

A Review of Methodology For Sample Size Calculations In Cluster Randomised Trials

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Cluster Randomised Trials Brief Overview

- Definition
 - In a cluster randomised trial groups, or clusters, of people are randomised to a treatment, with all members of the group receiving the same treatment
- Example
 - in a trial aimed at increasing GP recognition of domestic violence whole GP practices were randomised rather than individual GPs.

Why is the sample size different?

- A cluster randomised trial provides less information than an individually randomised trial of the same size
 - Outcomes are correlated within a cluster

- We could quantify the increase required by calculation of the design effect (DE)

$$1 + (n - 1) ICC$$

- n =cluster size
- ICC=a measure of similarity within a cluster

The assumptions

Assumption 1: All the clusters are the same size

Assumption 2: Simple random allocation
(i.e. no stratification or matching)

Assumption 3: Outcomes are continuous or binary

Assumption 4: ICC is constant

Literature Review

- Process and sources
- Status so far
 - 8697 results retrieved
 - 57 identified for inclusion
 - 23 (40%) in the previous 5 years
 - 38 (67%) in the previous 10 years

- **Assumption 1:** All the clusters are the same size
- To compensate for the loss in power calculate a measure of relative efficiency (RE) of unequal versus equal cluster sizes
 - You (2011), Breukelen (2007), Breukelen (2008), Candel (2009)
- Calculate a Design Effect which incorporates variable cluster size
 - Eldridge (2006), Kang (2003), Manatunga (2001), Kerry (2001)

Assumptions

- **Assumption 2:** Simple random allocation
 - Six papers (11%) dealt with stratified or matched designs
- **Assumption 3:** Outcomes are continuous or binary
 - 38 (67%) papers cover continuous outcomes
 - 18 also include binary outcomes
 - 1 also includes a rate outcome
 - 15 (26%) focus on binary outcomes
 - 4 (7%) focus on time to event outcomes

- Alternative analysis methods
- Varying cluster sizes
- Three level trials
- Incorporation of cost

Range of topics

- Matching and stratification
- Alternative measures of correlation
- Bayesian
- Dealing with attrition/non-compliance
- Stepped wedge/cross over design/adaptive designs/non-inferiority
- Simulation based approaches
- Incorporation of covariates

Potential barriers to use?

- Methodological
- Do methods reflect common trial designs?
- Information required
- Software/programming knowledge required

Potential Gaps?

- Small number of large clusters
- Ordinal and count data
- Restricted randomisation
- Alternative trial designs, cross-over, stepped wedge, non-inferiority
- Population averaged analysis approaches