Counterfactuals and directed acyclic graphs in epidemiology

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Motivation

AJPH PUBLIC HEALTH OF CONSEQUENCE

The C-Word: Scientific Euphemisms Do Not Improve Causal Inference From Observational Data

Causal inference is a core task of science. However, authors and editors often refrain from explicitly acknowledging the causal goal of research projects; they refer to causal effect estimates as associational estimates.

This commentary argues that using the term “causal” is necessary to improve the quality of

Miguel A. Hernán, MD, DrPH

See also Galea and Vaughan, p. 602; Begg and March, p. 620; Ahern, p. 621; Chiolero, p. 622; Glymour and Hamad, p. 623; Jones and Schooling, p. 624; and Hernán, p. 625.

You know the story:

> Dear author: Your observational study cannot prove causation. Please replace all references to causal effects by references to associations.

Confusion then ensues at the most basic levels of the scientific process and, inevitably, errors are made.

We need to stop treating “causal” as a dirty word that

glass of red wine per day versus no alcohol drinking. For simplicity, disregard measurement error and random variability—that is, suppose the 0.8 comes from a very large population so that the 95%

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Causal inference

- The goal of causal inference: to know how outcome Y would change if we changed exposure A from $a = 0$ to $a = 1$
- Y^a: the value outcome Y would take if we set A to a
- So $Y^{a=1}$ is the value Y would take if we set $a = 1$ (N.B.: this is not Y|A=1)
- Ideally, we would like to observe $Y^{a=1}$ and $Y^{a=0}$ for everyone
- But we observe *at most* half of the vector Y^a because we can only observe each person as $Y^{a=1}$ or $Y^{a=0}$
- We write the causal effect we're interested in as $\mathrm{E}[Y^{a=1} - Y^{a=0}]$ or $\mathrm{Pr}[Y^{a=1} = 1] - Pr[Y^{a=0} = 1]$ or $\frac{Pr[Y^{a=1}=1]}{Pr[Y^{a=0}=1]}$

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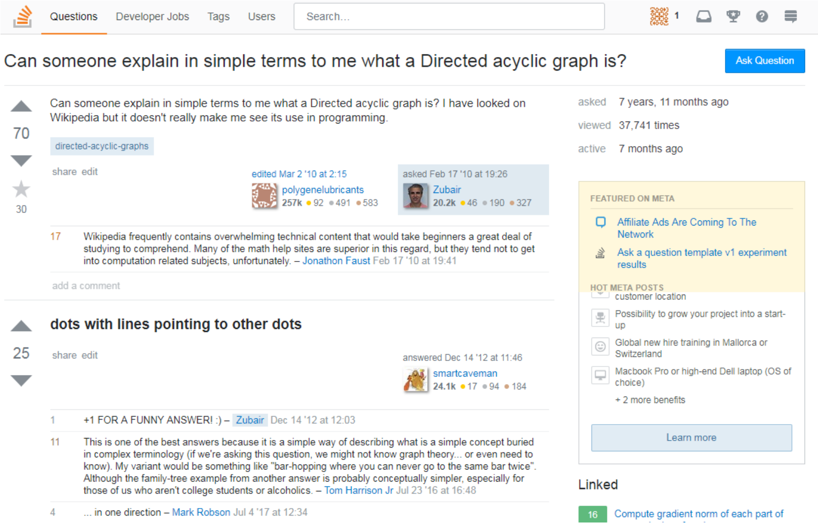
Counterfactuals

- Counterfactual notation has been used to achieve insight into estimation of longitudinal causal effects, instrumental variables and a number of other topics
- Some of the insight provided by counterfactuals can also be depicted in graphical form

Directed Acyclic Graphs (DAGs)



Directed Acyclic Graphs (DAGs)

