Site visits to initiate recruitment in a clinical trial: Does it matter who conducts the visit? Protocol for Implementation in Trials

Corresponding Author:

Ms Claire Nollett, Cardiff University

Co-authors:

Dr Mark Kelson, Cardiff University

Prof Kerenza Hood, Cardiff University

Address for Correspondence:

Centre for Trials Research

College of Biomedical and Life Sciences

7th Floor Neuadd Meirionnydd

Heath Park

CARDIFF CF14 4YS

Tel: 02920 687187 Fax: 0870 0241430

Email: nollettcl@cardiff.ac.uk

Accepted for publication in Journal of Evidence-Based Medicine

Abstract

The Study Within A Trial (SWAT) programme exists to 'embed research within research, so as to resolve uncertainties about the different ways of designing, conducting, analysing and interpreting evaluations of health and social care' (1). Published in this journal in 2013, a template for the first SWAT protocol outlined an investigation into the effects of site visits by the Principal Investigator on recruitment in multi-centre randomized controlled trials (1). We have now designed a SWAT protocol to extend this question and ask 'does it matter *who* conducts the site visit?' Our aim is to provide a protocol which trials can implement to address this research question.

Key Words

randomized controlled trials; recruitment; research design; SWAT; uncertainty

Introduction

Randomised controlled trials (RCTs) are commonly viewed as the 'gold standard' design for producing high quality evidence in medicine. However, recruiting participants to a trial or study can be a difficult process, and a high percentage fail to reach the recruitment target necessary for an adequately powered study (2, 3). This can result in uninterpretable/ambiguous findings or early closure of the trial (4) and create ethical issues.

One cause of under-recruitment may be lack of recruitment activity by clinicians. For example, in a large primary care cohort study of cough and respiratory tract infection in children (5) the authors reported that of the 247 practices that signed up to the trial,

as many as 1/5 did not start recruitment (reasons for non-recruitment were not stated). At best this represents a huge waste of resources and at worst, the failure of the study.

To address this common problem, Fletcher et al. conducted a systematic review of interventions aimed at improving recruitment activity of clinicians in RCTs (6). Effective interventions included the use of qualitative research to identify and overcome barriers to recruitment, reduction of the clinical workload associated with participation in RCTs and the provision of extra training and protected research time. However, the authors concluded that the interventions were tested mainly in low quality studies and no firm recommendations from the review could be made. They highlighted that many of the studies focused solely on under recruiters and suggested future studies examine factors associated with successful recruitment.

Subsequently, in their large primary care study, Redmond et al. focused on factors associated with high recruiting centres. Of the nine factors they examined, only three were significantly associated with high recruitment: longer duration of recruitment, higher number of recruiting clinicians per site, and shorter time taken to recruit first participant (5). The authors concluded that to maximise recruitment, trialists should ensure practices have a long duration of recruitment, at least four recruiting clinicians per practice and should monitor recruitment closely, addressing practices that fail to recruit within the first two weeks. Currently, it is common practice within our trial unit to monitor and visit sites which have been initiated but not started recruitment, or those with low recruitment rates, to problem solve any issues and encourage them to start/improve. However, we have yet to measure in a systematic way whether this site visit has any significant impact.

The results of a Study Within A Trial (SWAT-1) designed to assess the effectiveness of a ‘site visit’ intervention on recruitment rates in a multi-centre randomised trial were

recently published (7). The site visit and scheduled meeting had the sole purpose of discussing trial recruitment. The authors compared recruitment rates pre- and post-intervention in Site A who received the visit, against Sites B and C which did not. They found a significant increase in recruitment in the site that received the visit versus the controls, indicating that this maybe a useful method for addressing under-recruitment in trials.

This SWAT protocol extends the work of SWAT-1 by providing a protocol to examine whether site visits not only have the potential to improve recruitment, but also to initiate recruitment in those sites which have not yet started. However, the main aim of the SWAT protocol is to investigate: does it matter who conducts the visit?

The visits in SWAT-1 were made by the Principal Investigator (PI). PIs are can either be clinical staff who also conduct research eg. GPs, consultants or they might be non-clinical researchers, that is researchers who do not have a clinical background. In our unit, it would be common for the Trial Manager to make the site visits. Trial Managers are commonly non-clinical researchers. A systematic review summarising the evidence related to the impact of feedback on physicians' *clinical performance* found that the *source* of the feedback was important (8). Feedback had more effect on performance if it came from a professional or administrative group, than if it came from a researcher. Could this also apply to trial performance and activity, and if so, does it matter who conducts the site visit?

Aim

Our aim is to outline a protocol for a SWAT to investigate whether site visits intended to initiate recruitment in sites that are failing to recruit are more effective when conducted by a clinical peer rather than a non-clinical member of the research team. By clinical peer, we mean a person from the same professional group as the person in

charge of recruitment at the site eg. GP, nurse, consultant, who is affiliated with the central trial team running the study, but not a key research member of their team. We envisage that this SWAT protocol can be incorporated into trials in which some sites fail to commence recruitment, and the results can be pooled in a meta-analysis.

Theory

In Social Psychology, 'conformity' is the term used to describe the process in which a person alters their behaviour based on the influence of other people. One common reason for conforming is that we wished to be liked and accepted by others. This may lead us to change our behaviour to fit with theirs, or to match their positive expectations of us. We do what others do or ask of us so that we do not attract attention and to avoid getting into trouble. This is known as Normative Social Influence and is incorporated into Social Identity Theory [SIT: (9, 10)]. SIT describes how people identify themselves and respond to other. The theory suggests that:

1. People allocate themselves to groups they belong to (in groups) and groups they don't belong (out groups). For example, groups based on class, occupation, political orientation and hobbies.
2. People gain their identity and self-esteem from these groups.
3. People are more likely to conform to in groups (same group) than out groups (different group).

