Estimands

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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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We will consider two scenarios:

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

B- time-varying treatment.

Scenario A

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

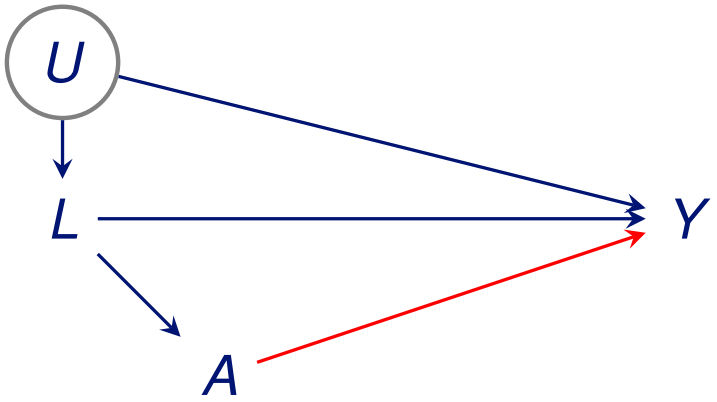


Figure: Directed Acyclic Graph (DAG) of a typical scenario for a time-fixed exposure.

Scenario B

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

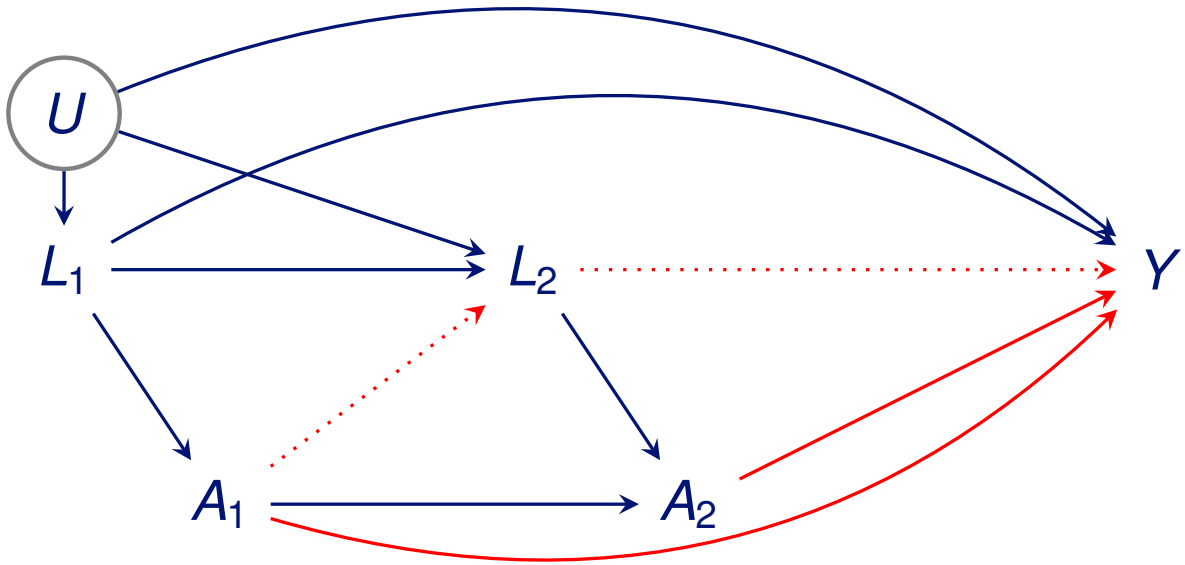
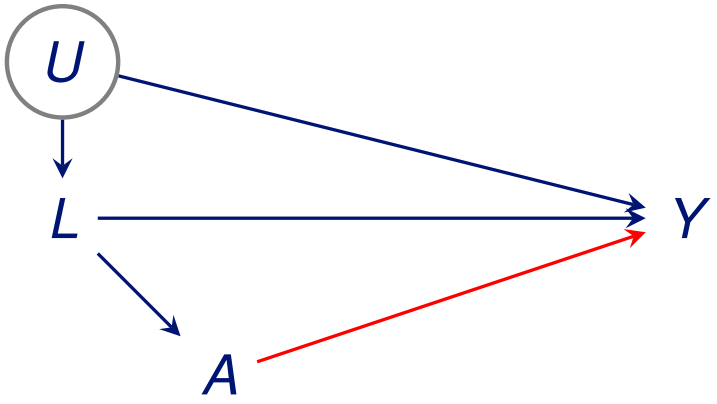


Figure: Directed Acyclic Graph (DAG) of a typical scenario for a time-varying exposure.

