Trial Forge Guidance 4: Ethical issues to consider when doing Studies within a Trial (SWATs)

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A list of study features routinely considered at research ethic committee meetings in the UK

- Social or scientific value; scientific design and conduct of the study
- Recruitment arrangements and access to health information, and fair research participant selection
- Favourable risk benefit ratio; anticipated benefits/risks for research participants (present and future)
- Care and protection of research participants; respect for potential and enrolled research participants' welfare & dignity
- Data protection & research participant's confidentiality
- Informed consent process and the adequacy and completeness of research participant information
- Suitability of the applicant and supporting staff
- Independent review
- Suitability of supporting information
- Other general comments

Example 1 of a Study Within A Trial (SWAT 24)

(full protocol is available here: https://www.qub.ac.uk/sites/TheNorthernIrelandNetworkforTrialsMethodologyResearch/FileStore/Filetoupload,545010,en.pdf)

SWAT Title

Using a theoretically informed cover letter to improve response rates to annual postal questionnaires

Status

This SWAT has been run in three different trials.

Participants

Anyone taking part in a trial where the main information for study is collected using a questionnaire.

Intervention

When trial participants are sent their questionnaire, a cover letter is included. In this instance the cover letter uses behavioural theory to identify practical steps that may help make it easier to send the questionnaire back.

Comparison

When trial participants are sent their annual questionnaire, a cover letter is included. In this instance the cover letter is the standard version, no practical steps for retuning it are included.

Outcomes

For both versions of the cover letter, the number of questionnaires sent and received back in the trial office will be counted. The rate of retuned questionnaires will be calculated and compared.

Example 2 of a Study within A Trial (SWAT 13)

(full protocol is available here: https://www.qub.ac.uk/sites/TheNorthernIrelandNetworkforTrialsMethodologyResearch/FileStore/Filetoupload,541985,en.pdf)

SWAT Title

Financial incentives to complete follow-up questionnaires in a randomised trial

Status

This SWAT has been run in one trial although slightly different SWATs, also using gift vouchers, have also been done.

Participants

Anyone taking part in a trial where the main information for study is collected using a questionnaire at two points in time.

Intervention

When trial participants are sent their questionnaire, a £5/€6/8CAD gift voucher is included with the questionnaire. The gift voucher is included for some participants at both time points or either one or the other time point.

Comparison

When trial participants are sent their annual questionnaire, no gift voucher is included. Some participants do not get gift vouchers while some do not get a voucher at one or the other time point.

Outcome

For both time points, the number of questionnaires sent and received back in the trial office will be counted. The rate of retuned questionnaires will be calculated and compared.

Abbreviation buster

CI – Chief Investigator

CTU – Clinical Trials Unit

GCP – Good Clinical Practice

HRA – Health Research Authority (based in UK and responsible for NHS Research Ethics Committees)

ICF – Informed Consent Form

IRB – Institutional Review Board (ethics committee)

PI – Principal investigator

PIL – (same as PIS) Participant Information Leaflet

PIS – (same as PIL) Participant Information Sheet

PPI – Patient and Public Involvement

REC – Research Ethics Committee

RCT – Randomised Controlled Trial

SWAT – Study Within A Trial

TFG4 – Trial Forge Guidance 4

UK – United Kingdom

Why should I consider embedding a SWAT in our trial?

What is a SWAT?

SWAT stands for a 'Study Within A Trial' and it is a research study that is embedded within a larger host trial.

The aim of a SWAT is to evaluate or investigate different methods of organizing or delivering a specific trial process such as recruitment or retention.

Why do we need to do SWATs?

Randomised trials are central to providing health care evidence that helps patients, clinicians and policy-makers to make evidence-informed choices about treatments and therapies. However, when it comes to making decisions about the design, conduct and reporting of randomised trials themselves, there is scant evidence to support them.

This means that trial process decision-making is largely based on instinct and experience, not evidence. Sometimes this is fine, sometimes it isn't. Without evidence it's hard to spot the difference before it's too late.

One way of building an evidence-base to support trial process decisions is to do a SWAT because they provide an opportunity to evaluate alternative options when conducting a trial process (e.g. patient recruitment, patient retention, reporting the findings) to provide much needed evidence about how the trial process can be improved.

Key features of a SWAT

- Embedded within a host trial.
- Aims to resolve crucial uncertainties about trial processes.
- Does not impact the scientific integrity or outcome of the host trial
- Has a formal protocol.
- Can be evaluated in one trial but is also suitable to be conducted across numerous host trials either simultaneously or sequentially.
- As well as generate data for the future design and conduct of trials, SWATs can also provide data to improve decisions about the host trial it is embedded within.

Health Research Board TMRN Trials Methodology Research Network

www.hrb-tmrn.ie

TRIAL FORGE

www.trialforge.org

Looking for SWAT inspiration? Have a look at the SWAT repository:

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

https://doi.org/10.1186/s13063-018-2535-5

@hrbtmrn @Trial_Forge #trialmethodology

Practical things to consider when planning a SWAT

Cost

- Relatively inexpensive. SWATs tend to cost between £5,000/€5,500 and £10,000/€11,000. Ideally, SWATs should be included in the host trial from the beginning.

Randomisation

- Depends largely on whether the SWAT question is focusing on measuring effect sizes. If it is looking at the effect of alternative methods of conducting a trial process, randomization should be considered. If the SWAT is not aiming to measure an effect size, it is highly likely there will be no need for randomisation.
- SWAT randomisation can be carried out separately to the host trial randomisation.

Ethics

- Ethical approval guidelines for conducting research in humans can differ between countries so it is advised that researchers check national guidance.
- Likely that some SWATs will require ethical approval.
- In the UK for instance, SWATs within non-medicinal product trials that involve only trial staff will not normally need UK NHS ethical approval (but may need institutional review).
- SWATs are generally low-risk and rarely add extra risk for participants so it is not normally necessary to get participant consent.
- SWATs focusing on staff but which directly impacts patients / participants (e.g. how information is delivered to participants), may require ethical approval.

Analysis

- May be simple and done by members of trial team rather than a senior member of the trial team (although they can, and often do, do SWATS!)
- If needed, SWAT sample size calculations can be done in the normal manner. SWATs are constrained by the size of host trials so single evaluations are often underpowered. SWATs are designed for replication and meta-analysis.
- For qualitative SWATs, a suitable qualitative methodological framework and methods should be applied.

Implementing the SWAT

- SWATs generally do not need to run for the full duration of the host trial so any extra work should be modest and short-term.

Publication

- SWAT findings should be put into the public domain and be accessible to others whether this is through being included in the host trial report, a separate publication or being included in a relevant systematic review.

Adapted from

Treweek S, Bevan S, Bower P, Campbell M, Christie J, Clarke M, Collet C, Cotton S, Devane D, El Feky A, Flemyng, Galvin S, Gardner H, Gillies K, Jansen J, Littleford R, Parker A, Ramsay C, Restrup L, Sullivan F, Torgerson D, Tremain L, Westmore M, Williamson PR. Trial Forge Guidance 1: what is a Study Within A Trial (SWAT)? Trials. 2018;19:139.

For further information or support on embedding a SWAT contact:

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