Marginal Structural Models

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Plan

Part 1. Marginal Structural Models - Steve Cole

A. Motivation by causal diagram
B. Simple example with potential outcomes

Part 2. A Case Study in Marginal Structural Cox Models - Daniel Westreich

(I will place key references, or remarks, here.)

G-methods

- G-formula, nonparametric/parametric
  - Parametric fit using Monte Carlo methods
  - Robins JM J Chronic Dis 1987; 40: 139S
  - Taubman SI, et al IJE 2009; In press
- Structural nested models, semiparametric
  - Fit by G-estimation
  - Robins JM Encyclopedia of Biostatistics 1998
- Marginal structural models, semiparametric
  - Fit using inverse probability weights
  - Robins JM et al EPID 2000; 11: 550

Let's place marginal structural models in some context

Part 1A: Motivation

A Review of Pearl's Causal Diagrams

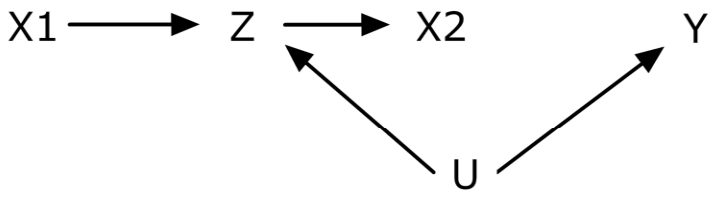
1. Nodes represent measured or unmeasured variables, including random error terms. (Random error terms are often omitted from causal diagrams.)
2. Nodes are placed in a box "□" when that variable is "conditioned" on. Conditioning occurs by restriction, stratification or regression.
3. Arrows represent direct causal effects in the study population. All arrows are solid, single headed. Arrows average over causal response types, and we assume (i.e., faithfulness) that there is no perfect cancelation of causation and protection for an arrow absent from a diagram.
4. Causal diagrams are acyclic; when cycles are needed because of feedback between variables over time we represent this by indexing the variables by time.
5. A path is a set of 2+ connected nodes. Paths represent associations, and do not respect arrowheads. Directed paths represent causal effects, and do respect arrowheads. Directed paths through intermediate nodes are indirect causal effects.
6. A path is closed at a colliding node "→Z←" on that path, otherwise the path is open.
7. An open path is closed at a conditioned node "□". (Partial closure is obtained by conditioning on a consequence of said node.)
8. Conditioning on a colliding node (or a descendent of a colliding node) opens that path.
9. For a diagram to be "causal" it must include exposure, outcome, and all common causes of any two or more variables on the diagram.

See Appendix of Hernán MA, et al AJE 2002; 155: 176

Some Notation

- X1 is exposure at time 1
  - eg use of anti-HIV drugs
- X2 is exposure at time 2
- Z is a covariate measured between times 1 and 2
  - eg HIV molecules detected in serum
- Y is an outcome measured after time 2
  - eg CD4 cell count/(mm^3 × 100), so 2.5 is 250 cells/mm^3
- U is an unmeasured common cause of Z and Y
  - eg immune function
- Uppercase letters are random variables, lowercase are possible values

Can We Estimate the X1,X2 Effect on Y?



- If we estimate the association of X1,X2 with Y without conditioning on Z, then there is confounding of the X2 component by Z-U
- If we estimate the association of X1,X2 with Y with conditioning on Z, then there is selection bias for the X1 component through Z-U

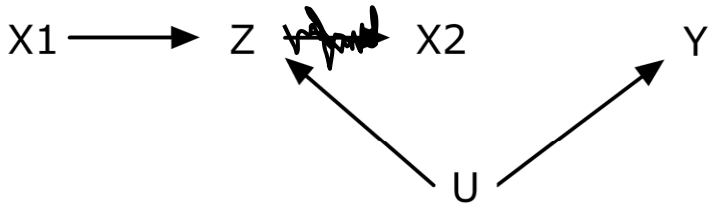
Damned if we do; damned if we don't

See Robins JM. J Chronic Dis 1987; 40: 139S

Caveats

1. Could estimate the separate individual effects of X1 and X2, but as the number of exposures grow (eg, X3-X9) we need to summarize exposure (eg, pack-years, other examples?)
2. Could estimate the "immediate" effect of X2 on Y conditioning on Z, but usually will also need to condition on X1 (ie, exposure history)
3. Does Z lie on a causal (ie, directed) path from X1,X2 to Y?
4. Others?

A Solution, Conceptually



- If we estimate the association of X1,X2 with Y without conditioning on Z, then there is **NO** confounding of the X2 component by Z-U
- If we estimate the association of X1,X2 with Y with conditioning on Z, then there is selection bias for the X1 component through Z-U

This is exactly what marginal structural models accomplish!

See Robins JM et al. EPID 2000; 11: 550

Conclusions, part 1A

Standard methods do not provide consistent estimates of causal effects when:

1. we have a time-varying exposure, and
2. one or more time-varying confounders, which
3. are affected by prior exposure.

A conceptual solution is to "excise" all arrows from (measured) confounders into subsequent exposures; next we will see that marginal structural models enact this conceptual solution

Part 1B: Example

Slides to come at SPER…