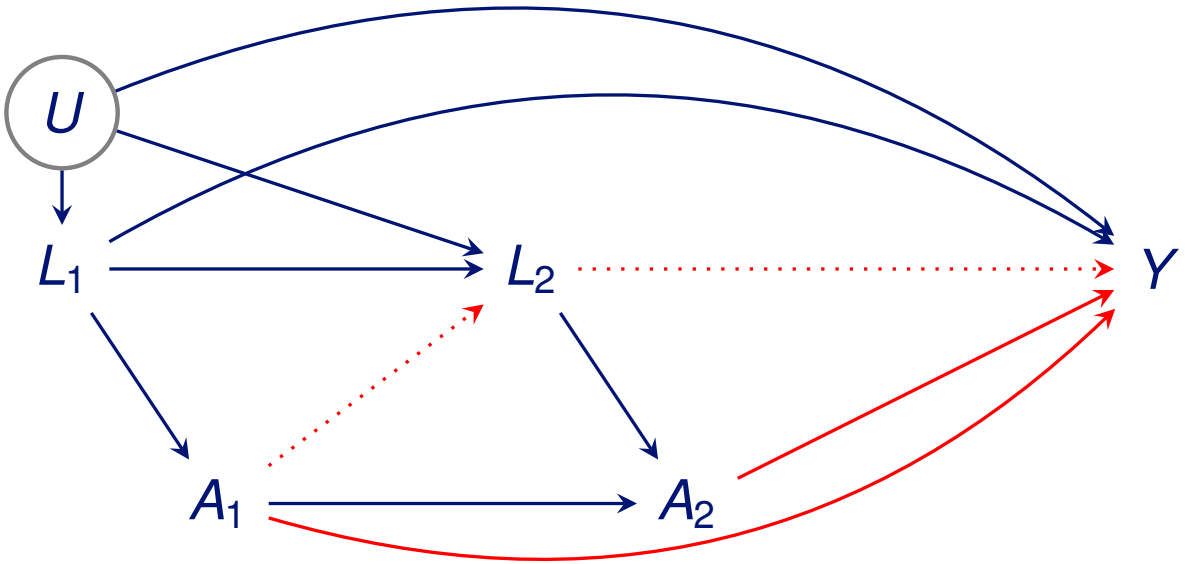
Comments

- 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).



Comments

- 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).

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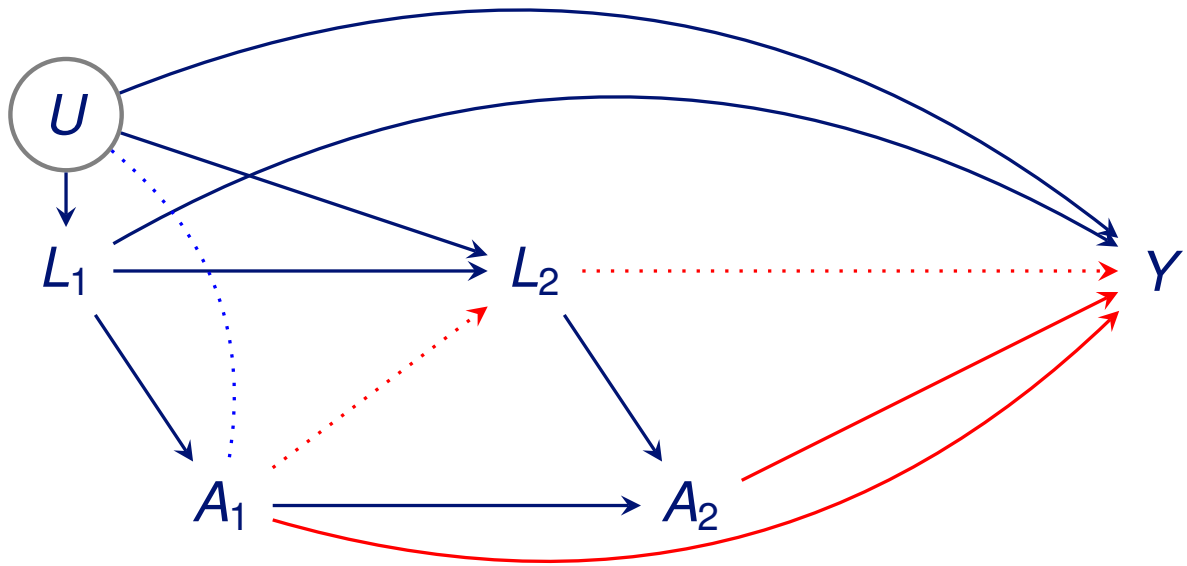

