MRC-NIHR Trials Methodology Research Partnership: Webinar recording

IMPLEMENT SWATs

Presented, on behalf of the UKCRC Registered CTU Network, by:

Adwoa Parker (University of York)

20 June 2024

The slides are available below.

For any queries, please contact uktmn@nottingham.ac.uk

https://youtu.be/t_w8mHzn1Dc

FUNDED BY
NIHR | National Institute for Health and Care Research

UNIVERSITY of York

Using IMPLEMENTation science and Studies Within A Trial to improve evidence-based participant recruitment and retention in randomised controlled trials

Adwoa Parker

NIHR Advanced Fellow & Assistant Professor

Lead, Trial Forge SWATs Centre, York Trials Unit, University of York

TRIAL FORGE

www.trialforge.org

A bit about how SWATs started

NIHR Doctoral Fellowship in 2012

MRC-START: Systematic techniques for assisting recruitment to trials

PROMETHEUS: PROMoting THE Use of SWATs

Current 10-year NIHR Advanced Fellow

Trials and tribulations

Trials are difficult to do, especially recruiting & retaining participants

Only 43% of UK trials recruit to target & on time (Jacques, 2022)

Affects internal & external validity

RECOVERY trial - dexamethasone arm: every 50-day delay in completion due to slow recruitment or retention led to ~450 more deaths in the UK alone (Knowlson & Torgerson, 2020)

Economic consequences: faster recruitment to RECOVERY dexamethasone arm (from 15% to 50%) could have generated an incremental net benefit of £17.2m (Gkekas, accepted)

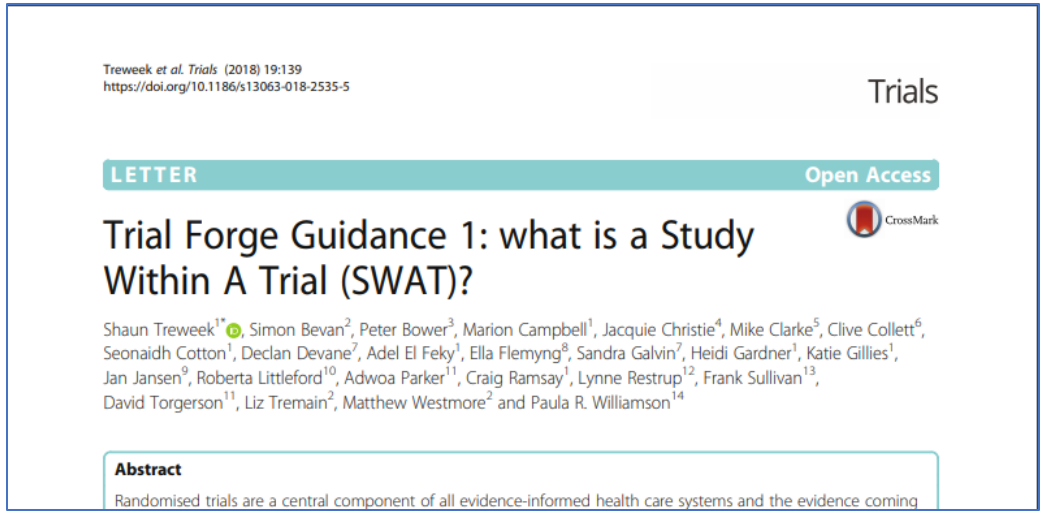
Huge amounts of research waste, affects bottom line & massive opportunity costs

Funders focusing on SWATs

What is a SWAT?

- A piece of methodological research nested into a 'host' trial.
- Can be randomised (i.e., trial within a trial) or non-randomised (e.g., qualitative, observational)

- *'A SWAT is a self-contained research study that has been embedded within a host trial with the aim of evaluating or exploring alternative ways of delivering or organising a particular trial process'.* (Treweek et al., 2018, Trials)



Treweek *et al. Trials* (2018) 19:139
https://doi.org/10.1186/s13063-018-2535-5

Trials

LETTER Open Access

Trial Forge Guidance 1: what is a Study Within A Trial (SWAT)?

Shaun Treweek[1*], Simon Bevan[2], Peter Bower[3], Marion Campbell[1], Jacquie Christie[4], Mike Clarke[5], Clive Collett[6], Seonaidh Cotton[1], Declan Devane[7], Adel El Feky[1], Ella Flemyng[8], Sandra Galvin[7], Heidi Gardner[1], Katie Gillies[1], Jan Jansen[9], Roberta Littleford[10], Adwoa Parker[11], Craig Ramsay[1], Lynne Restrup[12], Frank Sullivan[13], David Torgerson[11], Liz Tremain[2], Matthew Westmore[2] and Paula R. Williamson[14]

Abstract

Randomised trials are a central component of all evidence-informed health care systems and the evidence coming

TRIAL FORGE

Why do we need SWATs?

The most rigorous method to test strategies to improve trial conduct
They are useful
Conceptually simple
Generally cheap
Help generate evidence to reduce research waste
We need more robust evidence (and we need to use this evidence when we have it)

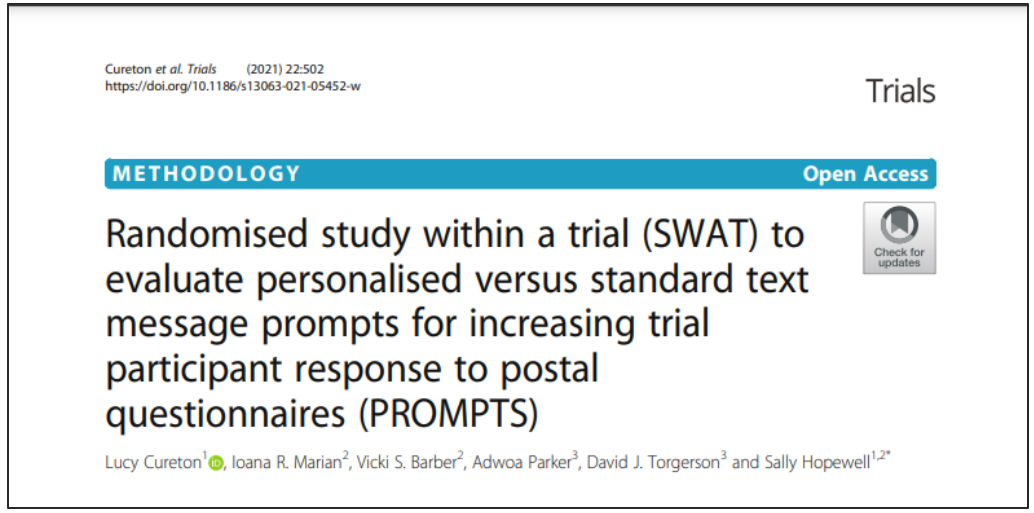
Key features of a SWAT

- 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
- Should have a formal protocol, just like the host trial
- Individual SWATs can contribute to systematic reviews of SWATs
- Can be evaluated in a single trial, but is preferably run across many trials
- Will inform how we do future trials, and might inform decisions about the host trial

Treweek et. al., 2018; Trials

SWATs can be randomised or non-randomised

- SWATs can be randomised trials (*i.e.*, trial within a trial) or non-randomised (*e.g.*, qualitative, observational or mixed methods)



Cureton *et al. Trials* (2021) 22:502
https://doi.org/10.1186/s13063-021-05452-w

Trials

METHODOLOGY Open Access

Randomised study within a trial (SWAT) to evaluate personalised versus standard text message prompts for increasing trial participant response to postal questionnaires (PROMPTS)

Lucy Cureton[1], Ioana R. Marian[2], Vicki S. Barber[2], Adwoa Parker[3], David J. Torgerson[3] and Sally Hopewell[1,2*]

Check for updates

JHP

Article

A qualitative investigation of reasoning behind decisions to decline participation in a research intervention: A study-within-a-trial

Journal of Health Psychology
2023, Vol. 28(4) 374–387
© The Author(s) 2021
Article reuse guidelines:
sagepub.com/journals-permissions
DOI: 10.1177/13591053211037736
journals.sagepub.com/home/hpq
SAGE

Christopher P Dwyer[1], Anusha Moses[1], Fionnuala M Rogers[1], Dympna Casey[1], Robert Joyce[1] and Sinéad M Hynes[1]

TRIAL FORGE

The EQUIP SWAT: an example

- **Aim**: to test the impact on recruitment of directly advertising patient and public involvement (PPI) to potential trial participants
- Embedded in host trial ('EQUIP') recruiting service users diagnosed with severe mental illness
- Co-designed recruitment strategy with PPI partners: a leaflet to advertise the PPI in EQUIP and sent potential participants invitations with the leaflet (intervention group) or not (control group)
- **Primary outcome**: proportion of patients enrolled into EQUIP

Hughes-Morley *et al. Trials* (2016) 17:586
DOI 10.1186/s13063-016-1718-1

Trials

RESEARCH Open Access

The impact of advertising patient and public involvement on trial recruitment: embedded cluster randomised recruitment trial

Adwoa Hughes-Morley[1,2*], Mark Hann[2], Claire Fraser[3], Oonagh Meade[4], Karina Lovell[3], Bridget Young[5], Chris Roberts[2], Lindsey Cree[3], Donna More[3], Neil O'Leary[6], Patrick Callaghan[7], Waquas Waheed[2] and Peter Bower[8]

Abstract

Background: Patient and public involvement in research (PPIR) may improve trial recruitment rates, but it is unclear how. Where trials use PPIR to improve design and conduct, many do not communicate this clearly to potential participants. Better communication of PPIR might encourage patient enrolment, as trials may be perceived as more socially valid, relevant and trustworthy. We aimed to evaluate the impact on recruitment of directly advertising PPIR to potential trial participants.

Methods: This is a cluster trial, embedded within a host trial ('EQUIP') recruiting service users diagnosed with severe mental illness. The intervention was informed by a systematic review, a qualitative study, social comparison theory and a stakeholder workshop including service users and carers. Adopting Participatory Design approaches, we co-designed the recruitment intervention with PPIR partners using a leaflet to advertise the PPIR in EQUIP and sent potential participants invitations with the leaflet (intervention group) or not (control group). Primary outcome was the proportion of patients enrolled in EQUIP. Secondary outcomes included the proportions of patients who positively responded to the trial invitation.

Results: Thirty-four community mental health teams were randomised and 8182 service users invited. For the primary outcome, 4% of patients in the PPIR group were enrolled versus 5.3% of the control group. The intervention was not effective for improving recruitment rates (adjusted OR = 0.75, 95% CI = 0.53 to 1.07, $p = 0.113$). For the secondary outcome of positive response, the intervention was not effective, with 7.3% of potential participants in the intervention group responding positively versus 7.9% of the control group (adjusted OR = 0.74, 95% CI = 0.53 to 1.04, $p = 0.082$). We did not find a positive impact of directly advertising PPIR on any other outcomes.

