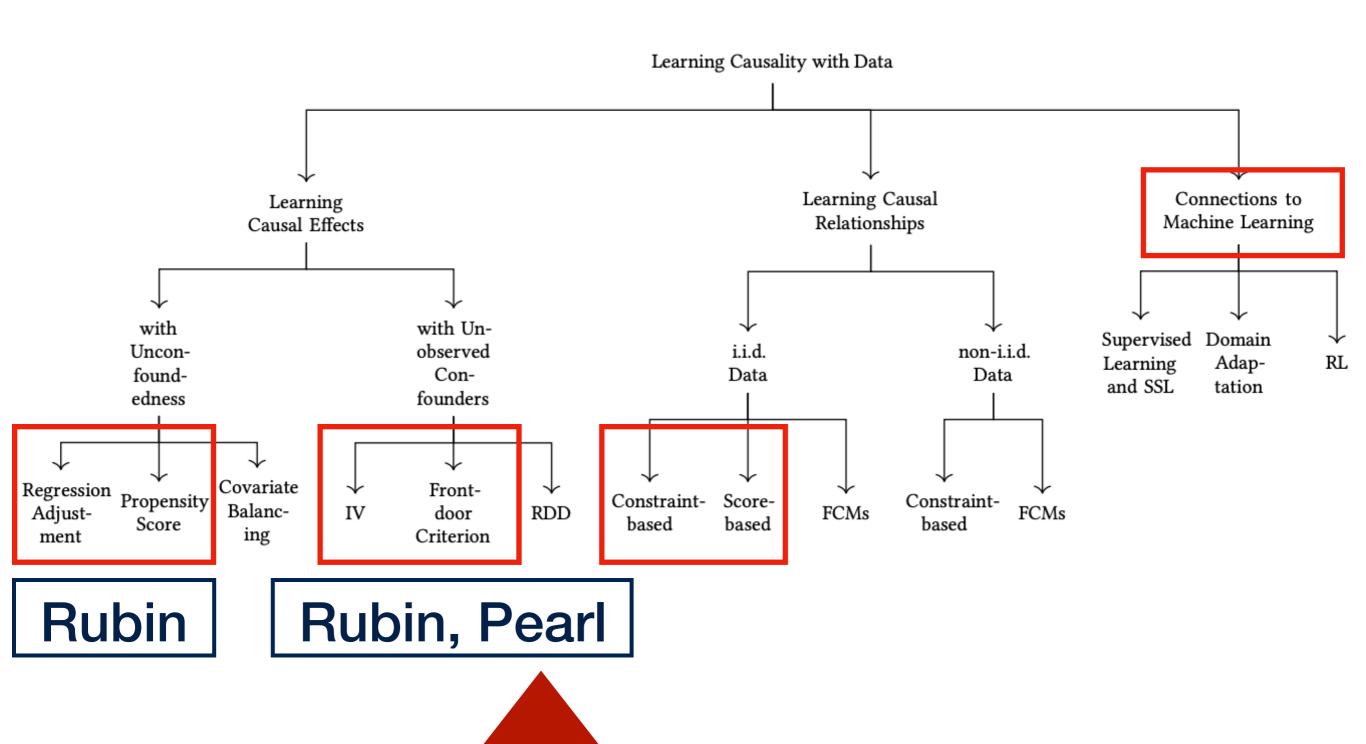
Causality in Biomedicine Lecture Series: Lecture 4

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12 Feb, 2020

Overview of the field



Pearl's framework Graphical models & Do-calculus

Causal Inference: DoWhy (a unifying language)

- Model a causal inference problem using assumptions, [Pearl's Causal Graphical Models]
- Identify an expression for the causal effect under these assumptions ("causal estimand"), [Pearl's Causal Graphical Models]
- Estimate the expression using statistical methods such as matching or instrumental variables, [Rubin's Potential Outcomes]
- Verify the validity of the estimate using a variety of robustness checks.