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Counterfactual Outcomes

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

- Let Y^a represent the value of the outcome under a hypothetical intervention that sets $A = a$:
  - Under the consistency assumption, for those treated, Y^1 is observed but Y^0 is not.
  - The reverse applies to those not treated.
- With two treatment periods the POs are: $Y^{1,1}$, $Y^{1,0}$, $Y^{0,1}$, $Y^{0,0}$.
  - Only those with the actual combination of treatments have their corresponding PO observed, while the other three are counterfactual.

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Questions and Estimands

Q: How would the outcome differ if treatment were given to everyone versus none?

- Using POs, we can expressed this question as a comparisons of mean POs:
  - Average Treatment Effect:

$$\text{ATE} = E[Y^1] - E[Y^0]$$

  - Risk Ratio:

$$\text{RR} = E[Y^1]/E[Y^0]$$

  - Average treatment in the treated:

$$\text{ATT} = E[Y^1|A = 1] - E[Y^0|A = 1]$$

Questions and Estimands in RCTs

Q: What is the effect of treatment assignment?

- The intention-to-treat (ITT) effect:

$$\text{ITT} = E[Y(Z = 1)] - E[Y(Z = 0)]$$

where Z represents randomization to treatment.

Q: What is the effect of sustained treatment?

- The per-protocol (PP) effect:

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

Questions and Estimands in Obs. Studies

- Similar estimands are targeted in TTE:
  - They are not identical given the observational nature of treatment assignment.
  - For this reason they are called "observational-analog".
- Interpretation:
  - Obs-analog ITT:
    What would be the effect of a policy that assigns a certain treatment regime to all?
  - Obs-analog PP:
    What would be the effect of that policy if all adhered to it?

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Assumptions for Identification

The most commonly invoked assumptions to identify these estimands from observational studies are:

1. Counterfactual Consistency
2. Conditional Exchangeability
3. Positivity

These were discussed by Michalis this morning (details in Appendix).

Assumptions: Motivation

For a time fixed exposure, with baseline confounder L_0:

- If individuals are conditionally exchangeable within strata of L_0, we can focus on each stratum:

$$\text{ATE}_{l_0} = E\left(Y^1 | L_0 = l_0\right) - E\left(Y^0 | L_0 = l_0\right)$$

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$E\left(Y^a | L_0 = l_0\right)$ can be replaced by $E\left(Y^a | A = a, L_0 = l_0\right)$, for $a = 0, 1$.

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Hence the stratum-specific causal effect is identified by:

$$\text{ATE}_{l_0} = E\left(Y \mid A = 1, L_0 = l_0\right) - E\left(Y \mid A = 0, L_0 = l_0\right).$$

Marginal vs. conditional effects
ATE

- ATE_{l_0} are conditional causal effects but we may be interested in the population average causal effect ATE.

- For a categorical L_0,

$$\text{ATE} = \sum_{l_0} \text{ATE}_{l_0} \Pr(L_0 = l_0)$$

i.e. ATE is found by standardisation of the conditional effects.

- This is an example of g-computation for the setting with a time-fixed exposure.

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Daniel will now give an overview of estimation methods.

Appendix

Consistency

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

$$Y(a) = Y \text{ for those with} a = A.$$

- 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:

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

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.