Conducting a Study Within A Trial (SWAT) in RCTs - What, why and how

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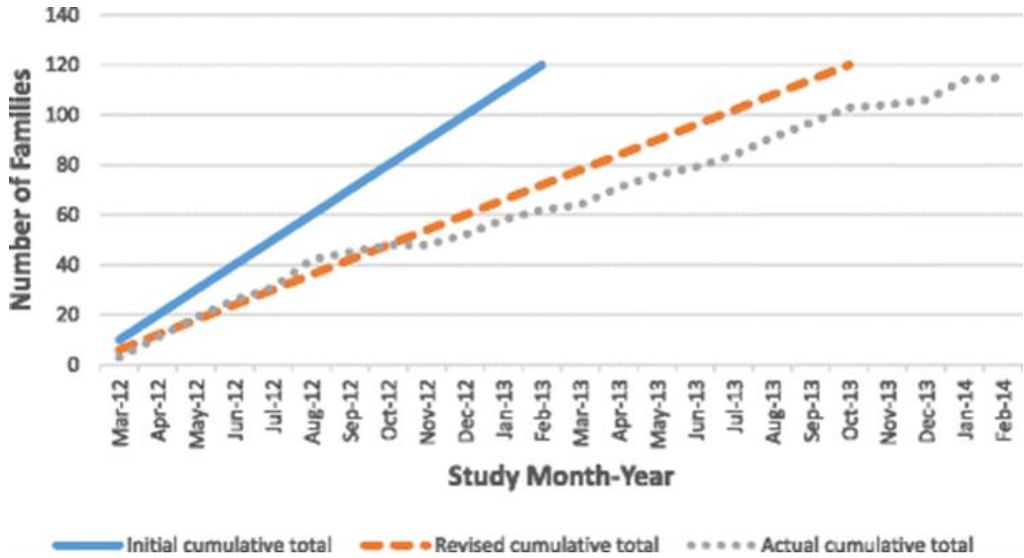
Summary

- What is a SWAT
- Why are SWATs important
- How to embed a SWAT
  - Designing a SWAT
  - Conducting a SWAT
  - Top Tips

Background

- Trial recruitment is known to be difficult
- Poor retention leads to missing outcome data affecting trial generalizability, validity and reliability
- Different strategies are used to try and improve recruitment and retention



Fleming et al, *Trials*, 2015, **16**:535

What is a SWAT?

What is a SWAT?

- A self-contained research study, embedded within a host trial, to evaluate or exploring delivery or organisation of trial processes
  - Also known as: ‘Nested trial’, ‘Trial within a trial’, Embedded trial’

- SWATs can use a range of methods (e.g., qualitative, mixed methods)
- SWATs can be randomised (i.e. trial within a trial) or non-randomised

- Often focus on testing recruitment or retention interventions but can focus on any trial process or stage

What is a SWAT continued

- Aim to resolve uncertainties about how to do trials
- Are embedded within a host trial, but do not affect the integrity of the host trial
- Will inform how we do future trials, and might inform decisions about the host trial
- Can be evaluated in a single trial, but is preferably run across many trials

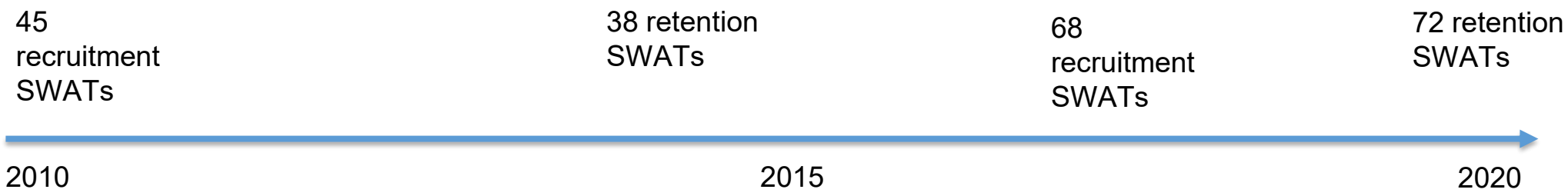
What a SWAT is not

- Embedded research to compare methods of assessing clinical changes (e.g., X ray vs MRI, blood vs urine sampling)
- Questionnaire validation studies
- Evaluation of service delivery

- A qualitative study exploring the trial or study (in relation to impact on clinical outcomes)

SWATs - Current Evidence

- Most SWATs focus on recruitment and retention strategies
- Number of SWATs has been increasing



- Impact of SWAT programmes, initiatives and funding

MRC START Developing the science of recr

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Health Research Board TMRN Trials Methodology Research Network

