Introduction to proximal causal inference

Non-parametric and parametric methods

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Known but unmeasured confounder

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How to survive in the presence of known unmeasured confounders?

Proximal causal inference helps! ... but where does it come from?

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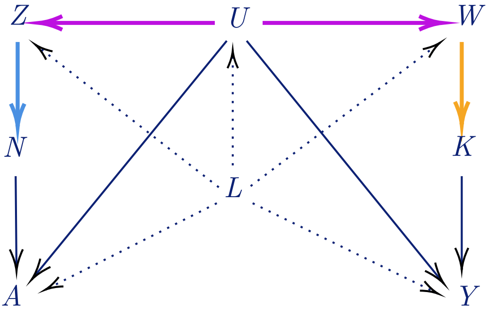
Let's first take a glance and then see how it's formulated...

First glance at proximal causal inference

Proximal causal inference strategy is dedicated to deal with such situation: a (set of) KU- (known but unmeasured) confounder(s).

ATE can be point-identified upon considering a treatment-side proxy Z and an outcome-side proxy W, with additional assumptions.



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- Instrument variable?
- Negative (population/outcome) control?
- Front door formula (causal mediation)?
- ...

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- **NOT** considering the “known” information for a KU-confounder; and are
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- altering the underlying population (*e.g.* monotonicity assumptions in NC/IV methods)

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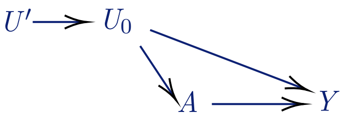
- altering the underlying population (*e.g.* monotonicity assumptions in NC/IV methods)

We therefore want another approach that integrates available information of "the known part" and does not add strong restrictions / strict assumptions that we don't believe either.

Proxy-based thinking

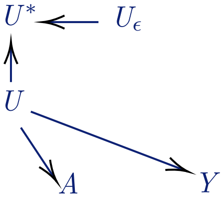
- When data for a confounder U_0 is not available, a natural alternative is to consider one measured proxy [2] of it, U';
- Intuitively, if $U' \propto U_0$ and U' is strictly only associated with U_0, the average treatment effect (ATE) can be point identified without additional assumptions.

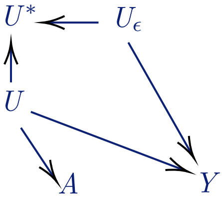


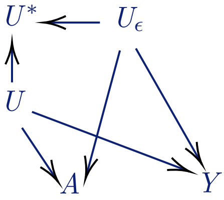
Proxy-based thinking

- However, we can never have a perfect proxy, otherwise it's equivalent to know everything about U_0.
- The actual proxies come with noises and lose information carried by the targeted confounder;
- Without additional **assumptions** a proxy may only mitigate but never eliminate bias [3];
- Error generating mechanism from targeted confounder to proxy is extremely important [2], *e.g.* coarsening, mismeasurement, etc.

Mismeasured variable as proxies

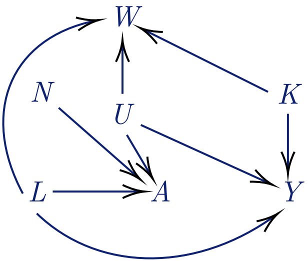


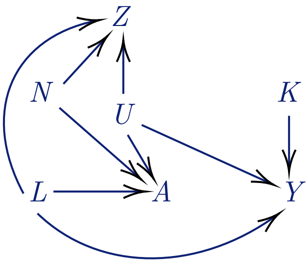




Approaching proxy-based inference (I)

- Negative control (NC) exposure (NC/e) and NC outcome (NC/o) are two most used proxy-based strategies.
- NC/o requires a proxy W that is U-comparable to Y but not caused by A or sharing a common cause [4];
- NC/e requires a proxy Z that is U-comparable to A but not causing Y or sharing a common cause [4].





