

REFORM Sub Study: A nested randomised controlled trial of a leaflet containing information on research to increase recruitment rates of potential REFORM trial participants.

1. Background

It is widely accepted that randomised controlled trials are the gold standard test for evaluations of interventions in the health care field and as a result, randomised controlled trials are frequently used in health care and health services research. A large number of randomised controlled trials are conducted each year, however, there is substantial information to indicate that recruitment to trials can be problematic. Research by McDonald et al (2006) indicates that 45% of trials “failed to recruit to within 80% of target”. Where trials do not achieve their full recruitment target this can mean the study is underpowered leading to non-significant findings which could mean that a trial of an effective intervention is abandoned before the true value of the intervention is assessed (Treweek et al, 2011). This is a critical issue in relation to health services research and its attempts to improve health care and available interventions for the general public.

Research by Ellis et al (2002), in relation to public understanding of health research, has found poor levels of understanding amongst the general public of i) the need for randomised controlled trials and ii) the way in which these trials are enacted. Furthermore this research indicates that participants would be “more willing to consider participating in a clinical trial once they were better informed” (Ellis et al, 2002). Additional research relating to information booklets and understanding of clinical trials has indicated that following general informed consent procedures, participants are often unable to recall information relating to the trial they are participating in (Ives et al, 2001). The work of Ives et al (2001) indicated that patients have found trial information sheets and booklets useful; enabling patients to read the literature in their own time, equipping them with knowledge of what might be involved in a trial should they decide to consent and enabling them to refer back to this information at any point. Prospective and current trial participants may therefore benefit from clear concise information on research and what their involvement can mean and involve; making their involvement in a clinical trial more informed.

A number of studies have discovered that pre-notification to increase questionnaire response rates has been successful. Angus et al (2003) have suggested that providing pre-notification in relation to the sending of a questionnaire increases the level of contact with the participant which subsequently increases response rates. The impact of pre-notification on questionnaire response rates is supported by the Cochrane systematic review by Edwards et al (2010). This review examined 45 health research trials with 40 trials investigating interventions targeting prospective participants and the remaining 5 focusing on the staff responsible for undertaking recruitment. With reference to the use of pre-notification, Edwards et al (2010) report that “the odds of response were substantially higher with pre-notification (1.45; 95% CI 1.29 to 1.63; $P < 0.00001$)”. This significant finding indicates that pre-notification has an impact on response rates and this has therefore exposed the potential to investigate this relationship for consent response rates.

A variety of ways to increase recruitment to randomised controlled trials have previously been investigated. Providing participants with financial incentives (Free et al, 2010), using telephone reminders to follow up non responders (Nystuen et al, 2004) and the use of existing trial participants to refer peers to trials (Larkey et al, 2002) have all been investigated and success of some of these interventions has been identified. Studies by Ellis et al (2002) and Ives et al (2001) have both investigated the provision of additional information in relation to participant's decisions to be involved in primary research. In both cases consent was obtained prior to information being provided and both involved participants experiencing complex conditions. These trials indicated there was little difference between the intervention and control groups in terms of understanding or willingness to consent to a future study, however, these studies may not have been sufficiently powered for detecting a significant difference due to their small sample sizes. Despite these studies it appears that little research has been conducted with regards the use of pre-notification to provide information to prospective participants in advance of invitation to consent. This method presents an opportunity to increase recruitment to randomised controlled trials and therefore warrants further investigation.

2. Aim of the Study

The aim of this study is to evaluate the effectiveness of providing prospective trial participants with a leaflet about health care research, prior to their receiving a consent pack, as a means of increasing the rate of recruitment to the REFORM (REducing Falls with ORthoses and a Multifaceted podiatry) Trial.

3. Method

3.1 Design

The proposed study is a nested randomised controlled trial.

3.2 Inclusion and Exclusion Criteria

The inclusion and exclusion criteria to be used in this study are the same as those used for the main REFORM trial. Patient lists will be screened by sites in accordance with criteria set out in section 5.1.2 of the REFORM Protocol.

Participants will be eligible for the sub study if they fulfil the following criteria:

1. Patient is 65 years of age and over.

Participants will not be eligible for the sub study if they fulfil any of the following criteria:

1. Patient has a life expectancy of less than six months.
2. Patient is known to have neuropathy.

3. Patient has had a lower limb amputation at or proximal to the level of the metatarsals.
4. Patient is known to have dementia.
5. Patient is known to be chair or bed bound.

