

## Evidence explained: Random error, bias and confounding

Before concluding that the results of a study are valid, three potential sources of error, which might provide an alternative explanation for the findings, should be considered.

- Random error
- Bias
- Confounding

This article aims to help you understand these sources of error. It's required knowledge for the AKT, but most importantly helps you to decide whether or not you'd want to apply the results of primary research to your clinical practice.

### **Random Error**

Error can be defined as the difference between the true value of a measurement and the recorded value. Random error is what it says on the tin – it occurs because of random variation or 'noise in the system'. There is always the possibility that if you toss a coin ten times in a row, it will fall on heads every time due to chance alone. For clinical trials, increasing sample size (the number of participants in the study), increases the statistical power to prove there is a true difference between an intervention we are testing and the control, reducing the likelihood that a study's results are due to chance. If we continue to toss the coin one hundred times, the chance of it always landing on heads decrease.

### **Bias**

In contrast to random error, bias refers to systematic errors – ones introduced by the way the study is designed, and that are not explained by chance. Bias can result in a distortion of outcomes, and can be introduced at all stages of the research process, from study design through interpretation of results, and even at publication. Because there is an error in the design of the study, increasing our sample size does not reduce the effect of bias on our results. A weighted coin will be more likely to fall on heads whether we toss it one hundred times or ten. The table below outlines some of the key types of bias to be aware of, but is not exhaustive.

**Table 1 – Types of bias**

Type of bias	What is this?
Selection bias	The selection of participants does not represent the target population, about which conclusions are to be drawn. This is avoided by adequate randomisation.

Healthcare access bias	Participants recruited from one healthcare setting do not represent the wider population, which the study is reporting on. This may be seen where studies recruit patients in hospital who might be expected to be sicker than those in the community, such as patients with acute compared to chronic heart failure.
Neyman bias	A type of selection bias where the very sick or very well are excluded from follow-up. Consider a study that assesses recovery following hospitalisation with an exacerbation of COPD by following up all those discharged one month later. Some of the most unwell patients may have died in hospital and will not be captured by this study design.
Detection bias	The expected outcome is sought more diligently in one group (usually the treatment group) compared to the other (usually the control). For example, a group of patients randomised to treatment with a new antihypertensive may receive more frequent follow-up to check their blood pressure levels than the control, leading to the impression blood pressure levels are lowered more quickly. This can be avoided by blinding.
Observer bias	A new antidepressant is being trialled and the researcher is questioning a participant who has taken the drug to gauge how his symptoms have responded. If the researcher knows the participant has had the new drug he may lead the interview or interpret the results in a different way. Blinding the observers to the participant group allocation can avoid this.
Response bias	Those who volunteer to participate in a study are not representative of the wider target population. Think NHS Health Checks...
Recall bias	Participants who know what treatment group they are allocated to may remember or report their symptoms differently. Those randomised to take statins in trials, tend to be more likely to report minor muscular pains given the widely publicised association with myopathy.
Hawthorn Effect	The process of follow-up and studying itself alters the course of a disease. For example chronic headache may improve in a study where the regular review and discussion around symptoms provides reassurance and a reduction in stress. Masking of study outcomes and use of control groups can prevent this.
Regression to the mean	Random chance can always produce an extreme outlying result, particularly if a small sample is used. Comparing subsequent results against this original may give the impression of a significant result or treatment effect as other results are likely closer to the mean. Use of control groups can protect against this effect.
Post-hoc analysis	A dataset is analysed retrospectively for a use other than that originally intended – so called data trawling. The risk is that the study was not designed to test this association and that if enough post-hoc analyses are run, some significant results will always occur due to chance alone.
Publication bias	Certain results, such as those with eye catching or positive results, are more likely to get published. If results with neutral or negative effects are not also published this will give a false impression of what the research in the field shows and can also skew subsequent systematic reviews or meta-analysis.

Lead time bias.	The added total duration of an illness by detecting it at an earlier stage. For example, screening may detect prostate cancer earlier. If patients remain on surveillance the outcomes will not change but five-year survival rates will seem to improve as diagnosis occurred earlier.
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### Confounding

Confounding occurs when the apparent observed association between our exposure and outcome is due to a different, unmeasured, variable. For example, a study may find that higher levels of smoking are associated with an increased risk of liver cancer. However, alcohol consumption may have confounded the association if it were not controlled for, as smoking is associated with higher levels of alcohol consumption, which is known to increase the risk of liver cancer. If we are aware of possible confounding factors, we can try to control for these by matching their frequency in both the intervention and control groups (e.g. similar levels of alcohol consumption in both groups). If we do not have this information at the outset, it may be possible to collect relevant data during the study (e.g. weekly alcohol intake) and control for this in the statistical analysis stage.

### Validity

If you are confident that the results of a study are not affected by any of these sources of error, then you can consider the study to have 'internal validity'. This means that the conclusions reached are likely to be correct for the circumstances of that particular study. This does not necessarily mean that the results can be generalised to other circumstances (external validity). For example, a study conducted to very high standards in the United States may not be directly applicable to the UK due to differences in the two populations or healthcare systems.

When reading a research paper it's good practice to consider these potential sources of error, together with what effect they might have had on the reported results and what steps the study

Where this fits in the RCGP curriculum: 2.04 Enhancing professional knowledge

- Making decisions

Acquire the research and academic skills required of a general practitioner that aid decision making which include a non-judgmental evidence- based approach to problem solving and recognising how individual bias may affect your interpretation

- Clinical management

Have the skills to appraise research findings critically with a working knowledge of statistics

- Managing medical complexity

Apply findings from multi-morbidity research, taking into account limitations in the evidence and the fact that certain groups, e.g. the elderly, are excluded from research trials

- Maintaining performance, learning and teaching

Understand how to critically appraise data. Extrapolate evidence using meta-analysis to individual patient care.

team have taken to protect against them. Never assume that because something has been published it is of high quality, or that the results are reliable. Also remember that there is often bias even in the choice of which papers are published. Developing your own critical appraisal skills, and learning about ways in which evidence can be synthesised (such as systematic reviews and meta-analyses, can help you take an informed approach to applying evidence to clinical practice.