Using Causal Graphs In Epidemiological Research

Dr David A. Stephens

Department of Mathematics & Statistics

david.stephens@mcgill.ca www.math.mcgill.ca/dstephens/SISCER2025/



- 1. Probability distributions for observed data.
- 2. Independence and conditional independence.
- 3. Graphical modelling.
- 4. Cause and effect: structural models.
- 5. Paths and how to block them.
- 6. d-separation.

Key objective: causal conclusions from observational data

- Experimental studies:
 - Treatment assigned by the researcher, independent of confounding factors;
 - Causal statements possible.
- Observational studies:
 - Treatment assignment dependent on confounding factors;
 - Causal statements not possible ?

The objective of *causal inference* is to quantify the effect of an *intervention*: in a multi-variable system

- suppose we are able to *manipulate* (i.e. alter the value of) one of the variables separately from all other variables;
- we wish to report the impact of that manipulation on one or more of the other variables.

In many scientific enterprises, this is a primary objective.

We will collect data

$$\{(x_i, y_i, z_i), i = 1, \ldots, n\}$$

which are observed values of the variables X, Y and Z.

- X predictors, covariates, *confounders*
- *Y outcome*, response
- *Z treatment*, exposure

Causal Effects and Counterfactual Outcomes

The *causal effect* of Z on Y is the amount to which an *intervention* to change Z from z_0 to z_1 modifies Y.

• The *potential* or *counterfactual* outcome is denoted Y(z), and is the outcome after an *intervention* to set Z = z.

For example, if $Z \in \{0, 1\}$, then

Y(0): outcome if intervention sets z = 0 ('Untreated') Y(1): outcome if intervention sets z = 1 ('Treated')

• The *observed* outcome *Y* is then

$$Y = (1 - Z)Y(0) + ZY(1) = \begin{cases} Y(0) & Z = 0 \\ Y(1) & Z = 1 \end{cases}$$

.

Hypothetical data generating mechanism:

- individual brings their characteristics X;
- for each **z**, the outcome *Y*(**z**) is determined by *X*;
- for *observed* treatment Z = z, we observe Y = Y(z).

In an *experimental study* precisely the right kind of 'intervention' to study causal contrasts is made:

- we randomly assign *Z*, *independently* of *X*;
- we *compare* the outcomes in the different groups indexed by different *Z* values.

Example: randomized controlled trials.

In an *observational study* we do *not* intervene to assign treatments, we observe it as part of the data collection process.

- we *cannot* treat *Z* as if it were independent of *X*;
- groups with different *Z* may have *different* distributions of *X*, so these groups are *not directly comparable*.

To study cause and effect, we need to have an understanding of the *probabilistic* relationship between all the variables we observe.

To gain statistical insights, we need to build probability models.

Example: HIV Study

- *C* CD4 count (continuous)
- *D* assignment of new HIV drug (binary)
- *H* underlying HIV severity (binary)
- *S* symptoms (binary)
- U follow up indicator (binary, U = 0 implies loss to follow-up)

We wish to examine the impact of the new drug on CD4 count:

Does intervening to change D affect outcome C?

We need to describe how these variables vary jointly in the study.

A *joint* probability distribution

 $f_{X,Y,Z}(x,y,z)$

describes how the data are generated. This model specifies

• the *marginal* distributions

$$f_X(x)$$
 $f_Y(y)$ $f_Z(z)$

that describe how the variables behave individually,

• the *conditional* distributions such as

 $f_{X|Y}(x|y) = f_{X|Z}(x|z) = f_{Y|X}(y|x) = f_{Y|X,Z}(y|x,z) = f_{Y,Z|X}(y,z|x)$

etc. that describe how the variables behave when one or more variable is *fixed*

We have the possible decompositions

$$f_{X,Y,Z}(x, y, z) = f_X(x) f_{Z|X}(z|x) f_{Y|X,Z}(y|x, z)$$
$$f_{X,Y,Z}(x, y, z) = f_Z(z) f_{Y|Z}(y|z) f_{X|Y,Z}(x|y, z)$$

and so on, for any ordering of the variables.

