Studies within a trial (SWAT)

Improving the evidence base for trial recruitment and retention

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Outline

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- Inefficiencies in two key clinical trial processes
  - Recruitment
  - Retention
- Evidence base for effective strategies
- Studies within a trial (SWAT)
- Summary
- ACTA webinar

Recruitment

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- Fewer than ½ of publicly-funded trials recruit their planned sample size and ¼ recruit at most half the planned sample size
- Failure to recruit to target may result in an underpowered trial
  - Unlikely to produce robust results
  - Promising treatment could be abandoned
- Typical responses are to add sites, extend recruitment period
  - Both increase trial costs
  - Still don't reach target recruitment numbers

Cochrane review - recruitment

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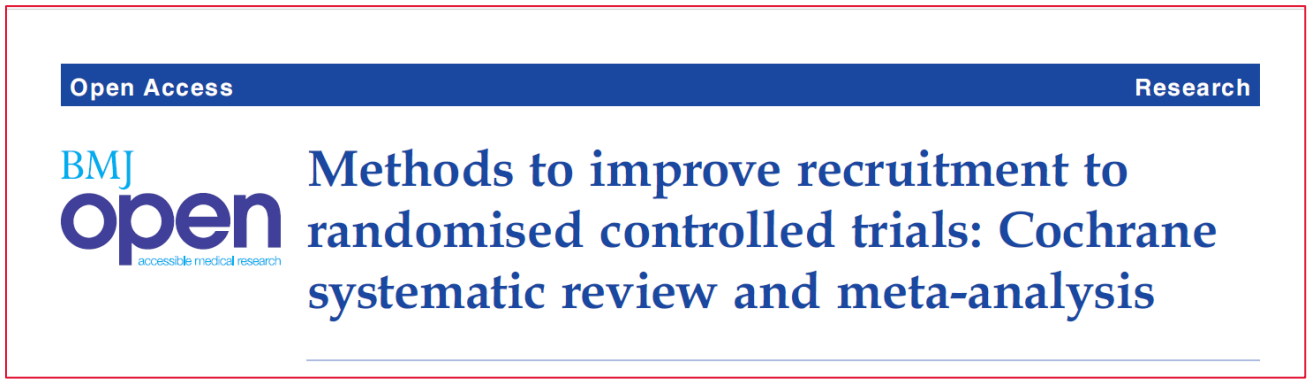

- 45 trials (recent update)
- Methods: trial design, obtaining consent, financial incentives, patient information leaflets
- Conclusions: Unblinded/open-label trial, opt-out consent, telephone reminders
- Most methods targeted participants, few aimed at recruiters
- 42% of studies used hypothetical scenarios

BMJ Open 2013;3:e002360
https://bmjopen.bmj.com/content/3/2/e002360

Retention

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- About ½ of clinical trials have at least 10% missing primary outcome data
- Loss of precision/power
- Potential bias
  - Especially if missing data related to treatment
  - 5% loss OK??
  - 20% loss can threaten trial validity
- Analyses in presence of missing data make assumptions – can never be sure these assumptions are correct

Cochrane review - retention

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- 38 trials
- Methods: vouchers, cash, enhanced letters, text/email reminders, questionnaire formats
- Monetary incentives to complete questionnaires
- Most strategies targeted participants, few aimed at recruiters, none at retaining sites
- Most evaluated return of questionnaires rather than returning to sites for follow-up visits

BMJ Open 2014;4:e003821
https://bmjopen.bmj.com/content/4/2/e003821

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Trial design and conduct decisions are generally uninformed by evidence because there is little relevant evidence to turn to.

