11.4: Blinding

Whenever possible, neither the participants nor the investigators should know to which intervention group each participant belongs until after the end of the trial. Such ‘double-blind’ designs (both the investigator and the participants are blind to the knowledge of who have received each intervention) eliminate the possibility that knowing to which intervention an individual is allocated may affect the way the individual behaves, is treated, or is monitored during the trial, or the way an individual is assessed at the end of the trial. Sometimes, a double-blind trial is not possible, and a ‘single-blind’ design might be used, in which the investigator knows to which group a participant belongs, but the participant does not.

‘Blinded’ designs are especially important when those in one of the groups under comparison are given an intervention that is expected to have no effect on the outcome of interest. To maintain blindness in these circumstances, a placebo should be used, if possible, which should look and smell as similar as possible to the intervention itself (and have a similar taste if it is being given orally). Sometimes, an identical-looking placebo cannot be obtained, and, in these circumstances, the investigator and the participants should be kept blind to which treatment is the active one. While this may be the best that can be done in some trials, it is generally undesirable. Either the participants or the investigator may form a view as to which the active treatment is (possibly erroneously), and this may affect differentially the amount of other care given to the participants or the likelihood that a participant reports apparently beneficial or harmful effects. For example, there is evidence that the colour of a tablet may affect the perceived action of a drug and seems to influence the effectiveness of a drug in some situations (de Craen et al., 1996).

For some interventions, it may be possible to preserve blindness in the initial phase of a trial, but this may be more difficult later. For example, in placebo-controlled studies of ivermectin against onchocerciasis, it was found that some participants were able to guess that they had received an active drug, rather than a placebo, because of the effect of ivermectin on other helminth infections, such as Ascaris, through the passage of worms in their stools, whereas those receiving placebo rarely experienced this effect. In placebo-controlled trials of BCG vaccination, most of those who have
received BCG develop a lasting scar, whereas those who have received placebo do not. The possible bias that this might induce in the assessment of whether or not a participant developed leprosy, following vaccination, was overcome in a trial in Uganda by covering the vaccination site with sticking plaster for all participants before each clinical examination (Brown and Stone, 1966).

For some intervention trials, in which the unit of randomization is the community, the use of a placebo is straightforward and is no different, in principle, from the situation for an individually randomized trial. This was the case, for example, in a cluster randomized trial to assess the impact of regular vitamin A supplementation on child mortality. Those in the control communities received supplementation with an inert liquid that was administered in such a way that it was indistinguishable from the administration of vitamin A (Ghana VAST Study Team, 1993). For some interventions, however, a suitable placebo may be impossible to find. What would be a suitable placebo for an improved water supply and sanitation programme in a village, for example?