Counterfactuals and Directed acyclic graphs in epidemiology

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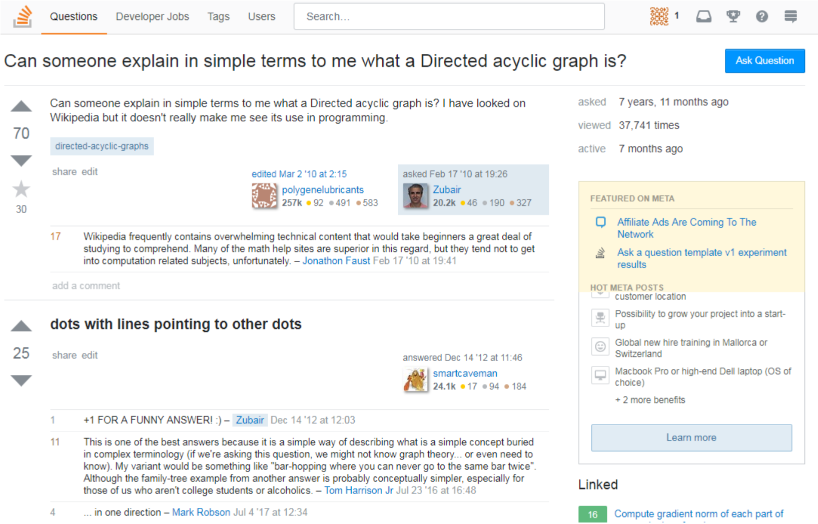
Causal inference

- 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)
- In a dataset 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 $Y^{a=1} - Y^{a=0}$ or $\frac{Pr[Y^{a=1}=1]}{Pr[Y^{a=0}=1]}$

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)



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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)

- $Y \not\perp\!\!\!\perp A$ and $Y^a \perp\!\!\!\perp A$

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

Directed Acyclic Graphs (DAGs)

- $Y \perp\!\!\!\perp A | L$ and $Y^a \perp\!\!\!\perp A | L$

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

Directed Acyclic Graphs (DAGs)

- $Y \perp\!\!\!\perp A$ and $Y^a \perp\!\!\!\perp A$

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

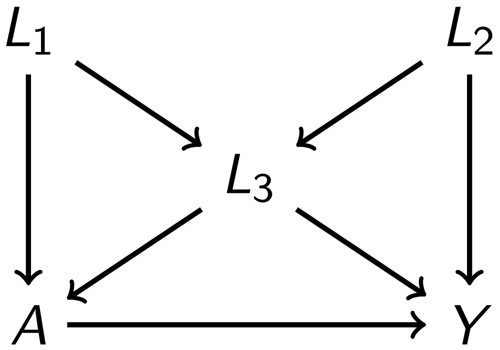
Directed Acyclic Graphs (DAGs)

- $Y \not\perp\!\!\!\perp A|S$ and $Y^a \perp\!\!\!\perp A|S$

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

Directed Acyclic Graphs (DAGs)

- With a DAG you can identify whether it's possible to achieve conditional exchangeability
- 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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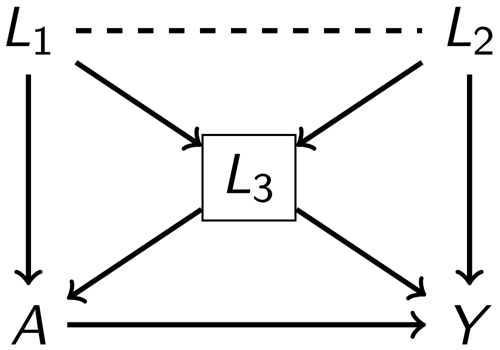

Directed acyclic graphs (DAGs)

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

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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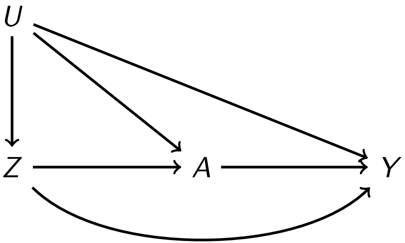
Showing the IV assumptions in a DAG

