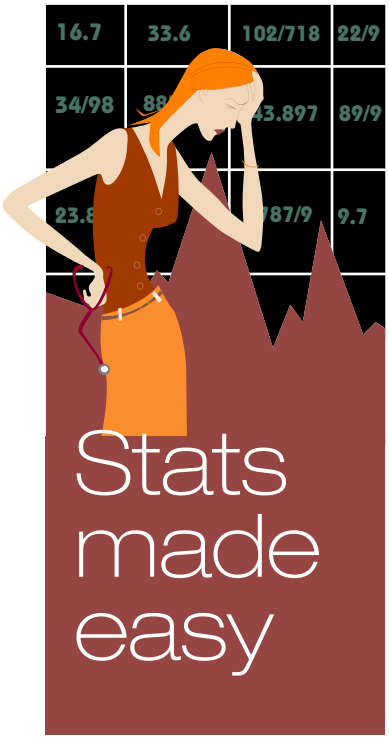
Randomised controlled trials

Why they are more reliable than observational studies



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Large randomised controlled trials (RCTs) are the most reliable way to test whether a treatment causes a benefit (or deterioration) in health.

While observational studies (see box) do not always give different results from subsequent RCTs, it is not possible to tell when selection bias is going to give the wrong answer.

The enthusiasts who promoted HRT for the prevention of heart disease in the 1990s took little notice of those who pointed out that the observational studies also found bizarre associations between taking HRT and lower rates of death from accidents and violence.

These associations suggest that HRT usage in the observational studies was confounded by something else (such as lifestyle) that decreased death from violence and heart disease.

People with low vitamin C levels are found to die more often from heart disease in observational studies, but we cannot assume that this means that the vitamin C is the cause of this difference, nor that giving extra vitamin C will change the risk.

The negative RCT evidence showed that giving people antioxidants did not improve their mortality, so vitamin C was more likely a marker for other risk factors, and it was not possible to allow for these adequately in the adjustments that were made.

Life-time social, developmental and behavioural differences are related to vitamin C levels, and these factors together can account for a four-fold increase in cardiovascular death between those with the best and worst risk-factor status.[1]

For this reason, Cochrane systematic reviews of treatments usually restrict the included studies to RCTs, and, moreover, the Cochrane Library has a controlled trial register (labelled CENTRAL) so that you can search for RCT evidence without being swamped by other less reliable types of data. Access is free to all UK users (go to www.nelh.nhs.uk/cochrane.asp).

Next month, I will discuss the differences between odds and risks.

REFERENCE

1. Lawlor DA, Smith GD et al. Lancet 2004; 363: 1724-7.

Observational

Observational studies include the types of study mentioned in the last three articles – cross-sectional surveys, case-control studies and cohort studies. In these, the participants have chosen their own treatment, leading to differences in characteristics between the two groups (selection bias), and researchers try to adjust for this. These studies are suitable to explore association but should not be assumed to prove causation.

Experimental

Experimental studies (or controlled clinical trials) are different because participants are allocated a particular treatment (preferably in a random fashion in which neither the participant nor the experimenter knows which treatment the patient will be allocated). In this way, the experimenter hopes that the groups of patients will have differences that are randomly distributed and that selection bias will be minimised, because if the number of patients being studied is large, the average characteristics in each group will be the same except for the treatment that is being studied.