- DAGs are diagrams with simple rules that allow us to clearly think about our causal questions to determine what sources of bias we might have and how we can avoid them
- DAGs are composed of two elements: nodes and edges
- Edges are directed (i.e. one causes the other)
- DAGs must be acyclic, no feedback loops are allowed
- The edges are not deterministic

$$\overset{\text{node}}{A} \xrightarrow{\qquad\text{edge}\qquad} Y$$

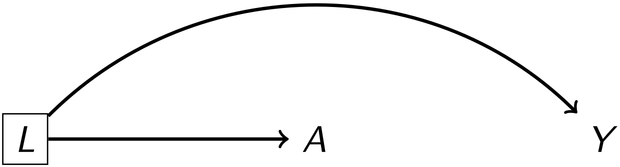
Directed Acyclic Graphs (DAGs)

- $E[Y^{a=1}] - E[Y^{a=0}] = 0$
- $E[Y|A=1] - E[Y|A=0] \neq 0$
- $A \not\perp\!\!\!\perp Y^a$

$$
\begin{tikzcd}
L \arrow[r] \arrow[rr, bend left] & A & Y
\end{tikzcd}
$$

Directed Acyclic Graphs (DAGs)

- $E[Y^{a=1}|L] - E[Y^{a=0}|L] = 0$
- $E[Y|A=1,L] - E[Y|A=0,L] = 0$
- $A \perp\!\!\!\perp Y^a|L$



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$$
\begin{tikzcd}
A \arrow[rr, bend left] & Y \arrow[r] & S
\end{tikzcd}
$$

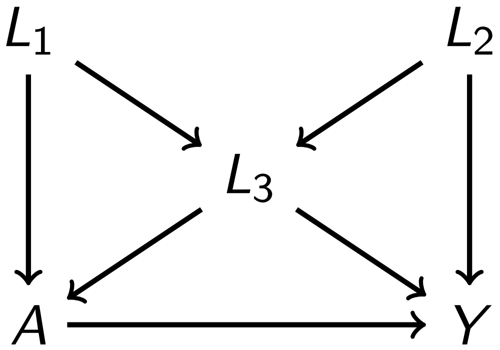
Directed Acyclic Graphs (DAGs)

- $E[Y^{a=1}|S] - E[Y^{a=0}|S] = 0$
- $E[Y|A=1,S] - E[Y|A=0,S] \neq 0$
- $A \not\perp\!\!\!\perp Y^a|S$

$$
\begin{tikzcd}
A \arrow[rr, bend left] & Y \arrow[r] & \boxed{S}
\end{tikzcd}
$$

Directed Acyclic Graphs (DAGs)

- With a DAG you can identify whether the causal question is identifiable and, if so, what must be adjusted for
- Here adjusting for L_1, L_3 or L_2, L_3 or L_1, L_2, L_3 are all sufficient adjustment sets



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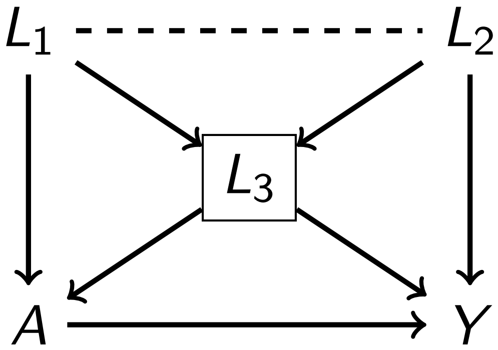

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Directed acyclic graphs (DAGs)


george davey smith
@mendel_random
Following

Epidemiologists rejoice! "'the task of selecting an appropriate set of covariates to control for confounding has been reduced to a simple "roadblocks" puzzle manageable by a simple algorithm" arxiv.org/abs/1801.04016 and

Epidemiology

Comments on: The tale wagged by the DAG | International ...
I am grateful to the editors for the opportunity to comment on Nancy Krieger and George Davey Smith's article, 'The tale wagged by the DAG', which appeared in t
academic.oup.com

This is true! But the DAG has to be correctly specified which is the hard (impossible) part.

