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

making the comparison unfair and the results misleading. A way to reduce differences between intended and actual treatment comparisons is to try to make the newer and older treatments being compared look, taste and smell the same.

This is what is done when a treatment with hoped-for beneficial effects is compared with a treatment with no active ingredients (a sham treatment, or placebo), which is designed to look, smell, taste and feel like the 'real' treatment. This is called 'blinding', or 'masking.' If this 'blinding' can be achieved (and there are many circumstances in which it cannot), patients in the two comparison groups will tend to differ in only one respect – whether they have been allocated to take the new treatment or the one with no active ingredients. Similarly, the health professionals caring for the patients will be less likely to be able to tell whether their patients have received the new treatment or not. If neither doctors nor patients know which treatment is being given, the trial is called 'double blind'. As a result, patients in the two comparison groups will be similarly motivated to stick to the treatments to which they have been allocated, and the clinicians looking after them will be more likely to treat all the patients in the same way.

Fair measurement of treatment outcome

Although one of the reasons for using sham treatments in treatment comparisons is to help patients and doctors to stick to the treatments allocated to them, a more widely recognized reason for such 'blinding' is to reduce biases when the outcomes of treatments are being assessed.

Blinding for this reason has an interesting history. In the 18th century, Louis XVI of France called for an investigation into Anton Mesmer's claims that 'animal magnetism' (sometimes called 'mesmerism') had beneficial effects. The king wanted to know whether the effects were due to any 'real force', or rather to 'illusions of the mind'. In a treatment test, blindfolded people were told either that they were or were not receiving animal magnetism when in fact, at times, the reverse was happening. People only reported feeling the effects of the 'treatment' when they had been told that they were receiving it.

For some outcomes of treatment – survival, for example –