# Modelos gráficos causales: introducción y algunos de nuestros resultados recientes sobre reglas gráficas sobre ajustes eficientes 

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> Based on

Rotnitzky and Smucler, 2020, Journal of Machine Learning Research, 21 188: 1-86,
Smucler, Sapienza and Rotnitzky, 2021, Biometrika, 109, 1, 49-65.
Smucler and Rotnitzky, 2022. Journal of Causal Inference, 10, 1, 174-189
Guo, Perkovic and Rotnitzky, 2022, https://arxiv.org/abs/2202.11994

Academia Nacional de Ciencias Economicas, 6 de Septiembre, 2022

## Causality in the 21st century

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- mediation analysis (origin in psychology and sociology),
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- mediation analysis (origin in psychology and sociology),
- instrumental variables (origin in economics and genetics), and
- marginal structural models (origin in epidemiology and biostatistics).
- "Causal revolution" in great part due to the emergence and adoption of two formalisms:
- Counterfactual Models
- Graphical Models


## Graphical Models

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## Graphical Models

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- Simple graphical rules exist to explain the potential biases of one's preferred estimation procedure and the possible remedial approaches.
- No graphical rules existed to explain efficiency (variance) in estimation
- In this talk: review graphical models and its use for understanding biases and summarize some of our own work towards filling this gap


## An adjustment set



## Another adjustment set



## Road map of the talk

- Gentle introduction to causal graphical models.
- Definition and properties
- Some examples of their use for detecting potential sources of bias
- Some of our results on efficient adjustment sets
- Rules for comparing adjustment sets for point exposure studies
- Summary of other results
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## Causal Graphical Models in a nutshell



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$$
\begin{aligned}
& V_{1}=f_{1}\left(\varepsilon_{1}\right) \\
& V_{2}=f_{2}\left(\varepsilon_{2}\right) \\
& V_{3}=f_{3}\left(\varepsilon_{3}\right) \\
& V_{4}=f_{4}\left(\varepsilon_{4}\right) \\
& V_{5}=f_{5}\left(V_{1}, \varepsilon_{5}\right) \\
& \vdots \\
& V_{11}=f_{11}\left(V_{5}, V_{7}, \varepsilon_{11}\right) \\
& V_{12}=f_{12}\left(V_{11}, V_{4}, \varepsilon_{12}\right) \\
& V_{13}=f_{13}\left(V_{8}, V_{10}, V_{12}, \varepsilon_{13}\right) \\
& \\
& \varepsilon_{1}, \ldots, \varepsilon_{13} \text { omitted } \\
& \text { non- common causes }
\end{aligned}
$$

## Causal Graphical Models in a nutshell



No omitted common cause assumption formalized as: the $\varepsilon_{j}^{\prime} s$ are mutually independent (Pearl, 1995)

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## Causal Graphical Models in a nutshell



- Graphical model with independent $\varepsilon_{j}^{\prime} s$ is tantamount to:

$$
p(\mathbf{v})=\prod_{j} p\left(v_{j} \mid p a_{\mathcal{G}}\left(v_{j}\right)\right)
$$

- The collection of laws for $V$ that factor like this is called a Bayesian Network $\mathcal{B}(\mathcal{G})$.


## Causal Graphical Models in a nutshell: counterfactual world static intervention



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Corollary: counterfactual law is identified and given by

$$
p_{\left(v_{11}=0\right)}(\mathbf{v})=\prod_{j \neq 11} p\left(v_{j} \mid p a_{\mathcal{G}}\left(v_{j}\right)\right) \times I_{\{0\}}\left(v_{11}\right)
$$

Causal Graphical Models in a nutshell: counterfactual world, deterministic dynamic intervention


$$
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& V_{1}=f_{1}\left(\varepsilon_{1}\right) \\
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& V_{4}=f_{4}\left(\varepsilon_{4}\right) \\
& V_{5}=f_{5}\left(V_{1}, \varepsilon_{5}\right) \\
& \vdots \\
& V_{11}^{g}=g\left(V_{9}\right) \\
& V_{12}^{g}=f_{12}\left(V_{11}^{g}, V_{4}, \varepsilon_{12}\right) \\
& V_{13}^{g}=f_{13}\left(V_{8}, V_{10}, V_{12}^{g}, \varepsilon_{13}\right)
\end{aligned}
$$