HRB Health Research Board

NIHR | National Institute for Health and Care Research

PROMETHEUS PROMOTING THE USE OF SWATS

ACT AEC Accelerating Clinical Trials Accélérer les Essais Cliniques

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SWATs - Current Evidence continued

Evidence for Recruitment strategies

- 68 randomised and quasi-randomised evaluations
- Just **three** interventions were supported by high-certainty evidence (GRADE)
  - Open trials vs blinded placebo trials
  - Telephone reminders to those not responding to postal invitation
  - Bespoke user tested PIS

https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.MR000013.pub6/full

Evidence for Retention strategies

- 70 randomised evaluations
- No interventions with high certainty evidence (GRADE)

- Three promising strategies
  - Self sampling kits
  - Monetary reward + reminder or prenotification
  - Pens with postal questionnaires

https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.MR000032.pub3/full

As an example…

- Recruitment SWAT investigating the effectiveness of an infographic plus information sheet vs. information sheet only

- **Population**: Patients with open surgical wounds, recruited face to face in clinic

- **Intervention**: Summary infographic provided with the participant information sheet

- **Primary Outcome**: Recruitment rate
- **Secondary Outcomes**: Proportion screened ineligible, proportion eligible but non consenting, cost effectiveness

SWAT 116: https://www.qub.ac.uk/sites/TheNorthernIrelandNetworkforTrialsMethodologyResearch/FileStore/Filetoupload,959361,en.pdf

Why are SWATs important?

'There is a peculiar paradox that exists in trial execution - we perform clinical trials to generate evidence to improve patient outcomes; however, we conduct clinical trials like anecdotal medicine.' *(Shah et al. Heart Failure Review (2014); 19: 135-52)*

- We should apply the same thinking used for clinical intervention assessment to research methodology to prevent research waste
- Help us conduct better trials
- Be more efficient in our use of time and resources

But why should I embed a SWAT?

- Contribute to building the evidence base
- Evidence based methods for trial processes
  - Inform current or future work

- Collaboration and network opportunities
  - Trial Forge SWAT Network
  - Share your expertise on design, conduct, delivery of SWATs

- Career development opportunities

How to embed a SWAT

General Things to Consider

- You will need a ‘host’ trial

- Embed a SWAT as soon as possible in the design process
  - But it’s never too late to implement one!

- You will need to consider costs and this can vary

- Should have a formal protocol, just like the host trial
- Ethical approval will likely be required

Picking the intervention(s)

- Many SWATs can fit within existing trials infrastructure

Consider:

- Trial Forge SWAT Centre priority SWATS

- PRioRiTy I and II

- SWAT repository
- https://www.qub.ac.uk/sites/TheNorthernIrelandNetworkforTrialsMethodologyResearch/SWATSWARInformation/Repositories/SWATStore/
- https://www.trialforge.org/swat-resources/

- Advice from the Trial Forge SWATs Centre: trial-forge-swat-centre@york.ac.uk

Trial Forge SWAT Priority Questions

https://www.trialforge.org/trial-diversity/press/

Recruitment

What is the most effective way of/strategy for:

1) Involving patients and the public in trials to improve participant recruitment
2) Using video(s) to support trial recruitment
3) Sending potential trial participants invitation letters by post to optimise recruitment
4) Using qualitative research to optimise recruitment rates
5) Recruiting underserved groups
6) Using incentives to support recruitment

Retention

What is the most effective way of/strategy for:

1) Offering flexibility to support participant retention
2) Involving patients and the public in trials to improve participant retention
3) Using participant reminders to support retention
4) Use financial incentives to support retention
5) Using routine data collection to support retention

Picking the intervention(s) continued

- Consider if another replication is needed
- Trial Forge SWAT Guidance 2 suggests considering:
  - GRADE
  - Cumulative evidence
  - Context
  - Balance – participants and host trials
  - Value of information
- Where evidence is accumulating evidence packs can help to outline where replication may be needed

Evidence Pack Ret3: Retention adding a pen

How big is the effect?	An increase of **1.9%** (95% confidence interval = 0.0% to 3.7%).
How certain are we?	GRADE **Moderate** certainty evidence. GRADE **High** certainty evidence for an older population.
Recommendation	We **recommend that trialists send trial pens to participants** to increase retention in trials that use questionnaires.

Evidence Pack Rec2: Recruitment letter highlighting health risks to particular ethnic groups

How big is the effect?	A reduction of **(-)3.8%** (95% confidence interval = -13.1% to 5.4%).
How certain are we?	GRADE **Low** certainty for trials in diabetes involving women. GRADE **Very low** for all other trials.
Recommendation	The intervention **needs input from public/patients across ethnic groups**. The resulting intervention **should be evaluated in a SWAT**.

