CLINICAL EVIDENCE MADE EASY

This book will help you to understand and appraise clinical research articles and guidelines and assess how they should influence your practice.

Assuming no prior knowledge, Clinical Evidence Made Easy starts by explaining the theory of evidence-based practice, including:
• understanding the hierarchy of evidence
• how to recognize bias
• assessing research papers
• making sense of qualitative research
• making use of clinical guidelines
• what to do with evidence from pharmaceutical companies
• how to apply the evidence in real life.

The book concludes with a section covering clinical evidence at work which:
• provides you with simple appraisal tools that you can use to evaluate research papers and clinical guidance
• uses extracts from original journal articles to show how you can put the appraisal tools and theory into practice.

This book will teach you the essential skills you need to get up to speed with assessing clinical evidence and improving your practice.

From the Foreword by Professor Paul Ewings
(Director of the Research Design Service South West):
“This is a great book for busy clinicians who want to learn how to deliver evidence-based practice and have at their fingertips the tools to make sense of the burgeoning research literature.”
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Chapter 5

Recognizing bias

There can be bias in the design, sampling, data collection, analysis, and publication phases of research. While there are standard techniques that researchers use to minimize the risk of bias, it may be impossible to avoid it completely.

Definition
Bias is a **systematic error** that causes inaccurate research findings.

How easy is this to understand?
Although the concept of bias is not difficult, there is a bewildering range of types of bias, and spotting unacknowledged bias in research papers can be difficult.

How important is it?
When critically appraising a paper, we need to assess to what extent the researchers were able to reduce bias. As it is difficult to eliminate bias completely, even in the most carefully planned of studies, we need to consider how it might have influenced the study’s conclusions.

There are many different types of bias. Here we discuss the most common ones and how researchers try to avoid or reduce them.

Avoiding bias by blinding
Patients who know that they are on an active treatment will be more likely to report an improvement or new symptoms (side-effects
for example) than those who are taking the standard treatment. Researchers avoid this bias by giving a control treatment or placebo to some patients and not telling any of the subjects whether they are on the active treatment or the control. This is called single-blinding.

Knowing whether or not the patient is taking active treatment may also bias the researcher’s observations. He may be convinced that the new treatment is better (or worse) than the control and be more (or less) likely to report improvements. Because of this, where possible there needs to be double-blinding, which means that both the patient and clinician are unaware of which of the trial treatments the patient is receiving (which trial arm the patient is in).

More detail on blinding is given in Chapter 8.

Randomization

Randomly selecting which patient goes into which arm of a trial is a way of avoiding bias. Without randomization, a researcher may, consciously or unconsciously, allocate patients who are more ill to the active treatment arm of a study, for instance.

One way to get comparable groups is to use a deterministic method: allocating alternate patients, or allocation by whether it is an odd or even date. However, the clinician recruiting the participants knows the next treatment and that may influence her in deciding which patient is recruited next.

**EXAMPLE**

A clinician is recruiting participants for a non-randomized trial. She wants a particular patient to have the new treatment, but that patient is due to be allocated to the control. She therefore decides to give it to the patient outside the study.

Randomization is typically carried out by computer, with the allocation concealed until the patient has been recruited.
Selection bias

Also known as sampling bias, this exists where there is bias in choosing the research participants.

EXAMPLE

A research project involves some patients travelling a long way to see the study nurse. This means that patients that are more frail or ill are unable to take part.

This may cause bias because they may respond differently to the treatment being investigated. One way that the investigator could avoid this would be for the nurse to travel to the patient for assessments, rather than the other way round.

Where research involves patients as subjects it can be difficult to eliminate bias completely, because those patients who consent to be in a trial may well differ from those who decline the invitation.

Procedural bias

This is when a research interview or questionnaire is administered in such a way that it may affect the outcome. A questionnaire that is completed when patients are immediately post-op, for example, may generate less useful answers than completion when patients have fully recovered from the after-effects of the anaesthetic.

Information bias

This happens when the accuracy of information collected is not equal between cases and controls. Patients with asbestosis are more likely to have thought about and remembered a history of asbestos exposure than controls without the disease.