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$$

## Causal Graphical Models in a nutshell: counterfactual world, random dynamic intervention



```
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$$
p_{\pi}(\mathbf{v})=\prod_{j \neq 11} p\left(v_{j} \mid p a_{\mathcal{G}}\left(v_{j}\right)\right) \times \pi\left(v_{11} \mid v_{9}\right)
$$

## Precursors, review papers in economics and an important reference

- Pearl's causal graphical model precursors:
- In biology: Sewall Wright's linear structural equations models with normal errors (geneticist) $\rightarrow$ path analysis
- In economics: Haavelmo's simultaneous structural equations model $\rightarrow$ allows non-recursiveness (simultaneous causation) and assumes parametric equations.
- For a review contrasting Pearl's and Haavelmo's models see Heckman and Pinto (2015). Causal Analysis After Haavelmo, Economic Theory.
- See also Imbens (2020) Potential Outcome and Directed Acyclic Graph Approaches to Causality: Relevance for Empirical Practice in Economics. Journal of Economic Literature
- For a unifying approach to potential outcomes and causal graphical models see T.S. Richardson, J.M. Robins (2013). Single World Intervention Graphs (SWIGs): A Unification of the Counterfactual and Graphical Approaches to Causality, In Foundations and Trends in Machine Learning, ISBN 13: 9781601988102


## Causal graphical models

## Causal graphical models

a. Factual world. The law $p$ of $\mathbf{V}=\left(V_{1}, \ldots, V_{J}\right)$ belongs to Bayesian Network $\mathcal{B}(\mathcal{G})$, i.e. it factorizes as

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p(\mathbf{v})=\prod_{j=1}^{J} p\left(v_{j} \mid p a_{\mathcal{G}}\left(v_{j}\right)\right)
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b. Counterfactual world. For any $\mathbf{A}=\left(A_{1}, \ldots, A_{s}\right) \subset \mathbf{V}$, the distrib. of the data when a regime that assigns $a_{t}$ to $A_{t}$ with prob. $\pi_{t}\left(a_{t} \mid \mathbf{Z}_{t}\right)$ is implemented in the population (where $\mathbf{Z}_{t}$ are non-descendants of $A_{t}$ ), is

$$
p_{\pi}(\mathbf{v})=\prod_{V_{j} \in \mathbf{V} \backslash \mathbf{A}} p\left(v_{j} \mid p a_{\mathcal{G}}\left(v_{j}\right)\right) \times \prod_{t=1}^{s} \pi_{t}\left(a_{t} \mid \mathbf{z}_{t}\right)
$$

So, $p_{\pi}$ is identified from $p$

## Bayesian Network

- Bayesian Network $\mathcal{B}(\mathcal{G})$ : collection of laws $p$ for $V$ that factorize as

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- d-separation: a sound and complete graphical rule for determining whether a conditional independence holds under any $p \in \mathcal{B}(\mathcal{G})$.


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$$

- Theorem (Geiger, Verma \& Pearl, 1990) :

$$
A \Perp_{\mathcal{G}} B \mid C \Leftrightarrow
$$

$A$ is cond. indep. of $B$ given $C$ under any $p \in \mathcal{B}(\mathcal{G})$

## d-separation

- $A, B$ single vertices, $C \subset V \backslash\{A, B\}$
- a path from $A$ to $B$ is blocked by $C$ if either
(1) at least one non-collider is in $C$

(2) $\exists$ at least one collider, such that neither itself nor its descendants is in $C$



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- $A$ and $B$ are d-separated by $C$ if all paths bw $A$ and $B$ are blocked by $C$
- A set $A$ is d-separated from another set $B$ by $C \subset V \backslash\{A, B\}$ if all $A_{j} \in A$ and $B_{k} \in B$ are d-separated by $C$, in which case we write

$$
A \Perp_{\mathcal{G}} B \mid C
$$

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## Two potential sources of bias in your causal analysis

NOT conditioning on common causes


Confounding bias

