Causal Modeling of Bias:
A graphical overview of concepts for methods

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I. Bias: **The** core problem (**Not** random error or fitting method)

State of epidemiology: Often called upon to give and has at times given "answers" to questions it can't reasonably answer due to uncontrolled (and often uncontrollable) sources of bias.

Example: Nutritional epidemiology.

- A worldwide epi study could not tell us whether observed associations are causal, because…
- We can never practically eliminate sources of **bias** (explanations other than direct causation, or lack thereof).
- All we can do is document how data were collected and what they look like, and then offer explanations of why they look that way.

Epidemiologic definition of bias:

- Nonrandom difference between an estimate and the true value of the target parameter,

Also known as

- systematic error
- invalidity

Can only be prevented or controlled by design and measurement strategies that are often infeasible (e.g., the RCT)

Statistics definition of bias:

- Difference between the average value of an estimator and the true value of the target parameter (e.g., a relative risk)

There are subtle differences between the epidemiologic and statistical definitions; statistical bias subsumes problems (such as sparse-data bias) that go beyond study methods missing data.

Types of bias

Epidemiologic categories (overlapping):

- Confounding (nonrandom exposure)
- Selection bias (nonrandom sampling)
- Bias from measurement error

There are many finer divisions, but they obscure the underlying deductive logic of the biases. All can be treated as missing-data biases.

Further statistical categories (often important but overlooked in epidemiology):

- Bias from use of a wrong model form (model-form mis-specification)
- Stat-method invalidity (e.g., ordinary stepwise selection)
- Method failure (e.g., sparse-data bias)
- Method misinterpretation (e.g., of null significance tests and post-hoc power)

Given bias, statistical analysis is never more than sensitivity analysis

- Logic is about conclusions that could be drawn regardless of the content
- Logical deduction concerns what must follow from what is assumed
- Deductions can only be hypotheticals of the form “If we assume this, we can deduce that…,” and some would say this is all science can offer beyond data

Expanding the model (weakening assumptions) to assess sensitivity

- Sensitivity analysis varies assumptions to see how deductions vary.

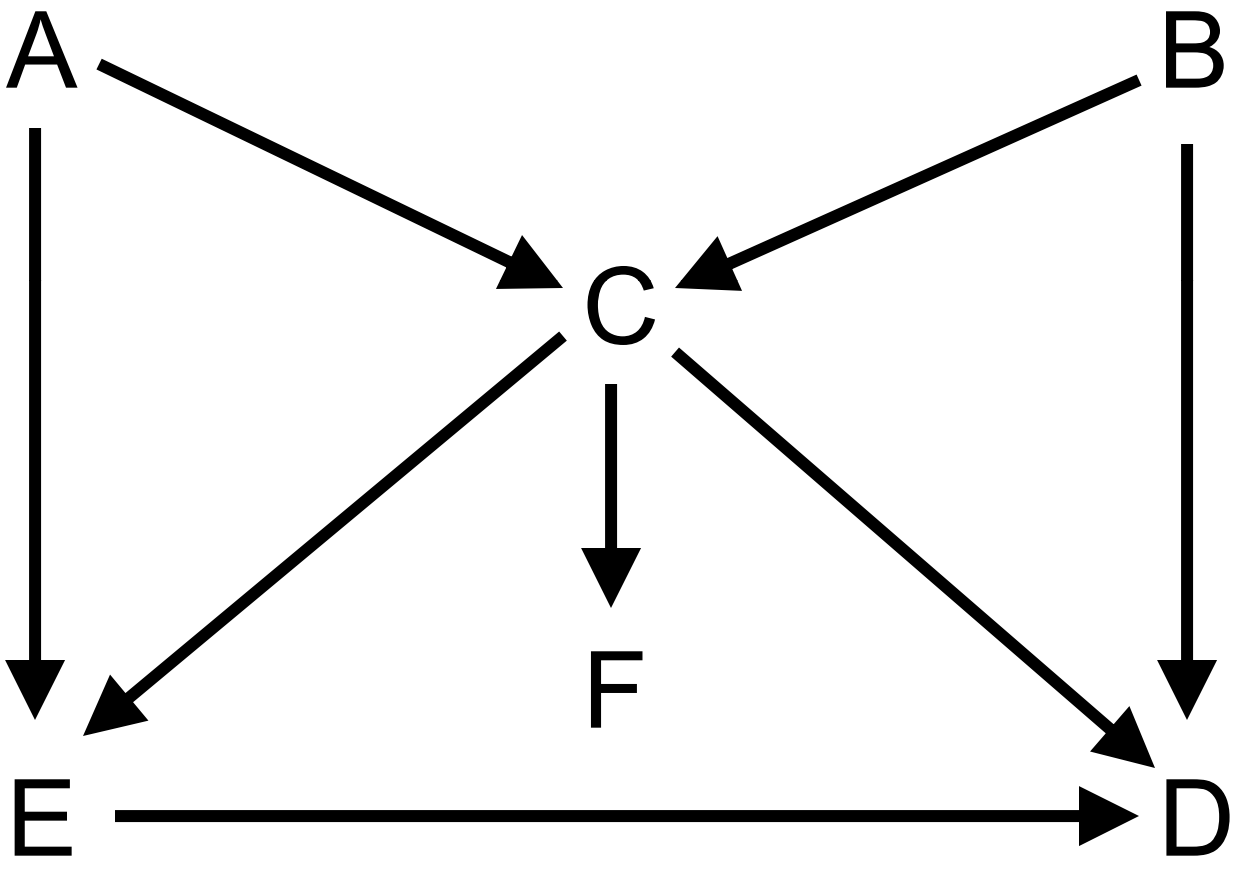
Only effective to the extent variations are

- **Plausible** (not contradicted by generally accepted theory and observation), and
- **Extensive** (cover many dimensions over their plausible range)

II. Causal diagrams: The easiest way to see and learn about bias sources

(The topology of causation and bias)

Example DAG
(directed acyclic graph)



Directed acyclic graphs (Bayes nets)

- A directed acyclic graph (DAG) shows the factors in the problem linked by arrows only, with no feedback loops.
- Have been used for decades to graph systems & conditional independencies, without explicit causal interpretations.
- Give independencies in joint distributions for the variables (nodes) that are **compatible** with the graph.

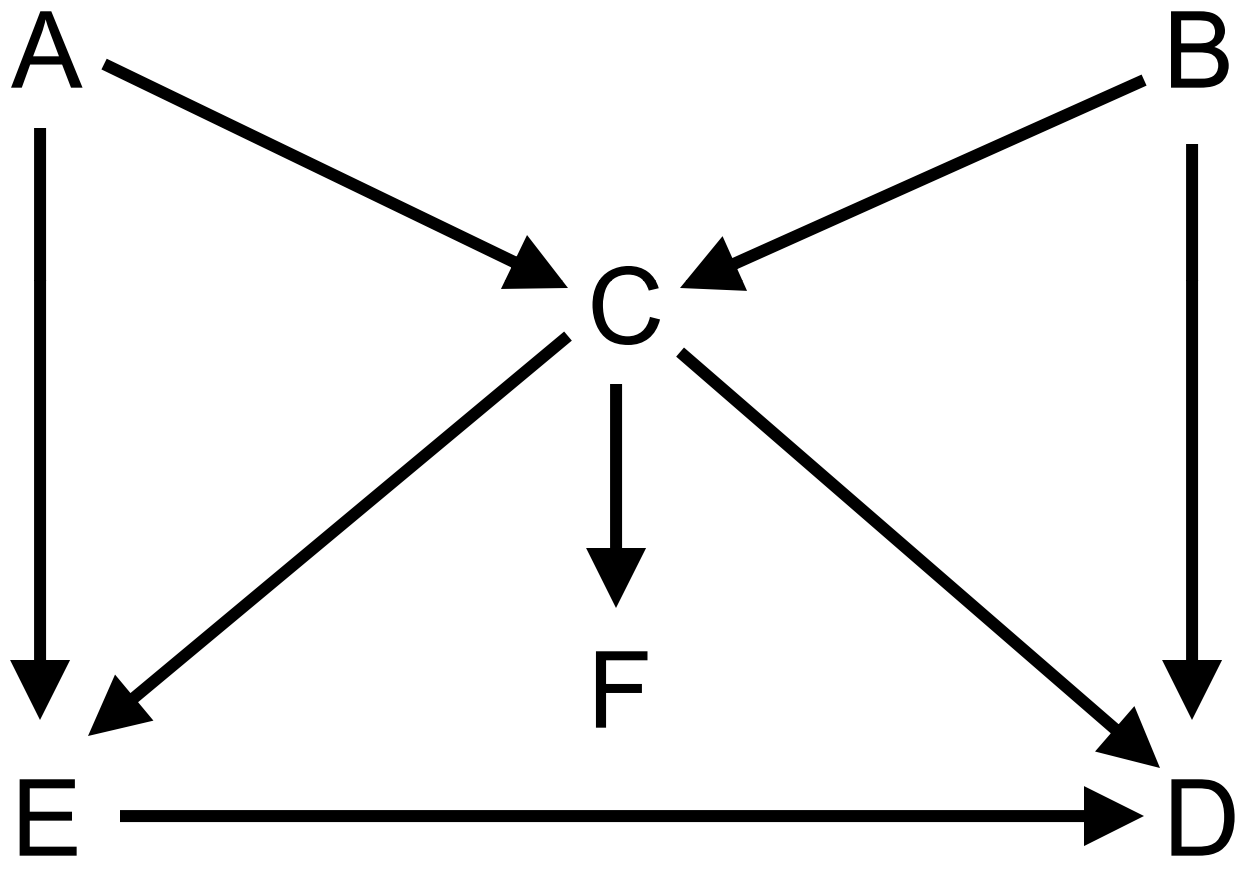
Compatible distributions

- Satisfy the Markov condition on the nodes **X**:

$$P(\mathbf{X}) = \Pi_j P(X_j|pa[X_j])$$

- Satisfy the condition that d-separated variables in the graph are independent.
- The converse (independent variables are d-separated = "faithfulness"), is not true for most compatible distributions (faithful distributions obey hard constraints).

Compatibility means P(A,B,C,E,F,D) = P(A)P(B)P(C|A,B)P(E|A,C)P(F|C)P(D|B,C,E)



Causal diagrams (path diagrams, causal Bayesian networks)

In a **causal diagram**, the arrows are interpreted as links in causal chains

- **Causal effects** of one variable on another are transmitted by **causal** sequences, which are **directed** (head-tail) paths:

  $X \rightarrow Y \rightarrow Z$ means X can affect Z

Concepts relative to a given DAG – these are **not** states of nature:

- "Direct cause": A causal arrow always represents a series of events that we have chosen not to model.
- "Endogenous": Has some causes (parents) in the graph.
- "Exogenous": Has no causes in the graph: We have chosen to take all its causes as independent random.

- Causal diagrams are schematics for causal explanations (e.g., “Process P may have caused bias B”) of multivariate associations (joint distributions).
- Diagramming a study can reveal avenues for bias that might be overlooked.
- “Faithfulness” is not used here! I only recommend diagrams to spot biases, **not** for “discovery.”

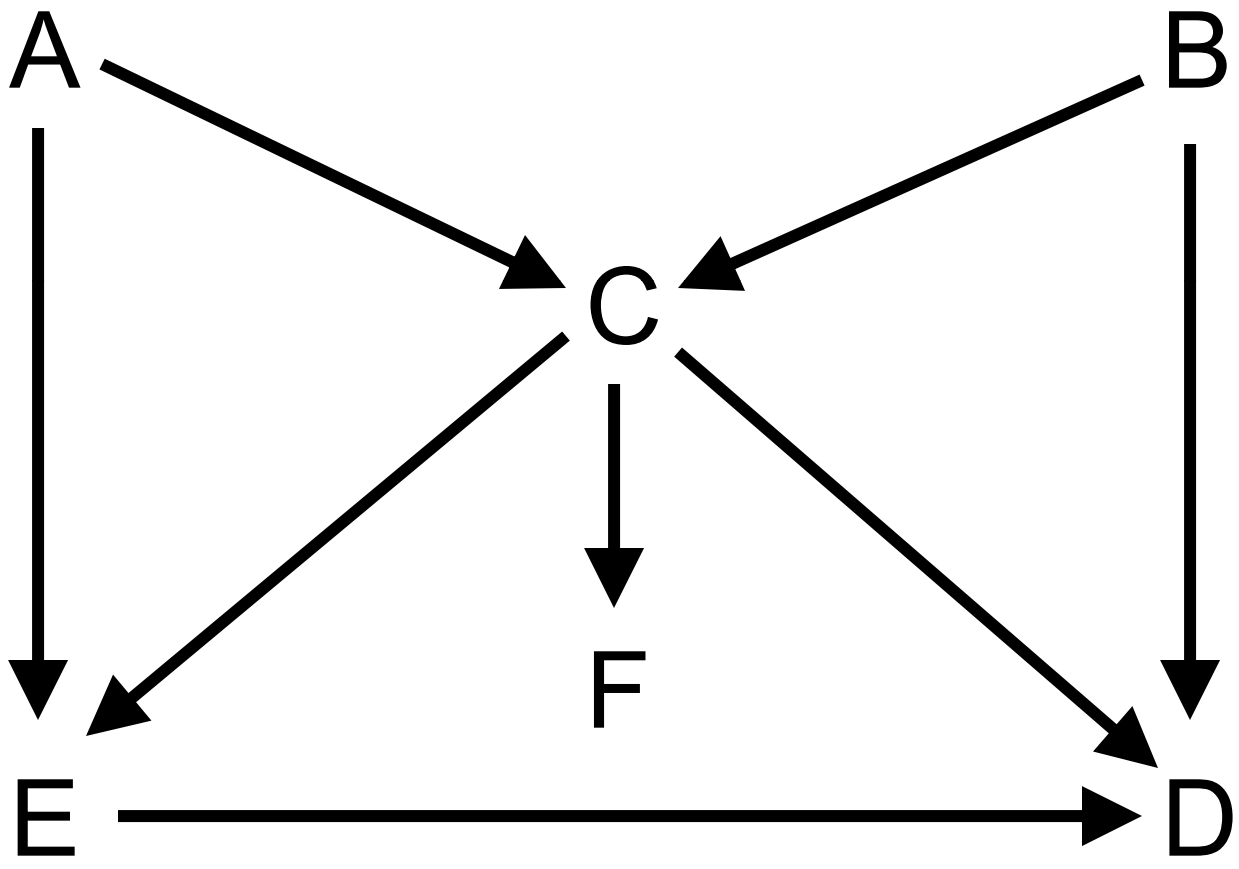
Assumptions coded in causal diagrams

Assumptions of a causal diagram are of two forms:

1) Arrow directions imply time ordering
2) Arrow absences imply null hypotheses:

No directed path from X to Y means that X and Y are independent given all direct causes ("parents") of X ("Causal Markov Condition")

Spot the implied causal nulls



Think of associations as signals flowing through the graph

- A variable may transmit associations along open (unblocked) directions but not along closed (blocked) directions.
- The open and closed directions are switched to closed and open by conditioning (stratifying) on the variable (and may be partially switched by partial or indirect conditioning)

Colliders **on a path**

Paths are **closed** (blocked) at colliders:

- Associations **cannot** be transmitted across a **collider** (→C←) on a path **unless** we at least partially condition (stratify) on it or something it affects (a descendent, such as F in C→F).