Designing – SWAT Methods

Individual

- Test interventions in a single host trial
- Requires replication and subsequent meta-analysis.
- Best for testing simple strategies or in specific populations

Individual Coordinated

- Test the same intervention in multiple host trials in staged approach over a period, using the same or a similar protocol.
- Best used in a dedicated programme of work or where collaboration is feasible

Coordinated SWATs

- Test the same intervention in multiple host trials at the same time with one protocol, ethical approval, analysis and write up.
- Requires significant coordination
- Best for evaluating complex or costly strategies

Designing - Randomisation and Sample Size

Randomisation

- Depends on your question
  - Randomised vs non randomised
  - Individual vs cluster randomisation
- Randomisation can be separate or combined with host trial randomisation

Sample size

- Usually constrained by the host trial sample size
- SWATs are designed for future meta-analysis.

Designing – Outcomes

Outcomes

Recruitment

- Eligible participants consented
- Consented participants randomised
- Cost

Retention

- Proportion of participants retained
- Data completeness
- Use of reminders
- Time to response
- Cost

Conducting a SWAT – Approvals & Registration

- REC committees frequently ask about consent or information provision
  - Clarify the who, what, when how
  - Note similar precedents
- Discuss consent requirements with your PPI group
  - Does existing consent cover the SWAT?

- SWAT Registration

Conducting a SWAT – Intervention fidelity

- Important to monitor intervention fidelity/adherence

- Consider how you will do this from the outset
  - Sites administering the intervention/control
  - Use of technology

Conducting a SWAT - Analysis and Reporting

Analysis

- An analysis plan is required
- Use outcomes and analysis methods like those in existing evidence/replications
  - Helps combination of results via meta-analysis
- Costs or cost analysis should be undertaken

Guidance for conducting cost analysis is available via: https://osf.io/sebnk/files/osfstorage

Publication

- Is important!
- The Trial Forge SWAT centre have developed a CONSORT compliant, short reporting guideline which may help

SWAT Reporting Guidelines

2b	Specific objectives or hypotheses for the SWAT	State SWAT question as objective *Does [insert SWAT intervention] increase/decrease [outcome] compared to [comparator] in [participants]?*
7a	How sample size was determined for the SWAT	SWATs are often individually underpowered due to the sample size being constrained by the host trial(s). A robust estimate of the effect of the SWAT intervention might therefore depend on the aggregation of replicated SWAT evaluations. It is not expected that a formal sample size calculation will always be done *The SWAT sample size depended on the host trial(s) [insert host trial name]; therefore, no formal sample size calculation was performed, which is in line with SWAT methodology*. [insert any reasoning for a subsample of the host trial(s) being used – e.g. SWAT was included midway through the trial]

https://doi.org/10.1186/s13063-024-08004-0

Conducting a SWAT – Process Evaluation

- As in trials, a SWAT identifies whether an intervention works but not why it does or does not
- Process evaluations are therefore also important in SWATs, but are rarely done
- Consider efficiencies for this e.g., existing qualitative sub study

SWAT – Top Tips!

- Start small – test a change to an existing document or process
- Consider a collaborative approach

- Use existing SWAT resources

- Resource the SWAT in the grant application

- Educate others about SWATs e.g., wider trial team, Sponsor
  - We have developed resources to help with this

- Join the SWAT network (trial-forge-swat-centre@york.ac.uk)

Conclusions

- The evidence for how to best design, conduct and disseminate trials is limited – this needs to change
- Building the evidence is the responsibility of everyone involved in research
- Plan to undertake SWATs routinely in your trials

References and Resources

- Trial Forge SWAT Centre priority SWATs: https://www.trialforge.org/trial-diversity/press/
- Recruitment SWATs: The Prioritising Recruitment in Randomised Trials study (PRioRiTy) https://priorityresearch.ie
- Retention SWATs: PRIORITY II https://www.trialforge.org/priority-two
- The SWAT repository: https://shorturl.at/gILX1

References and Resources continued

References

Treweek, S., Bevan, S., Bower, P. *et al.* Trial Forge Guidance 1: what is a Study Within A Trial (SWAT)?. *Trials* **19**, 139 (2018). https://doi.org/10.1186/s13063-018-2535-5

Treweek, S., Bevan, S., Bower, P. *et al.* Trial Forge Guidance 2: how to decide if a further Study Within A Trial (SWAT) is needed. *Trials* **21**, 33 (2020). https://doi.org/10.1186/s13063-019-3980-5