

TESTING TREATMENTS

Chapter 6, 6.3.6 6 FAIR TESTS OF TREATMENTS



Why all patients randomized should be included in the final outcome ('intention to treat').

figure are actually equal. However, if the two people allocated to surgery die before operation and are then excluded from consideration, the comparison of the two groups will be biased. It will suggest that surgery appears to be better when it is not.

Dealing with departures from allocated treatments

For all the reasons given so far in this chapter, you will have realized that fair tests of treatments have to be planned carefully. The documents setting out these plans are known as research protocols. However, the best-laid plans may not work out quite as intended – the treatments actually received by patients sometimes differ from those they were allocated. For example, patients may not take treatments as intended; or one of the treatments may not be given because supplies or personnel become unavailable. If such discrepancies are discovered, the implications need to be considered and addressed carefully.

During the 1970s and 1980s, there were remarkable advances in the treatment of children with acute lymphoblastic leukaemia,

the most common type of leukaemia in this age group. However, it was puzzling that American children were doing substantially better than British children who, on the face of it, were receiving exactly the same drug regimens.⁷ During a visit to a children's cancer centre in California, an astute British statistician noticed that American children with leukaemia were being treated far more 'aggressively' with chemotherapy than children in the UK. The treatment had nasty side-effects (nausea, infection, anaemia, hair loss, and so on) and when these side-effects were particularly troublesome, British doctors and nurses, unlike their American counterparts, tended to reduce or pause the prescribed treatment. This 'gentler approach' appears to have reduced the effectiveness of the treatment, and was probably a reason for the differences in British and American treatment success.

Helping people to stick to allocated treatments

Differences between intended and actual treatments during treatment comparisons can happen in other ways that may complicate the interpretation of tests of treatments. Participants in research should not be denied medically necessary treatments. When a new treatment with hoped-for, but unproven, beneficial effects is being studied in a fair test, therefore, participating patients should be assured that they will all receive established effective treatments.

If people know who is getting what in a study, several possible biases arise. One is that patients and doctors may feel that people allocated to 'new' treatments have been lucky, and this may cause them unconsciously to exaggerate the benefits of these treatments. On the other hand, patients and doctors may feel that people allocated 'older' treatments are hard done by, and this disappointment may cause them to under-estimate any positive effects. Knowing which treatments have been allocated may also cause doctors to give the patients who have been allocated the older treatments some extra treatment or care, to compensate, as it were, for the fact that they had not been allocated to receive the newer, but unproven treatments. Using such additional treatments in patients in one of the comparison groups but not in the other group complicates the evaluation of a new treatment, and risks