We can *always* consider this kind of sequential decomposition, which is termed a *chain rule factorization*.

Two random variables *X*, *Z* are *independent*

 $X \perp\!\!\!\perp Z$

if and only if, for all values (x, z),

$$f_{X,Z}(x,z) = f_X(x)f_Z(z)$$

$$f_{Z|X}(z|x) = f_Z(z)$$

$$f_{X|Z}(x|z) = f_X(x)$$

i.e. knowledge of *X* does not influence our assessment of *Z*.

We can consider *conditional independence*: say

 $Y \perp\!\!\!\perp Z \mid X$

if and only if, *for all* (x, z, y)

$$f_{Y,Z|X}(y,z|x) = f_{Z|X}(z|x)f_{Y|X}(y|x)$$

i.e. if we fix X = x

knowledge of Y does not influence our assessment of Z:

$$f_{Z|X,Y}(\boldsymbol{z}|\boldsymbol{x},\boldsymbol{y}) = f_{Z|X}(\boldsymbol{z}|\boldsymbol{x}).$$

• knowledge of *Z* does not influence our assessment of *Y*:

$$f_{Y|X,Z}(y|x,z) = f_{Y|X}(y|x)$$

Three variables

- X and Y vary continuously,
- Z is binary.

We can study the distribution of the data for X and Y

- for each level of Z separately,
- pooled over Z levels.

Z=0



Z=1





Pooled



We see that

- for Z = 0 and Z = 1 separately, X and Y are *uncorrelated*;
- overall *X* and *Y* are *positively correlated*.

Thus X and Y are

conditionally unrelated given Z

but are

unconditionally related.

This illustrates that conditioning can remove (or *block*) dependence.

We have a chain rule factorization

$$f_{X,Y,Z}(x,y,z) = f_X(x)f_{Y|X}(y|x)f_{Z|X,Y}(z|x,y).$$

We might then *assume* the *conditional independence*

 $Z \perp\!\!\!\perp Y | X$

so that

$$f_{Z|X,Y}(z|x,y) = f_{Z|X}(z|x)$$

and so

$$f_{X,Y,Z}(x,y,z) = f_X(x)f_{Y|X}(y|x)f_{Z|X}(z|x)$$

3. Causal graphs

We can depict the conditional independence using a graph:



This type of graph is sometimes called a *fork*.

The other common type of graph component is a *chain*



which implies the factorization

 $f_Z(z)f_{X|Z}(x|z)f_{Y|X}(y|x)$

and the conditional independence

 $Y \perp\!\!\!\perp Z | X$

That is, there are two ways the conditional independence

 $Y \perp\!\!\!\perp Z | X$

could be represented



 $\begin{array}{c} \text{Chain} & \text{Fork} \\ f_Z(z) f_{X|Z}(x|z) f_{Y|X}(y|x) & f_X(x) f_{Z|X}(z|x) f_{Y|X}(y|x) \end{array}$

- Nodes (\overline{X}) , (\overline{Y}) , (\overline{Z}) denote the variables;
- Edges with *arrows* indicate the nature of dependence in the chain rule factorization;
- *Directed* arrows specify the conditional independence assumptions;

Nodes without *incoming* edges are *founders*;



corresponds to

 $f_X(x)f_{Y|X}(y|x)$

Nodes with only *outgoing* edges act to *block* dependence.

For example, in



so that

$$f_{X,Y,Z}(x,y,z) = f_X(x)f_{Y|X}(y|x)f_{Z|X}(z|x)$$

it follows that

 $Z \perp \!\!\!\perp Y | X.$

However, it also follows that, in general

Y⊥Į́Z

(recall the earlier scatterplots)

- *Nodes* or *vertices*, *V*₁, *V*₂, . . . , represent variables.
- *Edges*, E_1, E_2, \ldots , represent dependencies.
- Two nodes are *adjacent* if there is an edge between them.
 - edges can be directed, denoted using arrows, or undirected;
 - if all edges are directed, the graph is directed.

