Critical appraisal of epidemiological studies

......and other helpful epi tips

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The basic epidemiological study
Bias towards the null

\[ RR = 1.9 \]

Bias away from the null

\[ RR = 0.55 \]

\[ RR = 1.9 \]
General strategy

- Use a systematic approach
- All studies will have strengths and weaknesses
- Look for the key issues for the particular type
- Those aspects done well will be important strengths
- Those aspects done poorly will be important weaknesses
- Try to predict the direction and size of any bias

What to look at

- Research question
- Study type
- Selection
- Measurement
  - Exposure, outcome, confounders
- Confounders
- Analysis
- Generalisability
Research question

— Is it clear?

— What is the study factor?

— What is the outcome factor?

Study type

— What is the study type?

— Is it appropriate for the study question?
Issues and study type

- Some issues will be more specific to, or more relevant to, particular study types
- Some issues will be common to many study types
- Try to work out if important bias is likely
- If it is, try to work out the direction and magnitude (size) of the bias
Selection issues

Selection – RCT and cohort 1

– Are the study groups at the BEGINNING of the study comparable in all relevant ways except the exposure?

– If not, is this likely to have resulted in important selection bias?

– Randomisation process (RCT)
– Selection process (cohort)
**Cohort study - selection of subjects**

- How do those who participated compare to those who didn’t participate? That is, are those who participated representative of those who didn’t participate?
- If not, did this vary between study groups?
- Is this likely to have resulted in important selection bias?
- Random selection?
- Were volunteers called for?
- Other approach?
- Information on (and comparison of) baseline characteristics

**Selection – RCT and cohort 2**

- Are the study groups at the END of the study comparable in all relevant ways except the exposure?
- If not, is this likely to have resulted in important selection bias?
  - Losses and intention to treat (RCT)
  - Losses (cohort)
  - Information on characteristics
  - Information on reasons for loss
  - Comparison of characteristics of final groups
Selection – case control 1

- Study base
- Is the study base well defined?
  - If not, is this likely to have resulted in important selection bias?

- Cases
- Are the cases representative of all cases?
  - all cases, random sample?

- Did all selected cases actually take part?
- If not, is this likely to have resulted in important selection bias?
  › What proportion participated?
  › Characteristics of those that did and didn’t.
  › Reasons for non-participation.
  › Likely effect on results.
Selection – case control 2

- Controls
  - Do the controls come from the same study base as the cases?

- Are the selected controls representative of all controls?
  - all controls, random sample?

- Did all selected controls actually take part?
  - If not, is this likely to have resulted in important selection bias?
    - What proportion participated?
    - Characteristics of those that did and didn't.
    - Reasons for non-participation.
    - Likely effect on results.

Selection – losses 1

- RCT and cohort
  - What proportion dropped out? Is this big enough to practically influence the results?
Selection – losses 1

- RCT and cohort
- What proportion dropped out? Is this big enough to practically influence the results?
- Did those who dropped out differ compared to those who didn’t drop out?
- If so, are these differences relevant (related to the probability of developing the outcome; related to the probability of exposure resulting in the outcome)?
  - Why did they drop out? What are their characteristics?
- If so, is this likely to have resulted in important selection bias?

Selection – losses 2

- Cases
- Did all selected cases actually take part?
- If not, what proportion didn’t? Is this big enough to practically influence the results?
- Did those who didn’t take part differ compared to those who did?
- If so, are these differences relevant (related to the probability of being exposed)?
  - Why did they not take part? What are their characteristics?
- Is this likely to have resulted in important selection bias?
Selection – losses 3

- Controls
- Did all selected controls actually take part?
- If not, what proportion didn’t? Is this big enough to practically influence the results?

- Did those who didn’t take part differ compared to those who did?

- If so, are these differences relevant (related to the probability of being exposed)?
  - Why did they not take part? What are their characteristics?

- Is this likely to have resulted in important selection bias?

Measurement issues
Measurement

– Exposure

– Outcome

– Confounders (and effect modifiers)

Measurement – key principles 1

– Was the measuring done without knowledge of other important study parameters (blinding).
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— Measure using the same person(s)/equipment/approach, or distribute subjects from different study groups equally between the various people/equipment/approaches.

— Use objective, standardised, validated approaches.
Measurement – key principles 1

– Do the measuring without knowledge of other important study parameters (blinding).

– Measure using the same person(s)/equipment/approach, or distribute subjects from different study groups equally between the various people/equipment/approaches.

– Use objective, standardised, validated approaches.

– Train measurers and confirm agreement (inter-rater and intra-rater) and validity (validated in previous studies or a pilot study).

Measurement – key principles 2

– Non-differential mis-classification of exposure or outcome (nearly) ALWAYS biases the measure of effect towards the null.
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– Non-differential mis-classification of exposure or outcome (nearly) ALWAYS biases the measure of effect towards the null.

– Differential mis-classification of exposure (case-control study) or outcome (RCT and cohort study) can bias the measure of effect towards OR away from the null.

– Any mis-classification of confounders can bias the measure of effect towards OR away from the null.
Measurement – key questions

– Is there important measurement error?

– If so, is it likely to be non-differential or differential?
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— If so, is it likely to be non-differential or differential?
  — Different error between study groups will be differential
  — The same error between study groups will be non-differential
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— If so, is it likely to be non-differential or differential?
  — Different error between study groups will be differential
  — The same error between study groups will be non-differential
  — Error before subjects are determined to be in their study groups will be non-differential

— Can have differential and non-differential error of the same parameter
Measurement – key questions

- Is there important measurement error?
- If so, is it likely to be non-differential or differential?
  - Different error between study groups will be differential
  - The same error between study groups will be non-differential
  - Error before subjects are determined to be in their study groups will be non-differential
  - Can have differential and non-differential error of the same parameter
- Which direction is this likely to have biased the estimate of effect (and by how much)?

Measurement – exposure 1

- RCT
  - any error in exposure will be non-differential
Measurement – exposure 1

– RCT
  - any error in exposure will be non-differential

– Cohort
  - any error in exposure will nearly always be non-differential
  - exception can occur if outcome known before exposure is determined (e.g. some retrospective cohort studies)
Measurement – exposure 2

- Case-control
  - error in exposure can be differential (recall bias)

- Cross-sectional
  - error in exposure can be non-differential or differential
Measurement – outcome 1

– RCT
  - error in outcome can be differential

– Cohort
  - error in outcome can be differential
Measurement – outcome 2

- Case-control
  - error in outcome will usually be non-differential
Measurement – outcome 2

- Case-control
  - error in outcome will usually be non-differential
  - exception can occur if exposure known before outcome is determined

- Cross-sectional
  - error in outcome can be non-differential or differential

Measurement – confounders

- Usually same issues as for exposure and outcome
Measurement – confounders

— Usually same issues as for exposure and outcome

— This may vary depending on when information on the confounder is collected.
Confounding

- Have the main potential confounders been considered?
- Have the main potential confounders been controlled?
- If not, is this likely to have resulted in important bias?

Analysis
Analysis

- Were the methods appropriate?

- Have the main potential confounders been controlled?

- (Was a dose-response analysis conducted?)

- Are there confidence intervals or p values?

- Is the power high enough (are the confidence intervals too wide)?

Generalisability
Generalisability

– To what extent is the study population similar (and different) to other relevant populations?

– To what extent is the relationship between exposure and outcome likely to be the same for other populations?
Summary

- Use a systematic approach
- All studies will have strengths and weaknesses
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- Those aspects done poorly will be important weaknesses
- Try to predict the direction and size of any bias