Conditioning on a common effect


Berkson's bias

## Berkson bias

Two variables that are marginally independent will typically be dependent if we condition on a common effect of both variables. (Berkson, 1946) Example


Suppose $P($ gene 1$)=P($ gene 2$)=0.02$, genes are marginally independent and Disease if and only if at least one of the two genes is present, i.e.

$$
X=1-(1-A)(1-Y)
$$

Then,

$$
\begin{gathered}
P(\text { Gene } 1 \mid \text { Disease, Not Gene } 2)=1 \\
P(\text { Gene } 1 \mid \text { Disease, Gene } 2)=P(\text { Gene } 1 \mid \text { Gene } 2)=0.02
\end{gathered}
$$

So, Gene 1 and Gene 2 are negatively correlated conditional on having the disease.

## M bias



## Time dependent confounders

Example: sequentially randomized trial of the effect of High vs Low dose of Highly Active Antiretroviral Therapy (HAART) at months 0 and 3 on Viral Load (high vs low) at month 6. (Assume in the graph all variables are binary)


## Time dependent confounders

Causal sharp null hypothesis $H_{0}^{\text {causal }}$ that $\left(A_{0}, A_{1}\right)$ has no causal effect on $Y$ is represented by the graph


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1. Regression controlling for $L$ fails: Suppose we fit a saturated (and hence correctly specified) logistic regression model

$$
\begin{aligned}
\operatorname{logit} \operatorname{Pr}\left(Y=1 \mid A_{0}, A_{1}, L\right)= & A_{0}\left(\gamma_{0}+\gamma_{1} L+\gamma_{2} A_{1}+\gamma_{3} A_{1} L\right) \\
& +\left(\eta_{0}+\eta_{1} L+\eta_{2} A_{1}+\eta_{3} A_{1} L\right)
\end{aligned}
$$

and to test $H_{0}^{\text {causal }}$ we test the null hypothesis

$$
H_{0}:\left(\gamma_{0}, \gamma_{1}, \gamma_{2}, \gamma_{3}, \eta_{2}, \eta_{3}\right)=(0,0,0,0,0,0)
$$

The test does not preserve the $\alpha$ - level because $H_{0}^{\text {causal }} \nRightarrow H_{0}$ since the path $Y-U-L-A_{0}$ is open when we condition on the collider $L$.

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## Time dependent confounders

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2. Regression that does not control for $L$ also fails: Suppose we fit a saturated (and hence correctly specified) logistic regression model

$$
\operatorname{logit} \operatorname{Pr}\left(Y=1 \mid A_{0}, A_{1}\right)=A_{1}\left(\alpha_{0}+\alpha_{1} A_{0}\right)+\left(v_{0}+v_{1} A_{0}\right)
$$

and to test $H_{0}^{\text {causal }}$ we test the null hypothesis

$$
H_{0}^{*}:\left(\alpha_{0}, \alpha_{1}, v_{1}\right)=(0,0,0)
$$

The test does not preserve the $\alpha$ - level because $H_{0}^{\text {causal }} \nRightarrow H_{0}^{*}$ since the path $Y-U-L-A_{1}$ is open when we fail to condition on $L$.

## Identification

- $Y_{a_{0}, a_{1}}$ : potential outcome when everybody in the study population takes treatment $A_{0}=a_{0}, A_{1}=a_{1}$.
- Result (Robins, 1986): under the causal graphical model represented by the graph

the probability $\operatorname{Pr}\left(Y_{a_{0}, a_{1}}=1\right)$ of high viral load in the counterfactual world in which everybody receives treatment $A_{0}=a_{0}, A_{1}=a_{1}$ is identified and given by
$\operatorname{Pr}\left(Y_{a_{0}, a_{1}}=1\right)=\sum_{l=0}^{1} \operatorname{Pr}\left(Y=1 \mid A_{0}=a_{0}, A=a_{1}, L=I\right) \operatorname{Pr}\left(L=I \mid A_{0}=a_{0}\right)$


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Counterfactual law under a point exposure intervention

- Counterfactual law.

$$
p_{\pi}(\mathbf{v})=\prod_{j: V_{j} \in \mathbf{V} \backslash A} p\left(v_{j} \mid p a_{\mathcal{G}}\left(v_{j}\right)\right) \times \pi(a \mid \mathbf{z})
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$$

- Then for $Y=V_{J}$,

$$