Note: we can use 'bidirected' (edges with an arrow at each end) to indicate general dependence between two variables

although these will be less important in causal settings.

- A *path* is a sequence of edges that connects two nodes;
 - a *directed* path is a path where the directions of arrows on edges are obeyed



Directed path from V_1 to V_4

whereas an *undirected* path is a path that is not directed.



Undirected path from V_1 to V_4

• two nodes are *connected* if a path exists between them, and *disconnected* otherwise.

In general, a graph may contain *cycles*, that is, directed paths that *start* and *end* at the *same* node.



Directed acyclic graph (DAG): a directed graph with no cycles.

Colliders: Suppose we have the DAG



 $f_{X,Y,Z}(x,y,z) = f_X(x)f_Y(y)f_{Z|X,Y}(z|x,y)$

In this DAG, we have $X \perp \!\!\!\perp Y$:

$$f_{X,Y}(x,y) = f_X(x)f_Y(y)$$

e.g. X and Y represent the scores on two dice rolled independently, Z is the total score

$$Z = X + Y.$$

We might observe

$$X = 2, Y = 3 \implies Z = 5.$$

However, conditioning on Z = z

$$f_{X,Y|Z}(x,y|z) \neq f_X(x|z)f_Y(y|z)$$

in general. Equivalently

 $f_{Y|Z,X}(y|z,x)$

depends on the value of *x*.

For example, if we observe Z = 5, and we know X = 2, then we know with certainty that Y = 3.

That is,

$X \perp\!\!\!\perp Y$

but

$X \not \perp Y \mid Z$

Conditioning on *Z* induces dependence; the node is termed a collider.

Example: Factorization



 $f_{X_1}(x_1)f_{X_2|X_1}(x_2|x_1)f_{X_3|X_1}(x_3|x_1)f_{X_4|X_2,X_3}(x_4|x_2,x_3)f_{X_5|X_4}(x_5|x_4)$

When we write


A structural interpretation states that we

- generate X independently,
- generate *Y* and *Z* independently as functions of the realized *X*, for example

Y = 3XZ = 4X + 9



For example

 $Y = X + U_Y$ $Z = X + U_Z$



Fixing X = x and Z = z fixes Y = g(x, z).



If we know X = x and Z = z, then we do not need to know the values of U_X and U_Z to determine Y. That is

$$Y \perp\!\!\!\perp (U_X, U_Z) \mid (X, Z).$$

We can interpret *causation* in terms of these functions.

- *X* causes *Y* if it appears in the function, *g*, that assigns *Y*s value;
- *X* causes *Y* if, in the graph representing the joint distribution, there is a *directed path* from *X* to *Y*;
- *X* is a *direct cause* of *Y* if there is an arrow from *X* to *Y*.

Note



$$X = g_1(U_X)$$

$$Z = g_2(U_Z)$$

$$Y = g(X, Z)$$

so that

$$Y = g(X, Z) = g(g_1(U_X), g_2(U_Z))$$

so both (X, Z) and (U_X, U_Y) can be interpreted as causes of Y.

- X and Z are direct causes,
- U_X and U_Y are indirect causes.

Note

We will proceed by assuming that in a practical setting, the structural relationship and the corresponding causal graph is *known* before any analysis can be carried out.

- Usually in practice this requires expert knowledge;
- Learning the causal graph from data is a hard problem.

Note

If we obtain all variables simultaneously, it is *not possible* to learn which of the possible factorizations is the data generating one.

For example, if we simply observe (X, Y) jointly, we cannot distinguish

 $f_X(x)f_{Y|X}(y|x)$ from $f_Y(y)f_{X|Y}(x|y)$

i.e. does X cause Y or does Y cause X?

Note

In order for X to cause Y, we must have that X precedes Y temporally.

The structural equations form the variables on the left hand side from the variables on the right hand side

$$Y = g(X, Z)$$

that is, we *first* generate *X* and *Z*, and *then* generate *Y*.

That is, there must be a *temporal* ordering.

