Estimating Treatment Effects

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One-day Course on Target Trial Emulation

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Overview

In this talk, we will discuss:

- Estimands of interest in TTE
- How to estimate these via g-methods.

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- Estimands of interest in TTE
- How to estimate these via g-methods.

We will consider two scenarios:

- single-point (“time-fixed”) exposure/treatment
- time-varying treatment.

Scenario A

Suppose we have a single treatment A, outcome Y, confounder L and unmeasured confounder U.

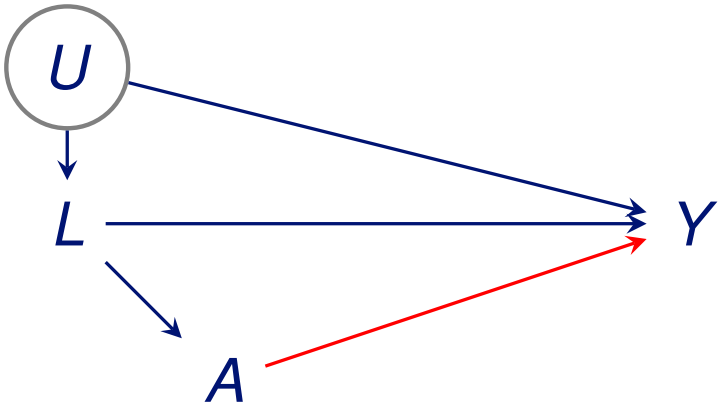

Figure: Directed Acyclic Graph (DAG) of a typical scenario for a time-fixed exposure.

Scenario B

Now suppose we have a time varying treatment $A = (A_1, A_2)$, outcome Y, unmeasured confounder U and time-varying confounder $L = (L_1, L_2)$.

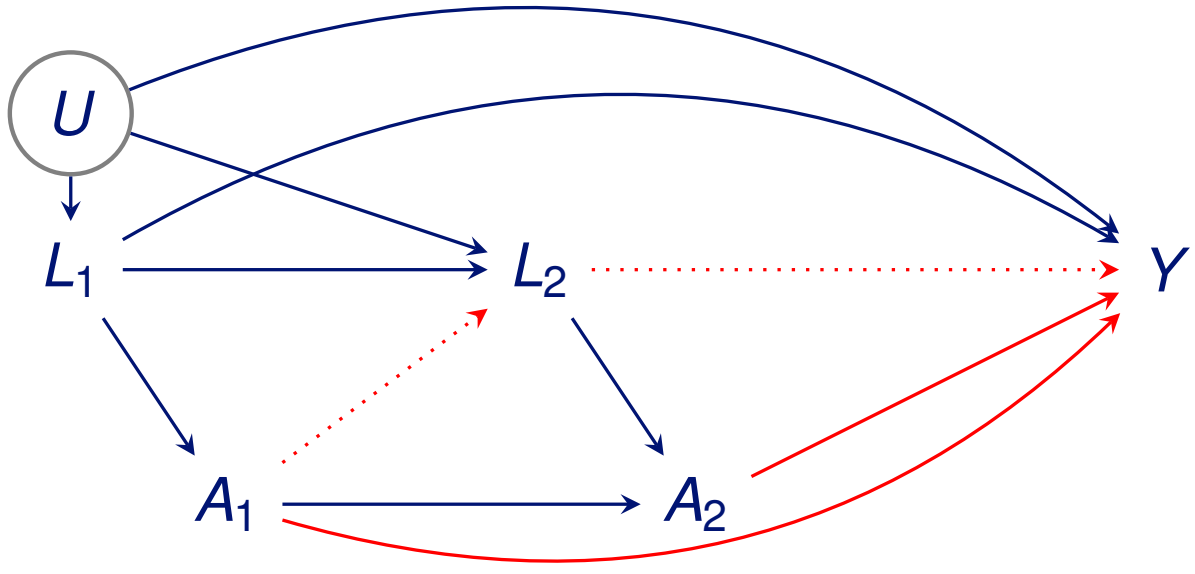

Figure: Directed Acyclic Graph (DAG) of a typical scenario for a time-varying exposure.

Comment

- The first scenario is simple: we can read the DAG and identify L as the variable needed to be controlled for in order to estimate the causal effect of A on Y (red line).
- The second scenario is more complex, primarily because of L_2. Controlling for L_2 (which is a confounder for the A_2–Y relationship) would block the effect of A_1 on Y that involves L_2 (dotted red lines).
- Furthermore, L_2 is a collider on the path from U to A_1, and conditioning on it would open a new confounding path from A_1 to L (A_1–L_2–U–Y).