Colliders **on a path**

Paths are **opened** (unblocked) at colliders by conditioning on them:

- Associations **may** be transmitted across a **collider** (→C←) on a path if we at least partially condition (stratify) on it **or something it affects** (such as F in C→F).

"(C)" = C unobserved

"[C]" = C conditioned

Noncolliders **on a path**

Paths are **open** (unblocked) at noncolliders:

- Associations **may** be transmitted across a **noncollider** (a **mediator** →C→ or a **fork** ←C→) on a path **unless** we completely condition (stratify) on it.

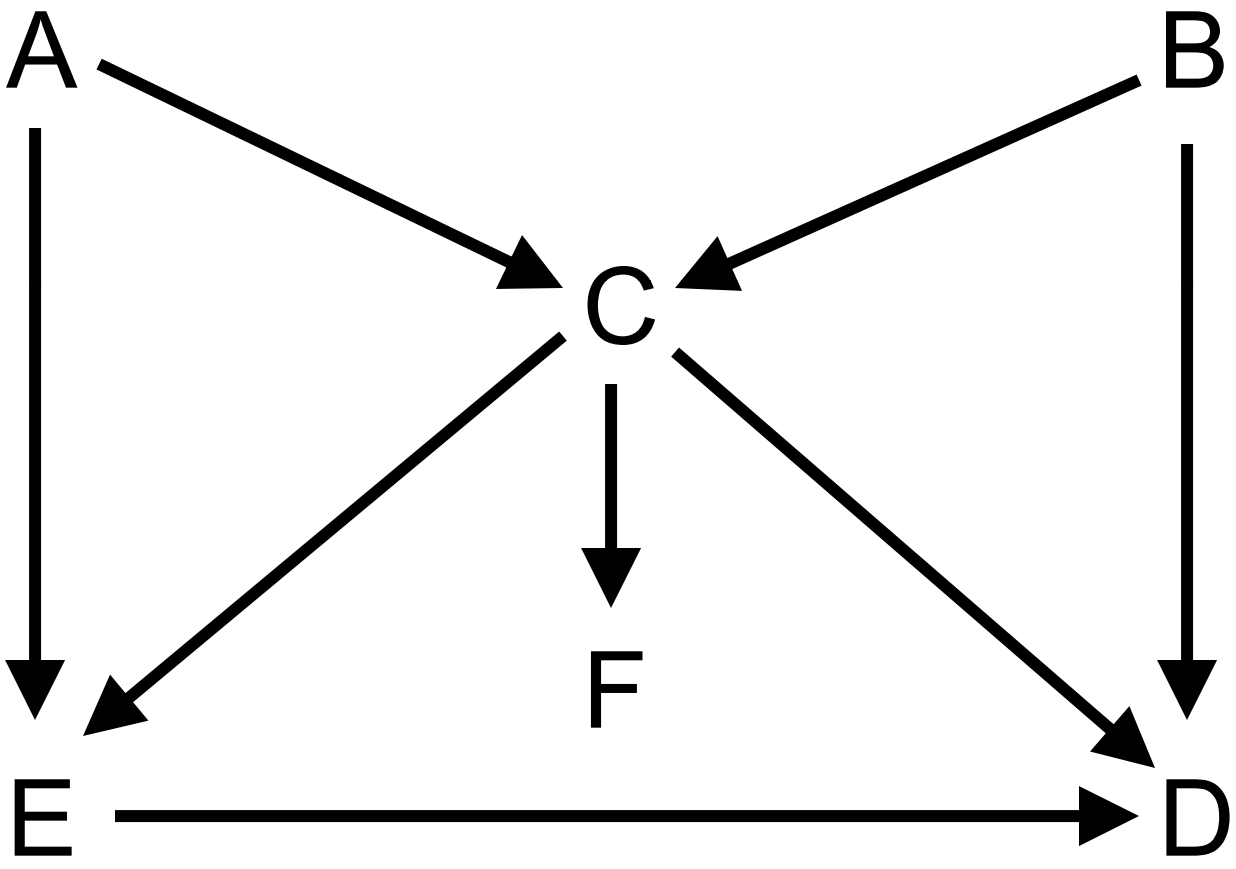
Noncolliders **on a path**

- Associations **cannot** be transmitted across a **noncollider** on a path if we **completely** condition (stratify) on it.

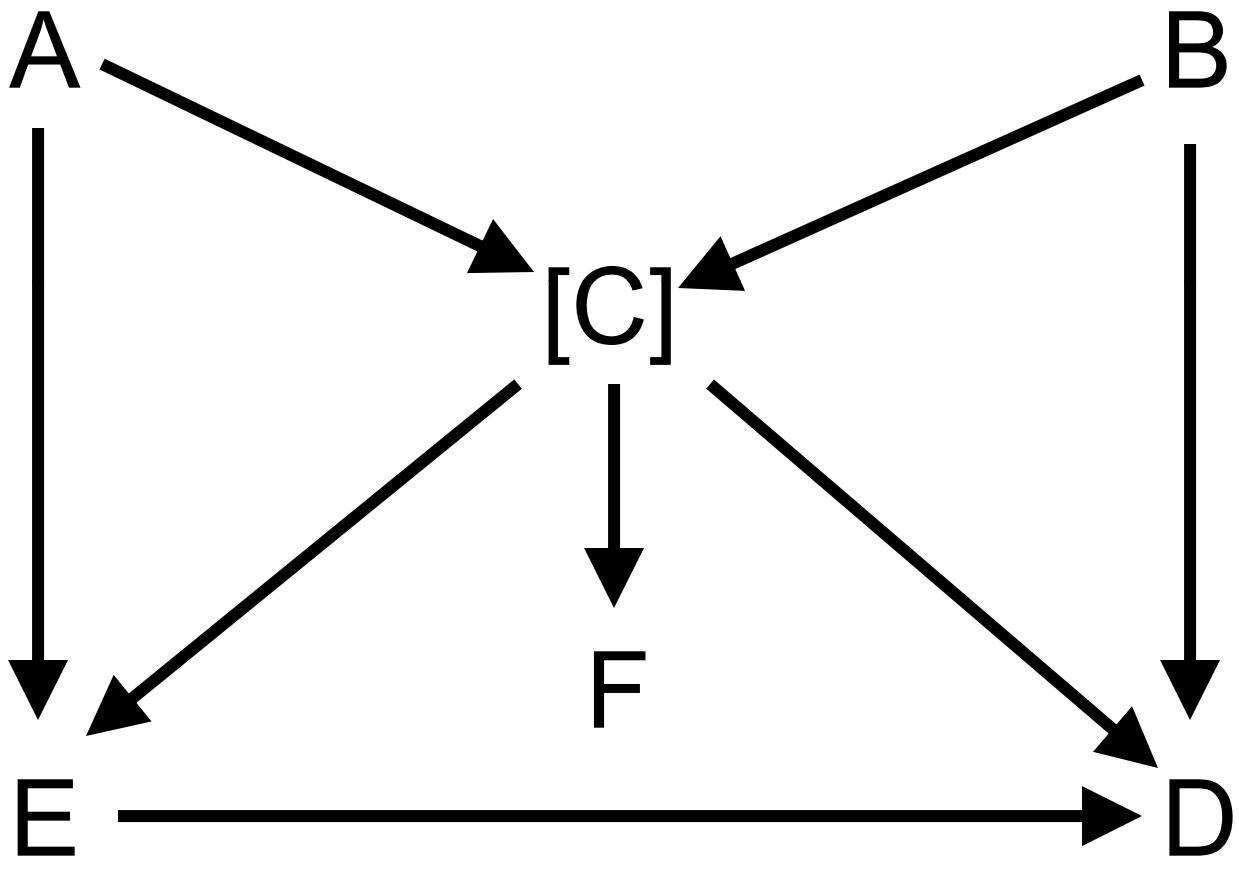
Partial conditioning (e.g., 10-year age categories, smoking yes/no) usually yields only partial control.

NOTE: A variable is a collider or noncollider **relative to a path** only

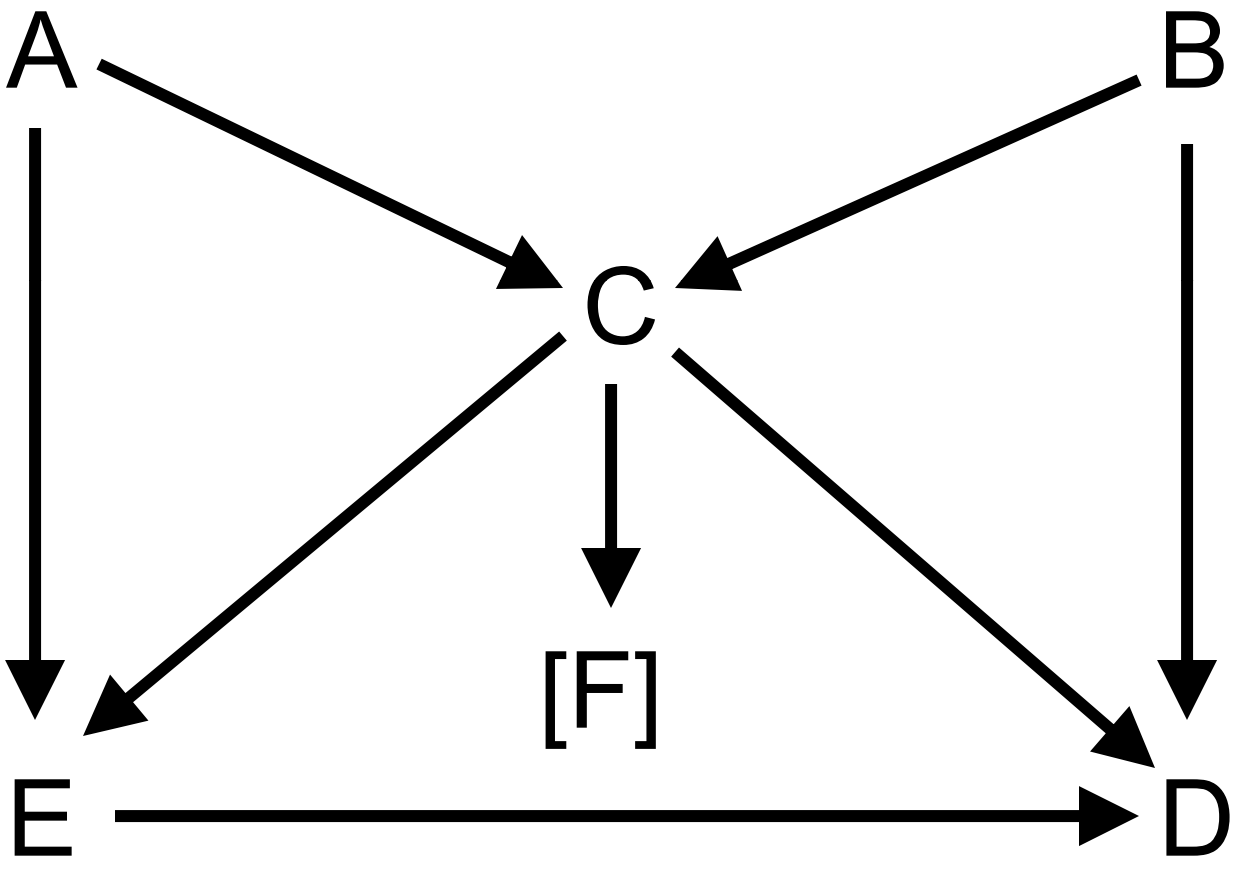
Spot the open and closed directions for C:



Spot the open and closed directions for C after conditioning on C:



Spot the open and closed directions for C given F:

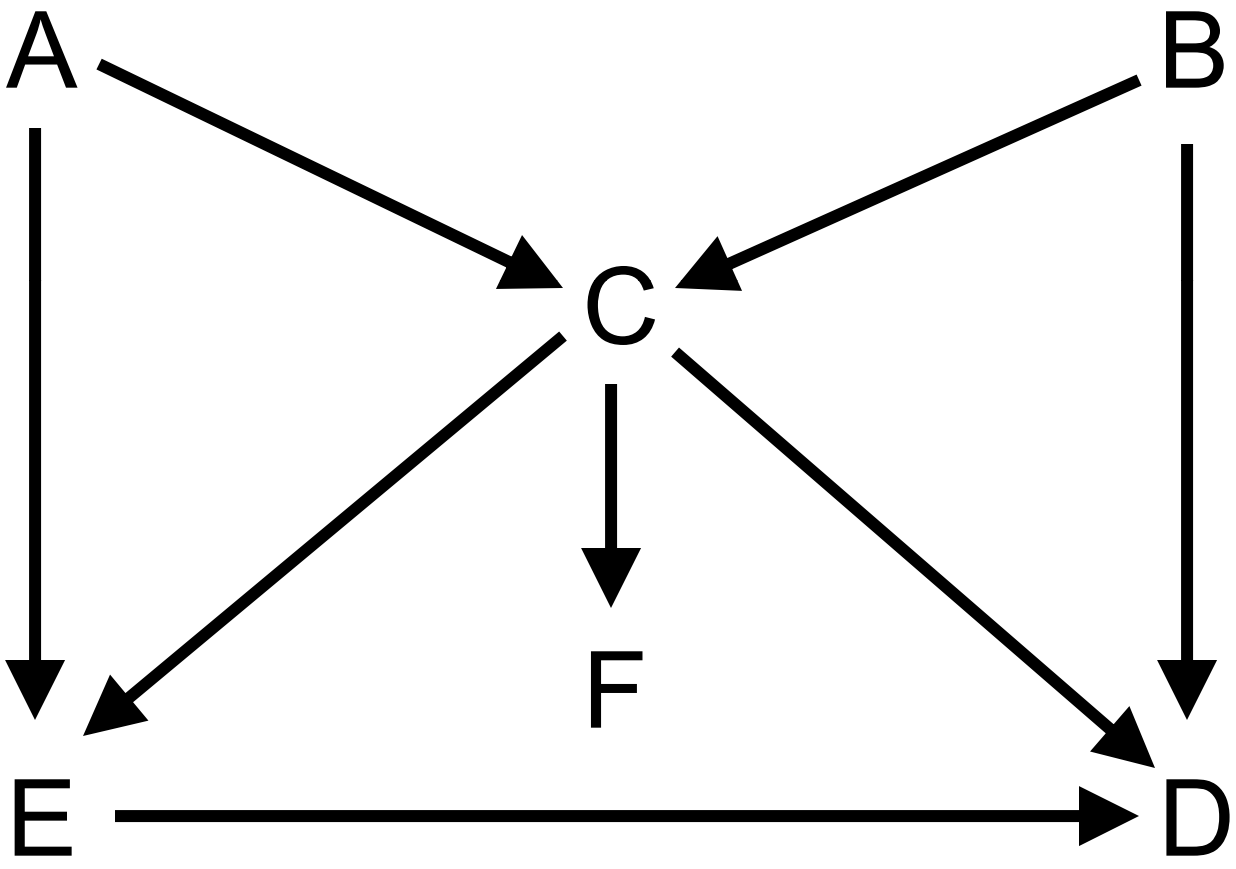


Closed and open paths

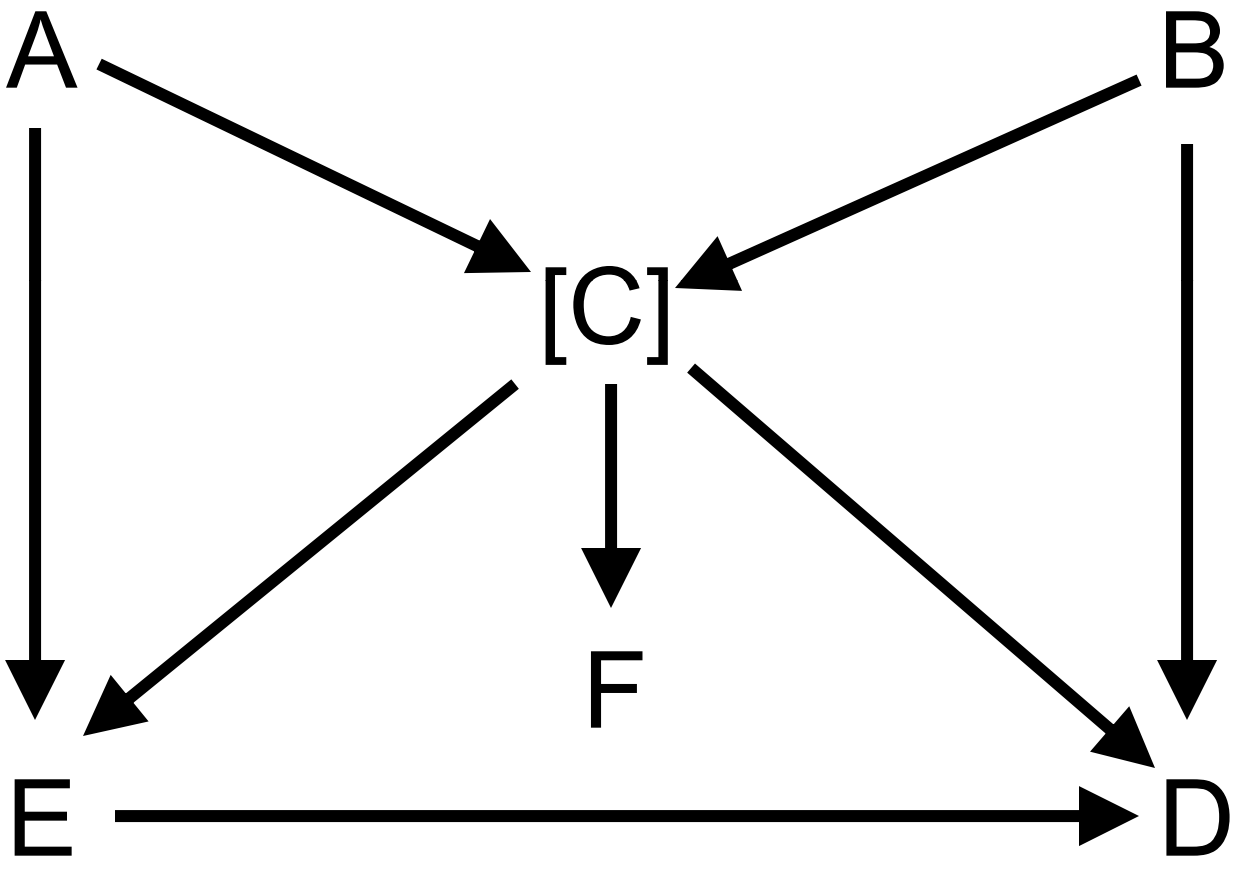
- Closed (blocked) path: Closed at **some** variable within the path, hence **cannot** transmit associations.
- Open (unblocked) path: Open at **all** variables within the path, hence **can** transmit associations.

Conditioning may open some closed paths and close some open paths

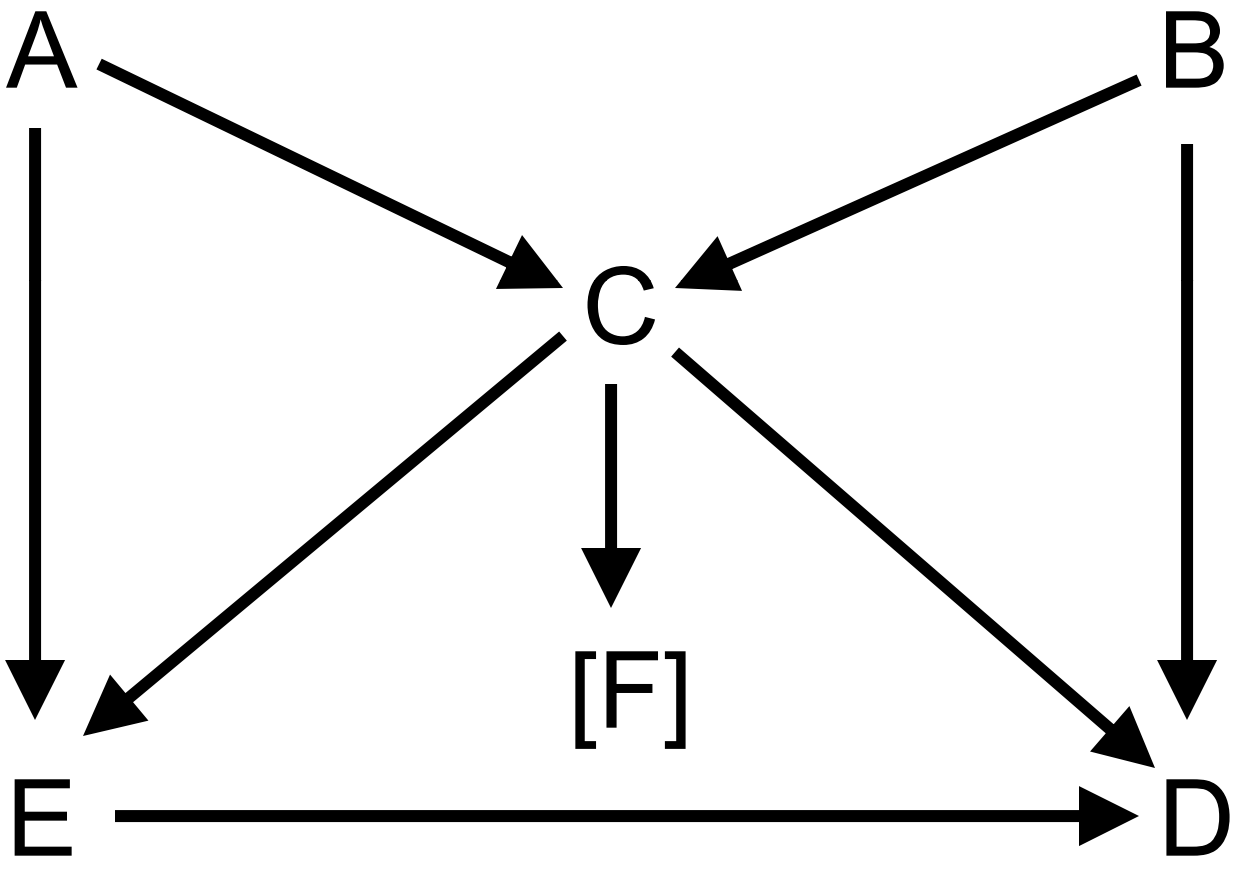
Spot the open and closed paths:



Spot the open and closed paths given C:



Spot the open and closed paths given F:

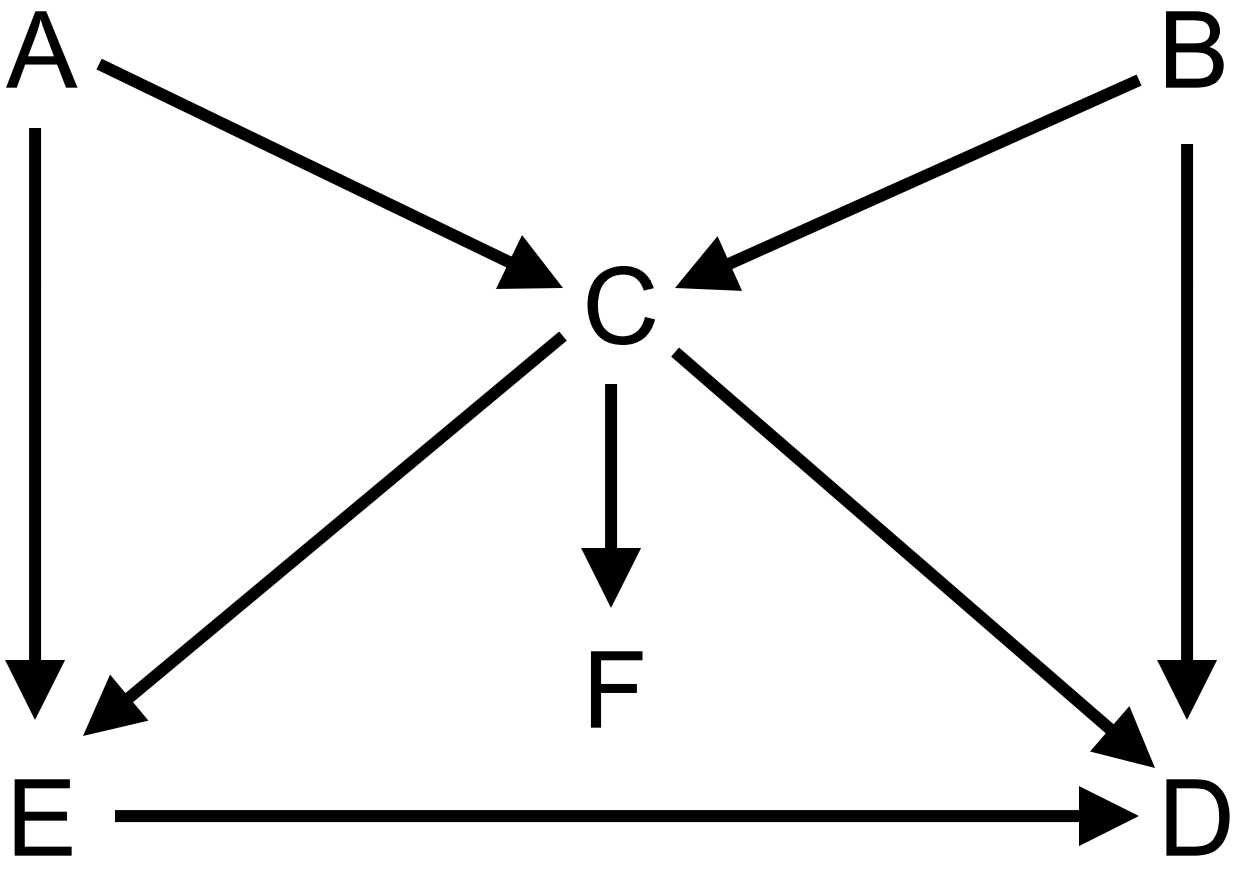


d-connectedness and d-separation

Two (sets of) variables are

- d-**connected** if there **is** an open path (association route) between them
- d-**separated** if there is **no** open path (no association route) between them

