Answering Clinical Questions

THE UNIVERSITY OF WESTERN AUSTRALIA
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Question of harm / aetiology – Advanced critical appraisal

1. Are the objectives of the study clearly stated?

The main question being addressed should be clearly stated. The question will often be expressed in terms of a simple relationship but may not fit a PICO question. The Title, Abstract, or final paragraph of the Introduction should clearly state the question.

This paper: Yes ☐ No ☐ Unclear ☐

Comments:

Question:

2. Were the patient groups clearly defined and similar in prognosis other than exposure to the treatment or aetiological factor?

Look in 'Patients and Methods' for a description of how the patient sample was selected. A randomised trial is the strongest design for studies of Harm or Aetiology, however it may not always be ethical to do a randomised trial in these types of questions. If it is not feasible or ethical to do a randomised trial, a cohort study may be the best design. Have the characteristics of the different cohorts been well described? Have statistical adjustments been performed for any differences?

This paper: Yes ☐ No ☐ Unclear ☐

Comments:

3. Was follow-up sufficiently complete and was it long enough?

The Methods and Results sections will tell you how follow-up was conducted, and how long participants were followed up for. A flow diagram may show loss to follow up. Would follow up have allowed sufficient time for the harm/outcome of interest to occur? Loss to follow-up may not be random and may be related to either an adverse or a good outcome. The study may have performed a 'sensitivity analysis' to investigate the effects of loss to follow up – the investigators may re-analyse the data assuming that patients lost to follow up all had the outcome of interest. This can help define the consequences of loss to follow-up on the study results.

This paper: Yes ☐ No ☐ Unclear ☐

Comments:

4. Were exposures and outcomes measured in the same way in the different patient groups?

The Methods section should define the outcomes and describe how exposures were assessed. In cohort studies and RCT, description of, and ascertainment of, outcomes is critical. In case-control studies, beware of recall bias (increased chance that cases will carefully examine and recall exposures) and interview bias (probing by interviewer in cases). Was the opportunity for exposure the same in cases and controls or were the groups dissimilar in this way?

This paper: Yes ☐ No ☐ Unclear ☐

Comments:

5. Is the temporal relationship plausible?

Did the exposure to the aetiological agent occur before the outcome/event? Did enough time elapse for the outcome to have plausibly been caused by the exposure?

This paper: Yes ☐ No ☐ Unclear ☐

Comments:

6. Is there evidence of a dose-response?

If the risk of an adverse outcome increases with the duration or dose of exposure, this provides stronger evidence of aetiology.

This paper: Yes ☐ No ☐ Unclear ☐

Comments:

7. Is the biological relationship plausible?

Does an association between the aetiological agent and the outcome make sense biologically?

This paper: Yes ☐ No ☐ Unclear ☐

Comments:

8. Is there evidence of causation from a withdrawal-rechallenge study?

If an outcome resolved on withdrawal of the exposure, and reoccurred on rechallenge, this provides stronger evidence of aetiology

This paper: Yes ☐ No ☐ Unclear ☐

Comments:

9. Was there adjustment for important differences between patient groups?

In a study of aetiology or harm, the clinical characteristics of the groups should be similar at baseline, or statistical adjustments should be made in the analysis for prognostic variables. This is simpler in a randomised controlled trial but more challenging for a cohort study or case-control study. Look in Statistical Methods

This paper: Yes ☐ No ☐ Unclear ☐

Comments:

10. Did the study have a sufficiently large sample size?

Larger samples usually mean more precise results. Look in Statistical Methods for sample size calculations.

This paper: Yes ☐ No ☐ Unclear ☐

Comments:

11. How strong is the association between exposure and outcome (harm, disease)?

Often expressed as a relative risk or odds ratio. Relative risk cannot be used for case-control studies, as the denominator of exposed people per case is unknown. In case-control studies, an odds ratio is used. Modest OR or RR are difficult to interpret from weaker study designs such as case-control or cohort studies, however very high OR or RR can be convincing even when the study design is not randomised. Look in results.

Odds ratio (OR):
The ratio of the odds of disease in an exposed group over the odds of disease in an unexposed group. The ratio will be greater than 1 if the exposure is harmful, less than 1 if the exposure is protective, and equal to 1 if the exposure carries no risk. The odds ratio is used for case-control studies and it is a useful estimate of the risk ratio if the risk of disease in the study population is low (e.g., less than 5%).

Relative risk (RR)
The ratio of risk in an exposed group to risk in an unexposed group. The ratio will be greater than 1 if the exposure is harmful, less than 1 if the exposure is protective, and equal to 1 if the exposure carries no risk.

This paper: Measure of association - _____

Comments:

12. How precise are the estimates of risk?

A 95% confidence interval should be given so that the reader can determine the precision of the result.

This paper: Yes ☐ No ☐

Comments:

13. Are the results discussed in relation to existing knowledge and is the discussion biased?

The discussion should place the results into a clinical context and the authors conclusions should be justified by the study results.

This paper: Yes ☐ No ☐ Unsure ☐

Comments:

14. What level of evidence does this paper give?

Can you assign a level of evidence using the Oxford CEBM Levels of Evidence Hierarchy?

Level of Evidence:

Comments:

15. Were the study patients and their management similar to those in my practice?

Can you generalise the study population to your patient? Does your patient have the same exposure? Do they have the same risk factors for the outcome of interest, other than the exposure?

This paper: Yes ☐ No ☐ Unsure ☐

Comments:

16. Are the results useful in your patient?

What is the magnitude of the risk in your patient? The OR and HR tell us about risk relative to an unexposed group. What is the baseline risk in your patient if he/she is not exposed? How does that change on exposure? Can you calculate a NNH?

Your Patient Expected Event Rate (PEER) without exposure:_____

$$\text{NNH} = \frac{\text{PEER (OR – 1) + 1}}{\text{PEER (OR – 1) x (1 – PEER)}} = \_\_\_\_\_$$

Comments: