Studies Within a Trial (SWATs)

An opportunity to reduce research waste

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Recruitment into a guided internet based CBT (iCBT) intervention for depression: Lesson learnt from the failure of a prevalence recruitment strategy

Joanne Woodford, Paul Farrand, Michael Bessant, Christopher Williams

Introduction: Internet based Cognitive Behavioural Therapy (iCBT) represents a significant development in the way psychological interventions are delivered. Studies tend to recruit via common media channels leading to criticisms of biased sample sizes and limited generalisability to primary care settings.

Aim: To evaluate the use of a prevalence recruitment strategy within primary care to recruit into an RCT examining a free to use iCBT intervention.

Methods: Fully randomised controlled trial (RCT), utilising a prevalence based recruitment strategy, comparing the iCBT intervention with telephone support provided by NHS Direct Health Advisors with treatment-as-usual (TAU) control.

Results: Recruitment rates were low with only 7 participants recruited over 8 months. Overall only 14% of expected study invitations were sent, with only 18% undertaking the consent and initial screening process.

Discussion: Key differences with successful prevalence recruitment strategies highlight four main issues to consider when recruiting participants from primary care into iCBT studies – lack of equipoise, a need for an assertive approach, coding of depression in GP databases and help seeking behaviour in depression which can all act as potential contributors to failure to recruit. However other non-primary care recruitment methods, such as the use of media channels,
Where it all started (for me)

Lack of public involvement
Lack of intervention acceptability work
Lack of feasibility work

Lack of attention to the evidence base concerning best practice in trial conduct
“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: (1) we do what we think works; (2) we rely on experience and judgement and (3) limited data to support best practices.”

Monica Shah, quoted in Gheorghiade et al. (2014)

- Lack of evidence to help inform trialists to make important decisions around trial processes spanning the trial lifecycle
- Examples include:
  - Recruitment
  - Site selection
  - Training trial staff
  - Retention
  - Reporting
- Need to fill the gap in evidence: Studies Within a Trial (SWATs) may represent a solution
Key features

- A research study embedded in a host trial, aiming to evaluate and/or explore a trial process
  - Resolve uncertainties concerning trial processes
- Should have a formal protocol (pre-registered)
- Host trial integrity should remain intact
- Can inform both the ongoing trial and decisions concerning future trials
- May use an RCT design. Other study designs possible i.e., Qual-SWATs (McCaffrey & Hunter, 2023)
- Replication essential to include in meta-analyses

Clark et al., 2022; Treweek et al., 2018
Some examples

- SWAT 116 (McCaffery et al., 2019)
  (https://www.qub.ac.uk/sites/TheNorthernIrelandNetworkforTrialsMethodologyResearch/FileStore/Filetoupload,959361,en.pdf)
  • To evaluate the effectiveness and cost-effectiveness of an infographic provided in addition to a standard patient information leaflet on recruitment to a clinical trial.

- SWAT 198 (Lidington et al., 2023)
  (https://www.qub.ac.uk/sites/TheNorthernIrelandNetworkforTrialsMethodologyResearch/FileStore/Filetoupload,1794815,en.pdf)
  • To evaluate the effect on participant retention of sending a newsletter, compared to not sending a newsletter, in randomised trials.
  • To evaluate the cost-effectiveness of sending a newsletter, compared to not sending a newsletter, in randomised trials.
The effect of personalised versus non-personalised study invitations on recruitment within the ENGAGE feasibility trial: an embedded randomised controlled recruitment trial

Ella Thiblin, Joanne Woodford, Mattias Ohman and Louise von Essen
A Swedish example from U-CARE

- Intervention group (n = 254) received a personalised study invitation letter.
- The control group (n = 255) received a non-personalised study invitation letter.
- Primary outcome was the proportion of participants in the intervention group and the control group enrolled into the ENGAGE host feasibility trial.
- Of the 509 potential participants, 56 (11.0%) were enrolled into the ENGAGE host feasibility trial:
  - Intervention group (personalized): 30/254 (11.8%)
  - Control group (non-personalized): 26/255 (10.2%)
  - No statistically significant effect on personalisation of enrolment was found (OR 1.18, 95% CI 0.68–2.06).
- Small sample size
- However, small effects on recruitment rates are important
- Need for additional studies
Pre-planned coordination

- SWATs can be conducted in a single trial, however pre-planned coordination of multiple SWATs beneficial

- For example:
  - Medical Research Council Systematic Techniques for Assisting Recruitment to Trials (MRC START) (Rick et al., 2014)
  - Medical Research Council-funded PROMoting THE USE of SWATs (PROMETHEUS) programme (Clark et al., 2022)
  - The Trial Forge SWAT Network

- Increased sample size, increased certainty of findings
- Cost-efficiency
- Speed up evidence generation
Some considerations

• Low cost (average cost SWATs funded through PROMETHEUS (PROMoting THE USE of SWATs) was £4,007

• Need for ethical review

• “When is enough, enough”
  • GRADE (certainty in the evidence)
  • Cumulated evidence
  • Context (Population, host Intervention, host Comparator, SWAT Outcome, Time)
  • Balance – participants
  • Balance – host trial

• Designing a SWAT

Treweek et al., 2020
Challenges

- Challenges finding eligible host trials (limiting pre-planned coordination)
- Lack of time and resources
- Not wanting to complicate already complex trials
- Lack of promotion/prioritisation by funders
- Lack of incentives
- Lack of qualified reviewers

Clark et al., 2022; Treweek et al., 2018
Some limitations

• Lack of SWATs on specific populations
• Ireland and UK centric (though growing internationally)
• SWAT intervention heterogeneity
• Sample size constrained by the host trial
• Heterogeneity in trial setting, population, condition/disease – can results be combined?