Spot the connected and separated variables:

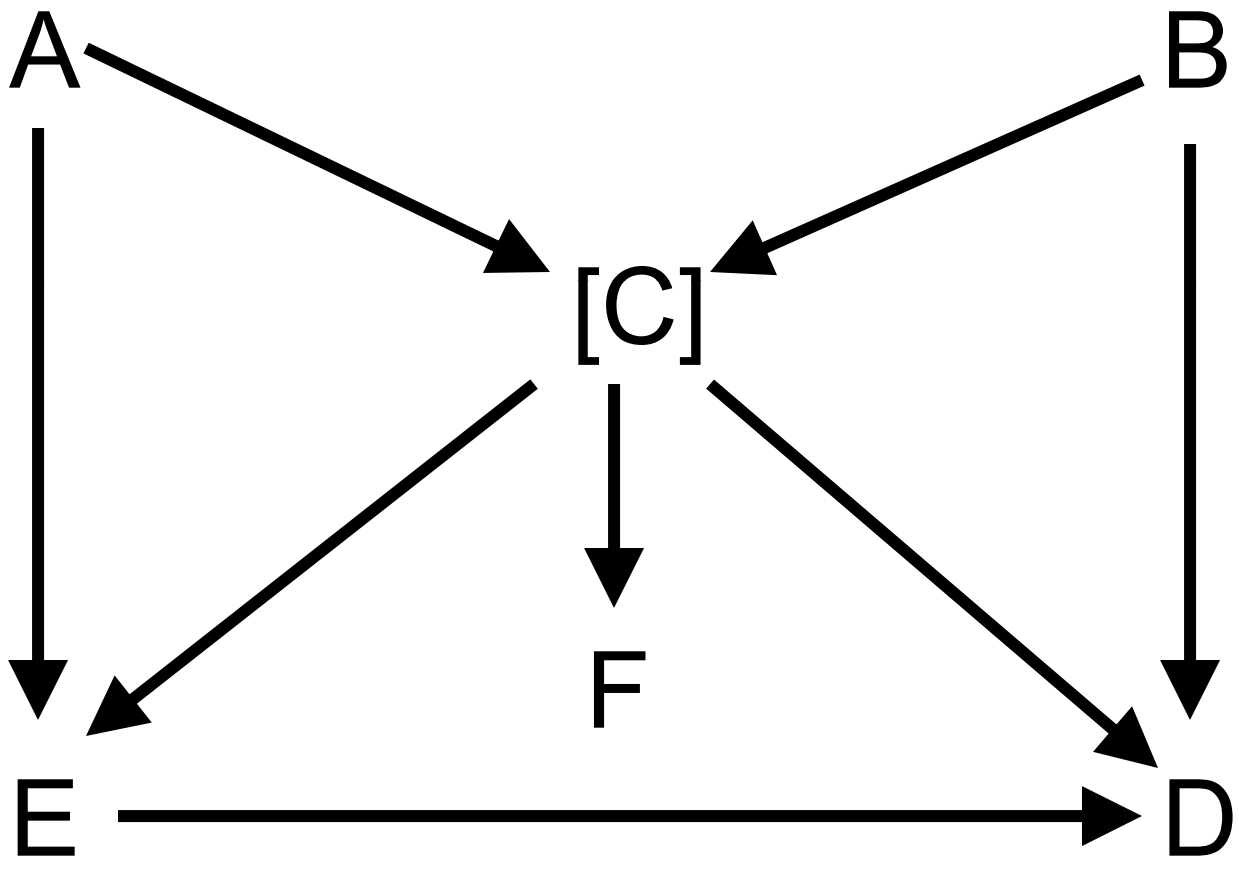


Conditional d-connectedness and d-separation

Two (sets of) variables are

- d-**connected** given (a set) S if there **is** an open path between them conditional on S
- d-**separated** given (a set) S if there is **no** open path between them conditional on S

Spot the connected and separated variables given various sets:



Separated → independent
Connected → **may** be associated

In the example, A and B are separated, hence independent, but

- are connected given C or given F, hence may be associated given C or F

E and D are connected, hence may be associated, and remain so given C, but

- If E has no effect on D, E and D are separated given A,C or given B,C, hence are independent given A,C or B,C.

Target paths vs. biasing paths

- **Target path**: A path that transmits some of the target association; in causal analysis, a target path must be a directed path from the posited cause to the posited effect.
- **Biasing path**: Any other open path; in causal analysis, any open undirected path between the posited cause and effect variables.

Objective: “Control” of bias

By judicious conditioning, we must close all biasing paths without closing target paths or opening new biasing paths.

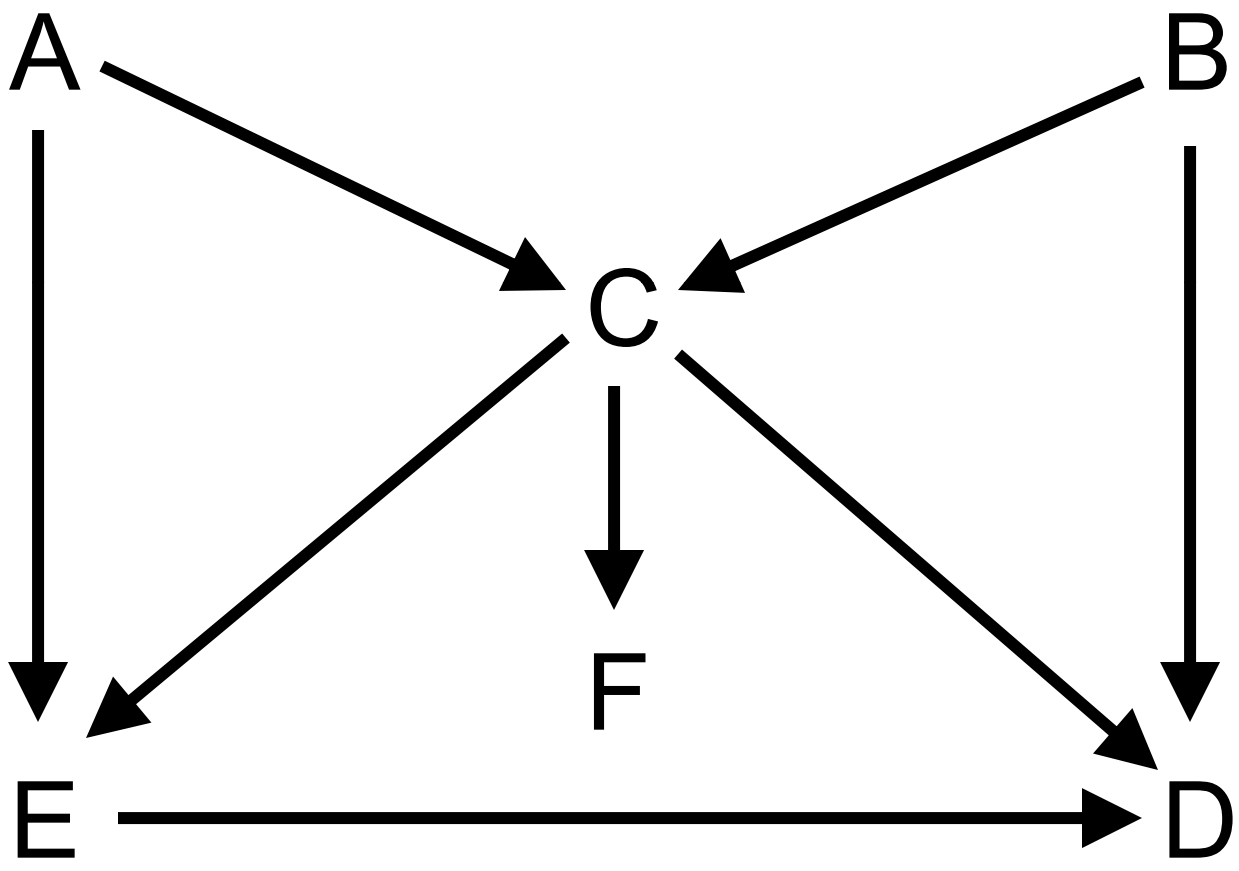
- **This isn’t always possible with available data.**

Sufficiency for “control” (conditioning)

A set Z of variables in the graph is **sufficient** for estimating a target effect of E on D (the net effect transmitted via all target paths) if, after conditioning on Z, the open paths are exactly the target paths (all biasing paths are closed and no target paths are open).

Z is **minimal sufficient** if no proper subset is sufficient.

Sufficient: A,B,C
Minimal sufficient: A,C and B,C



Confounding

There are many definitions, none universally accepted. My definition:

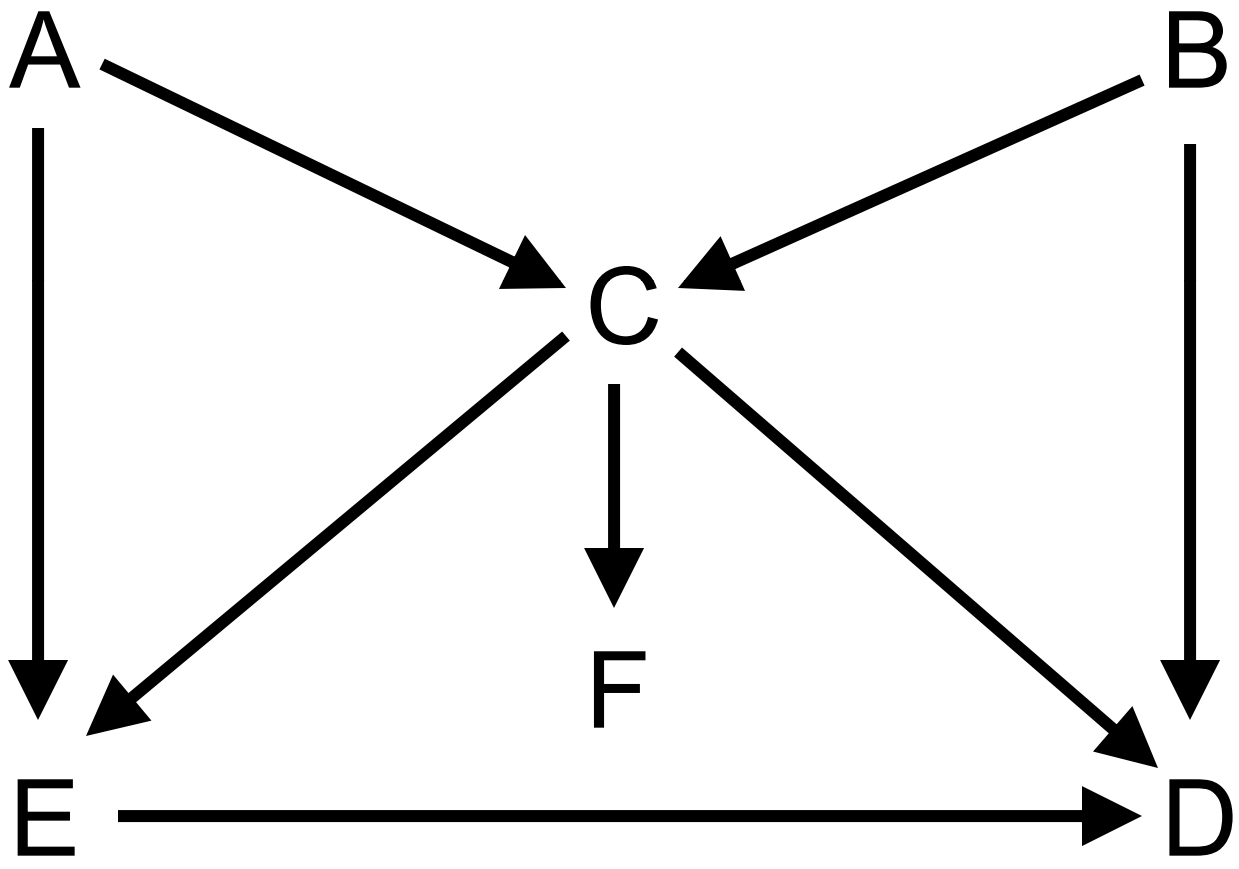
- Noncausal association transmitted via effects on the outcome

This definition appears to correspond best to the intuitive definitions given since the 19th century: Confounding is a mixing of the effect of interest with other effects on the outcome (Mill, 1843).