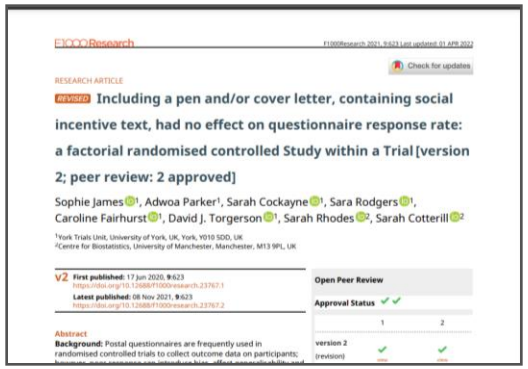
SWAT design choices are similar to other RCT design choices

- Individual randomised design: straightforward & efficient
- Factorial designs
  - 2x2 factorial SWATs can test the effectiveness of two strategies at the same time
  - Test for interaction effects
  - *OTIS retention SWAT*: Including a pen or no pen, with or without cover letter containing a social incentive text
- Cluster randomisation
  - May be more feasible for practical/logistical reasons
  - Minimises 'contamination' and dilution bias between intervention and control participants


Trials

RESEARCH Open Access

The effect of optimised patient information materials on recruitment in a lung cancer screening trial: an embedded randomised recruitment trial


F1000Research

RESEARCH ARTICLE

Including a pen and/or cover letter, containing social incentive text, had no effect on questionnaire response rate: a factorial randomised controlled Study within a Trial [version 2; peer review: 2 approved]


Trials

RESEARCH Open Access

The impact of advertising patient and public involvement on trial recruitment: embedded cluster randomised recruitment trial

TRIAL FORGE

SWATs can be co-ordinated

- SWATs nested in several host trials
- Similar protocols
- Pre-planned meta-analysis
- Bigger, better

Madurasinghe *et al. BMC Medicine* (2021) 19:218
https://doi.org/10.1186/s12916-021-02086-2

BMC Medicine

RESEARCH ARTICLE Open Access

Can we achieve better recruitment by providing better information? Meta-analysis of 'studies within a trial' (SWATs) of optimised participant information sheets

Vichithranie W. Madurasinghe[1], Peter Bower[2*], Sandra Eldridge[3], David Collier[4], Jonathan Graffy[5], Shaun Treweek[6], Peter Knapp[7], Adwoa Parker[8], Jo Rick[9], Chris Salisbury[10], Mei See Man[11], David Torgerson[12], Rebecca Sheridan[12], Frank Sullivan[13], Sarah Cockayne[12] and Charlotte Dack[14]

Madurasinghe *et al. BMC Medicine* (2023) 21:425
https://doi.org/10.1186/s12916-023-03081-5

BMC Medicine

RESEARCH ARTICLE Open Access

Can we achieve better trial recruitment by presenting patient information through multimedia? Meta-analysis of 'studies within a trial' (SWATs)

Vichithranie W. Madurasinghe[1], Peter Knapp[2], Sandra Eldridge[3], David Collier[4], Shaun Treweek[5], Jo Rick[6], Jonathan Graffy[7], Adwoa Parker[8], Chris Salisbury[9], David Torgerson[10], Kate Jolly[11], Manbinder S. Sidhu[12], Christopher Fife-Schaw[13], Mark A. Hull[14], Kirsty Sprange[15], Elizabeth Brettell[16], Sunil Bhandari[17], Alan Montgomery[15] and Peter Bower[18*]

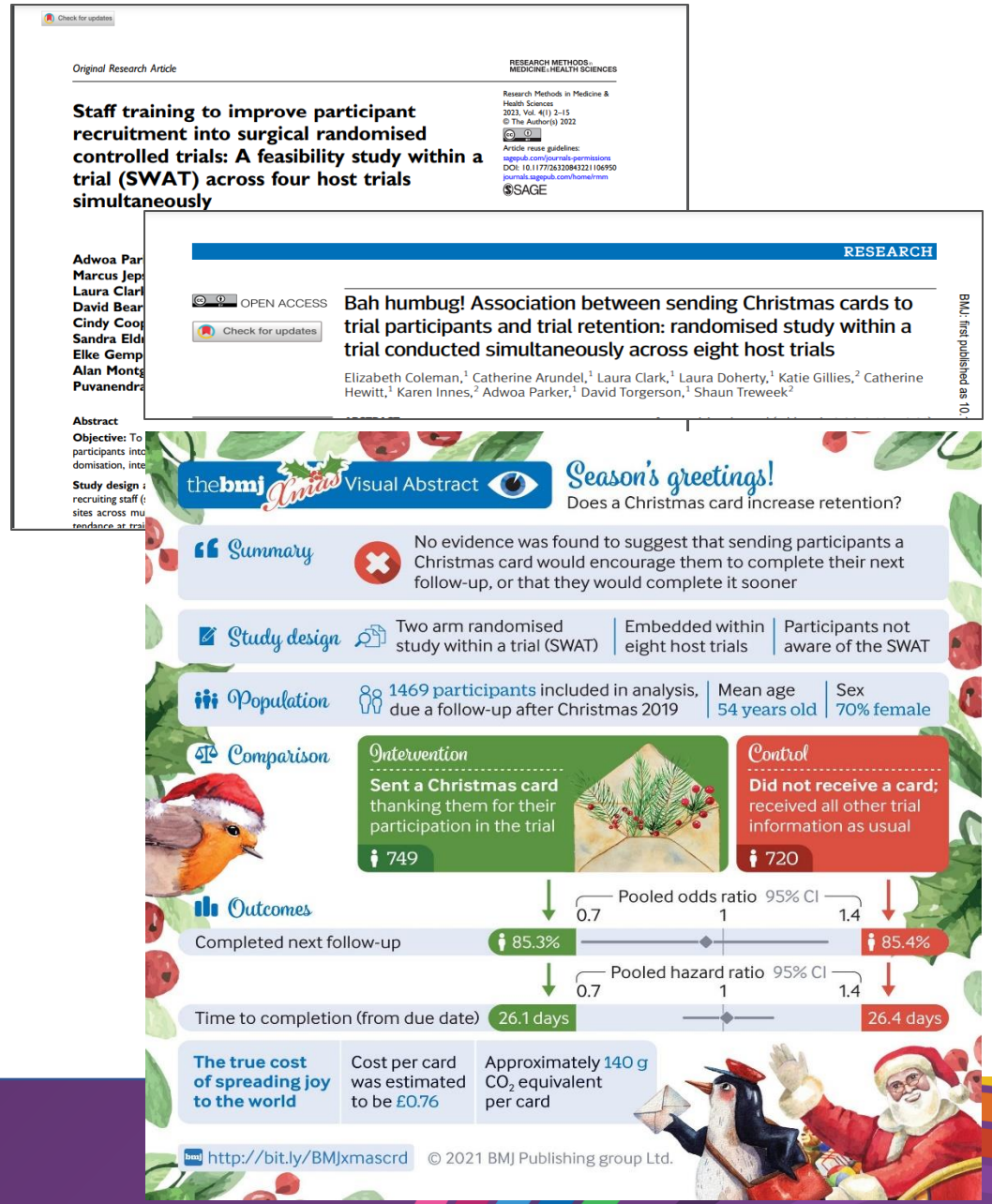
Multiple SWATs can be undertaken simultaneously

