIPEX charity which allows patients and the public to share peoples experiences of over 60 health related conditions and illnesses).

The structure and content of the multimedia resource have been developed based on:

- a review of research on patient decision making conducted by the research team
- a workshop run at the PCRN national conference (November 2012), led by a clinician with considerable PCRN expertise and attended by PCRN research staff
- input and feedback from our Patient and Public Involvement representatives from the University of Manchester PRIMER group (<http://www.population-health.manchester.ac.uk/primer/>) and
- expertise from within the MRC START project team which includes clinicians, psychologists and experts in clinical trials.

The website consists of three sections:

- (1) A home page identifying the STOP-ACEi trial and offering potential participants the options of more information on medical research in general or finding out more about their trial.
- (2) Generic pages on medical research consisting of edited video clips and infographics. The video clips, all from healthtalkonline, [www.healthtalkonline.org] are of patients talking about their experiences of medical research. The clips were selected and edited by our patient and public involvement representatives working directly with a GP from

healhtalkonline. They reflect the key concerns or issues raised by patients when talking about participation in research in the healtalkonline interviews. The infographics on these pages were developed by our digital partners based on material provided by the research team and our patient and public involvement representatives who then commented extensively on the finished product.

- (3) Study specific pages. The structure of the study specific pages was designed by the MRC START team and their PPI representatives. This section of the website is designed to host video and text specific to each host trial. The STOP-ACEi trial team will work with the MRC START team to produce content for this section.

It would be useful to know if the MMI in addition to the existing participant information sheet impacts on rate of recruitment, in comparison with the written patient information sheet alone. A nested randomised controlled trial would be the best approach to evaluate its effects. The STOP-ACEi study is one of six RCTs that will explore this as part of the wider MRC START research programme.

3. Study details

The STOP-ACEi study is a randomised controlled trial of a drug intervention to assess whether stopping existing ACEi or ARB treatment improves or stabilises renal function compared to that of a group of people who continue on the drugs. The population will be patients with advanced chronic kidney disease (CKD) who have stage 4 or 5 CKD who regularly attend hospital CKD clinics every three months.

In the STOP-ACEi study there will be approximately 20 UK centres. Potential participants will be identified (e.g. from medical records, clinical records, individual renal unit databases or other local registries) by the research team at each of the recruiting centres; more centres may join as the trial progresses. Potential participants will be sent an invitation letter and participant information sheet explaining the STOP-ACEi trial or approached whilst in clinic and given this information. Participating research sites will be randomised to use either the standard participant information or, additionally, give access to the MRC START MMI in a cluster randomised controlled design.

4. Research Objectives

4.1 To establish if the number of patients recruited in to the STOP-ACEi trial is improved by access and use of the MMI, compared to the participant information sheet.

4.2 To explore whether access and use of the MMI improves retention in the STOP-ACEi trial.

5. Method

5.1 Design

The nested RCT will be cluster randomised. The type of invitation and patient information received will be determined by random allocation of participating centres. As each centre is recruited, the STOP-ACEi team at BCTU will randomly allocate the centre to the intervention or control condition. The STOP-ACEi team will then provide the centre with the correct version of the covering letter and PIS to be provided to patients when they are approached about participation in the STOP-ACEi trial.

Those who are approached regarding participation in the STOP-ACEi trial will receive one of two participant information conditions depending on the centre they are recruited from:

- a) the intervention group will be sent the standard study participant information. In addition they will receive access to the MRC START MMI via a website link and QR code;
- b) the control group will be sent the standard study participant information only.

5.2 Inclusion/ exclusion criteria

The recruitment nested trial will include all patients identified as potentially eligible for the STOP-ACEi trial: there are no additional inclusion or exclusion criteria.

5.3 Recruitment and Randomisation

Participants in the START in STOP-ACEi sub-study will have been identified via medical records, clinical records, individual renal unit databases or other local registries in participating centres using the inclusion/exclusion criteria as detailed in the STOP-ACEi study protocol.

All potentially eligible patients for the STOP-ACEi trial will be sent or given a participant information sheet describing the trial and a covering letter from a research nurse inviting them to

take part. Potential participants in the intervention group will be given access to the MRC START MMI via a link and QR code on the covering letter and PIS.

