DESIGN CHALLENGES FOR CLUSTER RANDOMISED TRIALS IN STROKE REHABILITATION

Amanda Farrin and Ivana Holloway

for TRACS and LoTS Care trial teams

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Overview

- Cluster randomised trials (CRT)
- TRACS and LoTS Care trials
- Challenges in design
- Solutions
- Recommendations for future CRTs based on our experience

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Cluster randomised trials
(mini-revision)

- Randomised trials in which the unit of randomisation is a community, hospital, GP surgery etc.
- Reasons for adopting CRTs
- Ethical issues
- Implications of adopting CRT

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TRACS

RAINING CAREGIVERS AFTER STROKE

A cluster randomised controlled trial of a **structured training programme for caregivers of in-patients after stroke**

Aims and objectives:

- Does a structured, competency-based training programme for caregivers improve physical and psychological outcomes for patients and their caregivers after disabling stroke?
- Is such a training programme cost-effective?

Primary outcome

- NEADL score as completed by the patient at 6 months
- Caregiver Burden Scale as completed by the caregiver at 6 months

www.tracstrial.co.uk

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LoTS care

stroke system of care trial

A cluster randomised trial **evaluation of a patient and carer-centred system for longer-term stroke care**

Aims and objectives:

- Evaluate the clinical and cost effectiveness of a patient and carer-centred system of longer-term stroke care delivered by a stroke care co-ordinator (SCC)

Primary outcome

- GHQ12 score as completed by the patient at 6 months

www.lotscare.co.uk

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Challenges in design

Randomisation

- What criteria to use?
- How to balance clusters?

Recruitment

- How to avoid bias?
- Blinding – who? And to what?

Sample size

- How to achieve adequate power?

Response rates

- What rates to expect?
- How to boost them if low?

Unequal cluster size

- How to deal with it?

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Randomisation 1

Generally, in CRTs

- Only few clusters are randomised
- Danger of baseline imbalances

TRACS

- **stratification in blocks** was a method used for randomisation of 36 stroke rehabilitation units.
- A detailed overview of the stroke services was obtained prior to randomisation in order to inform stratification.

Reference: Raab, G.M. and Butcher, I. Balance in cluster randomized trials. *Statistics in Medicine*, 2001; 20:351-365

Randomisation 2

LoTS Care

- **Minimisation with a random element** was a method of randomisation of 32 services.
- Services were randomised in 2 blocks; 14 services were in phase 1 and 18 services in phase 2.
- R software was used.

Reference: Carter, B.R. and Hood, K. Balance algorithm for cluster randomized trials. *BMC Medical Research Methodology*. 2008,8; 65.

Recruitment

Need to **minimise** potential **selection bias** and potential alteration in clinical .

Clear **separation between**

- the **provision of the intervention** by clinical staff
- and the **recruitment and consent** of patients and caregivers by the research practitioners

in both TRACS and LoTS Care.

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Sample size

	Number of clusters	Predicted cluster size	Estimated ICC	Estimated loss to follow up	Power	Signif. level	Design effect	Sample size required
TRACS	36	25	0.05	25%	90%	5%	1.9	968(=382/0.75x1.9)
LoTS Care	32	25	0.05	25%	88%	5%	1.89	800(=316/0.75x1.89)

$$Design\ Effect\ (DE) = \frac{variance\ of\ cluster\ sampling}{variance\ of\ simple\ random\ sampling}$$

$$DE = 1 + (m-1)\rho, \qquad where\ \rho = ICC, m = cluster\ size$$

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Unequal cluster size 1

In reality, it is **unlikely to achieve equal cluster sizes, for example**:

- Services started recruitment at different times
- Partial service available for participants at times (e.g. researchers, SCCs on holidays, changes in their employment)

Solution

- Estimation of coefficient of variation of cluster size.
- We created various scenarios where we studied the possible effect of variable cluster size on power based on the recruitment figures in TRACS.

Unequal cluster size 2

When able to estimate likely min and max cluster sizes

$$cv = \left(\frac{max - min}{4}\right) / mean$$

$$DE = (1 + ((1 + cv^2)mean - 1)ICC$$

Reference: Eldridge, S. M., Ashby, D., Kerry, S. Sample size for cluster randomized trials: effect of coefficient of variation of cluster size and analysis method. *International Journal of Epidemiology* 2006;35:1292–1300

Response rates

In TRACS these were between **70 - 75%** in terms of returned questionnaires at 6 months.

Methods to **improve** response rates were instigated:

1. **Postal reminder** (2 weeks after questionnaire was sent to participants),
2. **Telephone reminder** (2 weeks after postal reminder),
3. **Collection of Primary outcomes over the phone** from patients who did not respond to postal and telephone reminders (labour intensive method).

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Recommendations for designs of CRTs based on our experience

- Choose adequate **method of randomisation** depending on information collected beforehand and estimation of whether centres can all start simultaneously.
- Try to **avoid selection bias** by employing independent researchers.
- Conduct extensive **literature review**, systematic review and meta-analysis of previous trials in the subject area.
- Prepare various **scenarios** for **sample size** calculations reflecting current clinical practice as realistic as possible. The same applies to estimation of **response rates**.

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Acknowledgments

TRACS team
Prof Anne Forster
Prof John Young
Prof Lalit Kalra
Dr David Smithard
Prof Martin Knapp
Anita Patel
Amanda Farrin
Dr Rachel Breen
Prof Jane Nixon
Dr Shamaila Anwar
Ivana Holloway

ISRCTN: 49208824
Funded by MRC.
The views and opinions expressed are the author's own and do not necessarily reflect those of the MRC .

LoTS Care team
Prof Anne Forster
Dr Kirste Mellish
Dr Katie Shorter

Amanda Farrin
Prof Jane Nixon
Dr Shamaila Anwar
Ivana Holloway

ISRCTN: 67932305
This trial is funded as part of a NIHR Programme Grant for Applied Research

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MRC Medical Research Council

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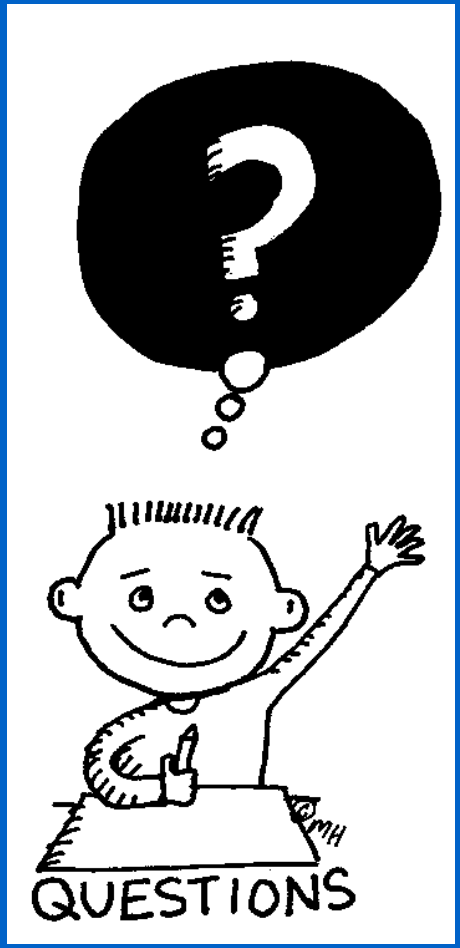
NHS National Institute for Health Research

King's College London University of London

The Stroke Association

Bradford Teaching Hospitals NHS Foundation Trust

Thank you.
Any questions ?



I.Holloway@leeds.ac.uk

ctru
University of Leeds