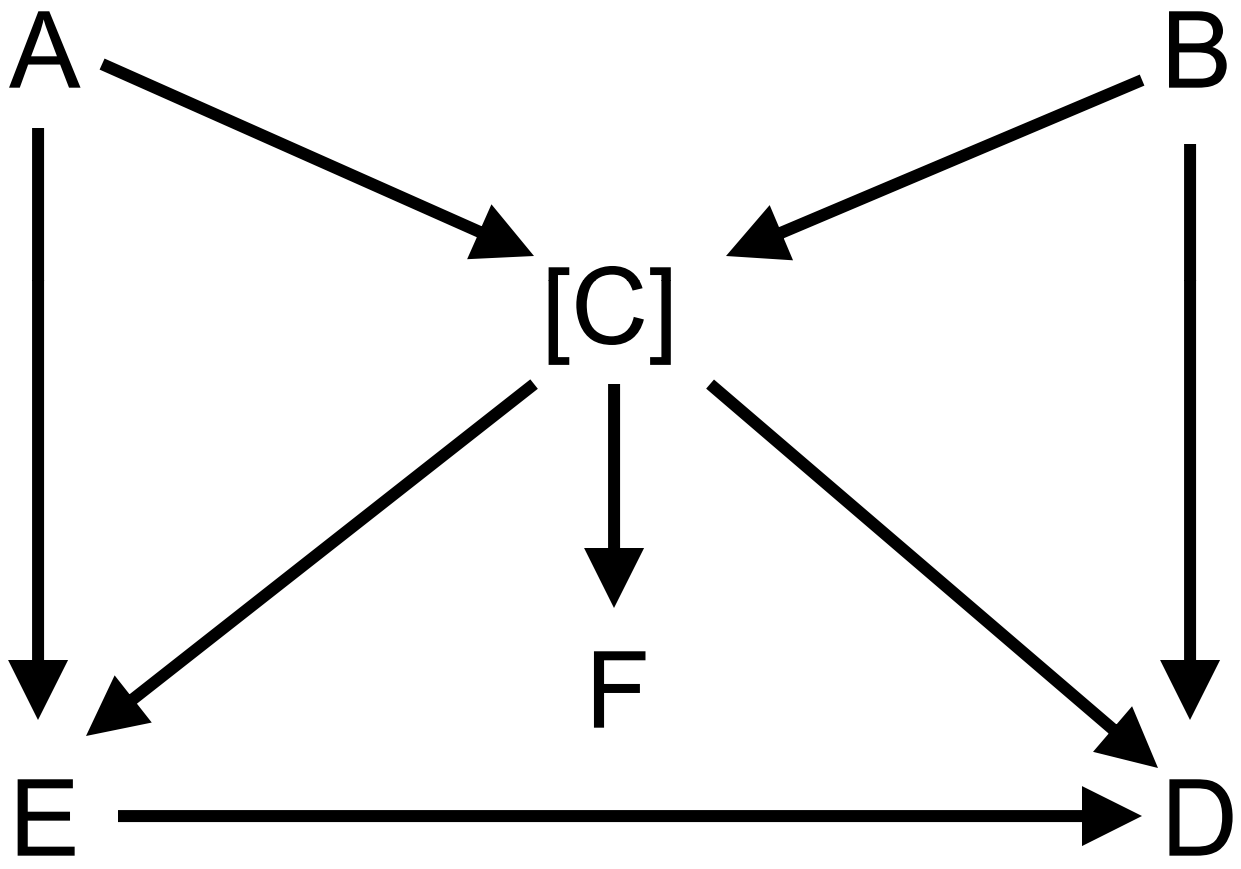
Confounding paths and confounders

- Confounding path: Any path capable of transmitting confounding
- Confounder: Any variable within a confounding path (one of many defs.)
- Without conditioning, all biasing paths in a DAG are confounding paths,
- HOWEVER, upon conditioning, other kinds of bias arise…

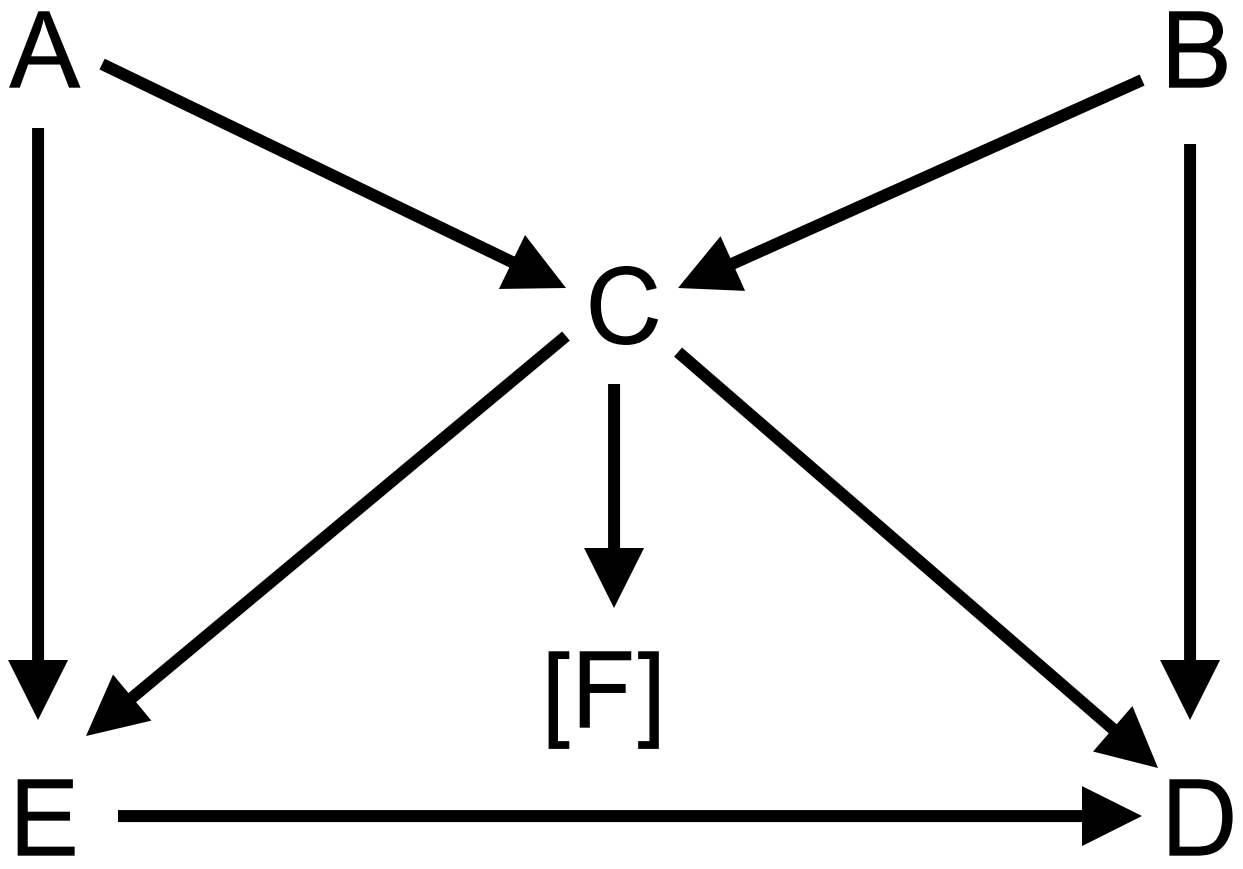
Confounding paths from E to D: EACD, ECBD, ECD



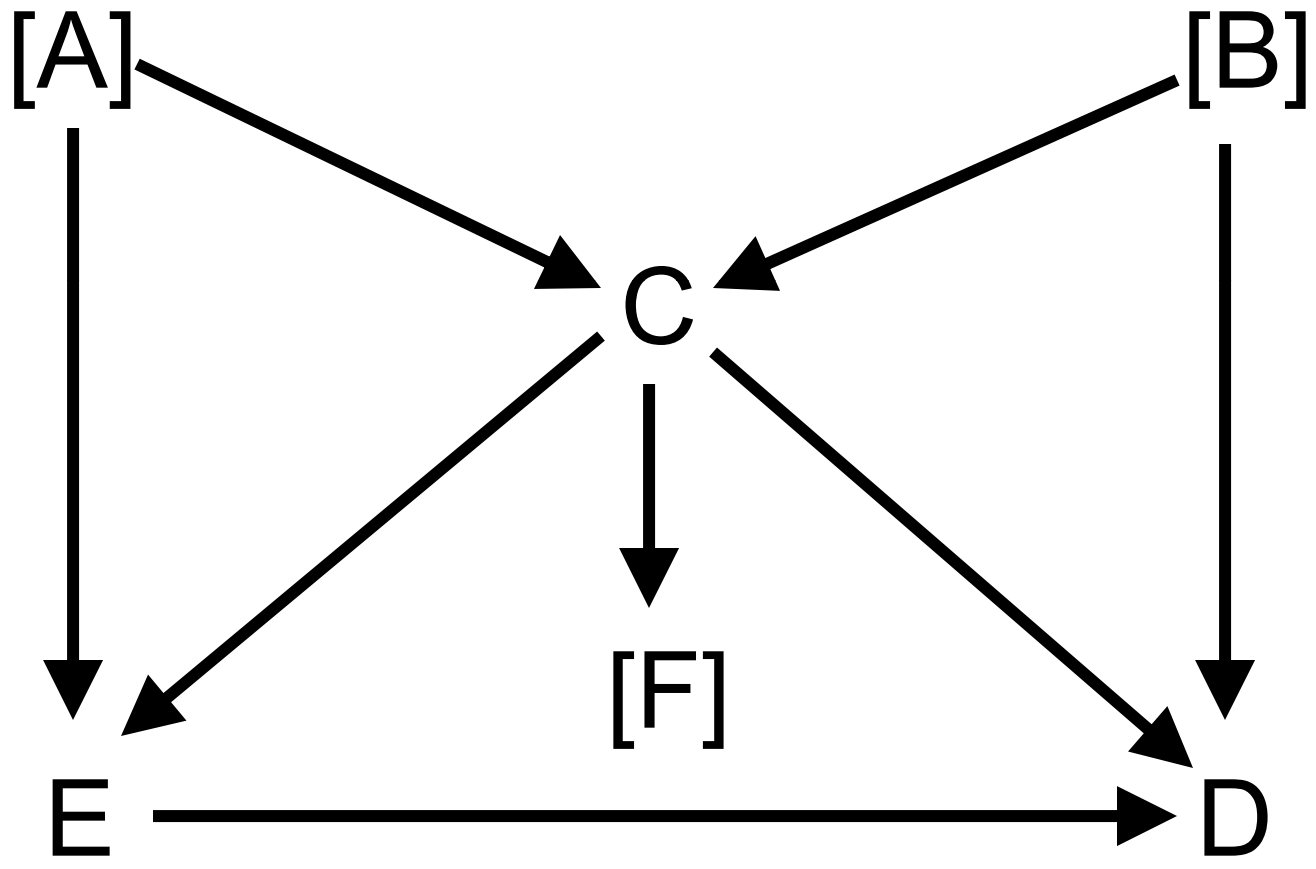
Confounding paths from E to D after conditioning on C: EACBD



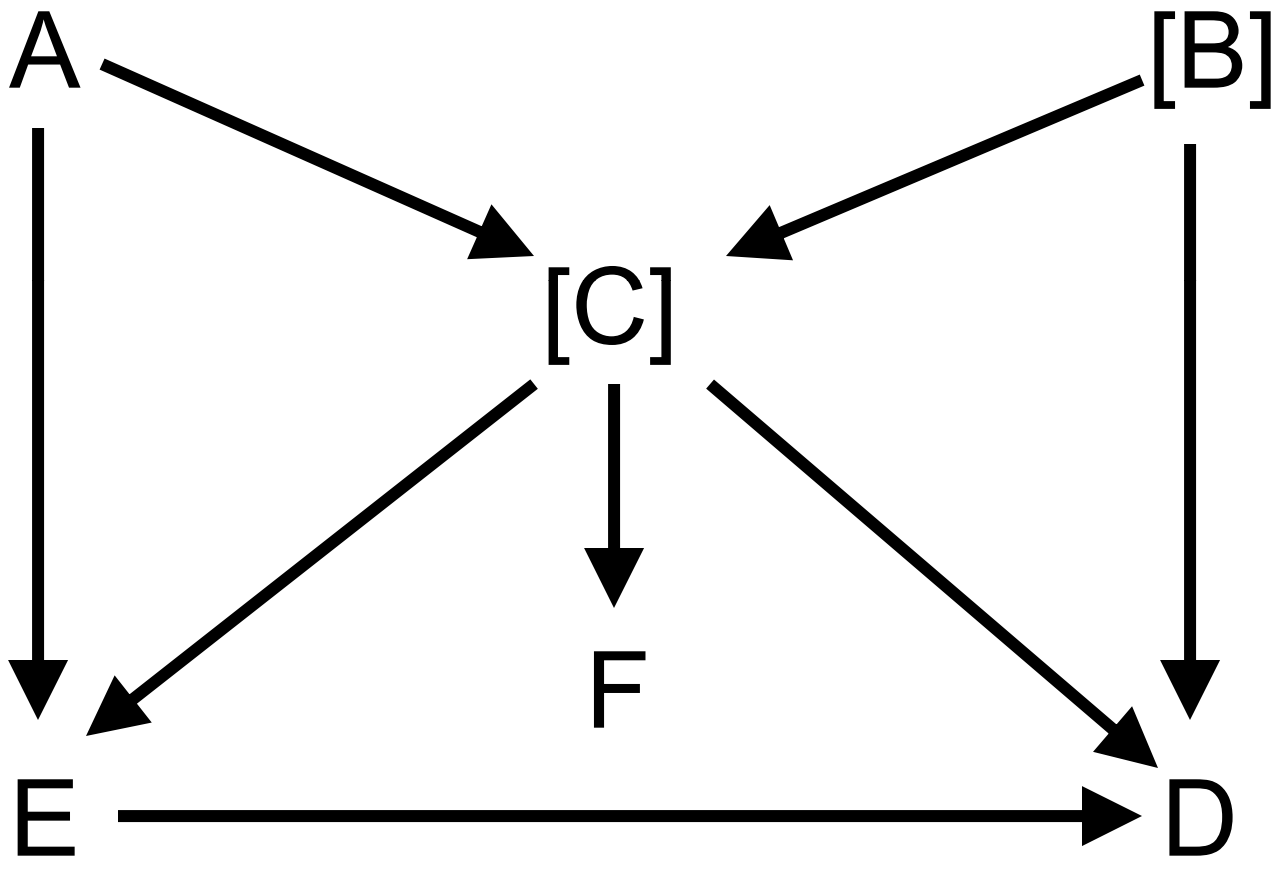
Confounding paths from E to D: EACD, ECBD, ECD, EACBD



