What is confounding .......... and what can we do about it?

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What is confounding?

Association, causes, causal studies, causal graphs

What is a confounder? … and what it isn’t

What can you do to prevent/reduce confounding?
   - by study design
   - by statistical analysis

Some fundamental problems & more difficult issues
Confounding

- One of the most important issues when considering the validity of observational research concerned with causes.

- Examples of causal questions from epidemiology:
  - Does HRT have a causal effect on cardiovascular risk?
  - Is the MMR vaccine a cause of autism?
  - Is (low) birth weight a cause of learning disability?
  - Is shift work a cause of heart disease?

In general: is E a cause of D?

where D is the outcome of interest
E is the factor/exposure under investigation
Confounding

is an attribute of a particular study of the E-D relationship

Definitions:

(i) **Confounding** is due to a lack of comparability between the Exposed and unexposed groups…

   because their disease risks would have been different even if no exposure took place.

(ii) **Confounding** is a situation in which a measure of the effect of an exposure, E, on disease risk is distorted/biased …

   because of the association of E with other factor(s) that influence risk
How big a distortion?

Confounding can

- cause a completely false association
  *in truth*, there is no causal relationship between E and D but there is an association in our data.

- can hide a true causal association
  *in truth*, there is a causal effect but there is no association in the data

- In extreme cases, can produce an association which is *in the opposite direction to the truth*.

But sometimes effects less dramatic: the measured associations are *slightly bigger* (*smaller*) than the true casual relationships.
Where/when should we worry about it?

Confounding is a **causal concept**: if you are not asking a question about cause, then no need to worry.

Therefore classification of your study objective/question is useful:

- Causal study: is E a cause of Y?
- Descriptive study: how does Y vary across areas of the UK?
- Predictive study: can we find a way of predicting Y from a set of variables $X_1, X_2, X_6$?
Relative risk
a measure of association between E=exp & D=disease risk

Suppose E is dichotomous

Relative Risk (RR) = \frac{\text{Risk of D inExposed (E=1)}}{\text{Risk of D in Unexposed(E=0)}}

- RR=1: suggests no effect of E on D
- RR>1 ...............E increases risk
- RR<1 ...............E decreases risk
HRT & cardiovascular disease: what is the true RR?

- Taken from BMJ 2004 (permission to reproduce requested)
The search for confounders....

HRT-CVD relationship:

is socio-economic status (SES) a ‘confounding factor’ in the unadjusted analysis?

- Confounders = factors which are jointly responsible for the distorted measure of the E-D relationship.

- How do we identify confounding factors?

- Adjusted’ analyses: the idea that we can, perhaps, remove the confounding bias by a statistical method.
Causal ‘graphs’
A pictorial method of showing our beliefs about causes…… & helping us to identify confounders

All the following imply **E is a cause of D:**

The last diagram will be used as a shorthand
In what situations will we see an association between E and D in a crude data analysis?

(i) E is a cause of D (see above)

(ii) D is a cause of E

(iii) D and E have at least one cause in common. Here there is one common cause, C:

(iv) We can also have (iii) with (i) or (iii) with (ii)
False association between E and D induced by C – and a solution

- In truth, NO causal relationship between E and D.
- The relationships C→E, C→D together will induce an association between E and D in a crude data analysis.
- C is a confounder in a crude analysis of E-D relationship.
- Solution: to undo/reduce the bias, adjust for C.

Figure 1
False assoc. between E and D induced by relationships, not all of which measured.....

Example: E is alcohol consumption, C = cigarette consumption. F might be a personal trait which tends to influence smoking and alcohol behaviours.

F, the common cause of E and D, is unmeasured.

However: Adjustment for C can undo the confounding.

Adjustment for C is like placing a ‘stopcock’ at C – which breaks the path between E and D.

