5.1: Introduction to trial size

One of the most important factors to consider in the design of an intervention trial (or indeed in the design of any epidemiological study) is the choice of an appropriate trial size to answer the research question. Trials that are too small may fail to detect important effects of an intervention on the outcomes of interest or may estimate those effects too imprecisely. Trials that are larger than necessary are a waste of resources and may even lead to a loss in accuracy, as it is often more difficult to maintain data quality and high coverage rates in a large trial than in a smaller one.

The choice of an appropriate trial size may be based on either the precision of outcome measures desired or the power of the trial wanted. In Section 2, there is a discussion of the criteria used to make this choice. In Sections 3 and 4, procedures are given for calculating trial size requirements in the simplest case where two groups of equal size are to be compared. More complex designs are considered in Section 5. Special methods are necessary when the interventions are allocated to groups (for example, communities, schools, or health facilities), rather than individuals, and these are described in Section 6. Following this, in Section 7, two other factors that may influence the choice of trial size are discussed—first, the need to allow for interim analyses of the results (see Section 7.1), and second, the effects of losses to follow-up (see Section 7.2). In Section 8, the consequences of trials that are too small are discussed. Computer programs can be used to carry out sample size calculations, and these are briefly discussed in Section 9.

The procedures described in this chapter should be regarded as providing only a rough estimate of the required trial size, as they are often based on estimates of expected disease rates, subjective decisions about the size of effects that it would be important to detect, and the use of approximate formulae. However, a rough estimate of the necessary size of a trial is generally all that is needed for planning purposes. More comprehensive reviews of methods for the determination of trial size requirements are available (Chow et al., 2008; Machin, 2009), but the methods given in this chapter should be adequate for most purposes.

Readers who are not familiar with methods for the statistical analysis of trial data and, in particular, with the concepts of
confidence intervals (CIs) and significance tests may find it helpful to read Chapter 21, Section 2, before embarking on this chapter, which is placed here because of the importance of considering trial size requirements at the design stage of a trial.

A principal objective of most intervention trials is to estimate the effect of the intervention on the outcome or outcomes of interest. Any such estimate is subject to error, and this error has two main components: bias and sampling error. Possible sources of bias and ways of avoiding them are discussed in Chapters 4, 11, and 21. The second component sampling error arises because the trial data come from only a sample of the population. This second component of error is the focus of this chapter. Sampling error is reduced when the trial size is increased, whereas bias generally is not.