Counterfactual Outcomes

Time-fixed exposures

As discussed this morning, we translate causal questions into targets of estimation by invoking the concept of potential outcomes (POs).

- We define $Y(a)$ as the value of the outcome if an individual were given treatment $A = a$.
- For individuals who did receive the treatment, $Y(1)$ is observed (under the consistency assumption discussed this morning)
- For individuals who did not receive the treatment, $Y(0)$ is observed.
- For each group the outcome under the alternative treatment is counterfactual.

Counterfactual Outcomes

Time-varying exposures

- With time-varying exposures, *e.g.* with two treatment periods, the POs becomes:
  - $Y(1,1)$
  - $Y(1,0)$
  - $Y(0,1)$
  - $Y(0,0)$
- As before, only those with the actual combination of treatments have their corresponding PO observed, while the other three are counterfactual.

Estimands

Many investigations concern hypothetical questions of the type: *How would the outcome differ if the exposure/treatment was given to everyone in the population versus none?*

This type of questions can be translated into comparisons of mean POs, as in the **Average Treatment Effect** (ATE):

- For a time-fixed exposure (scenario A):

$$\text{ATE}_{tf} = E[Y(1)] - E[Y(0)]$$

- For a time-varying exposure (scenario B):

$$\text{ATE}_{tv} = E[Y(1,\ldots,1)] - E[Y(0,\ldots,0)]$$

More Targeted Estimands

In TTE we often focus on other estimands when treatment is for time-varying.
When the focus is on:

Public health policies:

What would be the comparative effect of introducing (versus not introducing) a certain treatment regime on a particular health outcome?

→ Intention-to-treat (ITT) effect would address this

Effectiveness:

What would be the comparative effect of introducing (versus not introducing) a certain treatment among those who would adhere to the assigned treatment?

→ Per-protocol (PP) effect would address this

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ITT *vs.* PP Effects

- ITT ignores any treatment switching/drop-out:
  - This means it does not estimate the causal effect of treatment received but only of treatment assignment.
  - It also represents the “real world” (public health intervention) effect of treatment, accounting for people not always strictly following treatment.
- Per protocol asks a more strict causal question.
  - That is to say what is the effect of treatment provided that people strictly adhere to it from randomisation/initiation.

Assumptions for Identification

In TTE, the most commonly invoked assumptions to identify these estimands are:

1. Counterfactual Consistency.
2. Conditional Exchangeability.
3. Positivity.

I will go through all three in detail.

Consistency

- The Consistency assumptions states that a persons observed outcome is the same as their potential outcome under the observed treatment

$$Y^{obs} = Y(a) \text{ if } a = A \text{ for } Y^{obs}.$$

- The assumption amounts to having a well defined treatment, specifically one that can be administered in multiple different ways but that will still lead to the same PO.
- In other words, that different administrations do not affect the potential outcome.
- It would not be met if for example the same treatment administered orally or through an IV drip would lead to different outcomes.

Conditional Exchangeability

- This posits that an individuals counterfactual outcome is independent of actual exposure, given all confounders.

$$Y(a) \perp\!\!\!\perp A|L$$

- This is often called the “no unmeasured confounders” assumption.
- What it essentially means is that we can treat observed mean outcome of untreated individuals that share the same confounder values of treated individuals to represent the mean counterfactual outcome under no exposure for the treated:

$$[Y^{obs}_{Untreated}] \equiv E[Y(0)|A = 1].$$

Conditional Exchangeability

- This would be automatic if the treated and untreated were clones of each other ("exchangeable").
- This is exactly what randomization does in RCTs.
- With observational data we need to control (balance) for all relevant confounders.
- This is what g-methods attempt to do, for every stratum defined by the confounders:

	A=1	A=0
Treated	$Y^{obs}_{Treated} = Y(1)$	$Y(0)$
Untreated	$Y(1)$	$Y^{obs}_{Untreated} = Y(0)$

Positivity

- Positivity is invoked by estimation methods that use the propensity score (see “Estimation”).
- It means that all individuals in the target population have a non-zero chance of being assigned any treatment regardless of their characteristics.

$$P(A = a|L) > 0 \; \forall a$$

- In a well designed RCT, this automatically holds.
- This is sensible intuitively. In general, we cannot consider the outcome of the treated, had they been untreated, if they never could have been untreated.

G-methods

The three g-methods are broadly speaking

1. Inverse Probability of Treatment weighting (IPTW) of Marginal Structural Models (MSMs).
2. G-computation.
3. G-estimation of Marginal Structural Mean Models (MSMMs).