Bigger, better, faster: rapid, high-quality evidence at scale

Training workshop for staff recruiting participants - demonstrated feasibility of simultaneous SWATs

Simultaneous SWAT testing effectiveness of sending Christmas cards to participants on retention

A great way to collaborate!



Original Research Article

RESEARCH METHODS IN MEDICINE & HEALTH SCIENCES

Staff training to improve participant recruitment into surgical randomised controlled trials: A feasibility study within a trial (SWAT) across four host trials simultaneously

Research Methods in Medicine & Health Sciences
2023, Vol. 4(1) 2–15
© The Author(s) 2022

Article reuse guidelines:
sagepub.com/journals-permissions
DOI: 10.1177/26320843221106950
journals.sagepub.com/home/rmm

SAGE

Adwoa Par
Marcus Jep
Laura Clar
David Bear
Cindy Coo
Sandra Eld
Elke Gemp
Alan Montg
Puvanendra

Abstract

Objective: To
participants into
domisation, inte

Study design
recruiting staff (
sites across mu
tendance at trai

RESEARCH

OPEN ACCESS

Check for updates

Bah humbug! Association between sending Christmas cards to trial participants and trial retention: randomised study within a trial conducted simultaneously across eight host trials

Elizabeth Coleman,[1] Catherine Arundel,[1] Laura Clark,[1] Laura Doherty,[1] Katie Gillies,[2] Catherine Hewitt,[1] Karen Innes,[2] Adwoa Parker,[1] David Torgerson,[1] Shaun Treweek[2]

BMJ: first published as 10.

thebmj Xmas Visual Abstract

Season's greetings!

Does a Christmas card increase retention?

Summary

No evidence was found to suggest that sending participants a Christmas card would encourage them to complete their next follow-up, or that they would complete it sooner

Study design

Two arm randomised study within a trial (SWAT) | Embedded within eight host trials | Participants not aware of the SWAT

Population

1469 participants included in analysis, due a follow-up after Christmas 2019 | Mean age 54 years old | Sex 70% female

Comparison

Intervention

Sent a Christmas card thanking them for their participation in the trial

749

Control

Did not receive a card; received all other trial information as usual

720

Outcomes

Pooled odds ratio 95% CI

0.7 1 1.4

Completed next follow-up: 85.3% | 85.4%

Pooled hazard ratio 95% CI

0.7 1 1.4

Time to completion (from due date): 26.1 days | 26.4 days

The true cost of spreading joy to the world

Cost per card was estimated to be £0.76

Approximately 140 g CO_2 equivalent per card

http://bit.ly/BMJxmascrd

TRIAL FORGE

SWAT evidence: recruitment & retention

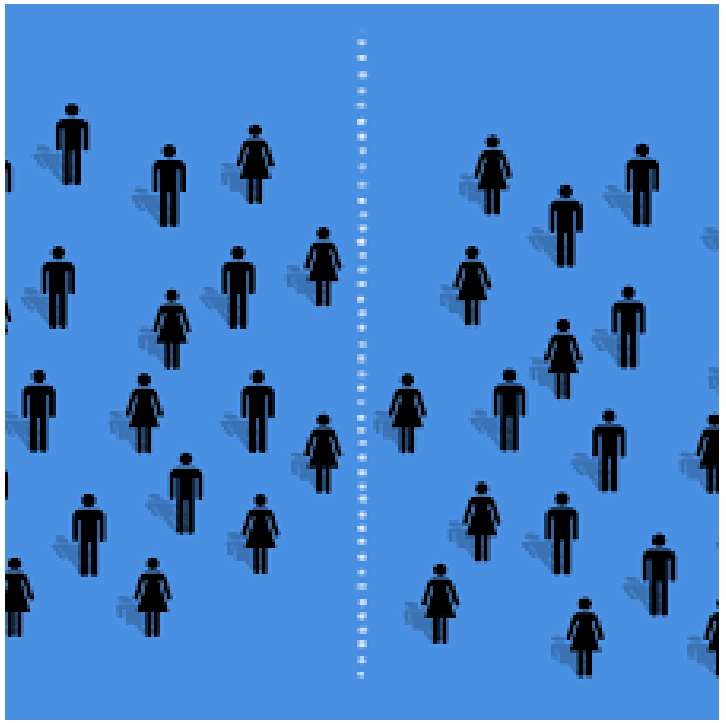
- 68 papers testing strategies to improve recruitment
- Quality of evidence: just **three** are supported by high-certainty evidence according to GRADE.