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



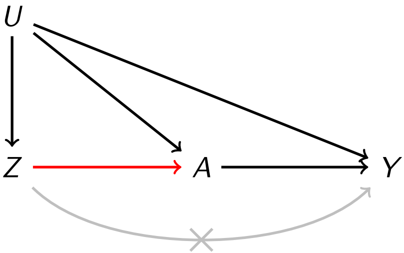
Showing the IV assumptions in a DAG

- The relevance assumption is represented by the red arrow, showing that there is a relationship between Z and A

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

Showing the IV assumptions in a DAG

- The exclusion restriction (ER) assumption assumes that the direct edge between Z and A is not present



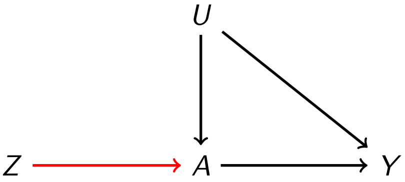
Showing the IV assumptions in a DAG

- The exchangeability assumption assumes that Z is not confounded with Y

$$
\begin{tikzcd}
U \arrow[d, "\times", gray] \arrow[dr] \arrow[drr] & & \\
Z \arrow[r, red] \arrow[rr, bend right, "\times", gray] & A \arrow[r] & Y
\end{tikzcd}
$$

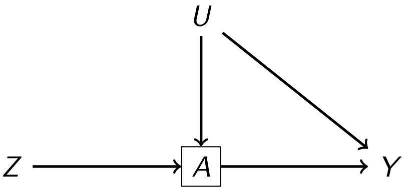
Showing the IV assumptions in a DAG

- With our three assumptions, we end up with our classic IV DAG
- This DAG implies that if $Z \not\perp\!\!\!\perp Y$ then it must also be that $A \not\perp\!\!\!\perp Y$[a]
- IV estimation requires monontonicity and homogeneity cannot be drawn on a DAG because they are parametric concepts



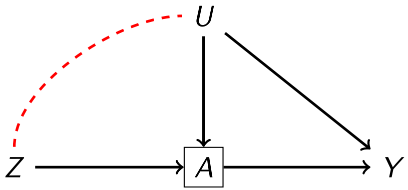
Conditioning on exposure in IV analyses

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



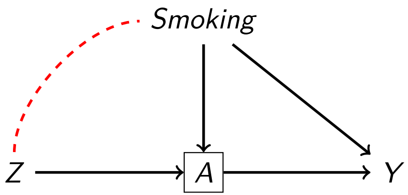
Conditioning on exposure in IV analyses

- We often draw this on DAGs using a dashed line to remind us that these variables are associated now



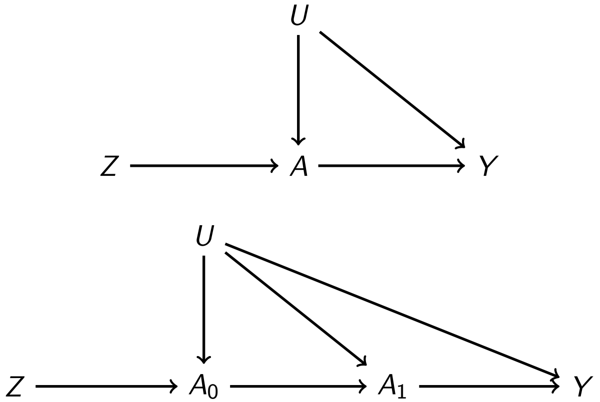
An example where a simple DAG could have helped

- "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?



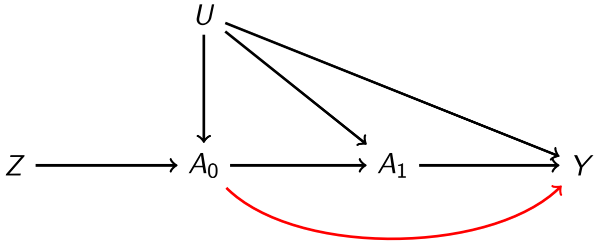
Using DAGs to think about IV longitudinally

- 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



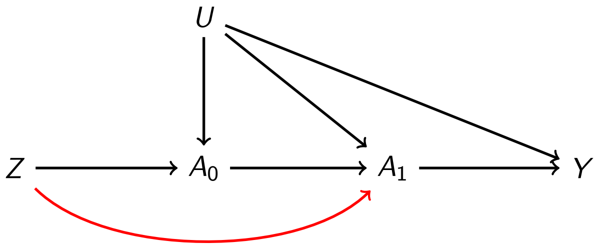
Using DAGs to think about IV longitudinally

- 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?