To assess whether

$Y \perp\!\!\!\perp Z$ or $Y \perp\!\!\!\perp Z \mid X$

for any distribution compatible with the DAG, we must assess whether there is any way for 'information' to 'flow' between Z and Y, maybe once X has been accounted for. First, recall the *collider* graph



X is a collider on the path between Z and Y. Therefore

 $Y \perp\!\!\!\perp Z$ but $Y \perp\!\!\!\perp Z \mid X$

Note that a *directed path* from one node to another *cannot* contain a collider.

The notion of being a collider is *path-specific*: for example



- X is a *collider* on path $Z \rightarrow X \rightarrow U$
- *X* is *not a collider* on path $Z \rightarrow X \rightarrow Y$.

Consider a general path (directed or undirected) between *Z* and *Y*. The path is *open* (or *unblocked*) if there is *no collider* on the path;

- if there is a collider, the path is *closed* (*blocked*).
- *Z* and *Y* are *d*-separated if there is no open path between them; If there is an open path, *Z* and *Y* are *d*-connected.
 - this path must comprise *chains* or *forks* only

Unconditional d-separation

Example: Diabetes example (Rothman et al. p 188)

- X₁ family income
- X₂ genetic risk
- W parental diabetes
- Z low educational attainment
- Y diabetes of subject



Example: Diabetes example (Rothman et al. p 188)

Z and Y are d-separated; there is one path between Z and Y, but it is blocked by the collider W.

 $f_{X_1}(x_1)f_{X_2}(x_2)f_{W|X_1,X_2}(w|x_1,x_2)f_{Z|X_1}(z|x_1)f_{Y|X_2}(y|x_2)$

and *Z* and *Y* are *independent*.

For a *non-collider X*: *conditioning* on *X*:



Conditioning *blocks* the path.

For a *collider X*: conditioning on *X opens* the path

$$(Z \longrightarrow X \longleftarrow Y) \qquad \qquad Z \not\perp Y \mid X$$

Conditional d-separation

Consider the following DAG:



and conditioning on *a descendant*, *W*, of *X*:

$$f_{Z,Y,W}(x, y, w) = f_Z(z)f_Y(y) \int f_{X|Z,Y}(x|z, y)f_{W|X}(w|x) dx$$
$$= f_Z(z)f_Y(y)f_{W|Z,Y}(w|z, y)$$

Therefore we have that



 $Z \not\perp Y \mid W$

and so *W* is a collider in the reduced graph.

Therefore

- (i) conditioning on a *non-collider X blocks* the path at *X*;
- (ii) conditioning on
 - a *collider* X or
 - a *descendant* W of X

opens the path at X;

Consider two nodes X and Y with possibly several open paths connecting them. Suppose S is a set of variables.

- *S* blocks a path if, after conditioning on *S*, the path is closed;
- *S* unblocks a path if after conditioning the path is open;
- If *S* blocks *every path*, then *X* and *Y* are *d*-*separated* by *S*.

• If *S* d-separates *X* and *Y*, then

$$X \perp\!\!\!\perp Y \mid S,$$

so that

$$f_{X|Y,S}(x|y,s) \equiv f_{X|S}(x|s) \quad \forall (x,y,s).$$

X and Y are *conditionally independent* given S.

Conditional d-separation

Example:



 $\{X_2\}$ and $\{X_3\}$ are d-separated by $\{X_1\}$, and $X_2 \perp \!\!\!\perp X_3 \mid X_1$.

- there are two paths between *X*₂ and *X*₃;
 - $X_2 \rightarrow X_1 \rightarrow X_3$: blocked by conditioning on X_1 .
 - $X_2 \rightarrow X_4 \rightarrow X_3$: blocked by the collider at X_4 , and $X_4 \notin \{X_1\}$.