Boxall et al., 2022, Treweek et al., 2018
What types of questions might we ask?

<table>
<thead>
<tr>
<th>Overall ranking</th>
<th>Research question</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>How can randomised trials become part of routine care and best utilise current clinical care pathways?</td>
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<tr>
<td>2</td>
<td>What information should trialists communicate to members of the public who are being invited to take part in a randomised trial in order to improve recruitment to the trial?</td>
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<tr>
<td>3</td>
<td>Does patient/public involvement in planning a randomised trial improve recruitment?</td>
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<td>4</td>
<td>What are the best approaches for designing and delivering information to members of the public who are invited to take part in a randomised trial?</td>
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<td>5</td>
<td>What are the barriers and enablers for clinicians/healthcare professionals in helping conduct randomised trials?</td>
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<td>6</td>
<td>What are the key motivators influencing members of the public’s decisions to take part in a randomised trial?</td>
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<td>7</td>
<td>What are the best approaches to ensure inclusion and participation of under-represented or vulnerable groups in randomised trials?</td>
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<td>8</td>
<td>What are the best ways to predict recruitment rates to a randomised trial and what impact do such predictions have on recruitment?</td>
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<td>9</td>
<td>What are the best approaches to optimise the informed consent process when recruiting participants to randomised trials?</td>
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<td>10</td>
<td>What are the advantages and disadvantages to using technology during the recruitment process?</td>
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Prioritising Recruitment in Randomised Trials (PRioRiTy) project (http://priorityresearch.ie/)

Healy et al., 2018
What types of questions might we ask?

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<td>What motivates a participant’s decision to complete a clinical trial?</td>
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<td>How can trials make better use of routine clinical care and/or existing data collection to improve retention?</td>
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<td>3</td>
<td>How can trials be designed to minimise burden on staff and participants and how does this affect retention?</td>
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<td>4</td>
<td>What are the best ways to encourage trial participants to complete the tasks (e.g. attend follow-up visits, complete questionnaires) required by the trial?</td>
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<td>5</td>
<td>How does involvement of patients/the public in planning and running trials improve retention?</td>
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<td>6</td>
<td>How could technology be best used in trial follow-up processes?</td>
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<td>What are the most effective ways of collecting information from participants during a trial to improve retention?</td>
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<td>8</td>
<td>How does a participant’s ongoing experience of the trial affect retention?</td>
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<td>What information should trial teams communicate to potential trial participants to improve trial retention?</td>
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<td>10</td>
<td>How should people who run trials plan for retention during their funding application and creation of the trial (protocol development)?</td>
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Prioritising Retention in Randomised Trials (PRioRiTy II) project (http://priorityresearch.ie/)

Brunsdon et al., 2019
A “mismatch” between SWATs and PRioRiTY 1 and 2 questions.
Recruitment and retention of participants in randomised controlled trials: a review of trials funded and published by the United Kingdom Health Technology Assessment Programme


ABSTRACT
Background: Substantial amounts of public funds are spent on healthcare research and randomised controlled trials (RCTs) and this is potentially wasted if a trial fails to recruit to time and target sample size. Trials and funders have highlighted recruitment and retention as a key issue for the conduct of RCTs.

This study reports the recruitment and retention rates for 151 single and multicentre randomised controlled trials funded by the UK’s National Institute for Health Research (NIHR) Health Technology Assessment (HTA) Programme and published in the HTA Journal between 2004 and 2016.

There is considerable variation in the consent, recruitment and retention rates in publicly funded RCTs.

Main outcome measures: Target sample size and whether it was achieved; recruitment rates (number of participants recruited per centre per month) and retention rates (participants withdrawn, withdrawn and lost to follow-up).
Useful resources

- Reporting checklist for embedded recruitment trials (Madurasinghe et al., 2016)

- Queen’s University Belfast in Northern Ireland SWAT repository (https://www.qub.ac.uk/sites/TheNorthernIrelandNetworkforTrialsMethodologyResearch/SWATSWARInformation/)

- Trial Forge SWAT Network (https://www.trialforge.org/2021/06/)

- The ORRCA project (Online Resource for Recruitment Research in Clinical trials) (https://www.orrca.org.uk/)

- MRC START: Systematic Techniques for Assisting Recruitment to Trials (http://research.bmh.manchester.ac.uk/mrcstart)
Conclusions

• To reduce research waste, it is essential trials are conducted efficiently
• However, we lack the best evidence regarding best practices in trial design, conduct, and reporting
• Embedding SWATs represents a solution
• Small effects (marginal gains) across the trial process can save resources and enhance trial efficiency (or inform what not to do)

• However:
  • Challenges regarding implementation
  • Currently a mismatch between SWAT activity and prioritised research gaps
  • Emerging evidence base currently UK-centric
Selected references

- Doherty L, Parker A, Arundel C, et al. PROMoting the use of studies within a trial (PROMETHEUS): Results and experiences from a large programme to evaluate the routine embedding of recruitment and retention strategies within randomised controlled trials routinely. Res Methods Med Health Sci. 2023;4(3):113-122
- McCaffrey J, Hunter A. Protocol development for a qualitative methodological study within a trial (Qual-SWAT): The KARMA-Dep-2 Trial. HRB Open Res. 2023;6:29