3.3 Randomisation

Simple randomisation will be used to allocate participants to one of two groups. This will be completed by means of a randomisation sequence, generated by computer at York Trials Unit, and will allocate participants to one of two groups in a 1:2 (intervention: control) ratio.

3.4 Intervention group

Participants randomised to the intervention group will be sent a leaflet providing information on, and detailing the importance of, taking part in research. The leaflet will be sent to the participant approximately 2 weeks prior to the REFORM consent pack being mailed to them.

3.5 Control group

Participants randomised to the control group will receive no literature regarding research. They will be contacted as per the REFORM protocol, when recruitment packs are mailed to prospective participants for the main trial.

3.6 Management of leaflets/consent forms

The REFORM trial team will liaise with the study site(s) in order to screen for participants who would be eligible for the REFORM trial. This will be done in advance of normal practice in order to allow sufficient time for leaflets to be sent to participants. The REFORM trial team will work with the study site(s) to assist with the mailing of the research leaflet to prospective participants. Records will be kept with regards which participants were sent a research leaflet and which were not. A screening log of trial ID number and patient's name and address will be kept at the NHS site to record which patients were sent the newsletter. The list of trial ID number and group allocation (Intervention: pre notification leaflet or control: usual recruitment procedure) will be held at the York Trials Unit. Consent forms returned to York Trials Unit will be handled in accordance with REFORM trial specific procedures and the REFORM protocol.

3.7 Primary Outcome

The primary outcome of this trial is the recruitment rate which can be defined as the proportion of people who are randomised in to the REFORM Trial.

3.8 Secondary Outcome

The secondary outcomes of this trial are:

- Time to response. This can be defined as the number of days elapsed between the consent pack being sent by the study site and the completed consent form being returned and recorded as such, at York Trials Unit.
- Rate of retention in the follow up phase of the study. This can be defined as the proportion of people who were provided with a research leaflet remaining in the study during the follow up phase of the REFORM trial.
- Recruitment rate to the cohort which can be defined as the proportion of people who agree to take part in the REFORM study.

4. Statistical Considerations

4.1 Statistical Power

This nested randomised controlled trial is designed to detect a 2% increase in participant recruitment rate in the REFORM trial.

To observe this 2% increase in recruitment from the observed pilot recruitment rate of 5% with 80% power and a 5% significance level requires, on the basis of unequal allocation (2:1) 3300 participants of which there would be 2200 participant's randomised to the control group and 1100 randomised to the intervention group.

4.2 Analysis

All analyses will be conducted on an intention to treat basis, including all randomised participants on the basis of the groups to which they were randomised. Analysis will be conducted using SPSS using 2 sided significance tests at the 5% significance level. The primary outcome is the proportion of people who are recruited to the REFORM trial. A chi squared test will be used to test for any statistically significant differences in the proportion of participants who responded. Logistic regression will be used to calculate odds ratios and corresponding 95% confidence intervals and P values.

The secondary outcome is time to response, calculated as the number of days from the date the leaflet was sent out to the date the consent form was returned to York Trials Unit. Cox's proportional hazards models for time to return will be used to analyse the differences between intervention and control groups.

The proportion of people, who were provided with a research leaflet, remaining in the study during the follow up phase of the REFORM trial will also be analysed as a secondary outcome. This will be analysed using the same methods as those used for the primary outcome.

5. Ethical Issues

NHS ethical approval has been granted for the REFORM Trial and an amendment will need to be made for this nested sub study. Prior to this, approval will need to be sought from the

University of York Health Sciences Research Governance Committee. Should the sub study be approved by both bodies, the study will also require R&D Governance approval from those study sites which may be involved in the sub study. These approvals will be sought before any trial activity commences.

Within this nested sub study, patients will not have opportunity to provide their informed consent for their involvement in this sub study. This is due to the fact that consent for the main REFORM trial will not have been obtained at the point of sending out a pre-notification leaflet. As this leaflet is designed to be non-invasive and will contain generalised literature with regards trials it is unlikely that this will pose a major ethical issue.

6. Financial and Insurance Issues

Funding for this sub study will be provided by the main REFORM study which is funded by NIHR Health Technologies Assessment Programme and is sponsored by the University of York. Normal NHS indemnity procedures will apply to this trial. Indemnity cover will also be provided by the University of York.

7. Dissemination of research

This research is being conducted for a dissertation project as part of an MSc in Health Services Research at the University of York. As a result, the findings of this trial will initially be detailed in a MSc dissertation thesis.

Results of this trial will also be published in a peer-reviewed journal and if possible will be presented at a conference or meeting suitable to this area of methodological research.

8. References

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