Study within a trial (SWAT)

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- Objective is to answer specific questions about trial conduct or trial methodology
- Embedded within one or more host trials
- Must not affect the rationale, outcomes or scientific integrity of the host trial(s)
- Aim to inform the design and conduct of future trials but can inform the ongoing host trial(s)

Trial Forge Guidance 1: What is a Study Within A Trial (SWAT)? Trials 2018;19:139

Example of a SWAT

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Advertising patient and public involvement in research (PPIR)

Host trial - EQUIP

- Enhancing the Quality of User Involved care Planning
- Community mental health teams allocated to a training intervention to improve user and carer involvement in care planning or to a no-training control group
- Participants - severely mentally ill, recruited by postal invitation
- Primary outcome – cost effectiveness of training program
- Multi-centre cluster randomised trial
- Patients and public involved in design of study

Hughes-Morley et al. Trials; 2016:586

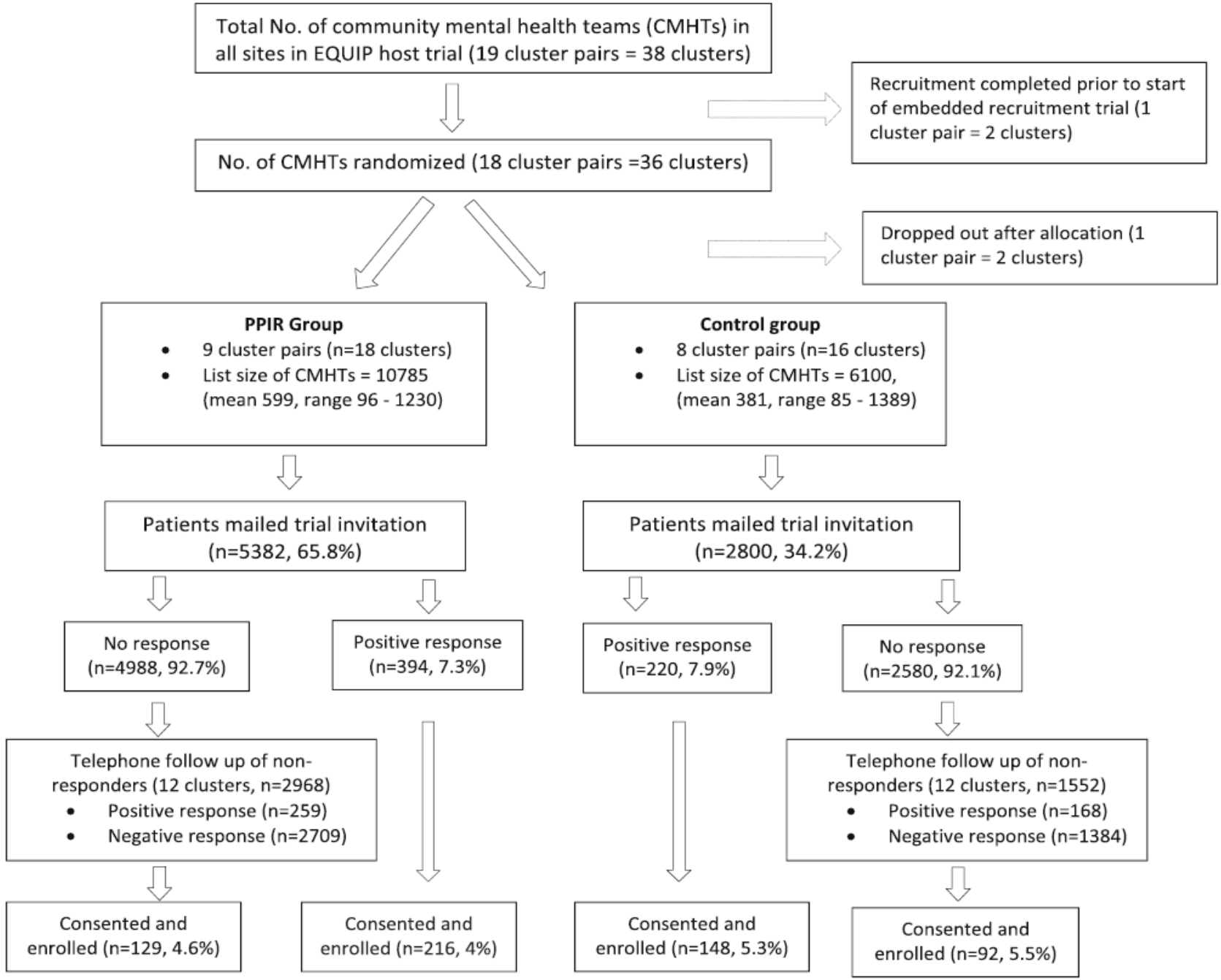
Example of a SWAT

Australian Clinical Trials Alliance

Advertising patient and public involvement in research (PPIR)

SWAT trial

- Aim - evaluate the impact on recruitment of directly advertising PPIR (via mailed glossy leaflet) to potential trial participants
- The cluster pairs of mental health teams were randomly allocated to the PPIR intervention or control (standard communication in the EQUIP trial)
- Primary outcome – proportions consented and enrolled into the host study EQUIP
- Secondary outcome – proportions responding positively to the invitation without telephone follow-up


Total No. of community mental health teams (CMHTs) in all sites in EQUIP host trial (19 cluster pairs = 38 clusters)
Recruitment completed prior to start of embedded recruitment trial (1 cluster pair = 2 clusters)
No. of CMHTs randomized (18 cluster pairs =36 clusters)
Dropped out after allocation (1 cluster pair = 2 clusters)
PPIR Group
9 cluster pairs (n=18 clusters)
List size of CMHTs = 10785 (mean 599, range 96 - 1230)
Control group
8 cluster pairs (n=16 clusters)
List size of CMHTs = 6100, (mean 381, range 85 - 1389)