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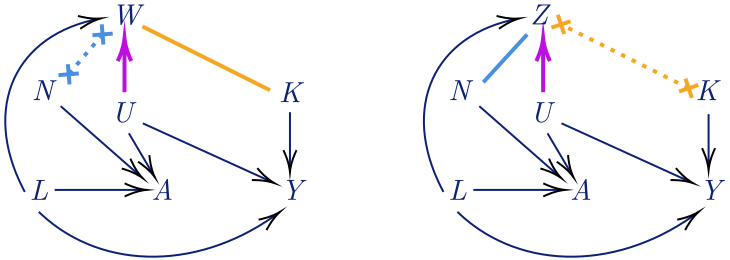

Left: NC/o proxy; proxy W is similar enough to Y, except that it is not caused by A or share common causes;

Right: NC/e proxy; proxy Z is similar enough to A, except that it cannot cause Y or share common causes.

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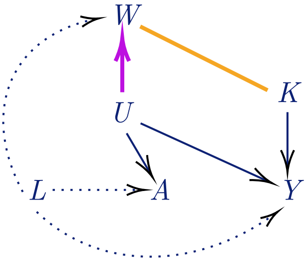
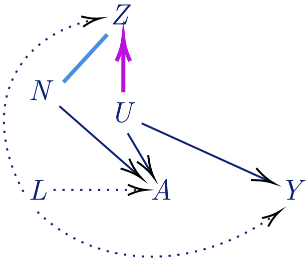


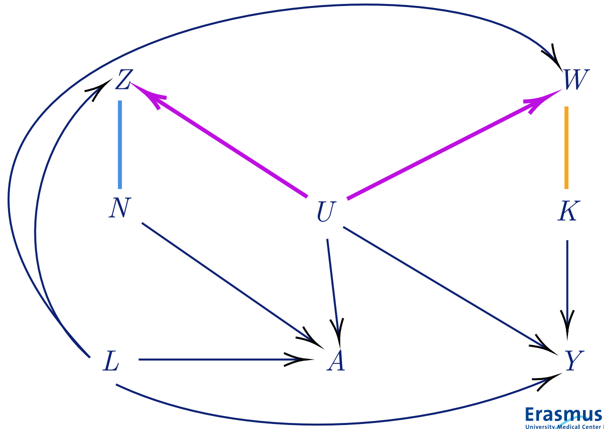


Left: NC/o proxy; proxy W is a child of U, and is (only) d-connected with Y;

Right: NC/e proxy; proxy Z is a child of U, and is (only) d-connected with A.

Approaching proxy-based inference (II)

Upon combining both the NC/o- and NC/e-proxies, we get...



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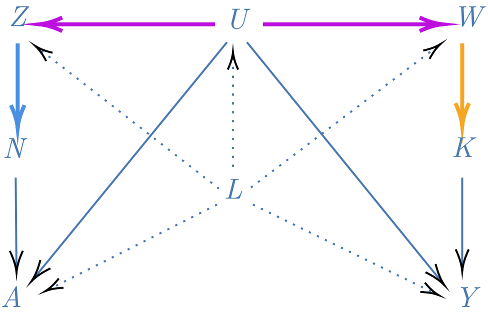

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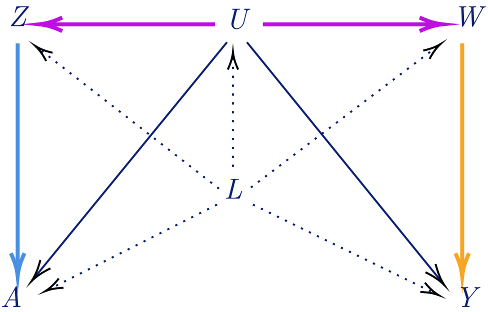


Nonparametric Identification (I)

Given observed individual level data with a binary treatment
$\mathcal{O}_i = \langle Y_i, A_i, \boldsymbol{L}_i, Z_i, W_i \rangle$,
an ATE $\psi = \mathbb{E}[Y^{a=1} - Y^{a=0}]$ is nonparametrically identified **without** the presence of U, if standard identifiability conditions **A1** through **A3** hold:

- **A1** Consistency: $Y_i^a = Y_i \;\; \forall a, \;\; a.s.$
- **A2** Treatment positivity over $\langle \boldsymbol{L}, Z, W \rangle$:
  $\Pr[A = a | \boldsymbol{L}, Z, W] > 0 \;\; \forall a, \;\; a.s.$
- **A3** Exchangeability over $\langle \boldsymbol{L}, Z, W \rangle$: $Y^a \perp\!\!\!\perp A | (\boldsymbol{L}, Z, W) \;\; \forall a$

Nonparametric Identification (I)

With KU-confounders $\boldsymbol{U}_i$, **A3** does not hold, and ATE cannot be identified given $\mathcal{O}_i$ and **A1**-**2**.