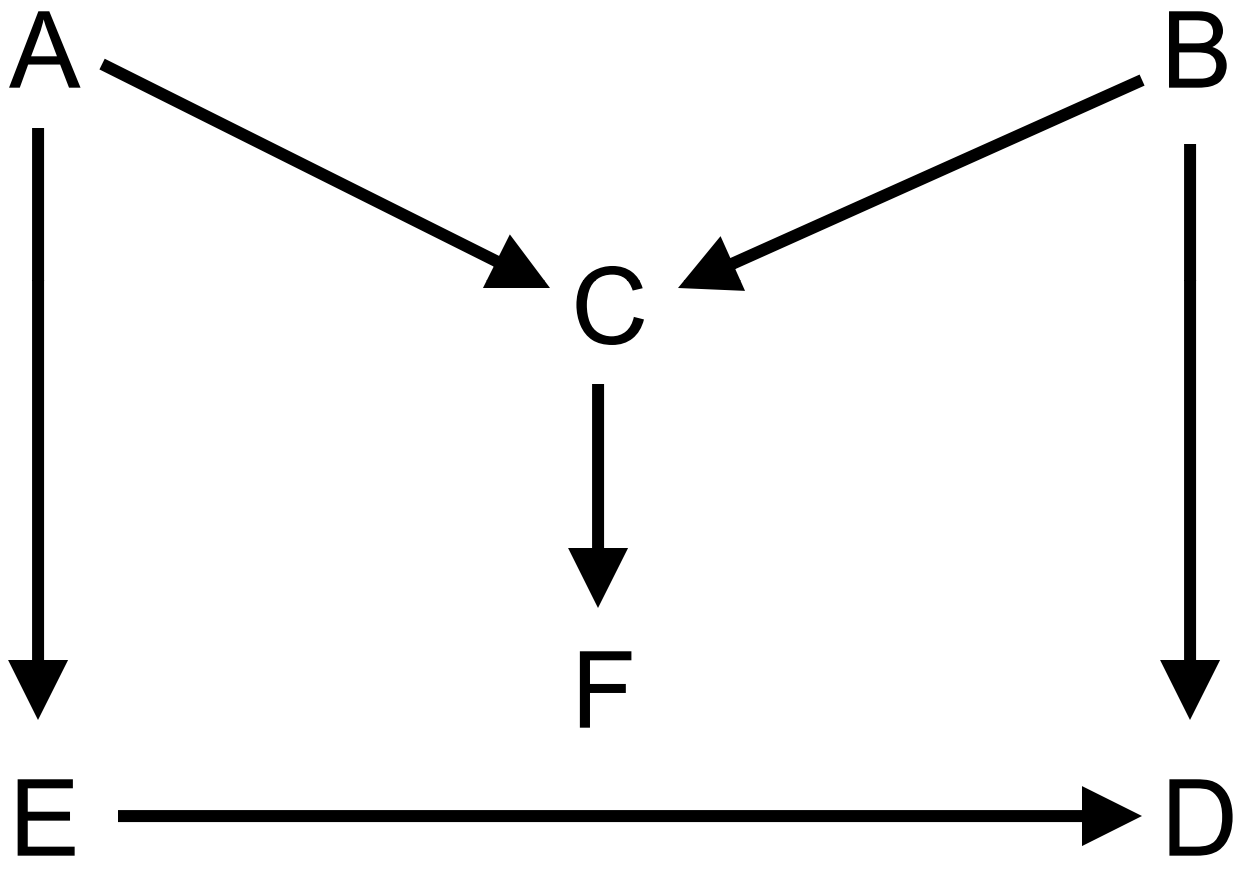
Confounding paths from E to D: ECD



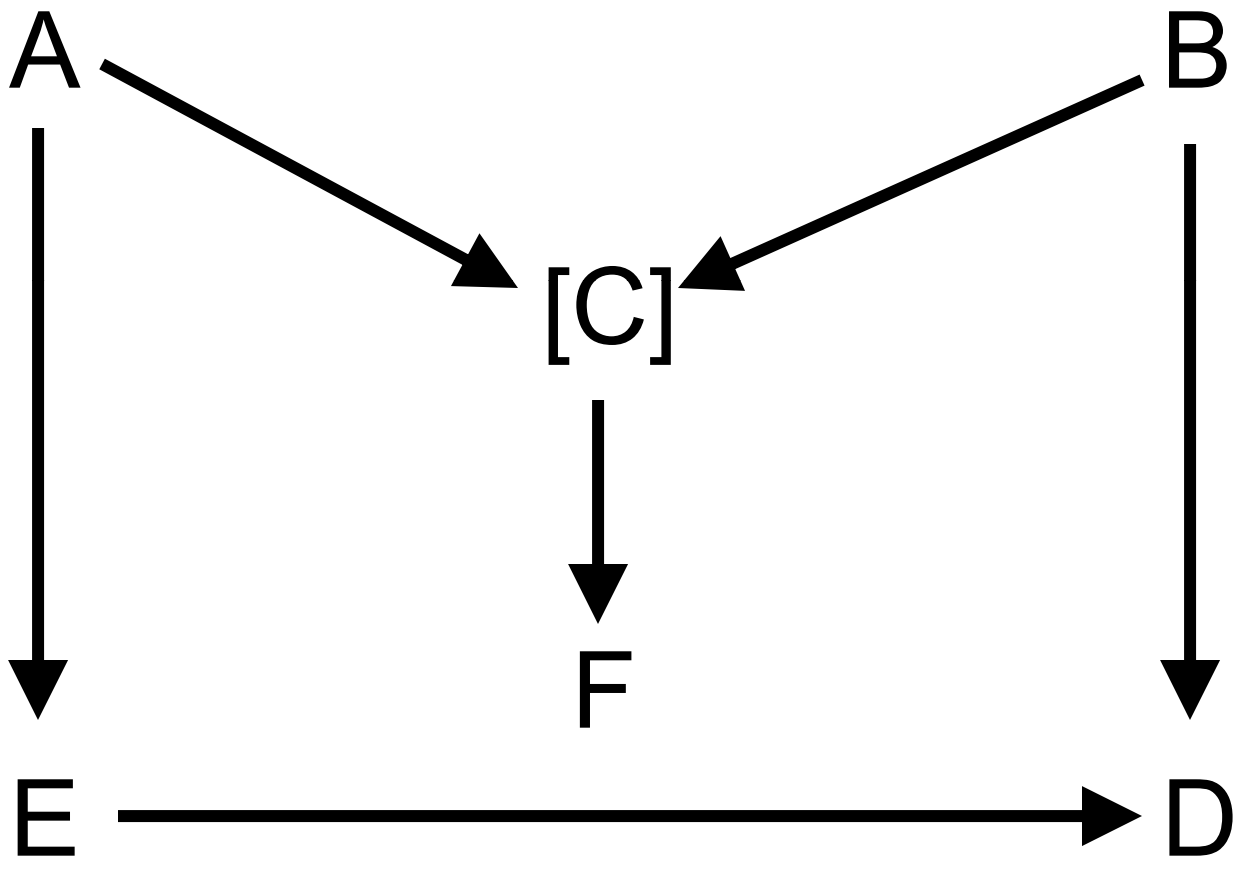
Confounding paths from E to D: None!



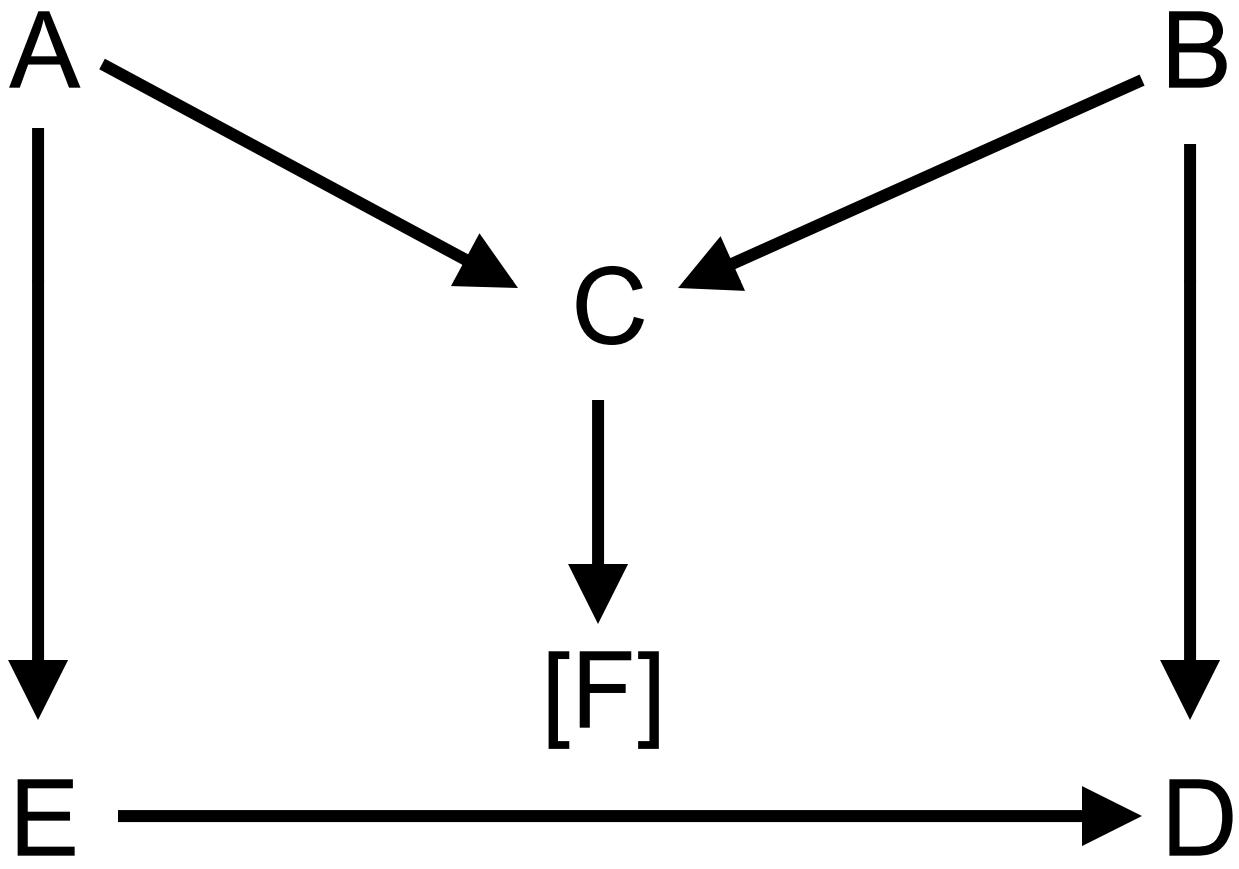
Confounding paths from E to D: None!



Confounding paths from E to D: EACBD ("M-bias")



Confounding paths from E to D: EACBD ("M-bias")



There are many definitions of "selection bias," none universally accepted.

