

3. Appendix 3 – Study Within A Trial (SWAT)

SWAT TITLE:	dOes ParTicipant InforMatIon ShEet Design affect the recruitment rate into an interventional trial? A Study Within A Trial (OPTIMISED)
SWAT Registration	This SWAT is registered as SWAT 101 on the MRC SWAT repository

Background and Rationale

Failure to recruit to time and target is a problem faced by many trials, including randomised controlled intervention trials. For studies to be considered a definitive trial, able to adequately explore a hypothesis, they must have an appropriate sample size; if too few participants are recruited, the chances of finding statistically significant results are lower and the study may fail to meet its objectives, posing the ethical issue that participants are taking part in a study that may have no tangible impact on healthcare (37). Problems in recruiting to studies can extend their duration making them more expensive or requiring agreement of collaborators to continue to work on the project with little or no additional funding.

There are many barriers to recruitment, not only from the perspective of the potential participant, but also for the clinician looking to involve patients in a study (38). Long and complex participant information sheets may effect a patient's decision to enter a trial, either based on a lack of understanding (39), or a lack of willingness to fully read the additional information alongside non-study information provided to the patient at the same time. This is particularly relevant in emergency settings, where decisions are time-sensitive and patients cannot be given as long to consider participation, compared to non-emergency settings where patients may take information away with them.

The information provided to participants plays an important role as a point of reference for them (40,41) therefore any decision to improve, or reduce the length of information provided should consider this, especially for trials that involve more complex interventions. There should be a balance between providing enough information to patients to inform their decisions whilst avoiding the use of long and complex sentences that might negatively impact on their decision to enrol (39).

A recent Cochrane review of studies testing recruitment and retentions interventions found that some were more effective than others, with studies evaluating the use of user-tested participant information leaflets showing that there was little or no difference to recruitment (42). Despite this, modification of participant information is still considered a priority for improving recruitment and retention into clinical trials (43,44). Such studies are embedded within larger trials (otherwise referred to as SWATs – “Study within a Trial”) and it is the focus of the MRC Start project and PROMETHEUS research group to increase the evidence base concerning recruitment to trials by conducting multiple SWATs that will contribute towards a meta-analysis (43,45) and future systematic reviews.

SWAT Objectives

The primary objective for this SWAT is to explore whether improving the readability of a participant information sheet (PIS) has an effect on the recruitment rate into an interventional trial.

The secondary objective of this SWAT will be to assess the impact, or “value”, of the PIS in the decision making of the patient.

Outcomes

The primary outcome will be the proportion of patients who consent to take part in the interventional trial (known as the host study). Secondary outcomes will be qualitative measures, whereby consenting participants will provide feedback about the PIS they were provided. A questionnaire provided by Peter Knapp used in the “TRECA” study (a study of digital, multimedia resources used in recruitment to trials with children and adolescents) will be used to inform the development of a similar, decision making questionnaire to assess the impact or value of the PIS in the decision making of the patient.

Study Design & Setting

This study will be a randomised study within a trial (SWAT) embedded within a host clinical trial of an investigational medicinal product (CTIMP). The study population will be the patients identified as eligible for the host study and approached by the local clinical team for inclusion. After approximately 6 months of recruitment, there will be a data cut to allow for an interim analysis which will be used for the write up for an MSc in Clinical and Health Sciences being undertaken by the Clinical Trial Manager, Rachelle Sherman. At this point, results will be shared with the SARC Trial Management Group (and Trial Steering Committee if appropriate) in case the outcome impacts the ongoing running of the trial. For example, if one PIS appears to significantly increase recruitment it might be considered necessary to remove randomisation and move forward with this one, as it would be unethical to continue to randomise.

Participants will be randomised to receive either the optimised PIS (PIS A) or conventional (PIS B). The optimised PIS (PIS A) will be designed with the following factors in mind:

- Improved readability by reducing the number of words per sentence, using familiar words and phrases, a columnar layout and clear headings (46)
- Templates used by other research groups including (39,47)
- The guidance provided by the EC on the readability of patient information leaflets for medicines (48)

The resulting optimised PIS will be reviewed by the Patient and Public Involvement (PPI) representatives involved in the host study, who will also review the conventional PIS. The PPI representatives will be informed of the intended SWAT and will be encouraged to comment on the design of the SWAT during the development of the host study.

The conventional PIS will be designed based on the template and guidance provided by the HRA (49) and will be subject to the expectations of the REC and HRA for approval, which includes adequate use of lay language and inclusion of appropriate information as deemed necessary for the study. The conventional PIS will be designed by a member of the Derby CTSU not involved in the development of the optimised PIS and the Chief Investigator for the host study as normal, before the development of the optimised PIS. This is to reduce the chance of unintentionally making the conventional PIS less readable than the optimised PIS due to prior knowledge of the design of the optimised PIS.

Patients considered eligible for the host study will be provided with either the optimised PIS or the conventional PIS. They will not be informed of the fact that they had been randomised to receive different information sheets, an approach deemed acceptable in other similar trials (47). Randomisation to the SWAT will be conducted using a randomisation list created by an online randomisation system (50) and the site staff will be provided with information packs in a given numerical order determined by this list. Each information pack envelope will be given a form of identification which will then be recorded on the host study’s screening log. The screening log will be anonymised and used to provide the information needed to determine the recruitment rate according to information received, for the primary analysis.

Patients who agree to take part in the study will then be asked to complete a questionnaire designed to assess the impact of the PIS on the patient's decision making to enter the trial. This will be provided to them at the 2 hour follow up visit.

The proportion of patients who consented to the host study will be compared between the two groups – those who received the conventional PIS and those who received the optimised PIS – using either an independent Chi-squared test or Fisher's exact test for categorical data.

The data to inform the secondary objectives will be composed of as questionnaire responses that are a mixture of closed questions and a Likert scale to provide scores to the questions asked, designed to provide feedback on the PIS design, feasibility and general provision of information.

Sample size calculation

The sample size calculations for the SARC trial have been outlined in the main trial protocol. As is usual with a SWAT, we did not undertake a formal power calculation to determine the sample size (51), since the sample size is constrained by the number of patients being approached in the SARC host trial. The sample size will therefore be the total number of patients invited into the SARC trial during the SWAT recruitment period. Based on response rates achieved in existing emergency trials, we estimate we will need to invite approximately 236 patients in order to recruit 118 to the host trial, representing a recruitment rate of approximately 50%.

The sample size for the secondary outcome measure, the decision-making questionnaire, will be smaller as this will consist of a cohort of patients who consent to the trial and who agree to complete the questionnaire (a maximum of 118).

Statistical analyses

Analyses will be conducted on an intention to treat basis, including all randomised participants on the basis of the PIS groups to which they were randomised. Analysis will be conducted using 2 sided significance tests at the 5% significance level. For analysis of the primary outcome, Chi-squared test and logistic regression will be used to produce odds ratios and their associated 95% confidence intervals and p-values. Interim analysis of the primary outcome will be performed to assess whether one arm is clearly outperforming the other and allow the host trial to benefit from the improved overall consent rate.

Dissemination

The results of the SWAT will be shared with the Prometheus group of trial methodologists and contribute towards an increasing evidence base for recruitment intervention strategies. The study will be presented at appropriate trial methodology conferences, including the UK Trial Manager's Network Annual Meeting as well as being submitted for publication in an appropriate methodology journal, for example *Trials*. At the very least, if no significant difference is seen between the two groups for the primary analysis, the secondary objectives might inform the choice of PIS style for future studies ran by the researchers and sponsor of the host study.

15. REFERENCES

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