- 70 papers testing strategies to improve retention.
- Quality of evidence: **NONE** were supported by high-certainty evidence as determined by GRADE assessment.

Advice on doing a SWAT: things to consider

You will need a ‘host’ trial

- Often this is pragmatic: usually your own trial or that of a collaborator or colleague



You will need to consider costs

Costs vary

- Can be ~£3-30k+ for a single randomised SWAT
- Qualitative SWATs cost more
- Will cost a lot more for a programme of SWATs

Choosing your SWAT question

"The literature on interventions to improve recruitment to trials has plenty of variety but little depth"

Important to replicate existing SWATs

- Power & generalisability

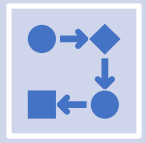
Choosing your SWAT question

- We have prioritised 11 broad recruitment and retention strategies to be tested using randomised SWATs:
  - https://www.trialforge.org/2024/02/a-list-of-11-priority-recruitment-and-retention-swats/
- The Prioritising Recruitment in Randomised Trials study (PRioRiTy) https://priorityresearch.ie
- PRioRiTy II: Prioritising Retention in Randomised Trials study
  - https://www.trialforge.org/priority-two
- There is a repository of SWATs. You can adopt or adapt any of these SWATs

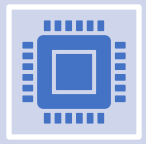
Developing protocols & resources to test these priority strategies using SWATs (PRESS)

- 11 SWAT Protocols & resources to support trial teams to do these SWATs, inc. these templates:
  - Grant application text
  - ethics application
  - Statistical Analysis Plan
  - Cost-effectiveness templates
- Available Jan 2025

When to embed the SWAT



The earlier the better (and easier): we often plan SWATs at the design stages of our trials



But it is (almost) never too late to implement a SWAT.

E.g., A randomised SWAT testing a retention strategy can be implemented up until the last follow-up time-point.

Ethical approval

- SWATs are low risk studies
- Most SWATs will need ethical approval
- For recruitment and retention SWATs, participants are not be informed about being included in a SWAT
    - This is because it is not be possible to get individual consent from participants as it may confuse them as to what they are consenting to and may impact on their behaviour
- Our team has worked with the Health Research Authority in the UK to develop a streamlined approvals process and guidance for SWATs

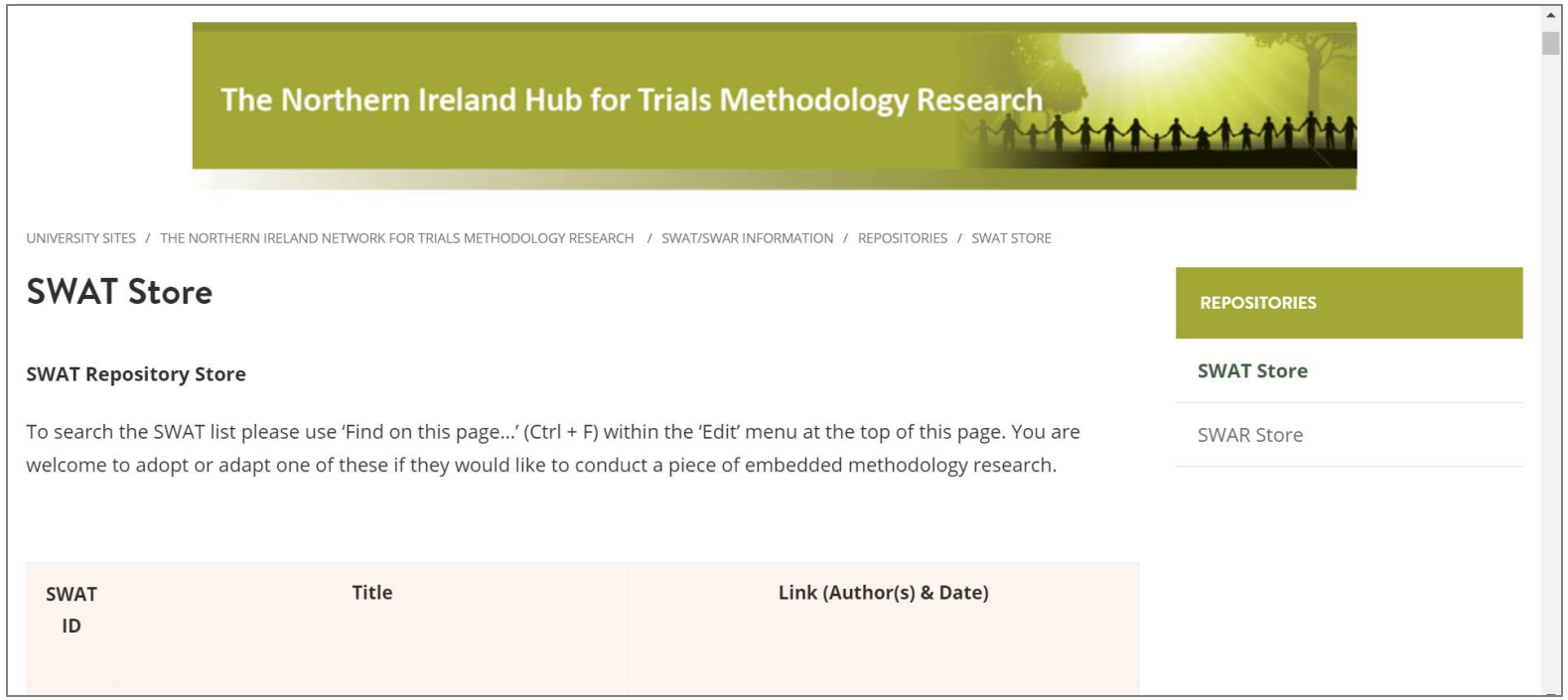
Sample size

- For some SWATs (such as recruitment SWATs), the sample for the SWAT will actually be much larger than the host trial
- Other SWATs are constrained by host trial size - a separate power calculation may not be useful
- Meta-analysis of several SWATs testing the same intervention can provide powerful evidence