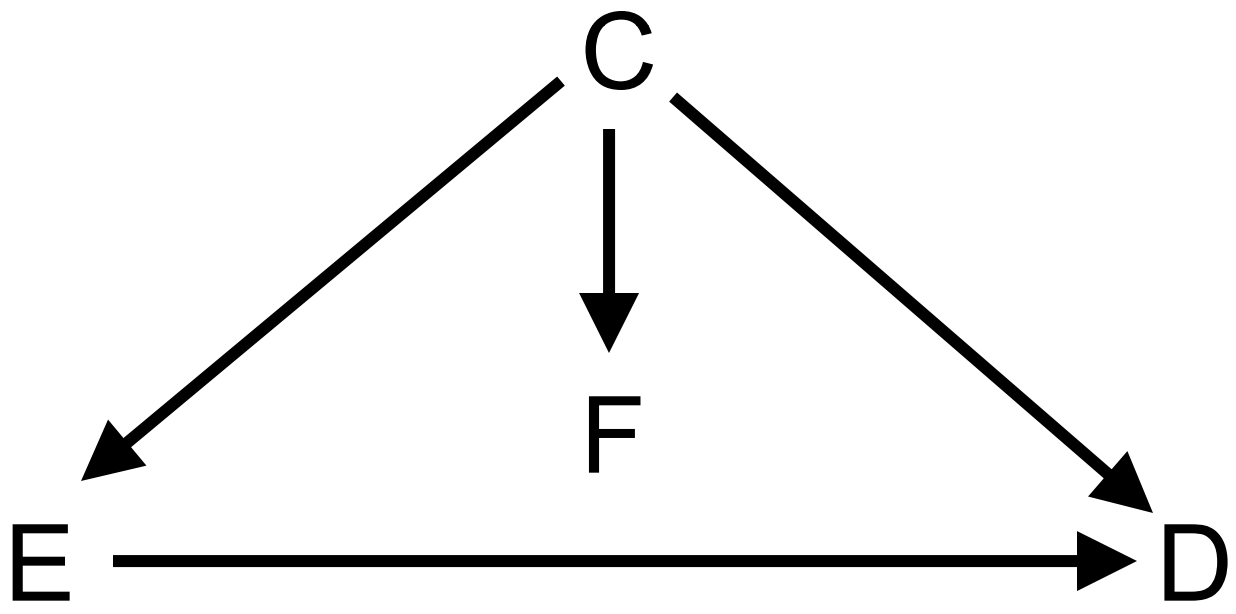
My definition:

- Noncausal association created by nonrandom selection into the **analysis**.

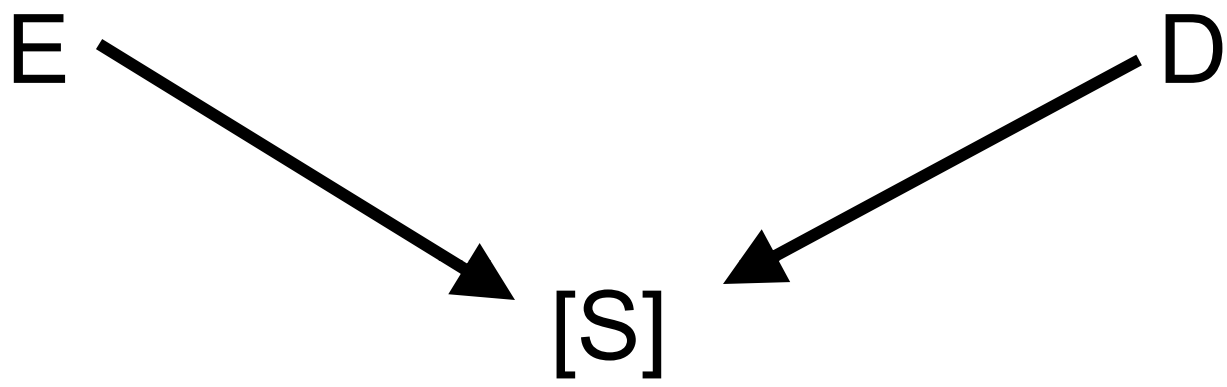
This definition appears to correspond best to the intuitive definitions given in epid texts since the mid-20th century.

- Confounding and selection bias overlap, but one is not always the other. (Using graphs, the distinction is not important.)

Confounding that is not selection bias: ECD



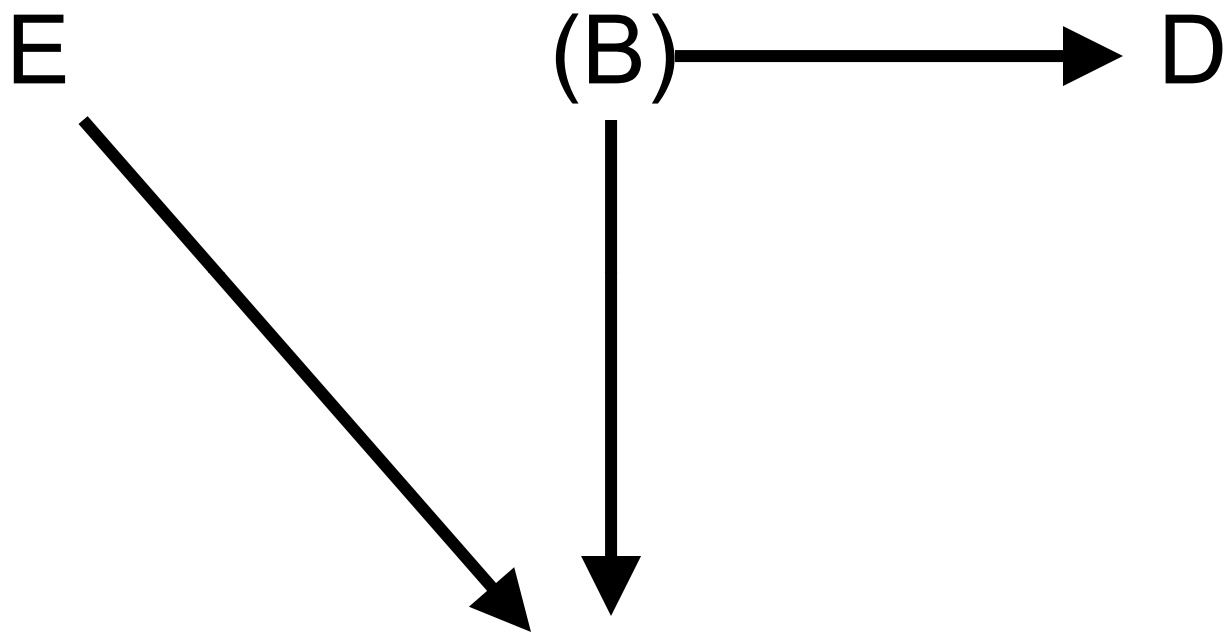
Selection bias that is not confounding: Berksonian bias



Uncontrollable biasing path: ESD

In Berkson's 1948 example, S was hospitalization.

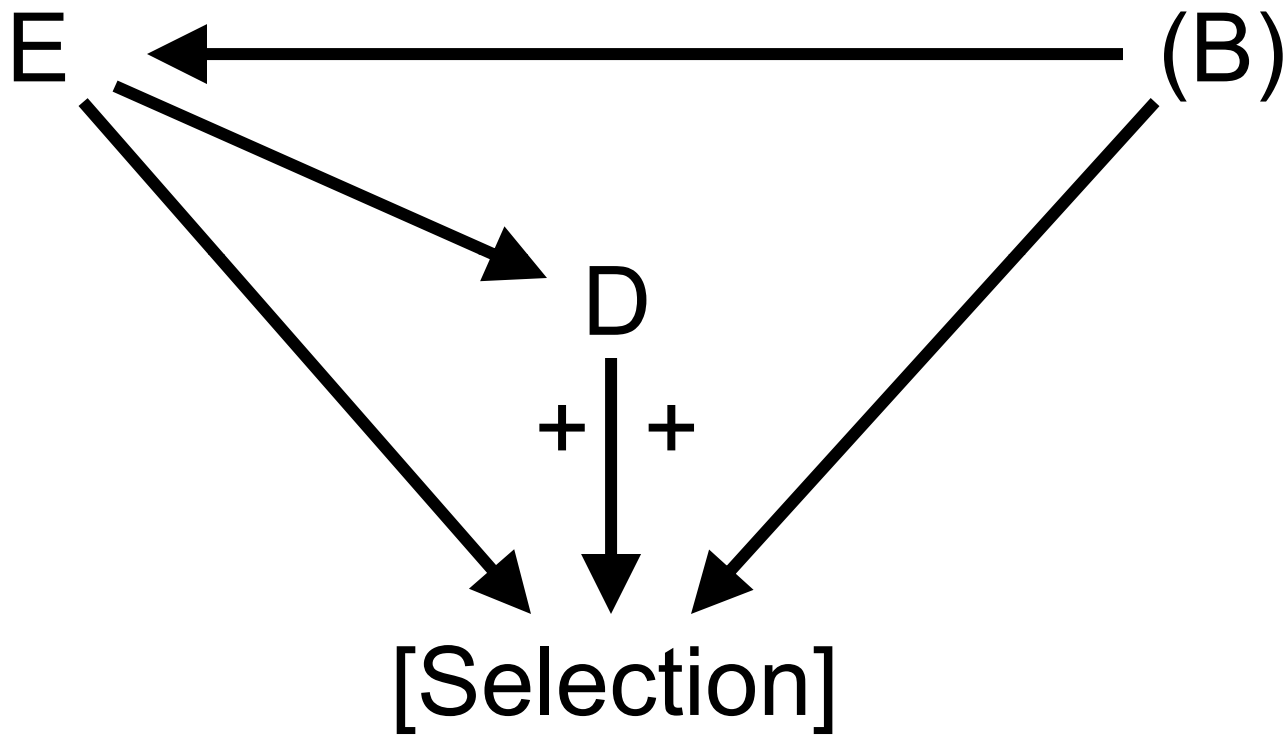
Why “as-treated” and “per-protocol” analyses can create bias:



[C = Compliance or Censoring]

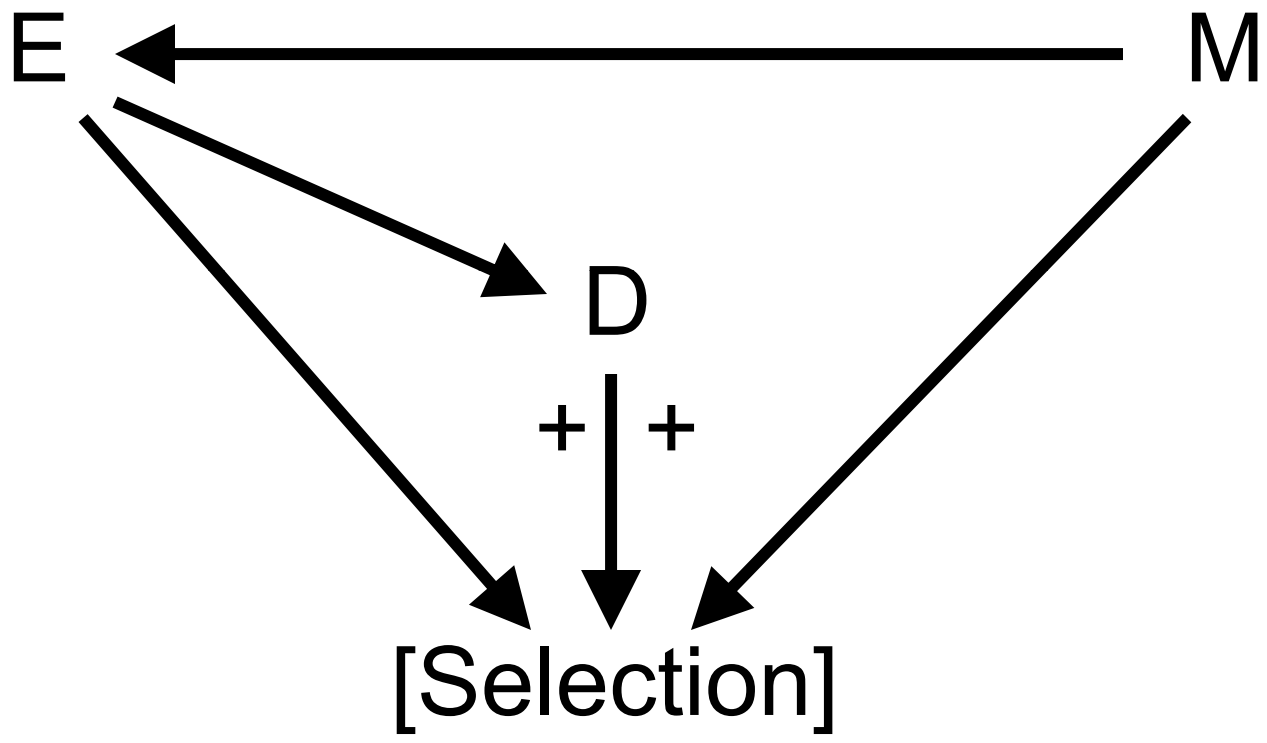
Biasing path if E and B or D affect C

Why case-control (choice-based) studies are more vulnerable than cohort studies to selection bias