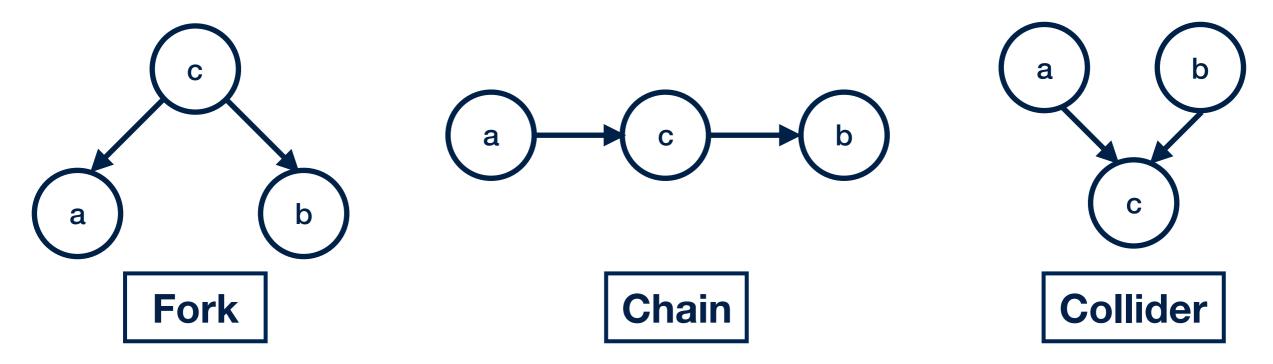
DAG contains more info than joint probability

$$p(a,b,c)=p(c|a,b)p(a,b)=p(c|a,b)p(b|a)p(a)$$
 b a
$$p(a,b,c)=p(a|b,c)p(b,c)=p(a|b,c)p(c|b)p(b)$$
 c Symmetric in a, b, c

- Probabilistic notations are not enough to describe causal aspects
- Using repeated application of Bayes' rule, one can write any joint probability distribution in terms of its marginals
- A graph is fully connected if there is a link between every pair of nodes
- The interest lies in the absence of a link and link direction.

This lecture:

- Conditional independence via graphs and D-separation
- 3 main graph structures:

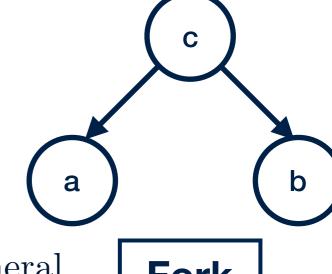


Do-calculus and causal identification

Fork

$$p(a, b, c) = p(a|c)p(b|c)p(c)$$

Case 1: No conditioning



$$p(a,b) = \sum_{c} p(a,b,c) = \sum_{c} p(a|c)p(b|c)p(c) \neq p(a)p(b)$$
 in general

$$\Rightarrow a \not\perp \!\!\!\perp b | \emptyset$$

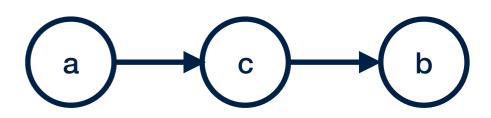
Case 2: Conditioning on c

$$p(a,b|c) = \frac{p(a,b,c)}{p(c)} = \frac{p(a|c)p(b|c)p(c)}{p(c)} = p(a|c)p(b|c)$$

 $\Rightarrow a \perp\!\!\!\perp b | c$ c blocks (d-separates) the path from a to b

Chain

$$p(a, b, c) = p(a)p(c|a)p(b|c)$$



Case 1: No conditioning

Chain

$$p(a,b) = \sum_{c} p(a)p(c|a)p(b|c) = p(a)\sum_{c} p(b|c)p(c|a) = p(a)p(b|a) \neq p(a)p(b)$$

$$\Rightarrow a \not\perp \!\!\!\perp b | \emptyset$$

Case 2: Conditioning on c

$$p(a,b|c) = \frac{p(a,b,c)}{p(c)} = \frac{p(a)p(c|a)p(b|c)}{p(c)} = \frac{p(a)p(b|c)}{p(c)} \frac{p(a|c)p(c)}{p(a)} = p(a|c)p(b|c)$$