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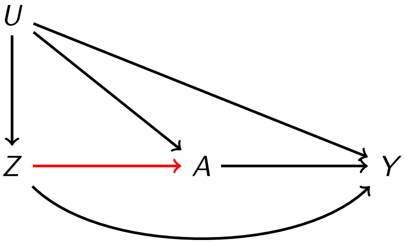
Showing the IV assumptions in a DAG

- This DAG makes the least amount of assumptions about the observed data. Every node is connected to every other

$$
\begin{tikzcd}
U \arrow[d] \arrow[r] \arrow[rr] & & \\
Z \arrow[r] \arrow[rr, bend right] & A \arrow[r] & Y
\end{tikzcd}
$$

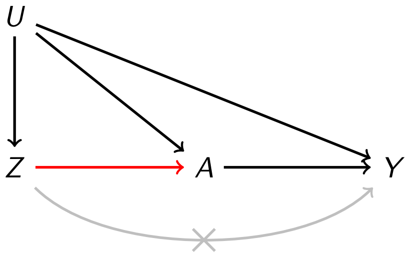
Showing the IV assumptions in a DAG

- The relevance assumption is represented by the red arrow, showing that there is a relationship between Z and A
- $Z \not\perp\!\!\!\perp A$



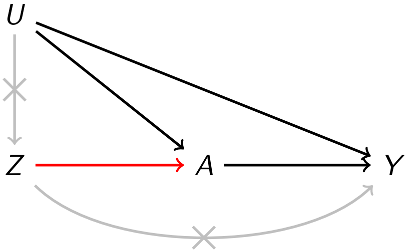
Showing the IV assumptions in a DAG

- The exclusion restriction (ER) assumption assumes that the direct edge between Z and A is not present
- $\mathrm{E}[Y^{z,a}] = \mathrm{E}[Y^{z',a}]$



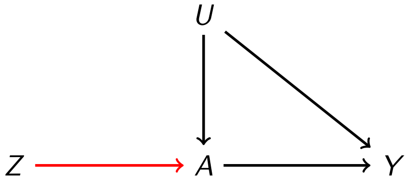
Showing the IV assumptions in a DAG

- The exchangeability assumption assumes that Z is not confounded with Y
- $Y^{a,z} \perp\!\!\!\perp Z$



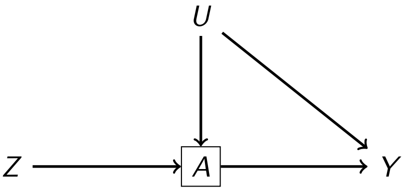
Showing the IV assumptions in a DAG

- With our three assumptions, we end up with our classic IV DAG which implies that $Z \perp\!\!\!\perp Y^a$
- Therefore if $Z \not\perp\!\!\!\perp Y$ then it must be that $\mathrm{E}[Y^a - Y^{a'}] \neq 0$
- IV estimation requires monontonicity and homogeneity cannot be drawn on a DAG because they are parametric concepts



Conditioning on exposure in IV analyses

- Sometimes people like to stratify or restrict on exposure
- But if we do, now $Z \not\perp\!\!\!\perp U$ and therefore $Z \not\perp\!\!\!\perp Y^{z,a}$, AKA, the exchangeability assumption is violated
- Swanson et al, Am J Epi, 2015



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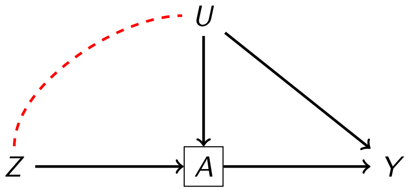
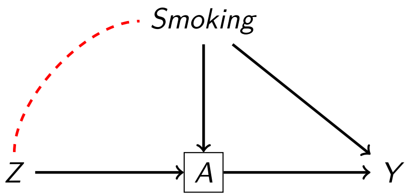


An example where a simple DAG could have helped

- "Strong evidence of collider bias was observed for smoking behaviour" (Cho et al, Sci Rep, 2015)
- "To minimize the effect of risk factors susceptible to collider bias, associations between the SNP and cardiovascular outcomes were then assessed with adjustments for smoking"
- By saying smoking is what drives collider bias, they are implying smoking is the only confounder alcohol and cardiovascular outcomes. Better off simply adjusting then?