Another possibility is measurement error, where there is a systematic difference among the measurements recorded in the different study arms.
EXAMPLE

In a cluster randomized trial (see Chapter 8), hypertensive patients who have been allocated to Treatment A have their blood pressures checked with different sphygmomanometers to those who are having Treatment B. The researchers need to ensure that the equipment is calibrated regularly.

Attrition effect

When patients drop out of studies, this is called attrition. There are many reasons why patients leave studies. For example, patients may leave a study because the treatment made them feel worse, and this means that their data do not contribute to the estimation of the treatment effects. Conversely, subjects may drop out because the treatment has made them feel better and they no longer see the need to continue the study.

As well as causing bias, attrition reduces statistical power (see Chapter 7) by decreasing the sample size.

Researchers need to explain what their attrition rates were. The more patients that were lost to follow-up, the more risk that the attrition has caused bias. We may spot that the rates of loss to follow-up were different in the different arms of the trial, or that there was a difference between the baseline characteristics of participants who were lost to follow-up and those of the patients remaining.

Bias in questionnaires

Non-response bias

This is where, in questionnaire research, respondents differ systematically from non-respondents. Because people who are more interested in a subject are more likely to respond to a survey about it, their responses will not reflect the views of the whole population. It may be that researchers need to make more attempts to contact initial non-responders to try to address this bias.
Response bias

Surveys can have additional potential biases, collectively known as ‘response bias’. Note that this is not the opposite of non-response bias.

Bias may arise from how the whole questionnaire is designed. The layout of a survey can cause confusion or affect the way that questions are answered, or respondents may give up halfway through a survey that is too long.

The way individual questions are constructed can also introduce bias, for example when a leading question unduly favours one response over another.

**EXAMPLE**

In a survey that asks “Are you (a) very satisfied, (b) satisfied or (c) dissatisfied with this treatment?” the mid-point, and therefore default, response is ‘Satisfied’.

Changing the question to “Are you (a) satisfied, (b) neither satisfied nor dissatisfied, or (c) dissatisfied?” is likely to give a less biased response.

Another type of response bias is when people feel that they need to give socially desirable answers or ones that they think will please the researcher: a face-to-face questionnaire about alcohol intake over the previous 24 hours may predispose to answers suggesting a safe level of intake.

Poor statistical analysis

The statistical analysis is central to the paper’s conclusions, but there are many ways in which a poor statistical approach can itself erroneously influence the conclusions. Details of statistical approaches are given in Chapters 6 and 7.

Researchers may favour analyses that support their pre-conceived ideas. We need to watch out for researchers who, in the absence of any significant effect on primary outcomes (i.e. the outcomes which represent the greatest therapeutic importance), write up their results in a way that concentrates on successful secondary outcomes (data used
to evaluate the additional effects of an intervention, for instance side-effects or less important therapeutic effects).

**Publication bias**

Research is less likely to be published if it shows no statistically significant results or is considered by journal editors to be lacking in interest. Also, researchers’ sponsors are less likely to support the publication of results that don’t show them, or their product, in a good light.

Some journals and regulators encourage both the registration and the publication of trial protocols before the studies start so that unfavourable results are not withheld from final publication.

**Conflicts of interest**

This happens when financial or other personal considerations may affect the objectivity of the researcher. A clinician whose funding or status is dependent on a medical charity, for example, may consciously or unconsciously favour results that are attractive to that sponsor. Potential or actual conflicts therefore need to be recognized by the researcher and explicitly disclosed in their publications, so that we can take them into account.

**Watch out for...**

In qualitative research, the investigator is an integral part of the data collection and interpretation process. This means that her own background and beliefs will inevitably affect her interpretation of the data. However, this researcher bias does not mean that this type of study is less ‘valid’ than quantitative research, because qualitative researchers use special techniques to minimize and acknowledge the effect of bias. These are explained in detail in Chapter 12.

Author acknowledgement of bias does not only apply to qualitative papers. If quantitative researchers are aware of bias that they have been unable to control for, they should state this in their ‘Discussion’ or ‘Strengths and weaknesses’ sections. This shouldn’t necessarily make us decide that the findings are invalid, but it does mean that we need to take it into account when appraising the paper.