 $\Rightarrow a \perp \!\!\! \perp b | c$ c blocks (d-separates) the path from a to b

Collider

$$p(a, b, c) = p(a)p(b)p(c|a, b)$$

Case 1: No conditioning

$$p(a,b) = \sum_c p(a)p(b)p(c|a,b) = p(a)p(b)\sum_c p(c|a,b) = p(a)p(b)$$
 Collider

 $\Rightarrow a \perp \!\!\! \perp b | \emptyset$ with no conditioning, a and b are independent

Case 2: Conditioning on c

$$p(a,b|c) = \frac{p(a,b,c)}{p(c)} = \frac{p(a)p(b)p(c|a,b)}{p(c)} \neq p(a)p(b) \text{ in general}$$

 $\Rightarrow a \not\perp \!\!\! \perp b | c$ c unblocks the path from a to b

B: State of battery, B=1 charged, B=0 flat

F: State of fuel tank, F=1 full, F=0 empty

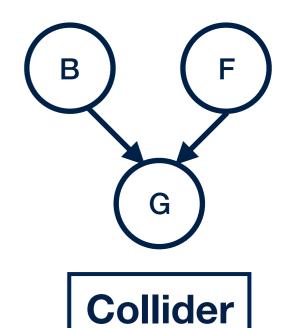
G: State of electric fuel gauge, G=1 full, G=0 empty

Given Info:

$$p(B = 1) = 0.9$$

 $p(F = 1) = 0.9$
 $p(G = 1|B = 1, F = 1) = 0.8$
 $p(G = 1|B = 1, F = 0) = 0.2$
 $p(G = 0|B = 0, F = 1) = 0.2$

$$p(G = 1|B = 0, F = 0) = 0.1$$



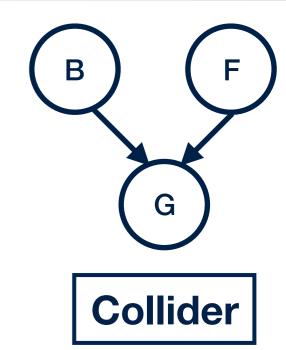
B: State of battery, B=1 charged, B=0 flat

F: State of fuel tank, F=1 full, F=0 empty

G: State of electric fuel gauge, G=1 full, G=0 empty

(1) Before any conditioning (before observing):

$$p(F=0) = 0.1$$



B: State of battery, B=1 charged, B=0 flat

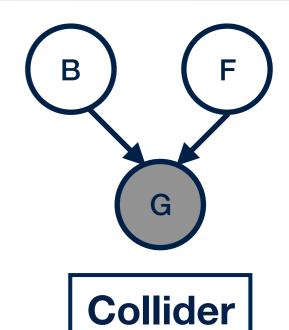
F: State of fuel tank, F=1 full, F=0 empty

G: State of electric fuel gauge, G=1 full, G=0 empty





$$p(F = 0|G = 0) = \frac{p(G = 0|F = 0)p(F = 0)}{p(G = 0)}$$



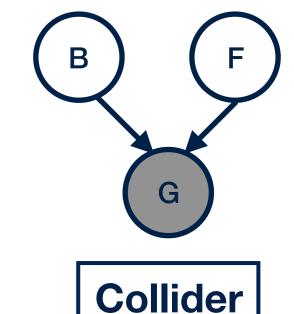
B: State of battery, B=1 charged, B=0 flat

