How to cite this document: McKenzie J, Ryan R, Di Tanna GL; Cochrane Consumers and Communication Review Group. 'Cochrane Consumers and Communication Review Group: cluster randomised controlled trials'. http://cccrg.cochrane.org, December 2016 (accessed DATE).

Cochrane Consumers and Communication Group:
Cluster randomised controlled trials

Please note that the advice in this document is adapted directly from the Cochrane Handbook for Systematic Reviews of Interventions, particularly section 16.3.

Analysing cluster RCTs

Compared with individually randomized trials, cluster RCTs randomize groups of people (rather than individual people) to groups to be studied. The way this is described is that the 'unit of allocation' in these trials is the groups, or cluster, of people. Clusters can be based on many different groupings, such as clinics, communities or towns, schools, or families.

Cluster RCTs may be used for a variety of reasons. These include: to avoid contamination (eg. some of the people randomized to the control group receive some or all of the intervention) that might occur if individuals in the same group were randomized to different study arms, because the intervention may be targeted at the cluster, or for logistical, feasibility or ethical reasons (Donner A, Klar N. *Design and analysis of cluster randomization trials in health research.* London: Arnold Publishing, 2000.) Cluster RCTs provide a valid design to investigate the effectiveness of an intervention, but have additional issues compared with individually- randomized trials that need to be addressed.

One key issue relates to analysing data from a cluster RCT. Participants within the same cluster may be more similar than those from different clusters, which may lead to correlation of observations within the clusters. This feature of the data needs to be accounted for in the analysis and standard statistical methods (such as ANCOVA or a difference in means) do not appropriately account for this correlation. When the correlation is not accounted for, the resulting standard error of the intervention effect will be too small, along with the confidence interval and P value. This error will propagate through to any meta-analysis that includes the trial, with the trial receiving too much weight in the meta-analysis, and the standard error of the pooled intervention effect being too small (ie. the confidence intervals around the effect estimate will be narrower than they should be, based on the sample size).

When including cluster-RCTs in a meta-analysis, review authors need to make an assessment as

to whether the trial has been analysed in such a way as to account for clustering, and if not, they need to make an adjustment to the trial results using one of several available approaches (outlined in the next section). A common problem in the analysis of cluster RCTs is that the data is analysed according to individuals, rather than clusters of individuals (referred to as a 'unit of analysis error'). It is advisable to seek statistical advice as to whether the cluster RCT has been appropriately analysed. Cluster level analyses, analyses of individual level data that are adjusted for the design effect (see next section), or regression analyses of individual level data using methods for clustered data (e.g. random effects models, marginal modelling using generalised estimating equations (GEEs)) are all valid.

In the review, authors must consider and report any impacts (on the analysis) of including cluster RCTs.

Approaches to incorporate results from cluster RCTs in meta-analyses

See the Cochrane Handbook sections 16.3.3-16.3.7.

Cluster RCTs may be combined in a meta-analysis with individually-randomised trials, but cluster RCTs should always be clearly identified in a review, and the way that data have been dealt with should be described. In circumstances where a cluster RCT has not been appropriately analysed, one of the following approaches may be used to reanalyze the data to provide an approximately correct analysis.

Approach 1: Calculating effective sample sizes

This approach can be used if the following data are available:

- number of clusters per intervention group; total number of participants per intervention group
- outcome data (number of events, or means and standard deviations by intervention group) and
- an estimate of the intracluster correlation coefficient (ICC).

Often an ICC will not be available from a study, but a suitable ICC can be selected from other cluster RCTs included in the review, or external sources (see list below).

Using this information, an effective sample size (ie reduced sample size to take account of clustering) can be calculated. To calculate an effective sample size, a quantity known as the design effect must first be calculated.

Design effect = 1 + (M-1) ICC, where M is the mean cluster size (ie average number of people in each cluster).

The design effect is then used to adjust the study data:

- For **dichotomous** outcomes, both the number of participants and the number of events in each intervention group should be divided by the design effect.

- For **continuous** outcomes, only the number of participants in each intervention group needs to be divided by the design effect (means and standard deviations need no adjustment).

For a step-by-step explanation of calculating an effective sample size, with a worked example, please see the Cochrane Handbook section 16.3.4 and 16.3.5.

Approach 2: Inflating standard error

An alternative approach to reducing the sample size is to inflate the standard error of the estimated intervention effect (see section 16.3.6).

This approach also requires calculation of a design effect, and therefore, an estimate of the ICC (see below). The adjustment is computed by multiplying the standard error by the square root of the design effect. An example using this approach is available in section 16.3.6.

Intracluster correlation coefficient (ICC) resources

- Adams G, Gulliford MC, Ukoumunne OC, Eldridge S, Chinn S, Campbell MJ (2004). Patterns of intra-cluster correlation from primary care research to inform study design and analysis. *Journal of Clinical Epidemiology* 57(8): 785-94.

- Bell ML, McKenzie JE: Designing psycho-oncology randomised trials and cluster randomised trials: variance components and intra-cluster correlation of commonly used psychosocial measures. *Psycho-oncology* 2013, 22(8):1738-47.

- Campbell M, Grimshaw J, Steen N. Sample size calculations for cluster randomised trials. *Journal of Health Services Research and Policy* 2000, 5(1): 12-16.

- Elley CR, Kerse N, Chondros P, Robinson E: Intraclass correlation coefficients from three cluster randomised controlled trials in primary and residential health care. *Australian and New Zealand Journal of Public Health* 2005, 29(5):461-7.

- Ukoumunne OC, Gulliford MC, Chinn S, Sterne JA, Burney PG: Methods for evaluating area-wide and organisation-based interventions in health and health care: a systematic review. *Health Technology Assessment 1999*, 3(5):iii-92.