E_{\pi}[Y]=\int y \prod_{j: V_{j} \in \mathbf{V} \backslash A} p\left(v_{j} \mid p a_{\mathcal{G}}\left(v_{j}\right)\right) \times \pi(a \mid \mathbf{z}) d v
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- But under the Bayesian Network $E_{\pi}(Y)$ is equal to many other functionals


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## Adjustment formula and adjustment sets

- Adjustment formula:

$$
\begin{aligned}
\underbrace{E_{\pi}[Y]}_{\text {rvention mean }} & =\underbrace{\sum_{a=0}^{1} \int E[Y \mid A=a, \mathbf{L}=\mathbf{I}] \pi(a \mid \mathbf{z}) p_{\mathbf{L}}(\mathbf{I}) d \mathbf{l}}_{\text {g-functional }} \\
& =E_{p}\left[\frac{\pi(A \mid \mathbf{Z})}{p(A \mid \mathbf{L})} Y\right]
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- Definition: A $\mathbf{Z}$ - adjustment set for a single trx $A$ and outcome $Y$ is any $\mathbf{L}$ disjoint with $A$ and $Y$ such that
- $\mathbf{Z} \subset \mathbf{L}$ and,
- Under the causal graphical model, for any regime $\pi(A \mid \mathbf{Z}), E_{\pi}[Y]$ is equal to the corresponding adjustment formula.


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- $\mathbf{Z} \subset \mathbf{L}$ and,
- Under the causal graphical model, for any regime $\pi(A \mid \mathbf{Z}), E_{\pi}[Y]$ is equal to the corresponding adjustment formula.
- If $\mathbf{Z}=\varnothing$, then we say $\mathbf{L}$ is a static adjustment set .


## Characterization of Z-adjustment sets

- Generalized adj. criterion for static (i.e. $\mathbf{Z}=\varnothing$ ) treatments (Shpitzer. et. al., 2010, Perkovic et. al., 2015, 2018): L is static adj. set iff


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- L blocks all non-causal paths between $A$ and $Y$.


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- $\mathbf{L}$ is neither a mediator, nor descendant of $Y$ or of a mediator
- L blocks all non-causal paths between $A$ and $Y$.
- Result (Smucler and Rotnitzky, 2020):

Class of all $\mathbf{Z}-\operatorname{adj}$ sets $=\{\mathbf{L}: \mathbf{L}$ is a static adj. set and $\mathbf{Z} \subset \mathbf{L}\}$

## Static adjustment set



## Another static adjustment set



## An invalid Z-adjustment , $\mathrm{Z}=$ previous injury



## A valid $Z$-adjustment set, $Z=$ previous injury



## L-NPA estimators of a counterfactual mean

- Recall: a $\mathbf{Z}$ - adj. set $\mathbf{L}$ satisfies that for any regime $\pi(A \mid \mathbf{Z})$, the counterfactual mean $E_{\pi}(Y)$ is equal to

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- Is there a universally optimal adjustment set and, if so, what graphical rules determine it?


## Related literature

- Henckel, Perkovic and Maathuis (2019) provided graphical rules
- for comparing certain pairs of static adjustment sets
- for determining the globally optimal static adjustment set
- Also, Kuroki and Miyakawa, 2003 and Kuroki and Cai 2004.
- These works assume:
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- Works connected with efficiency implications of inclusion of overadjustment and precision variables in regression and in semip. estimation of ATE:
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## Supplementing adjustment sets with precision variables.

- Lemma 1. Suppose $\mathbf{B}$ is a $\mathbf{Z}$-adj. set and $\mathbf{G}$, disjoint with $\mathbf{B}$, satisfies

$$
A \Perp_{\mathcal{G}} \mathbf{G} \mid \mathbf{B}
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then, $\mathbf{G} \cup \mathbf{B}$ is also a $\mathbf{Z}$-adj. set and for all $p \in \mathcal{B}(\mathcal{G})$ and all regimes $\pi(A \mid \mathbf{Z})$

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- In particular, for the static regime $\pi$ that sets $A$ to $a$,

$$