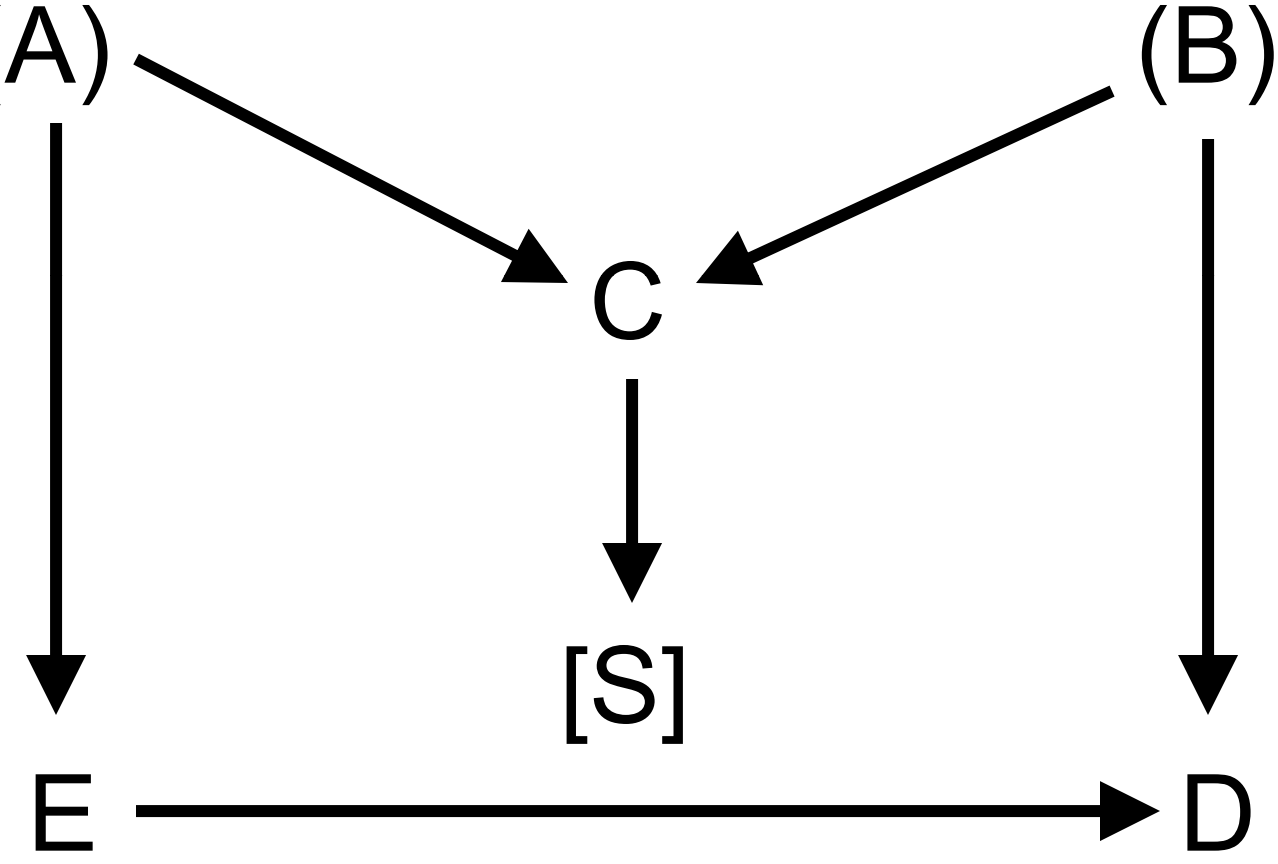
By definition, D **massively** affects selection

Why matched case-control studies need matching-factor control for validity



By definition, M affects selection

M-bias that is both confounding and selection bias (via EACBD)



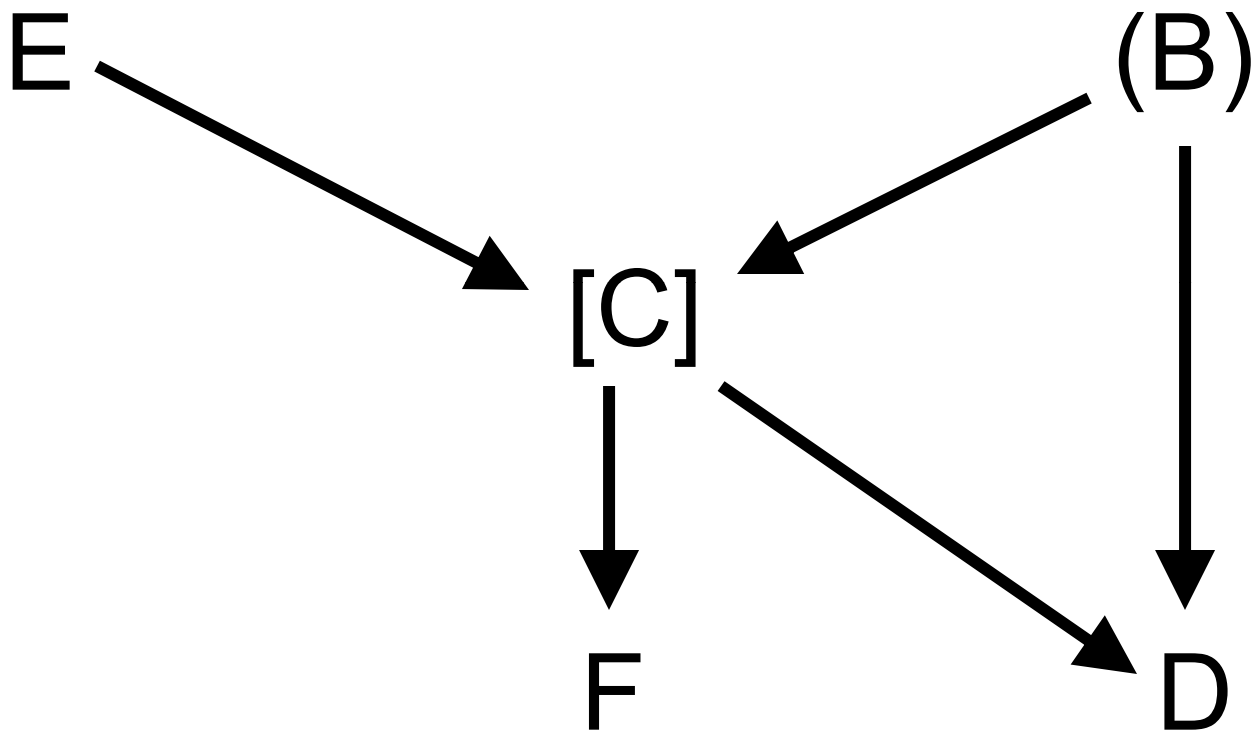
Collider bias: Selection bias and confounding induced by conditioning

Many variations:

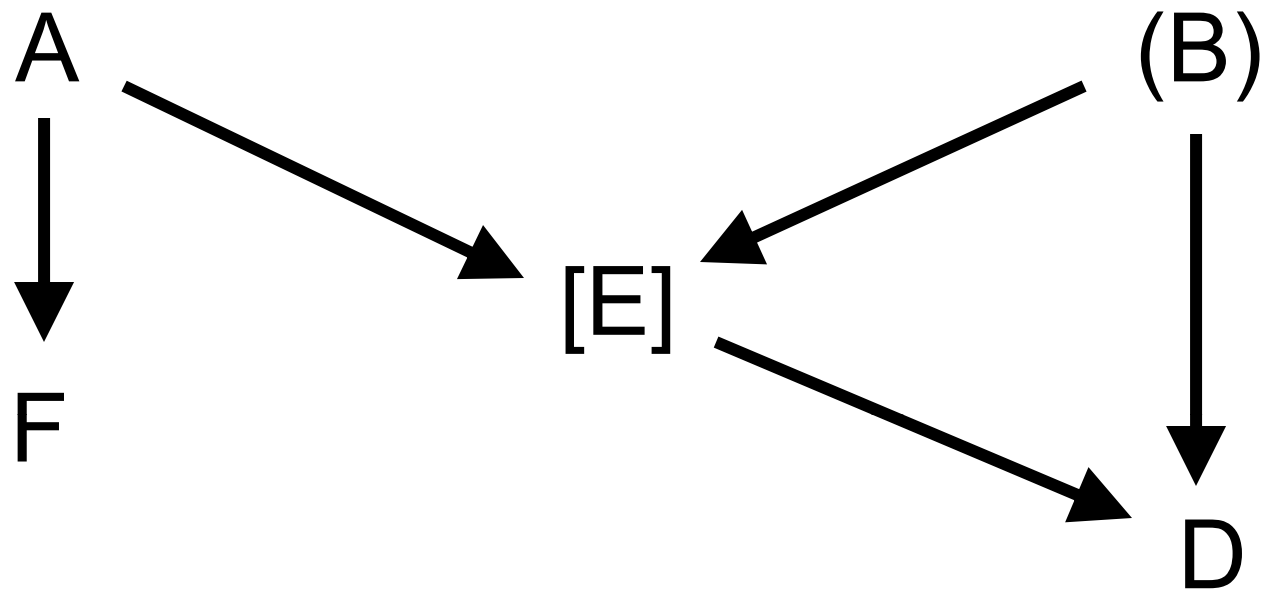
- Beksonian bias
- M-bias
- Confounding produced by control of intermediates to estimate direct effects, or by intermediates that affect selection

NOTE: By definition, analyses **always** condition on selection!

E has no direct effect on D, but control of C or F can make it appear so (via ECBD)



Bias from conditioning on an instrument A



Conditioning on A or F while examining E effects changes the ED estimate (via AEBD), making A look like a confounder, but inflating bias (Pearl, 2010).

Caution: Causal DAGs are chock full o' null hypotheses:

For **every** node pair A,B, a cDAG assumes:

1) No shared ancestor not in graph (not A↔B) and

2) No shared conditioned descendant not in the graph (not A–B).

3ab) For every nonadjacent node pair A, B with no arc (edge) between them (neither A→B nor B→A), no mechanism exists that leads directly from one node to the other.

Unfortunately, few if any of these nulls will have convincing support

- In observational HSS, many if not most arrows shown in diagrams encode no data other than an observed conditional sequential association (as per Hume), which may be due to A↔B or A─B.
- **Absence** of arrows encodes strong mechanistic nulls that usually lack supporting data.

Realistic causal graphs for HSS…

- Will have numerous unobserved (latent) nodes, often more of them than observed nodes.
- Will have few node pairs without an arc between them.
- Will provide **no** observed set of variables sufficient for bias control.
- Will have a selection node potentially affected by most other nodes.

Consider a vaguely realistic causal model for a single exposure-disease analysis:

X = Exposure, X*: measured X

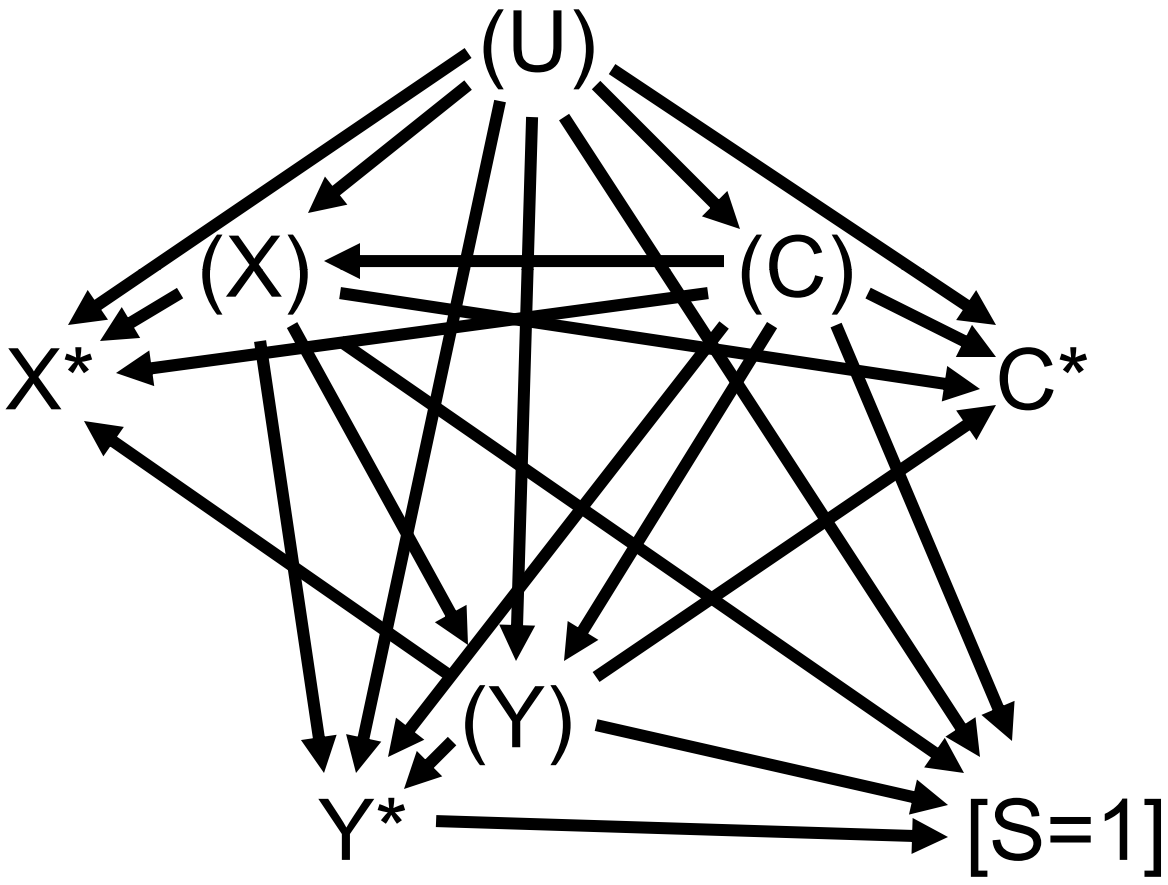
Y = Outcome, Y*: measured Y

C = Known antecedents, C*: measured C

U = Unmeasured or ignored antecedents

S = Selection into the **analysis**: analysis is **always** conditioned on S=1, so we should always show [S=1] on the graph

What might be a MINIMAL realistic causal graph for a case-control study of nicotine X and Alzheimer's Y (23 of 28 possible adjacencies):



Further reading

Basic:

- Greenland S, Pearl J, Robins JM. Causal Diagrams for Epidemiologic Research. Epidemiology 1999; 10: 37-48 (downloadable from JSTOR), and
- Glymour M, Greenland S. Causal Diagrams. Ch. 12 in Modern Epidemiology, 3rd ed., Lippincott, 2008.

Advanced:

- Pearl J. Causality, 2nd ed. Cambridge U Press, 2009.