F: State of fuel tank, F=1 full, F=0 empty

G: State of electric fuel gauge, G=1 full, G=0 empty



Since B and F are independent



(2) Now suppose we observe G=0

$$p(F = 0|G = 0) = \underbrace{\frac{p(G = 0|F = 0)p(F = 0)}{p(G = 0)}}_{p(G = 0)} \sum_{B,F \in \{0,1\}} p(G = 0,B,F)$$

$$= \sum_{B,F \in \{0,1\}} p(G = 0|B,F)p(B|F)p(F)$$

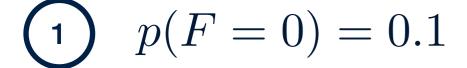
$$= \sum_{B,F \in \{0,1\}} p(G = 0|B,F)p(B)p(F) = 0.315$$

 $B, F \in \{0,1\}$

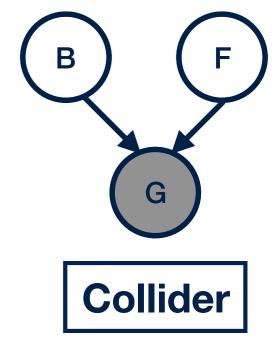
B: State of battery, B=1 charged, B=0 flat

F: State of fuel tank, F=1 full, F=0 empty

G: State of electric fuel gauge, G=1 full, G=0 empty







$$p(F=0) < p(F=0|G=0)$$

Observing that gauge reads empty makes it more likely that the tank is indeed empty.

B: State of battery, B=1 charged, B=0 flat

F: State of fuel tank, F=1 full, F=0 empty

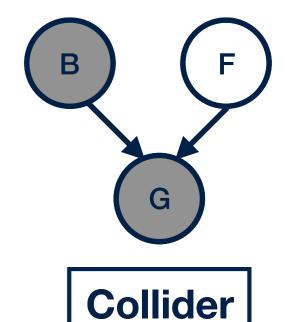
G: State of electric fuel gauge, G=1 full, G=0 empty





$$p(F = 0|G = 0, B = 0) = \frac{p(F = 0, G = 0, B = 0)}{p(G = 0, B = 0)}$$

$$= \frac{p(G = 0|B = 0, F = 0)p(F = 0)p(B = 0|F \neq 0)}{\sum_{F \in \{0,1\}} p(G = 0|B = 0, F)p(F)p(B \neq 0|F)} = 0.111$$



B: State of battery, B=1 charged, B=0 flat

F: State of fuel tank, F=1 full, F=0 empty

G: State of electric fuel gauge, G=1 full, G=0 empty



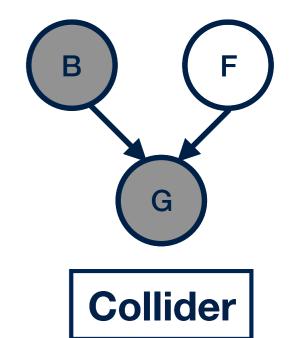


$$p(F = 0|G = 0, B = 0) = \frac{p(F = 0, G = 0, B = 0)}{p(G = 0, B = 0)}$$

$$= \frac{p(G = 0|B = 0, F = 0)p(F = 0)p(B = 0|F \neq 0)}{\sum_{F \in \{0,1\}} p(G = 0|B = 0, F)p(F)p(B \neq 0|F)} = 0.111$$

$$p(F = 0|G = 0) > p(F = 0|G = 0, B = 0)$$

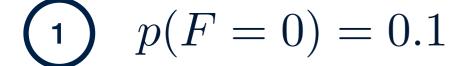
Probability that tank is empty F=0 has decreased with extra information on the state of the battery



B: State of battery, B=1 charged, B=0 flat

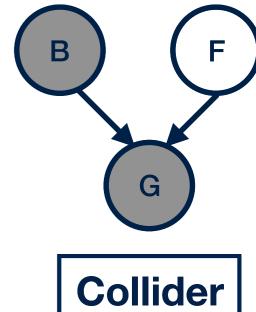
F: State of fuel tank, F=1 full, F=0 empty