Randomisation & analysis

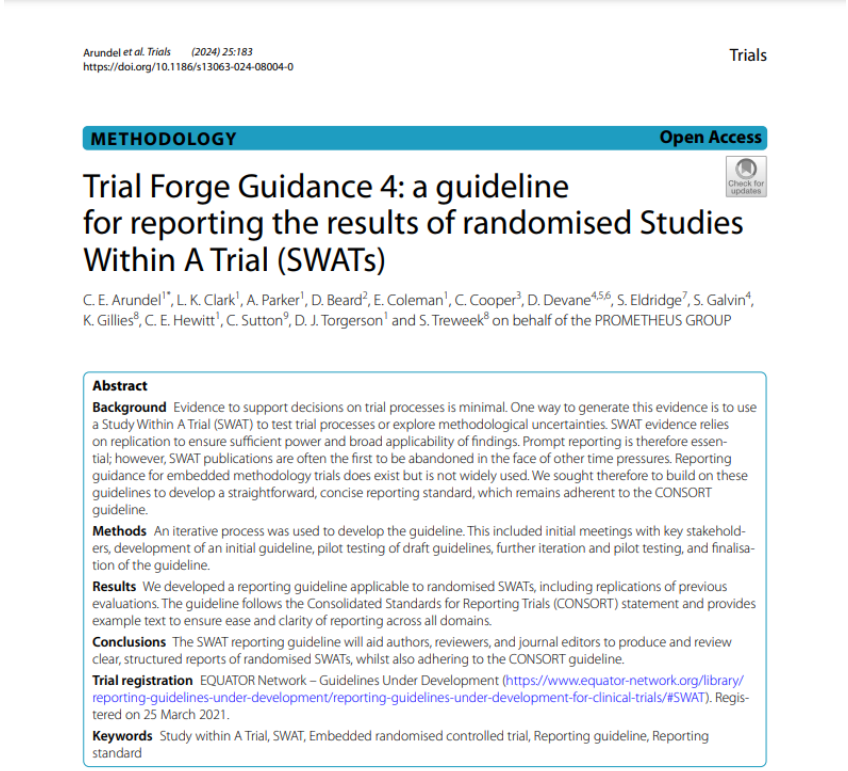
- Randomisation
  - Randomisation can be separate to that used for the host trial randomisation
  - Individual randomisation is preferable, but may not always be practical. Cluster randomisation can be used.
- Analysis
  - The analysis will be simple for primary outcome (comparison of two proportions)
  - Qualitative SWATs will use a suitable qualitative analysis method

Registering your SWAT



Dissemination

- The findings should be published as soon as possible
- Reporting guidelines for randomised SWATs



Arundel et al. Trials (2024) 25:183
https://doi.org/10.1186/s13063-024-08004-0

Trials

METHODOLOGY Open Access

Trial Forge Guidance 4: a guideline for reporting the results of randomised Studies Within A Trial (SWATs)

C. E. Arundel[1*], L. K. Clark[1], A. Parker[1], D. Beard[2], E. Coleman[1], C. Cooper[3], D. Devane[4,5,6], S. Eldridge[7], S. Galvin[4], K. Gillies[8], C. E. Hewitt[1], C. Sutton[9], D. J. Torgerson[1] and S. Treweek[8] on behalf of the PROMETHEUS GROUP

Abstract

Background Evidence to support decisions on trial processes is minimal. One way to generate this evidence is to use a Study Within A Trial (SWAT) to test trial processes or explore methodological uncertainties. SWAT evidence relies on replication to ensure sufficient power and broad applicability of findings. Prompt reporting is therefore essential; however, SWAT publications are often the first to be abandoned in the face of other time pressures. Reporting guidance for embedded methodology trials does exist but is not widely used. We sought therefore to build on these guidelines to develop a straightforward, concise reporting standard, which remains adherent to the CONSORT guideline.

Methods An iterative process was used to develop the guideline. This included initial meetings with key stakeholders, development of an initial guideline, pilot testing of draft guidelines, further iteration and pilot testing, and finalisation of the guideline.

Results We developed a reporting guideline applicable to randomised SWATs, including replications of previous evaluations. The guideline follows the Consolidated Standards for Reporting Trials (CONSORT) statement and provides example text to ensure ease and clarity of reporting across all domains.

Conclusions The SWAT reporting guideline will aid authors, reviewers, and journal editors to produce and review clear, structured reports of randomised SWATs, whilst also adhering to the CONSORT guideline.

Trial registration EQUATOR Network – Guidelines Under Development (https://www.equator-network.org/library/reporting-guidelines-under-development/reporting-guidelines-under-development-for-clinical-trials/#SWAT). Registered on 25 March 2021.

