6.1: Introduction to ethical considerations

For any research investigation involving human subjects, there must be careful consideration of ethical issues that may arise in the planning, conduct, and reporting of the study. With very few exceptions, such research is not permitted unless the study has been approved by at least one formal ethics review committee (ERC). All research funding agencies require approval of the research by the appropriate ERC(s) before they will confirm an award for an intervention study. Often ethical review will be required from more than one such committee, for example, by both an institutional and a national ethics review committee, and/or in each of the countries involved in a trial. The ethics committee(s) will not only review the study protocol but usually will require full details of the study plan and procedures and will usually have specific application forms that must be completed. They may require payment of an administration fee for considering an application, irrespective of the outcome of the application. The committee will pay particular attention to informed consent documents and how consent to take part in the research will be obtained from potential study participants. Any significant changes in the study plan, either before it starts or during the conduct of the study, such as adding new objectives, extending the trial catchment area, or adding/removing inclusion or exclusion criteria, require approval by the ERC.

It is important that the ethical aspects of a research study are considered from its inception; for that reason, this chapter is placed early in the book. An underlying philosophy in this chapter is that it is difficult, and often inappropriate, to lay down ethical rules that apply to all studies in all places; each study should be judged in the context of the circumstances in which it will be conducted. A study judged unethical in one place might be considered ethical in another, and both of these might be ‘correct’ judgements.

Most ethical issues arise from conflicts between competing sets of values. For example, the medical practitioner is dedicated to the provision of the best medical care for an individual who is his or her patient. However, this dedication may be in direct conflict with that of the public health professional whose goal is to achieve maximum health benefits in a community with the limited resources available, which may entail restricting resources available to any one patient.
Consuming large amounts of resources on one patient may deprive others of benefit. The appropriate balance between benefit for the individual and benefit for the community depends very much on the particular situation. The conflict is most obvious in situations of poverty and deprivation—just those conditions in which most field trials are conducted in LMICs. Those conducting field trials of interventions against diseases associated with poverty are likely therefore to be faced with especially difficult ethical dilemmas. Resolution of such dilemmas often depends upon where the investigators place their horizon of responsibility. If they consider their responsibility is confined to the participants in a trial, then some studies to resolve important public health issues might be viewed as unethical. But to assess the likely public health impact of an intervention in the wider community, it may be important to continue a trial beyond the point when it is established that one intervention is superior to another, in order to obtain a better estimate of the magnitude of the beneficial effect. Knowledge of the extent of benefit is needed, in order to make an informed decision about whether the benefit is sufficient to introduce the intervention on a widespread basis, especially if it is more expensive than the intervention that is currently available. If the investigators consider their responsibility is extended to the entire population, then they may regard it as unethical to stop a trial before a reasonable estimate of that benefit is obtained.

It is important to recognize that the primary purpose of an intervention trial is not to benefit the specific participants in the trial, but rather to obtain information about the effects of the intervention that will inform decisions about whether the intervention should be introduced on a widespread basis. Although trial participants may derive benefit, for example, they might receive better medical care in the trial than they would with the normal medical services, this is incidental to the main purposes of the trial.

Although intervention trials are not conducted with the prime aim of benefiting those in the trial, investigators have a specific responsibility for participants in a trial and must ensure that they are not harmed as a consequence of taking part in the trial and might derive some benefit. In so far as is possible, at a minimum, participants in a trial should be placed in no worse a situation than would have been the case had they not participated in the trial. It is, of course, not always possible to guarantee this, as sometimes there may be unexpected adverse events associated with an intervention, but it is important to minimize the possibility of harm to trial participants.

There is sometimes a conflict between what is best for the ‘future population’ and what is best for those participating in a trial. Such conflicts may pose serious ethical dilemmas, for which there are few ‘cookbook’ solutions. Each situation has to be considered individually and preferably during the planning of the trial, so that potential ethical issues can be thought through in advance and, where necessary, guidance can be sought from properly constituted ethics committees. This issue is discussed further in Section 2.

It is not the purpose of this chapter to provide comprehensive guidance on all of the ethical considerations that must be considered in designing and conducting a field trial. Substantial sets of ethical guidelines have been published by a number of international bodies, and we give reference to these in the chapter, especially in Section 2.8. Rather we highlight some of the basic ethical principles related to randomized trials in Section 2 and then focus on some of the particularly difficult, and sometimes controversial, issues that arise in field trials in LMICs.