DESIGN CHALLENGES FOR CLUSTER RANDOMISED TRIALS IN STROKE REHABILITATION

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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
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
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
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
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?
Randomisation

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.

Randomisation

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.

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.
## Sample size

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

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

\( DE = 1 + (m - 1)\rho, \) where \( \rho = ICC, m = \text{cluster size} \)
Unequal cluster size

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

When able to estimate likely min and max cluster sizes

\[ cv = \frac{(\text{max} - \text{min})}{4 \times \text{mean}} \]

\[ DE = (1 + (1 + cv^2) \times \text{mean} - 1) \times \text{ICC} \]

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).
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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Any questions?

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