Using DAGs to think about IV longitudinally

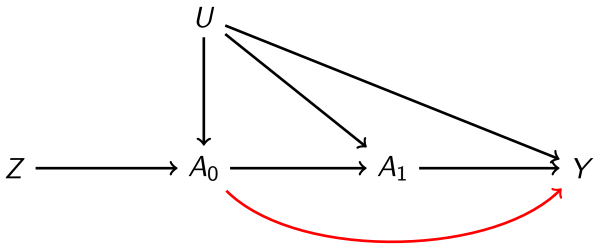
- We can depict a time-varying exposure by splitting the A node into separate nodes for each time point
- We are still assuming the IVs assumptions but splitting A into two nodes adds assumptions to the DAG
- Labrecque and Swanson (under review at Am J Epi)

$$
\begin{tikzcd}
 & U \arrow[d] \arrow[dr] & \\
Z \arrow[r] & A \arrow[r] & Y
\end{tikzcd}
$$

$$
\begin{tikzcd}
 & U \arrow[d] \arrow[dr] \arrow[drr] & & \\
Z \arrow[r] & A_0 \arrow[r] & A_1 \arrow[r] & Y
\end{tikzcd}
$$

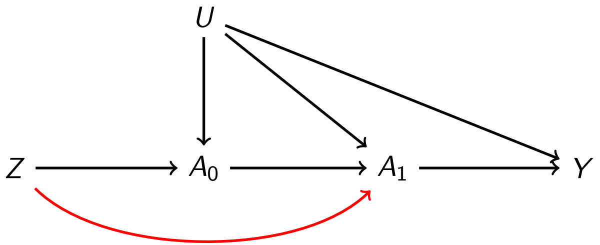
Using DAGs to think about IV longitudinally

- We have assumed that A_0 does not have a direct effect on Y
- If A_0 does affect Y then we can no longer estimate the effect of A_1 ony Y
- This is because, although the ER holds for A as a whole, it does not hold for A_1
- So if we measure A_0 we're alright?



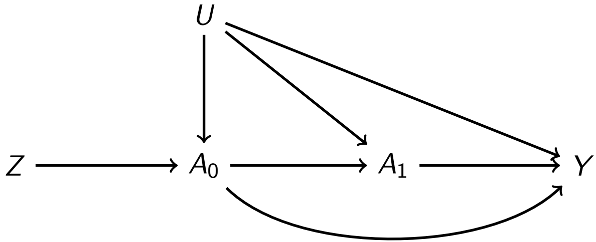
Using DAGs to think about IV longitudinally

- We have also assumed that Z does not have a direct effect on A_1
- If Z does affect A_1 then we can no longer estimate the effect of A_0 ony Y
- This is because, although the ER still holds for A as a whole, it does not hold for A_0
- All this to illustrate that, in contexts such as Mendelian randomization, important thought must be given to how exposures change longitudinally



Using DAGs to think about IV longitudinally

- What if we think about joint effects?
- First, though “lifetime effects” is often used in Mendelian randomization, it has no precise defintion
- We propose $\mathrm{E}[Y_k^{\bar{A}+\bar{1}} - Y_k^{\bar{A}}]$
- Only identifiable with IV if the effect of the Z on A does not change with time (N.B.: A can change as long as the effect of G doesn’t)
- This also has implications for which null hypotheses are testable (Swanson et al, Eur J Epi, 2018)