\sigma_{\pi, \mathbf{B}}^{2}(p)-\sigma_{\pi, \mathbf{G} \cup \mathbf{B}}^{2}(p)=E\left[\left\{\frac{1}{P(A=a \mid \mathbf{B})}-1\right\} \operatorname{var}\{E(Y \mid A=a, \mathbf{G}, \mathbf{B}) \mid A=a, \mathbf{B}\}\right]
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## Deleting overadjustment variables

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If $\mathbf{Z} \subset \mathbf{G}$, then $\mathbf{G}$ is also a $\mathbf{Z}$-adj. set and for all $p \in \mathcal{B}(\mathcal{G})$ and all regimes $\pi(A \mid \mathbf{Z})$

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## Comparing two arbitrary adjustment sets

- Corollary: Suppose that $\mathbf{G}$ and $\mathbf{B}$ are two $\mathbf{Z}$-adj. sets such that

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- Proof:

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## Not all adjustment sets are comparable



- $\left(O_{1}, W_{2}\right)$ is preferable to $\left(O_{2}, W_{1}\right)$ if green association stronger than brown, and blue association weaker than red
- $\left(O_{2}, W_{1}\right)$ is preferable to $\left(O_{1}, W_{2}\right)$ if brown association stronger than green, and red association weaker than blue
- but... $\left(O_{1}, O_{2}\right)$ is more efficient than both


## Optimal adjustment set

- Theorem: (Henckel, et. al. (2019)). The set

$$
\begin{aligned}
\mathbf{O}= & \text { non-descendants of } A \text { that are parents of } Y \text { or } \\
& \text { of vertices in the causal path bw } A \text { and } Y
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is a static adjustment set. Furthermore, for any other static adjustment set $\mathbf{L}$,

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- Corollary (Rotnitzky and Smucler, 2020): O is the globally optimal static adjustment set.
- Lemma (Smucler, Sapienza and Rotnitzky, 2021): $\mathbf{O} \cup \mathbf{Z}$ is the globally optimal Z - adjustment set


## Globally optimal static adjustment set



## Optimal personalized adjustment set



## Road map of the talk

- Gentle introduction to causal graphical models.
- Definition and properties
- Some examples of their use for detecting potential sources of bias
- Some of our results on efficient adjustment sets
- Rules for comparing adjustment sets for point exposure studies
- Summary of other results
- Final remarks


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- $\mathbf{L}=\left\{L_{1}\right\}$ is another adj. set but is dominated by $\mathbf{L}=\varnothing$
- In Smucler, Sapienza and Rotnitzky (2021) we characterize sufficient conditions for an optimal observable adjustment set to exist


## Time dependent treatments

- Suppose $A_{1}$ and $A_{2}$ are two treatments, $A_{1} \in \operatorname{nd}_{\mathcal{G}}\left(A_{2}\right)$. Under a causal graphical model represented by a graph $G$, the mean of $Y_{a_{0}, a_{1}}$ when the static regime that sets $A_{0}$ to $a_{0}$ and $A_{1}$ to $a_{1}$ is

$$
\begin{aligned}
E\left(Y_{a_{0}, a_{1}}\right) & =E\left\{\frac{l_{a_{0}}\left(A_{0}\right)}{p\left(a_{0} \mid p a_{\mathcal{G}}\left(A_{0}\right)\right)} \frac{l_{a_{1}}\left(A_{1}\right)}{p\left(a_{1} \mid p a_{\mathcal{G}}\left(A_{1}\right)\right)} Y\right\} \\
& =E\left\{E\left[E\left[Y \mid a_{0}, a_{1}, p a_{\mathcal{G}}\left(A_{0}\right), p a_{\mathcal{G}}\left(A_{1}\right)\right] \mid a_{0}, p a_{\mathcal{G}}\left(A_{0}\right)\right]\right\}
\end{aligned}
$$

- Definition: $\mathbf{L}=\left(\mathbf{L}_{0}, \mathbf{L}_{1}\right) \subset \mathbf{V}$ is a static time dependent adjustment set relative to trxs $\left(A_{0}, A_{1}\right)$ and outcome $Y$ in $G$ iff for all $P \in \mathcal{B}(\mathcal{G})$,

$$
