Statistical approaches to computing sample size in cluster randomized trials: a simulation study

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Abstract
Background: Cluster randomized trials, which randomize groups of individuals to an intervention, are common in health services research when one wants to evaluate improvement in a subject's outcome by intervening at an organizational level. For many such trials sample size calculation is performed under the assumption of equal cluster size. Many trials that set out to recruit equal clusters end up with unequal clusters for various reasons. This leads to a misalignment between the method used for sample size calculation and the data analysis, which may affect trial power. Various weighted analysis methods for analyzing cluster means have been suggested to overcome the problem introduced by unbalanced clusters; however, the performance of such methods has not been evaluated extensively.

Methods: We examine the use of the general linear model for analysis of clustered randomized trials assuming equal cluster sizes during the planning stage but ending up with unequal clusters. We demonstrate the performance of three approaches using different weights for analyzing the cluster means: (1) the standard analysis of cluster means, (2) weighting by cluster size, and (3) minimum variance weights. Several distributions are used to generate cluster sizes to cover a wide range of patterns of imbalance. The variability in cluster size is measured by the coefficient of variation (CV).

By means of a simulation study, we assess the impact of using each of the three analysis methods with respect to type I error and power of the study and how it is affected by the variability in cluster size.

Results: Analyses that assumes equal clusters provide a reasonable approximation when cluster sizes vary minimally (CV < 0.30). In an analysis weighted by cluster size type I errors were inflated, and that worsened as the variation in cluster size increases. However, a minimum variance weighted analysis best maintains target power and level of significance under all degrees of imbalance considered.

Conclusion: The unweighted analysis works well as an approximate method when the variation in cluster size is minimal. However, using minimum variance weights performs much better across the full range of variation in cluster size and is recommended.

Full-text
Due to technical limitations, full-text HTML conversion of this manuscript could not be completed. However, the manuscript can be downloaded and accessed as a PDF.

Figures

Figure 1
Distribution of type I error (left) and power (right) for three categories of CV: (a) (b) and (c). The reference line for nominal type I error and target power are shown by a dotted line at 0.05 and 0.80 respectively.