Patients mailed trial invitation (n=5382, 65.8%)
Patients mailed trial invitation (n=2800, 34.2%)
No response (n=4988, 92.7%)
Positive response (n=394, 7.3%)
Positive response (n=220, 7.9%)
No response (n=2580, 92.1%)
Telephone follow up of non-responders (12 clusters, n=2968)
Positive response (n=259)
Negative response (n=2709)
Telephone follow up of non-responders (12 clusters, n=1552)
Positive response (n=168)
Negative response (n=1384)
Consented and enrolled (n=129, 4.6%)
Consented and enrolled (n=216, 4%)
Consented and enrolled (n=148, 5.3%)
Consented and enrolled (n=92, 5.5%)

SWAT – some practical issues

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- Statistical power dependent on size of host study
  - Multi-centre
  - Meta-analysis
- Extra burden on host study participants and staff
- Timing of introduction into the host trial
- Funding – separate or conjoint?
- Ethics approval – (where needed) separate or conjoint?

UK-based initiatives

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- The SWAT Store
  - Online library of methodology studies – 82 studies (25/11/2018)
  - http://www.qub.ac.uk/sites/TheNorthernIrelandNetworkforTrialsMethodologyResearch/SWATSWARInformation/Repositories/SWATStore/
- Trial FORGE
  - Promotes a systematic approach to making trials more efficient
  - www.trialforge.org
- PROMETHEUS
  - PROMoting THE USE of SWATs
  - www.york.ac.uk/healthsciences/research/trials/research/swats/prometheus/

Summary

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- Urgent need to make clinical trials more efficient
- Recruitment and retention are two trial conduct areas in need of improvement
- Numerous untested theories on strategies to improve recruitment and retention in clinical trials
- SWATs can help fill the evidence gaps in our recruitment and retention knowledge
- Clinical trial networks could play a role in making embedded recruitment/retention trials a routine activity

Webinar

Australian Clinical Trials Alliance

Studies Within A Trial: How they can help to make trial process decisions more evidence-based

Wednesday 17 April 2019, 5pm AEST

Professor Shaun Treweek
Health Services Research Unit
University of Aberdeen

Leads Trial Forge (http://www.trialforge.org)

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