E\left(Y_{a_{0}, a_{1}}\right)=E\left\{E\left[E\left[Y \mid a_{0}, a_{1}, \mathbf{L}_{0}, \mathbf{L}_{1}\right] \mid a_{0}, \mathbf{L}_{0}\right]\right\}
$$

## Time dependent treatments

- Example:

- $X_{0}$ is a time 0 adjustment set $\left(=\mathbf{L}_{0}\right)$
- $X_{1}, U$ and $\left(X_{1}, U\right)$ are time 1 adjustment sets $\left(=\mathbf{L}_{1}\right)$
- In Rotnitzky and Smucler, 2020, we derived rules for comparing static time dependent adjustment sets and showed by example that an optimal adjustment set need not exist.


## Study design.

- Assign cost to each graph variable and find the adjustment set leading to smallest estimation variance:
- subject to a cost constraint $\rightarrow$ a universal solution does not exist

- among adjustment sets of minimum cost $\rightarrow$ for point exposure we provide the universal solution in Smucler and Rotnitzky, 2022, and graphical rules for finding it


## Semip. efficient estimation vs optimal non-parametric adjusted estimation



- The interventional mean $E\left(Y^{a}\right)$ is

$$
E[E(Y \mid A=a, V, W)]=\int E(Y \mid A=a, V=v, W=w) \underbrace{p(v) p(w)}_{=p(v, w)} d v d w
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- Optimal non-parametric adjusted estimator ignores restrictions on the marginal law of covariates, i.e. that $V$ and $W$ are marginally independent.
- Semiparametric efficient (SE) exploits these restrictions and can be much much more efficient than optimally adjusted NP estimator.


## However ... in some graphs the optimally adjusted estimator is efficient



- With discrete data the MLE of $p_{a}(y)$ under $\mathcal{G}$ is

$$
\hat{p}_{a, M L E}(y)=\sum_{m, o} \mathbb{P}_{n}(y \mid m, a) \mathbb{P}_{n}(m \mid a, o) \mathbb{P}_{n}(o)
$$

- Surprisingly, $\widehat{p}_{a, M L E}(y)$ is asym. equivalent to the MLE of $p_{a}(y)$ under $\mathcal{G}^{*}$ is

$$
\tilde{p}_{a, M L E}(y)=\sum_{o} \mathbb{P}_{n}(y \mid o, a) \mathbb{P}_{n}(o)
$$

- In Rotnitzky and Smucler (2000) we characterized the graphs in which the optimally adjusted estimator is semiparametric efficient


## Graph reduction for semiparametric efficient estimation of a counterfactual mean

- In Guo, Perkovic and Rotnitzky, 2022, we derived the following.
- Given a graph $\mathcal{G}$ we derived an algorithm that outputs another graph $\mathcal{G}^{*}$ over a subset of the variables in $\mathcal{G}$ such that
- the semiparametric variance bound for estimation of $E\left(Y_{a}\right)$ in model $\mathcal{B}(\mathcal{G})$ and in model $\mathcal{B}\left(\mathcal{G}^{*}\right)$ agree
- $\mathcal{G}^{*}$ is the smallest such possible graph in the sense that all variables in $\mathcal{G}^{*}$ are informative. More precisely, the efficient influence function for $E\left(Y_{a}\right)$ is a function of every variable in $\mathcal{G}^{*}$ for at least one $P$ in $\mathcal{B}\left(\mathcal{G}^{*}\right)$


## Final remarks

- Estimation via adjustment vs semip. efficient estimation:
- Usual variance/bias trade-off: adjustment relies on less model assumptions
- Equally or perhaps even more importantly: efficient estimation requires estimation of each cond. density $p\left(V_{j} \mid p a_{\mathcal{G}}\left(V_{j}\right)\right)$. Even debiased, influence-function based, i.e. one-step estimation, will hardly control the estimation bias of these densities.


## Open problems

- Inference about the functional returned by the ID algorithm when no observable adj. set exists
- Some special cases have been studied, e.g. the generalized front door formula, (Fulcher, et. al. 2019). General theory for an arbitrary functional not yet available.
- Optimal adj. sets and efficient estimation for other parameters e.g., trx effect on the treated, and natural direct and indirect effects

THANKS!