Keywords Study within A Trial, SWAT, Embedded randomised controlled trial, Reporting guideline, Reporting standard

Dissemination: Cochrane reviews

- Share your findings with me, so I can include them in future updates of the Cochrane recruitment & retention reviews
- As evidence builds, these reviews will be modified into ‘living reviews’

FUNDED BY
NIHR | National Institute for Health and Care Research

implement SWATs

Using IMPLEMENTation science and Studies Within A Trial to improve evidence-based participant recruitment and retention in randomised controlled trials.

https://www.implementswats.org

The need to improve efficient trial conduct

Trial teams do not use evidence to inform recruitment and retention decisions (Gardner, 2019)

Emerging SWAT activity, no guidelines to support evidence-based decisions for conducting trials

How we make trial process decisions is a largely evidence-free zone

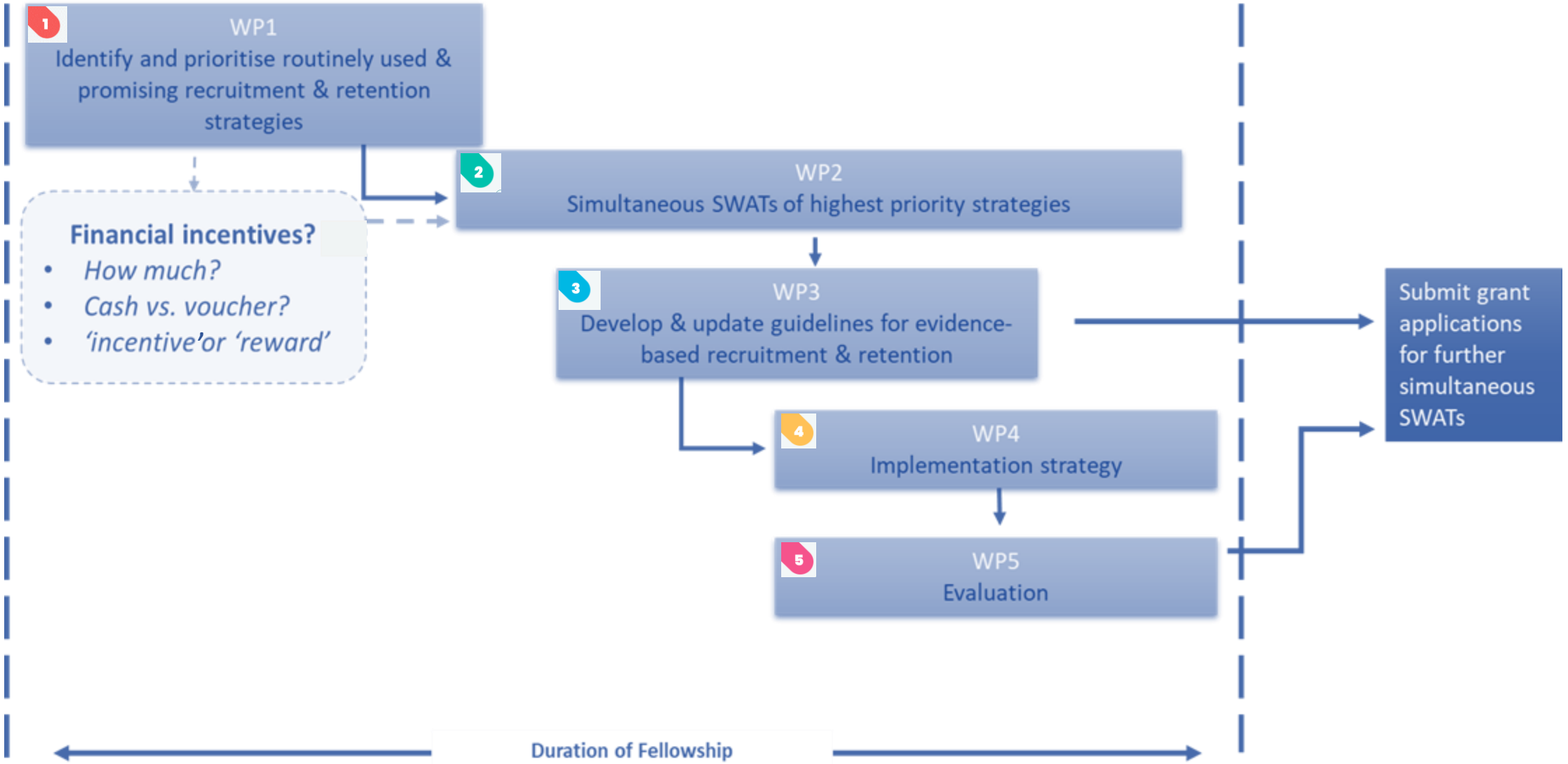
Implementation science is the study of methods that support the use of evidence-based practice.