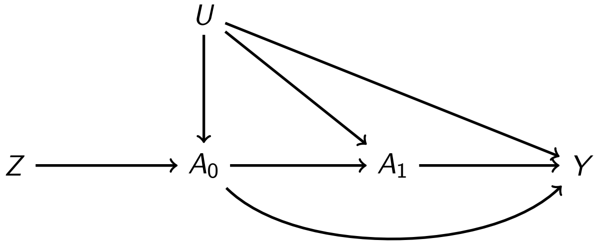
Using DAGs to think about IV longitudinally

- 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



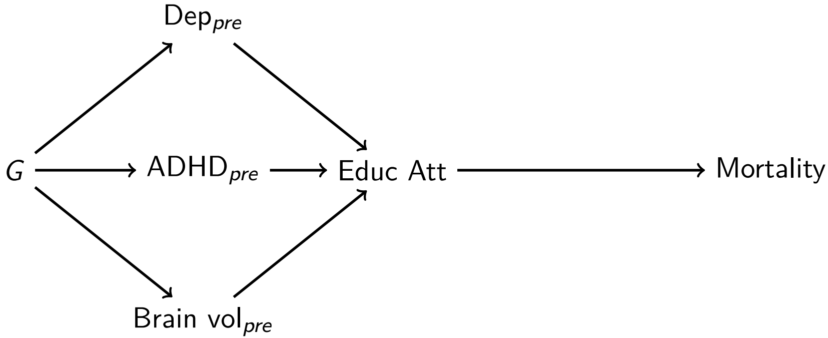
Using DAGs to think about IV longitudinally

- 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)



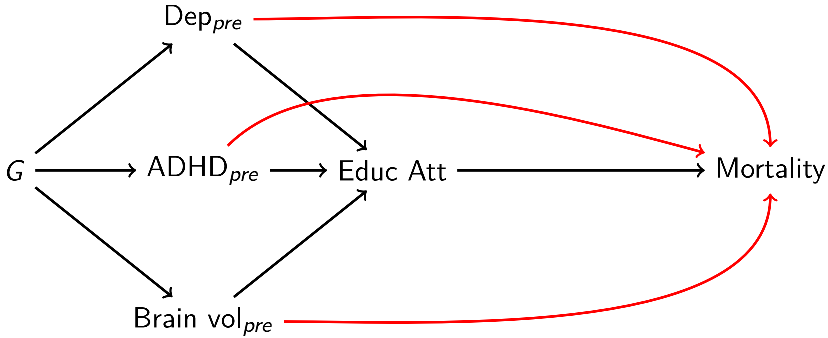
Using DAGs to think about Mendelian randomization

- 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?



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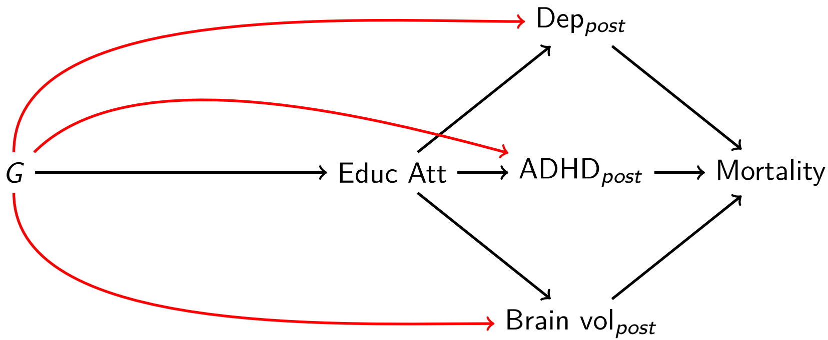
Using DAGs to think about Mendelian randomization

- 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