Conditional d-separation

Example:



 $\{X_2\}$ and $\{X_3\}$ are *not* d-separated by $\{X_1, X_5\}$:

- $X_2 \not\perp X_3 \mid (X_1, X_5).$
- X₅ is a descendant of collider X₄;

Conditioning on the common effect of two causes renders the two causes dependent;

- this is known as *selection bias* or *Berkson bias*
- it is the effect we observe in the collider graph





Here $Z_1 \perp \!\!\!\perp Z_2$: there are two paths to consider

•
$$Z_1 \to X \to W \to Z_2$$

•
$$Z_1 \to W \to Z_2$$

both blocked by collider *W*. Therefore $Z_1 \not\perp Z_2 \mid \{W\}$.



Here $Z_1 \perp \!\!\!\perp Z_2$: there are two paths to consider

• $Z_1 \rightarrow X \rightarrow V \rightarrow W \rightarrow Z_2$ is blocked by the collider *X*.

• $Z_1 \to X \to W \to Z_2$ is blocked by the colliders X and W. Therefore $Z_1 \not\perp Z_2 \mid \{X, W\}.$ If X and Y are d-separated by S then

$X \perp\!\!\!\perp Y \mid S$

for *all* distributions compatible with the graph; conversely, if they are not d-separated, then X and Y are *dependent* given S for at least one distribution compatible with the graph.

Intervening set the level of Z to z has the effect of

- removing all *incoming* arrows to Z
- switching the marginal for Z to the *degenerate distribution* $f_Z^*(.)$

$$f_Z^*(z) = \mathbb{1}_{\{\mathbf{z}\}}(z) \quad z \in \mathbb{R}.$$

That is, Z takes the value z with probability 1.

In the earlier example





 $f_X(x)f_{Z|X}(z|x)f_{Y|X,Z}(y|x,z)$

 $f_X(x)f_Z^*(\mathbf{z})f_{Y|X,Z}(y|x,\mathbf{z})$

Consider the DAG



 $f_{X_1}(x_1)f_{X_2|X_1}(x_2|x_1)f_{X_3|X_1}(x_3|x_1)f_{X_4|X_2,X_3}(x_4|x_2,x_3)f_{X_5|X_4}(x_5|x_4)$

Suppose we *intervene* to set $X_3 = x_3$. The relevant DAG is



 $f_{X_1}(x_1)f_{X_2|X_1}(x_2|x_1)f_{X_3}^*(\mathsf{x}_3)f_{X_4|X_2,X_3}(x_4|x_2,\mathsf{x}_3)f_{X_5|X_4}(x_5|x_4)$ and X_1 is *no longer a cause* of X_3 . We aim to understand the effect of Z on Y.

• An *open undirected path* between *Z* and *Y* allows for the association between *Z* and *Y* to be modified by the presence of other variables.

This is known as a *biasing* path.

- By 'association', we mean some form of *correlation*.
- Usually association is estimated using regression,

Graphical representation of bias

• The association between *Z* and *Y* is *unbiased* for the effect of *Z* on *Y* if the only open paths between them are *directed paths*.



Consider a set of nodes *S*:

- *S* is *sufficient* to control bias in the association between *Z* and *Y* if after conditioning on *S* the remaining *open* paths between *Z* and *Y* are precisely the *directed* paths between *Z* and *Y*;
- *S* is *minimally sufficient* if it is the *smallest* sufficient set.

Note: Conditioning on descendants of ${\cal Z}$

(i) *blocks* directed paths


Graphical representation of bias

(ii) may *create* paths that lead to *biasing* of the effect of *Z* on *Y*.



In this graph,

- the only open path between *Z* and *Y* is the *direct* path;
- conditioning on *X* opens a *biasing* path.

(iii) may be unnecessary in statistical terms: for example



In this graph, conditioning on *X* will not affect bias.

Undirected paths from *Z* to *Y* are termed *backdoor* paths (relative to *Z*) if they *start* with an arrow pointing *into Z*.



The only path from Z to Y is a backdoor path; however, it is not open because of the collider W.

Before conditioning

- *all biasing* paths in a DAG are backdoor paths, and
- all *open* backdoor paths are biasing paths.

To obtain an unbiased estimate of the effect of Z on Y, all backdoor paths between Z and Y must be *blocked*.