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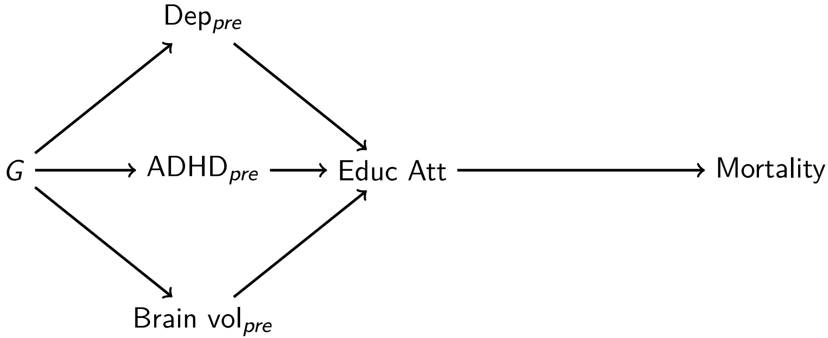
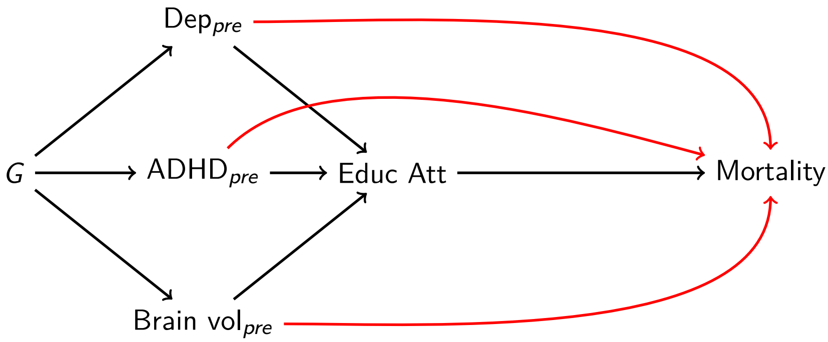
Using DAGs to think about Mendelian randomization

- DAG for a MR study of the effect of educational attainment on mortality



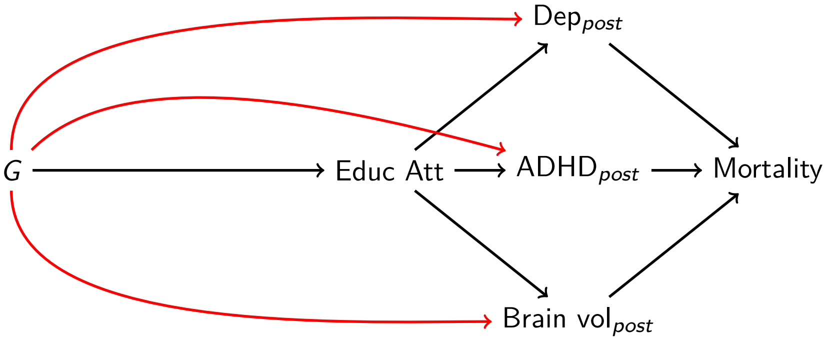
Using DAGs to think about Mendelian randomization

- But what if the intermediates between G and education attainment have a direct effect on mortality?



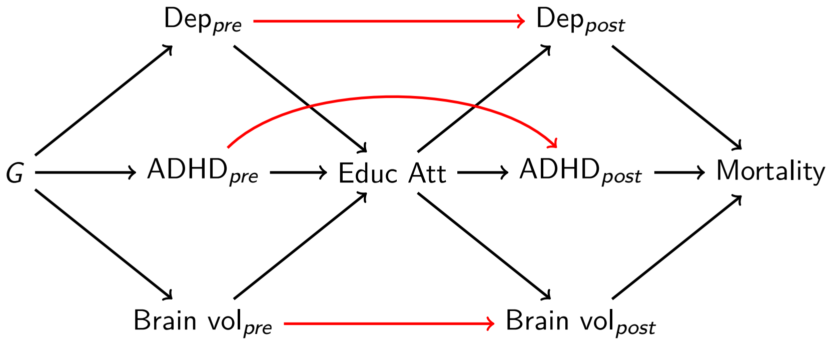
Using DAGs to think about Mendelian randomization

- Or what if G has a direct affcect on the intermediates after educational attainment



Using DAGs to think about Mendelian randomization

- We have also assumed that Z does not have a direct effect on A_1



Thank you

- We are Erasmus MC Causal Inference Group (we don't have a name yet)
  - Sonja Swanson (assistant professor): Instrumental variable analysis, target trial emulation, causal inference
  - Jeremy Labrecque (postdoc): Instrumental variable analysis, target trial emulation, causal inference
  - Elizabeth Diemer (PhD student): Methodological issues in perinatal MR
  - Paloma Rojas Saunero (PhD student): Target trial emulation using data from the Rotterdam Study
- Email us at: s.swanson@erasmusmc.nl or j.labrecque@erasmusmc.nl

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