

Study within a trial protocol: Same-day consent vs. delayed consent in a randomized trial

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Abstract

Background: Randomized trials are designed to evaluate the effects of health care interventions. The recruitment process in a randomized trial can be challenging. Poor recruitment can have a negative impact on the allocated budget and estimated completion date of the study and may result in an underpowered research that will not adequately answer the original research question.

Aim: We aim to perform a Study Within A Trial (SWAT) to evaluate the impact of same-day consent or delayed consent on recruitment and retention in the host trial.

Methods: This SWAT is designed as an observational study. However, the host trial is a randomized controlled trial evaluating the effectiveness of an intensive lifestyle modification program in patients with peripheral arterial disease. For this trial and SWAT, same-day consent is defined as the patient giving consent on the same day, after the investigator has fully explained the pre-designed information leaflet for the host trial. Delayed consent is defined as the patient feeling they still need further time to consider their decision to participate or not.

Swat registration: The SWAT was registered on the Northern Ireland Network for Trials Methodology Research.

KEYWORDS

consent, delayed, PAD, same day, SWAT

1 | Background

Randomized controlled trials (RCTs) are widely acknowledged as the design of choice for evaluating the effectiveness of health care. Methods to increase recruitment in randomized trials are priorities for methodological research. The success of RCTs depends on the recruitment and retention of trial participants. However, the recruitment process in RCTs can be challenging for the researcher. At least 50% of trials fail to recruit the required sample size, leading to an underpowered study.

The consenting process is both legal and ethical requiring a lot of consideration during the trial design phase^{1,2,3,4}. According to the International Conference on Harmonization Guideline for Good Clinical Practice (ICH GCP),⁵ trialists should ensure that patients being recruited to join a study should be given adequate and reasonable time to think, before consenting to join the study. There is no clarification

as to what is considered to be a reasonable time. The timing of the consenting process and its impact on recruitment and retention in a trial is not well understood.

Retention during trial follow up can introduce attrition bias and can affect the reliability and validity of outcomes.^{6,7} Attrition bias may occur if the characteristics of participants were lost in follow up between the arms of the RCT.⁸ If retention is less than 5% it may not result in concerning bias, and if retention is between 5% and 20% it may cause a minor bias, but if retention is higher than 20%, it can risk the validity of the trial.⁶ Poor recruitment and loss of participants can result in increasing the budget and time and may result in an underpowered study that will not adequately answer the original research question.²

There is an argument to be made that patients who consent on the same day could be more determined to join as they already understand the benefits of the study. In contrast, undecided patients would tend to

delay their joining and probably not be fully convinced of the benefits, causing higher attrition rates. There is, however, a counter-argument that patients who took longer to give their consent, only gave their consent after full studying of the material and without feeling coerced thus enabling the participant to make an informed decision to participate into joining, making them more determined to continue with the study with less attrition.

More studies are required to identify strategies to improve recruitment and the consent process within randomized trials. While these studies may only be moderately active, yet they could have a crucial impact on the costs or duration of a study.²

2 | AIM OF THE SWAT

We aim to perform a Study Within A Trial (SWAT) to evaluate the impact of same-day consent or delayed consent on recruitment and retention in the host trial.

3 | SWAT METHOD

This SWAT⁹ is designed as an observational (nonrandomized) study, observing the impact of same-day consent versus delayed consent on the recruitment and retention in the host trial. The host trial is an RCT evaluating the effectiveness of an intensive lifestyle modification program in patients with peripheral arterial disease.

Intervention 1 is same-day consent, and this is where the participant gives consent on the same day after the investigator has fully explained the predesigned information leaflet for the host trial.

Intervention 2 is delayed consent, and this is where the participant will give consent on the next day or following the initial meeting after the predesigned information leaflet for the host trial has been fully explained by the investigator, they are given an unsigned consent form, with an addressed and stamped envelope. Patients are allowed time to discuss with family and friends and will be advised to ring the investigators with their verbal consent and send back the signed written consent form, only when they feel comfortable joining the study. The investigator will call the patient on the third day after the initial meeting (if the returned envelope has not arrived), to ask if they have decided to join or not. Patients will not be coerced to consenting to participate at any time.

3.1 | PRIMARY OUTCOME

The primary outcome will measure the proportion of patients who withdraw consent at the recruitment phase of the host trial before randomization in the host RCT.

3.2 | SECONDARY OUTCOMES

The secondary outcomes will include:

- (1) Reasons for withdrawing consent; this stage can be at the time of randomization or baseline assessment before commencing treatment in either intervention or comparator arm in the host study. Patients who contact the investigators, to withdraw consent, will be asked at the same setting about the reason for removing the consent. However, if the patient does not wish to disclose the reason for consent withdraw, that will also be noted.
- (2) Retention rates within the host study; after the subject has commenced the treatment in either intervention one or intervention 2 in the host study.
- (3) Reasons for drop-out from host study
- (4) Compliance with host study intervention.

3.3 | ANALYSIS

The primary outcome will be analyzed through quantitative analysis using chi-square. Similarly, retention rates and compliance rate will be assessed via quantitative analysis.

Reasons for consent withdraw and drop-out will be analyzed through qualitative analysis.

4 | POSSIBLE PROBLEMS

A priori, we do not know the impact of same-day or delayed consent on recruitment and retention in clinical trials. Hence, our reasoning for undertaking this SWAT. Participants may decide not to join the study or leave the study for other reasons that are not related to the timing of their consent. We will endeavor to establish this information. Still, there is a possibility that patients who withdraw their consent or drop-out from the host trial may not be comfortable to convey the real reasons for doing so.

FUNDING

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SWAT REGISTRATION

The SWAT was registered on the Northern Ireland Network for Trials Methodology Research.¹⁰ The host trial was registered (11/07/2017) on the European Clinical Trials Database (EudraCT number 2017-002964-41) and ClinicalTrials.gov (NCT03935776)

ETHICS APPROVAL

Ethical approval has been obtained from the Clinical Research Ethics Committee at University Hospital Galway (approval number: C.A. 1973).

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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