Proximal causal inference nonparametrically identifies ATE if additional conditions hold [1]:

- **A4** Independence of Y and Z: $Z \perp\!\!\!\perp Y|(A, \boldsymbol{U}, \boldsymbol{L})$
- **A5** Independence of W and A, W and Z: $W \perp\!\!\!\perp (Z, A)|(\boldsymbol{U}, \boldsymbol{L})$
- **A6** Exchangeability over $\langle \boldsymbol{L}, \boldsymbol{U} \rangle$: $Y^a \perp\!\!\!\perp A|(\boldsymbol{U}, \boldsymbol{L}) \ \ \forall a$
- **A7** Treatment positivity over $\langle \boldsymbol{L}, \boldsymbol{U} \rangle$: $\Pr[A = a|\boldsymbol{L}, \boldsymbol{U}] > 0 \ \forall a, \ \ a.s.$
- **A8** Statistical completeness for $\boldsymbol{U}$ given Z: $\mathbb{E}[g(\boldsymbol{U})|Z, A = a, \boldsymbol{L} = \boldsymbol{l}] = 0 \ a.s. \Leftrightarrow g(\boldsymbol{U}) = 0, \ \forall \ a, \boldsymbol{l}, $ and a square-integrable function g

G-formula (II)

Suppose there exists an function $h = h(w, a, l)$ that solves the equation *a.s.*:

$$\mathbb{E}[Y|A, Z, L] = \int h(w, A, L)\,\mathrm{d}F(w|A, Z, L)$$

then if **A1-2, A4-8** holds, ATE is nonparamentrically identified by: (outcome-side proximal g-formula)

$$\psi = \int_{\mathcal{L}} \int \Big[h(w, a = 1, l) - h(w, a = 0, l)\Big]\,\mathrm{d}F(w|l)\,\mathrm{d}F(l)$$

G-methods are all compatible and can be used for estimation.

G-formula (II)

Assumption **A9** suffices for the existence of such a "bridge" function $h = h(w, a, l)$:

A9 Statistical completeness for Z given W:
$\mathbb{E}[g(Z)|W, A = a, L = l] = 0 \ a.s. \Leftrightarrow g(Z) = 0, \ \forall \ a, l,$ and a square-integrable function g

G-formula (II)

Note: There are alternatives to completeness assumptions **A9** and/or **A8** upon considering different "flows of information" and starting points [5].

With $U|W$ completeness (alternative to **A8**) and $W|Z$ completeness (alternative to **A9**), a treatment bridge function $q = q(z, a, l)$ is valid, and ATE is identified by:
(treatment-side proximal g-formula)

$$\psi = \int_{\mathcal{L}} \int (-1)^{1-a} q(z, a, l) y \, \mathrm{d}F(y, z, a|l) \, \mathrm{d}F(l)$$

Parametric assumptions

Two-stage least squares (2SLS) are implemented the most for parametric estimation of an ATE via proximal causal inference approach.

Given that assumptions **A1, A4-6** hold, and that no structural violation of treatment positivity over $\langle \boldsymbol{L}, \boldsymbol{U} \rangle$, with additional parametric assumptions:

P1 $\mathbb{E}[Y^a | A, Z, L, U] = \beta_0 + \beta_a A + \beta_l L + \beta_u U$;

P2 $\mathbb{E}[W | A, Z, L, U] = \alpha_0 + \alpha_l L + \alpha_u U$

Parametric estimation

P1 and **P2** can be rewritten as:

$$\begin{aligned}
\mathbb{E}[Y^a|A,Z,L,U] &= \beta_0 + \beta_a A + \beta_l L + \beta_u U \Rightarrow \\
\mathbb{E}[Y^a|A,Z,L] &= \beta_0 + \beta_a A + \beta_l L + \beta_u \,\mathbb{E}[U|A,Z,L]; \\
\mathbb{E}[W|A,Z,L] &= \alpha_0 + \alpha_u \,\mathbb{E}[U|A,Z,L] + \alpha_l L \Rightarrow \\
\mathbb{E}[U|A,Z,L] &= -\alpha_u^{-1}\alpha_0 - \alpha_u^{-1}\alpha_l L + \alpha_u^{-1}\,\mathbb{E}[W|A,Z,L]; \\
&\Rightarrow \\
\mathbb{E}[Y^a|A,Z,L] &= (\beta_0 - \beta_u\alpha_u^{-1}\alpha_0) + \beta_a A + (\beta_l - \beta_u\alpha_u^{-1}\alpha_l)L \\
&\quad + \beta_u\alpha_u^{-1}\,\mathbb{E}[W|A,Z,L] \\
&= \beta_0^* + \beta_a^* A + \beta_u^*\,\mathbb{E}[\hat{W}|A,Z,L] + \beta_l^* L
\end{aligned}$$

Parametric estimation

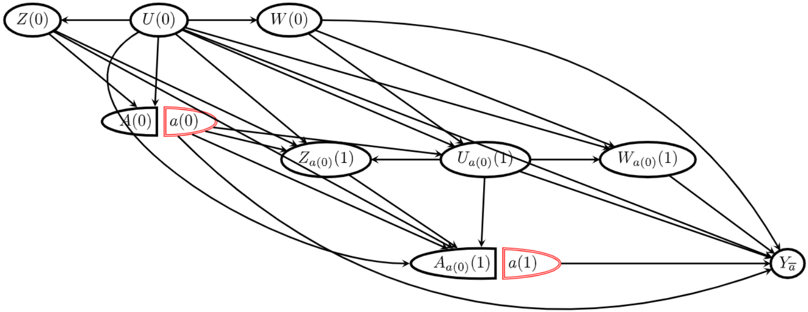
An ATE is then parametrically identifiable through a 2SLS approach [6], estimated by the coefficient β_a^* in a 2SLS regression:

$$\mathbb{E}[Y^a|A, Z, L, \hat{W}; \beta] = \beta_0^* + \beta_a^* A + \beta_u^* \mathbb{E}[\hat{W}|A, Z, L] + \beta_l^* L$$
$$\mathbb{E}[W|A, Z, L; \alpha] = \alpha_0^* + \alpha_a^* A + \alpha_z^* Z + \alpha_l^* L + \epsilon_w$$

Note: Statistical and modelling constraints/assumptions (*e.g.* distribution; the existence of MGF for error term, etc.) apply for different types of Y and W. This approach can be generalized in the presence of effect measure modification [7].

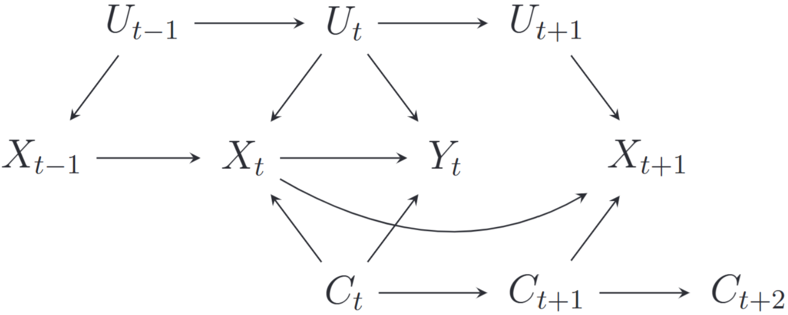
Time-varying settings

Sequential proxies can be used in a time-varying setting to allow that sequential exchangeability assumption over L not hold [7]:



Time-varying settings

Future exposures and past outcomes can serve as valid proxies [8]:



Closing and take-home message

1. PCI deals with **KU**-confounders.
2. PCI has its root in **measurement error**-based thinking and **proxy**-based approaches.
3. PCI combines **negative control** outcome and exposure proxy.
4. PCI makes the use of the residual information carried by measured proxies around the unmeasured things.
5. Nonparametric estimation of ATE via PCI is flexible and requires additional statistical assumptions (completeness); 2SLS can be used for parametric estimation.
6. Finding valid proxies is challenging. Mismeasured versions, future exposures, and past outcomes can sometimes serve as proxies.

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Thanks!