The third point indicates that people are more likely to conform, that is, alter their behaviour, when asked to do so by people they identify with, from the same group as themselves. The implication for this SWAT is that recruiting clinicians are more likely to conform to encouragement to commence recruitment from fellow clinicians (peers) with whom they identify (in group) than they are to requests from non-clinical researchers (out group). Therefore a visit from a clinical peer may be more effective at changing the clinician's recruitment activity than a visit from a non-clinical member of the research team.

Design

Intervention and Comparator

The intervention will be a face-to-face site visit and meeting by a clinical peer to sites that fail to recruit a participant within a specified time frame following site initiation. The choice of clinical peer will be study specific and reflective of the person to be visited. As an example, if GPs are the main recruiters in a study, a GP trained in the study procedures and working with the study team would be asked to visit the non-recruiting site. The control will be a face-to-face site visit and meeting by a non-clinical research member of the trial team, for example, a Trial Manager or possibly the Principal Investigator (as long as they are not also a clinical peer). Details of what the visit would entail will change depending on the type of study, nature of practice and recruitment process, but examples include reviewing study specific SOPs with the recruitment team, ensuring they have up-to-date contact details in the event of queries, checking that recruitment materials are readily available and that promotional posters and leaflets are being displayed.

Allocation to Intervention and Comparator

Recruiting sites who fail to recruit a participant within a pre-agreed time period after initiation would be randomly allocated to intervention or control via simple randomization. The main trial statistician should perform the allocation using any valid simple randomisation method. The pre-agreed time frame will vary depending on the nature of the condition under investigation, with some conditions being very common and others rarer. As an example, in GP practices recruiting to a respiratory tract infections study, Redmond et al (2015) have recommended addressing practices that fail to recruit within the first two weeks following initiation.

Primary Outcomes

The primary outcome measure will be the number of days to first recruit following the site visit.

Secondary Outcomes

The secondary outcome measure will be the total number of participants recruited at the end of the study.

Analysis

The primary outcome would be compared between groups (those receiving a visit from a clinical peer or a non-clinical member of the research team) using survival analysis. The unit of analysis is site. Hazard ratios with associated 95% confidence intervals would summarise the results. Descriptive statistics will compare the total number of recruits between trial arms.

Possible Problems

Studies would need to be large enough to have sufficient sites to randomize non-recruiting sites to two arms. This may be more feasible in large primary care studies than in secondary care studies with fewer sites. However, whilst small studies may not be able to definitively demonstrate effectiveness, they could contribute to a meta-analysis, which demonstrates the importance of using a standard protocol such as this one. Another issue to consider is that the research teams would also need an available peer clinician, willing and able to make site visits.

Link to the SWAT Repository

http://www.qub.ac.uk/sites/TheNorthernIrelandNetworkforTrialsMethodologyResearch/SWATSWARInformation/Repositories/SWATStore/

Version information

Source of idea: Ms Claire Nollett and Prof Kerry Hood

Revised by: Dr Mark Kelson

Acknowledgements

None

References

1. Smith V, Clarke M, Devane D, Begley C, Shorter G, Maguire L. SWAT-1: what effects do site visits by the principal investigator have on recruitment in a multicentre randomized trial? *Journal of Evidence-Based Medicine* 2013; 6: 136-137.

2. Bower P, Wilson S, Mathers N. Short report: How often do UK primary care trials face recruitment delays? *Fam Pract* 2007; 24: 601-3.

3. Raftery J, Bryant J, Powel J. Payment to healthcare professionals for patient recruitment to trials: systematic review and qualitative study. *Health Technol Assess* 2008; 12: 1-28, iii.

4. Campbell M, Snowdon C, Francis D, Elbourne, D, McDonald AM, Knight R, Entwistle V, Garcia J, Roberts I, Grant A. Recruitment to randomised trials: strategies for trial enrolment and participation study. The STEPS study (the STEPS group). *Health Technol Assess* 2007*;* 11: No. 48

5. Redmond N, Turnbull S, Thornton H, et al. Can predictors of successful clinician and GP practice recruitment be established? Analysis from a large primary care prospective cohort study of children with acute cough and RTI. Presented *at The South West Society for Academic Primary Care Annual Scientific Meeting*; March 2015; Birmingham; Abstract No. P3.32.

6. Fletcher B, Gheorghe A, Moore D, Wilson S, Damery S. Improving the recruitment activity of clinicians in randomised controlled trials: a systematic review. *BMJ Open* 2012; 2: e000496. doi: 10.1136/bmjopen-2011-000496

7. Smith V, Clarke M, Begley C, and Devane D. SWAT-1: The effectiveness of a 'site visit'intervention on recruitment rates in a multi-centre randomised trial. Trials 2015; 16: 211-217. DOI 10.1186/s13063-015-0732-z

8. Veloski J, Boex J, Grasberger M, Evans A, Wolfson D. Systematic review of the literature on assessment, feedback and physicians' clinical performance: *BEME Guide No 7. Medical teacher* 2006; 28,2: 117-128.

9. Tajfel H, Turner J. An integrative theory of intergroup conflict. In: Austin WG, Worchel S, eds. *The social psychology of intergroup relations*. Monterey, CA: Brooks/Cole, 1979; 33-48.

10. Turner JC. *Social influence*. Milton Keynes: Open University Press, 1991.