Figure 2
Conditions (ABC) for a single variable to be treated as a confounder of E-D relationship

A. C must be a cause of D

AND

B. C must be correlated with E in the study dataset.

AND

C. C is **not** caused by E - see below where it is

![Diagram](image)

**Figure 3:** C is not a confounder

eg E = smoking, C = Blood pressure, D = heart disease.
**Joint effect of confounders is what matters**

Suppose we have two variables, \( C_1, C_2 \) which satisfy the confounder conditions.

If the direction of bias (i.e., distortion) for \( C_1 \) alone is opposite in direction to that for \( C_2 \), then the joint bias could, in principle be 0!

**Example** (health study comparing Exp and Unexposed):

<table>
<thead>
<tr>
<th></th>
<th>Exposed</th>
<th>Unexposed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Younger</td>
<td>Older</td>
</tr>
<tr>
<td>SES</td>
<td>Higher</td>
<td>Lower</td>
</tr>
</tbody>
</table>

*This possibility means that we should be cautious about using previous criteria (ABC) to label variables unanimously as confounders .......

Nevertheless these criteria remain useful .....*
More complex causal scenarios……..

Key
- Smoking = Confounder
- Smoking = Mediator
- Smoking = Risk Factor only
- ETS- Environmental tobacco smoke

Thanks to KH for her picture!
The appeal of causal graphs for inferring confounding in complex problems

- Causal graphs* can tell us whether we can remove confounding by adjusting for a given set of variables....
  - no calculation involved!
  - no statistical knowledge needed!

- Graphs may show that adjustment for a subset of variables is enough ...because it blocks the paths of all others
  - .....think of the stopcock analogy

- * assuming graph is correct
Dealing with confounding: statistical methods of adjustment

For measured variables $C_1, C_2$ etc

- Via regression models
- Via stratification
- Via propensity scores

For unmeasured confounders

- Instrumental variable (IV) methods: main issue here is whether we can identify a suitable IV....
Recall:

**confounding** is a lack of comparability between the Exposed and unexposed groups…

*because their disease risks would have been different even if no exposure took place.*

- Statistical methods try to deal with consequences -retrospectively

- Can we achieve comparability by study design?

- **Meaning of group comparability** : the groups would have the same outcome – on average- if no exposure took place.
The idea is to find E and not-E groups that are ‘comparable’

- **Randomisation:** randomly allocate individuals to E and not-E gps.

- **Restriction.** restrict study to subjects with a particular value of C. e.g. restrict study to women.

- **Matching.** for each E individual, find a not-E with same C.
Some fundamental problems

- **Unmeasured confounders** in observational studies:
  
  *just because we don’t know about them, doesn’t mean they don’t exist!*

  *(Only in randomised studies, can we feel more secure).*

- **Measurement error** in confounders:

  *Imprecise measurement of C means inadequate adjustment: there will still be ‘residual confounding’ by C*

- A decision to treat C as a confounder of an E-D relationship .......... *(correctly) depends on making causal assumptions about C!*
There is no foolproof statistical ‘test’ for confounding: we should be guided by external knowledge and data, not data alone.

It is possible to create confounding by adjusting for the wrong thing.

Time dept confounding: standard statistical approaches for dealing with confounders are invalid & special methods needed!

*If your Es and Cs change over time, & you have a longitudinal study, you need to consider this possibility*
Some references


Also see
http://www.population-health.manchester.ac.uk/biostatistics/research/causalgroup/
A (hypo) causal graph for HRT/CVD relationship

- SES
- Education/knowledge
- Healthiness
- Use of HRT
- CVD
Why do X and Y show an association in a crude data analysis?

3 reasons:

(i) X is a cause of Y

(ii) Y is a cause of X:

(iii) X and Y have at least one cause in common. Here there is one common cause, Z:
Association vs causation

**Association**: a statistical term referring to observed data: it does not carry any causal meaning.

(Measures of association: correlation coefficients, mean differences, RR, etc)

Example:

**RR** measured from study data = **RR**\textsubscript{observed}, say

If **RR**\textsubscript{observed} $\neq$ 1, there is an association between E & D.

**Confounding**: **RR**\textsubscript{observed} $\neq$ **RR**\textsubscript{true}