Statistics notes

Trials randomised in clusters

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In most randomised trials each subject is individually assigned at random to an intervention group. The intervention is applied directly to the subject and observations are made on each individual to determine the outcome of the intervention. Sometimes subjects cannot be allocated independently, or they may interact with one another during the treatment period.

In trials of population screening, for example, screening centres may be set up in some districts and not in others. This may be necessary because widespread publicity is needed to encourage subjects to come for screening, or because members of the screening group might pass on information to neighbours who have been allocated to the control arm (no screening), leading them to demand screening.

In the Swedish two county trial of breast cancer screening the county of Kopparberg was divided into seven geographical areas.[1 2] Each was then subdivided into three units, either parishes or municipalities, two of which were randomly allocated to screening and the other to control. The county of Östergötland was divided into 12 areas, each of which was subdivided into two experimental units, one allocated to screening and the other to control. The subjects within a unit are called a cluster, and the trial used cluster randomisation. Cluster randomisation is used especially in public health and general practice research.

A price must be paid

There is a price to be paid for this design at the analysis stage. We cannot think of our trial subjects as independent individuals but must do the analysis at the level of the experimental unit.[3] In the two county trial women within a parish will be more alike than a random sample of women from the two counties. We have two sources of variation: that between people in a parish and that between parishes. The variability between parishes must be taken into account in the analysis.

The effect of cluster randomisation is to increase the size of standard errors and hence widen confidence intervals and increase P values compared with a study of the same size using simple randomisation. The effective sample size is reduced and power is lost. The larger and fewer the clusters are, the more important and greater the effect becomes.

Many cluster randomised trials ignore this design effect in the analysis. Early reports of the two county trial[1 2] did this, although more recent analyses have taken it into account.[4] In a review of 16 non-therapeutic intervention trials employing cluster randomisation only eight allowed for the clusters in the analysis.[5] Ignoring the correct unit of analysis in this way may lead to spurious positive findings.[3]

Health promotion is another area where cluster randomised designs are common. For example, in the evaluation of a health education programme schools may be randomly allocated to receive the education programme or to act as control. The subsequent behaviour and knowledge of the children can be compared. As children may influence each other children within a school cannot be regarded as independent of one another and the school should be the unit of analysis.

Use the right unit

Patients are often allocated so that all the patients of one general practitioner receive the same treatment. In a trial of terminal care coordination, for example, general practices were allocated into two groups and the patients of doctors in one group were offered the extra intervention.[6] All the patients needing terminal care in a practice formed a single cluster. In this example the treatment was applied directly to the patient, who received visits from the care coordinators. Sometimes the treatment is applied to the provider of care rather than to the patient directly; and here the effect of the clustering may be much larger. For example, to improve the treatment of asthma in general practice general practitioners were allocated randomly to three groups.[7] The first group was given an intensive programme of small group education, the second a lesser intervention, and the third no intervention at all. A sample of each general practitioner's asthmatic patients was selected. These patients received questionnaires about their symptoms, and the prevalence was compared between the groups. The experimental unit was the general practitioner, not the patient. The proportion of patients who reported symptoms was used as a measure of the general practitioner's effectiveness and the three groups of doctors compared by analysis of variance.[8]

We shall discuss the design and analysis of cluster randomised trials in future statistics notes.

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