G: State of electric fuel gauge, G=1 full, G=0 empty



(2)
$$p(F=0|G=0)=0.257$$

(3)
$$p(F=0|G=0,B=0)=0.111$$



Conditioning on G, finding out the battery is flat, 'explains away' the observation that the fuel gauge reads empty. The state of the fuel tank and the battery have become dependent:

$$p(F = 0|G = 0) \neq p(F = 0|G = 0, B = 0)$$

D-separation

A path p is **blocked** by a set of nodes Z if and only if:

- 1) p contains a **chain** of nodes A -> B -> C or a **fork** A <- B -> C such that the middle node B is in Z (i.e. B is conditioned on), or
- 2) p contains a **collider** A -> B <- C such that the collision node B is not in Z, and no descendant of B is in Z.

Observation (conditioning) vs intervention

Distinguish between: a variable T takes a value t naturally and cases

where we **fix** T=t by denoting the latter do(T=t)

$$p(Y = y|T = t)$$

Probability that Y=y **conditional** on finding T=t i.e., population distribution of Y among individuals whose T value is t (subset)

$$p(Y = y|do(T = t))$$



Probability that Y=y when we **intervene** to make T=t

i.e., population distribution of Y if everyone in the population had

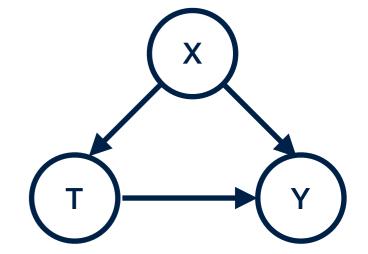
their T value fixed at t.

Graph surgery

T: Drug usage

X: Gender

Y: Recovery



To know how effective the drugs is in the population, compare the **hypothetical interventions** by which

- (i) the drug is administered uniformly to the entire population do(X=1) vs
- (ii) complement, i.e., everyone is prevented from taking the drug do(X=0)

Aim: Estimate the difference (Average Causal Effect ACE)

$$p(Y = 1|do(T = 1)) - p(Y = 1|do(T = 0))$$

Using a **causal theory**, we aim to write p(Y = y | do(T = t)) in terms of quantities we can compute from the data, i.e., conditional probabilities.

The causal effect $\ p(Y=y|do(T=t))$ is equal to conditional probability $p_m(Y=y|T=t)$ in the manipulated graph

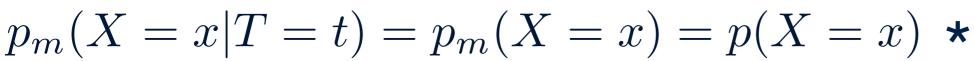
Key observation: p_m shares 2 properties with p:

(i) $p_m(X = x) = p(X = x)$ is **invariant** under the intervention, X is not affected by removing the arrow from X to T, i.e. the proportion of males and females remain the same before and after the intervention

(ii)
$$p_m(Y = y|X = x, T = t) = p(Y = y|X = x, T = t)$$
 is invariant

Moreover, T and X are d-separated in the modified model:





Putting these together:

$$p(Y = y|do(T = t)) = p_m(Y = y|T = t)$$
 by definition

$$\sum p_m(Y=y|T=t,X=x)p_m(X=x|T=t) \text{ law of total prob}$$

$$\sum_{x} p_m(Y=y|T=t,X=x)p_m(X=x) \star$$

Using the two invariance relations, we have the adjustment formula:

$$p(Y = y|do(T = t)) = \sum_{x} p(Y = y|T = t, X = x)p(X = x)$$

$$p(Y = y|do(T = t)) = \sum_{x} p(Y = y|T = t, X = x)p(X = x)$$

Adjusting for X (controlling for X) ... seen before?