Set *S* satisfies the *backdoor criterion* with respect to *Z* and *Y* if

- (i) *S* contains no descendant of *Z*, and
- (ii) there is *no open backdoor path* from *Z* to *Y* after *conditioning* on *S*.

A *confounding path* between Z and Y is

- (i) a *biasing* path (that is, an *undirected open path*) that
- (ii) *ends* with an arrow into *Y*.

Variables on a confounding path are termed *confounders*.



X is a confounder in both cases.



W is a collider on the undirected path from Z to Y

Path 1:
$$Z \to X_1 \to W \to X_2 \to Y$$

and hence this path is blocked.

However unconditional on W, the effect of Z on Y is confounded by the backdoor path

Path 2:
$$Z \to X_1 \to W \to Y$$
.

Conditioning on W alone opens Path 1, therefore to block both paths, we need to condition on

 $S \equiv \{W, X_2\}.$



Conditioning on *W* opens the confounding path. Therefore $Z \perp \!\!\!\perp Y$ (as there is no open path between them), but

 $Z \not\perp Y \mid W$

Further conditioning on either $\{X_1\}$ or $\{X_2\}$ blocks the path.



Conditioning on W blocks the confounding path. Therefore conditioning on any one of

$$\{X_1\}, \{W\}, \{X_2\}$$

will block the path.

For the effect of *Z* on *Y* relative to *X*:

- *Direct effect:* A direct effect of *Z* on *Y* is the effect captured by a *directed* path from *Z* to *Y* that does not pass through *X*.
- *Indirect effect:* An indirect effect of *X* on *Y* that is captured by directed paths that pass through *X*.
 - *X* is termed an *intermediate* or *mediator* variable.

Direct and indirect effects





Indirect effect

Direct (D) & Indirect effect

X is a mediator of the indirect effect

Direct and indirect effects



No indirect effect

Direct effect is not confounded

X is a collider, so there is no other open path from Z to Y.

Suppose that in reality there is a further variable U that is a confounder, but is unmeasured in the observed data.



There is a hidden confounding path $Z \rightarrow U \rightarrow Y$. Conditioning on *U* is not possible, as we are unaware of its existence.

With two unmeasured confounders:



We have that X, Y and Z are *independent*; the (true but hidden) path between Z and Y is blocked at collider X.

Unmeasured confounding

Suppose we condition on *X*:



In the modelled DAG, $Y \perp Z \mid X$; however, conditioning on *X* opens the *hidden* path through U_1 and U_2 , so there is now an open biasing path.

This is sometimes referred to as the *M*-bias phenomenon.

We have seen that conditioning on variables can close biasing paths, allowing an unbiased assessment of the causal effect of Z on Y.



The open, undirected path

$$Z \to X \to Y$$

can be blocked by conditioning on *X*.

If all the variables are jointly Normally distributed, then this conditioning can be achieved by including X as a predictor in a linear regression model of Y on Z.

That is, we can fit the linear model where

$$\mathbb{E}[Y|X=x, Z=z] = \beta_0 + \beta_1 x + \psi z$$

and estimate the direct effect of *Z* on *Y* by estimating ψ .

Note

Blocking confounding paths (e.g. by conditioning) is not quite the end of the story.

Typically we need to utilize *parametric* inference, and there is usually a requirement that certain parametric models are *correctly specified*.

In a statistical formulation of a causal inference problem

- 1. We identify *treatment Z* and *outcome Y*
- 2. We form the *DAG* representing the relationships between Z and Y which contains other measured variables X.
- 3. The causal effect of *Z* on *Y* flows down *open* and *directed* paths from *Z* to *Y*;
 - there may be a *direct* effect if there is an arrow from Z into Y;
 - there may also be *indirect* effects if the directed path passes through *mediating* variables.

- 4. If there are *undirected* paths from *Z* to *Y* that are open, then these paths may induce *bias* in estimation of the effect of *Z* on *Y*.
- 5. In order to obtain unbiased estimation, the open undirected (biasing) paths must be *blocked*; typically this is done by *conditioning* on variables on those paths.
- 6. A *collider* node blocks a path; however, conditioning on the collider *opens* the path at that node.