The type of invitation received will be determined by random cluster allocation of the participating centres using a method which is robust and ensures concealment of allocation, conducted by someone independent from those undertaking recruitment at the STOP-ACEi trial office. Centres will be randomised to use either the control patient information or patient information with access to the MMI. Centres will be randomised using a random number list with variable block length, stratified by size of recruiting centre, to ensure a balance in the number of small (patient recruitment target <15) and large (patient recruitment target >15) centres since there is considerable variability in the size of patient population at each centre..

The research nurse will record the following data for each participant using a log:

- whether they are actually recruited into STOP-ACEi.
- whether they are not eligible and specify failed criterion;
- whether they declined to enter the trial and any reasons volunteered
- the patient ID number linked to each patient recruited;

5.4 Intervention

The resource consists of three sections:

1. a home page identifying the STOP-ACEi trial and offering potential participants links to:
2. generic pages on taking part in medical research, and
3. study specific pages providing information about the STOP-ACEi trial.

Currently the blank development site can be viewed at:

<http://mrcstart.reasondigital.com/blank-template/>

5.5 Outcome measures

The primary outcome will be the number of patients recruited to the STOP-ACEi trial. The host trial team will keep a record of all patients who were identified as potential participants and which recruitment intervention group they were in.

Secondary outcomes will be:

- the proportion of patients in each intervention group who agree to participate in the STOP-ACEi trial (where this differs from the number actually recruited, due to e.g. screening or exclusion criteria);
- the proportion of recruited patients who are retained to the end of the STOP-ACEi trial.

5.6 Sample size

The sample sizes used in START nested studies are not calculated a priori, as the sample size is dependent on the host trial. To guide recruitment of host trials, nested studies are broadly powered on an estimated increase in recruitment of 10% from a baseline of 50%, which requires 400 patients per arm to provide 80% power (alpha 0.05). Note this is the number approached, not the number randomised: the former will often be many times higher than the latter.

However it is anticipated that across the 12 host trials there will be variation in the numbers approached.

STOP-ACEi is a randomised controlled trial recruiting 410 participants. The STOP-ACEi team have estimated that larger centres will approach 60 patients over the two year period and smaller centres over 30 patients. We know that research nurses have had 70% success rate using a similar recruitment approach, therefore we estimate we will need to approach 585 potential participants to recruit 410 participants.

6. Analysis

Anonymised data from STOP-ACEi will be sent to the MRC START team in accordance with the MRC START data sharing agreement (see Appendix 2).

The research centres will be screening eligibility before approaching a patient, so theoretically no ineligible patients will be given a PIS and those that are given a PIS would only not be entered if they decided they didn't want to. A recruitment log will be kept by the research nurse

who will record why they weren't entered and there are options for "not eligible/error in screening" and for "not interested". The proportion of patients who express an interest in participating, attend screening and are ultimately randomised in to the main trial will be calculated for the two intervention groups (original and revised PIS). The differences between the two proportions at each point will be calculated along with the corresponding 95% confidence intervals.

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 nested study, using the recruitment method described above.

MRC START has received full ethical approval (REC Reference 11/YH/0271) from NRES Committee Yorkshire and the Humber – South Yorkshire, and an MRC START Multimedia Substantial Amendment (covering the generic content in the MMI): REC Reference 11/YH/0271 Substantial amendment 2, 31/10/13).

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 – but is simply a supplementary form of presentation.

The nested study (MRC START in the STOP-ACEi trial) will be registered by the STOP-ACEi study team as a sub-study on ISRCTN.

8. Financial and Insurance Issues

The multimedia resource intervention 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 STOP-ACEi Trial, which is sponsored by Hull and East Yorkshire Hospitals NHS Trust. Normal NHS indemnity procedures will apply.

9. Project Timetable

Date	Action
10.05.14	Documentation for the nested study agreed & signed off
Dec 2014	Submission to REC of application for substantive amendment
10.06.14	Discuss/approve scripts with host trial and plan process of filming bespoke content with external digital media company
07.06.14	On-site filming of bespoke content
01 Oct 2014	Recruitment to the nested trial begins
01 Aug 2016	Recruitment to the nested trial ends
01 Oct 2016	Data cleaning and submission of data set to MRC START team or the Cochrane collaboration
01 Dec 2016	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 STOP-ACEi study team – the START team will provide a template to assist in the drafting of an individual paper. 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 3).

11. References

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