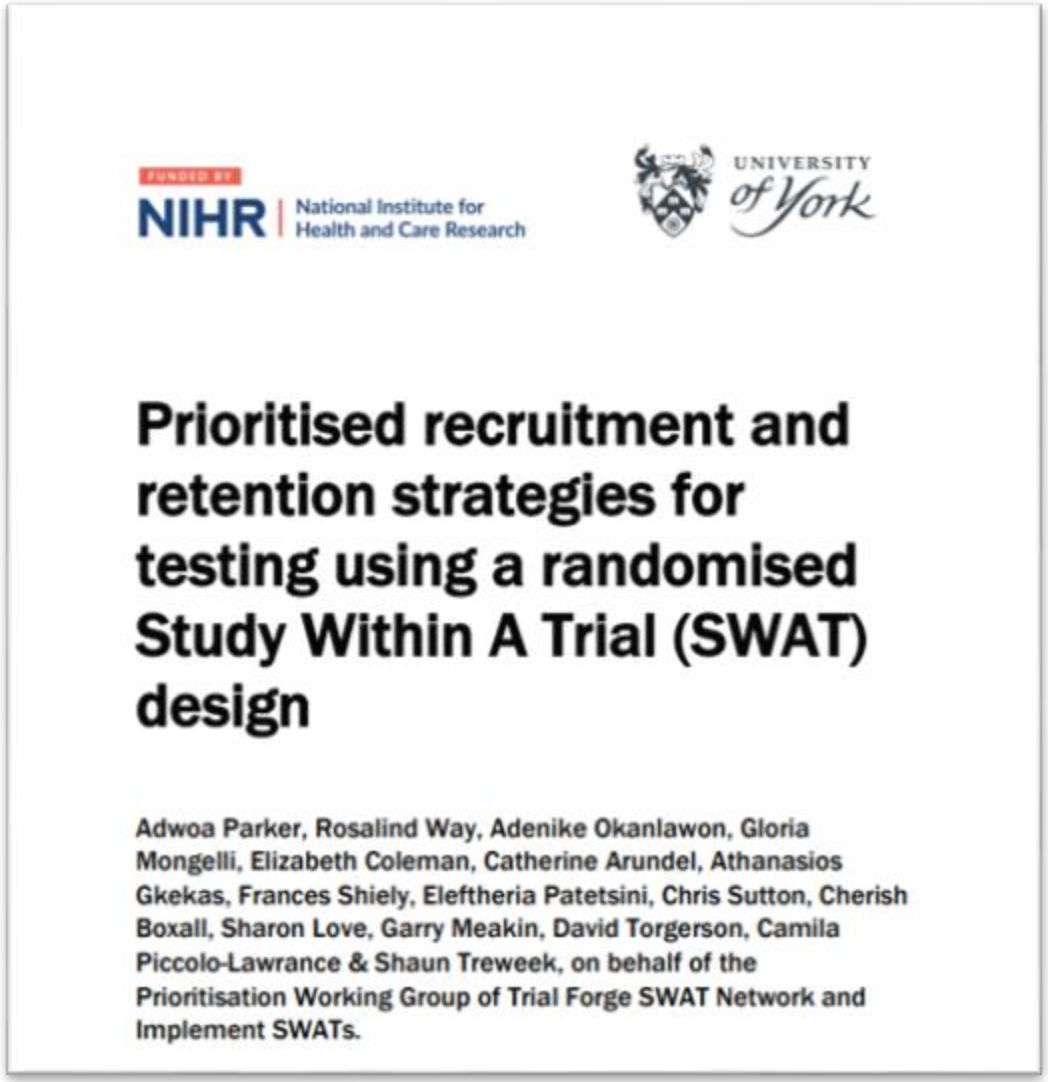
Implement SWATs: overarching aims

1. To test the effectiveness and cost-effectiveness of routinely used and promising trial recruitment and retention strategies, using simultaneous SWATs

2. To develop, implement, and test guidelines for evidence-based recruitment and retention in trials

Overview of methods





implement SWATs

TRIAL FORGE

Simultaneous SWATs of monetary incentives

Aims: rapidly build the evidence-base for the effectiveness and cost-effectiveness of monetary incentives for recruiting and retaining trial participants by undertaking simultaneous SWATs, alongside a process evaluation.

Priority questions: What is the most effective way to use monetary incentives to support recruitment & retention?

What are the optimal values of incentives for recruitment and retention?

What is the optimal format (cash *vs.* voucher)?

Unconditional incentive, or conditional reward?

Incentives will likely range between £10 and £50.

Monetary incentive SWATs

- Host trial eligibility
  - Recruitment: host trials will be eligible if using individual randomisation
  - Retention: host trials will be eligible if using individual randomisation and participants have at least one follow-up remaining
- We will fund up to £10,000
- We will provide methodological support & study materials
- We are interested in collaborating with trial teams for these SWATs.
- Email: swats-group@york.ac.uk

SWAT Resources [1]

- Treweek S. et. al. Trial Forge Guidance 1: what is a Study Within A Trial (SWAT)? Trials. 2018 Feb 23;19(1):139. https://trialsjournal.biomedcentral.com/articles/10.1186/s13063-018-2535-5
- Parker A., et. al. Undertaking Studies Within A Trial to evaluate recruitment and retention strategies for randomised controlled trials: lessons learnt from the PROMETHEUS research programme. Health Technol Assess 2024;28(2). https://doi.org/10.3310/HTQW3107
- SWAT resources: introductory videos and documents on doing SWATs: https://www.york.ac.uk/healthsciences/research/trials/swats/swatresources/
- Trial Forge Guidance for writing a SWAT in Stage 1 and Stage 2 NIHR applications: https://www.nihr.ac.uk/documents/trial-forge-additional-guidance/32778

SWAT Resources [2]

- Interest in doing a recruitment or retention randomised SWAT? Here's the 2024 priority list of questions to test: Parker, A., et al. (2024, February 8). WP1: Identifying and prioritising trial recruitment and retention strategies. https://doi.org/10.17605/OSF.IO/CZ829
- Interest in collaborating to test the effectiveness and cost-effectiveness of monetary incentives for recruiting and retaining participants in trials? Further information here: https://docs.google.com/document/d/1LNHxvUyhxKSexLvboiSHCpm5ySuqJOjO/edit?usp=sharing&ouid=117279899757688883871&rtpof=true&sd=true
- There is a repository of SWATs to help link with the work others are doing
- For specific advice about which SWAT might work for specific trials, contact: adwoa.parker@york.ac.uk / swats-group@york.ac.uk

Acknowledgements

Implement SWATs is funded by the National Institute for Health and Care Research (Advanced Fellowship, reference: NIHR302256). The PRESS project is funded by the Medical Research Council - National Institute for Health - Research Trial Methodology Research Partnership (MRC-NIHR TMRP) and the Health Research Board Trials Methodology Research Network (HRB-TMRN)] in a joint(HRB-TMRN/MRC-NIHR-TMRP) Working Group Project Seed Co-Funding Award 2023. The views expressed are those of the authors and not necessarily those of the NIHR or the Department of Health and Social Care.

Massive thanks to all our collaborating partners, host trial teams and to my mentors: Profs Jeremy Grimshaw, Mike Clarke, David Torgerson and Shaun Treweek.

Thank you for listening!

adwoa.parker@york.ac.uk / swats-group@york.ac.uk

@adwoa_parker