12.1: Introduction to outcome measures and case definition

Field trials of health interventions are designed to assess the impact of one or more interventions on the incidence, duration, or severity of specified diseases, or on intermediate variables or risk factors considered to be closely related to these measures of disease (for example, hygiene behaviours for diarrhoeal diseases, reduction in density of parasite vector, reduction of indoor air pollutants for pneumonia, or reduction of salt intake for hypertension). The measures chosen to assess the impact of the interventions are called the outcome measures in the trial (or the trial endpoints). Such measures should be defined at the time the trial is designed and should be specified in detail in the study protocol. The outcomes should be compared between those in the different intervention groups and should be measured in a consistent way during the course of the trial in the different groups. Clear definitions are also necessary, so that the measures can be replicated in other trials and meaningful comparisons made between trials. Failure to pay sufficient attention to the precise definition of the primary outcome measures at the start of a trial may lead to confusion in interpreting the results or can even invalidate them.

As discussed in Chapter 4, Section 5, several different outcome measures may be employed in a trial. It is important to decide which is of most interest (primary outcome), as this has major design implications, particularly in terms of the study size and duration. Trials may have other outcomes (secondary or tertiary) that may be important to measure, although they will generally not determine the size of the trial. In Table 12.1, there are some examples of primary and secondary outcomes for trials of different interventions.

In this chapter, different types of outcome measures are reviewed in Section 2, and factors influencing the selection of these are discussed in Section 3. The importance of standardizing measurements between different observers is stressed in Section 4.1, and there is a discussion of how the results of a trial may be influenced by poor sensitivity or specificity in the outcome measures in Section 4.2. Finally, ways of avoiding bias and maintaining quality control (QC) in case ascertainment methods are reviewed in Sections 4.3 and 4.5.
### Table 12.1 Examples of primary and secondary outcomes for trials of different interventions

<table>
<thead>
<tr>
<th>Intervention trial</th>
<th>Primary outcome(s)</th>
<th>Secondary outcomes</th>
<th>Comment</th>
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<tbody>
<tr>
<td>Phase III trial of 9-valent conjugate pneumococcal vaccine in The Gambia (Cutts et al., 2005)</td>
<td>First episode of radiological pneumonia</td>
<td>- Clinical or severe clinical pneumonia</td>
<td>The main purpose of the trial was to evaluate the public health impact of the vaccine. First episodes of radiological pneumonia were reduced by 37% (and all-cause mortality by 16%—not a primary endpoint in the trial). Highest efficacy was expected against invasive pneumococcal disease due to serotypes in the vaccine, but the aetiology of most cases of pneumonia is difficult to establish.</td>
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| Cluster randomized trial to assess the impact of an adolescent sexual health intervention in Tanzania (Ross et al., 2007) | Incidence of HIV infection Prevalence of herpes simplex type 2 (HSV-2) infection at end of trial | - Six biological measures (for example, syphilis and gonorrhoea prevalence at end of trial)  
- Five behavioural endpoints (for example, use of condoms during sexual intercourse)  
- One attitudinal endpoint  
- Three knowledge endpoints (for example, how HIV is transmitted) | The intervention was designed to reduce HIV incidence through behaviour change brought about by sexual health education. A substantial number of secondary outcomes were included to facilitate understanding of the main results. This was important, as the intervention was shown to substantially improve knowledge, reported attitudes, and some reported sexual behaviours but had no consistent impact on biological outcomes. |
| Trial of intermittent treatment of infants for malaria and anaemia control at time of routine vaccinations in Tanzania (Schellenberg et al., 2001) | First or only episode of clinical malaria                                                                 | - Multiple malaria episodes  
- Fever episodes  
- Severe anaemia  
- Admissions to hospital  
- Outpatient attendances | This was a test of a new approach to malaria control by administering anti-malarial drugs routinely to infants attending clinics for vaccination. Clinical malaria was reduced by 59%, and severe anaemia by 50%                                                                 |