Example: T=1 taking the drug, X=1 male, Y=1 recovery

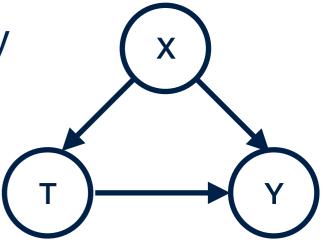


Table 1.1 Results of a study into a new drug, with gender being taken into account

	Drug	No drug
Men	81 out of 87 recovered (93%)	234 out of 270 recovered (87%)
Women	192 out of 263 recovered (73%)	55 out of 80 recovered (69%)
Combined data	273 out of 350 recovered (78%)	289 out of 350 recovered (83%)

$$p(Y = y|do(T = t)) = \sum_{x} p(Y = y|T = t, X = x)p(X = x)$$

T=1 taking drug

X=1 male

Y=1 recovery

$$p(Y = y|do(T = 1)) = p(Y = 1|T = 1, X = 1)p(X = 1) + p(Y = 1|T = 1, X = 0)p(X = 0)$$

$$p(Y=1|do(T=1)) = \frac{0.93(87+270)}{700} + \frac{0.73(263+80)}{700} = 0.832$$

$$p(Y = 1|do(T = 0)) = \frac{0.87(87 + 270)}{700} + \frac{0.69(263 + 80)}{700} = 0.7818$$

$$ACE: p(Y=1|do(T=1)) - p(Y=1|do(T=0)) = 0.832 - 0.7818 = 0.0505$$



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X=1 male

Y=1 recovery

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$$p(Y=1|do(T=1)) = \frac{0.93(87+270)}{700} + \frac{0.73(263+80)}{700} = 0.832$$

Stratification!

$p(Y = 1|do(T = 0)) = \frac{0.87(87 + 270)}{700} + \frac{0.69(263 + 80)}{700} = 0.7818$

Note equivalence to Rubin's FW

$$ACE: p(Y = 1|do(T = 1)) - p(Y = 1|do(T = 0)) = 0.832 - 0.7818 = 0.0505$$



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Pearl & Rubin

Pearl

$$\mathbb{E}(Y|do(T=1)) = \mathbb{E}(Y|T=1, X=1)p(X=1) + \mathbb{E}(Y|T=1, X=0)p(X=0)$$

$$\mathbb{E}(Y|do(T=0)) = \mathbb{E}(Y|T=0, X=1)p(X=1) + \mathbb{E}(Y|T=0, X=0)p(X=0)$$

$$\mathbb{E}(Y|do(T=1)) - \mathbb{E}(Y|do(T=0))$$

Rubin

recall potential outcomes $y_0^{(i)}$ and $y_1^{(i)}$ and ATE:

$$\tau = \hat{\mathbb{E}}[\tau^{(i)}] = \hat{\mathbb{E}}[y_1^{(i)} - y_0^{(i)}] = \frac{1}{N} \sum_{i=0}^{N} \left(y_1^{(i)} - y_0^{(i)} \right)$$

Pearl & Rubin

Pearl

$$\mathbb{E}(Y|do(T=1)) = \mathbb{E}(Y|T=1, X=1)p(X=1) + \mathbb{E}(Y|T=1, X=0)p(X=0)$$

$$\mathbb{E}(Y|do(T=0)) = \mathbb{E}(Y|T=0, X=1)p(X=1) + \mathbb{E}(Y|T=0, X=0)p(X=0)$$

$$\mathbb{E}(Y|do(T=1)) - \mathbb{E}(Y|do(T=0))$$

Rubin

recall potential outcomes $y_0^{(i)}$ and $y_1^{(i)}$ and ATE:

$$\tau = \hat{\mathbb{E}}[\tau^{(i)}] = \hat{\mathbb{E}}[y_1^{(i)} - y_0^{(i)}] = \frac{1}{N} \sum_{i=0}^{N} \left(y_1^{(i)} - y_0^{(i)} \right)$$

$$= \frac{1}{N} \left(\sum_{i \in \text{males}} \left(y_1^{(i)} - y_0^{(i)} \right) + \sum_{i \in \text{females}} \left(y_1^{(i)} - y_0^{(i)} \right) \right)$$

Pearl: To adjust or not to adjust

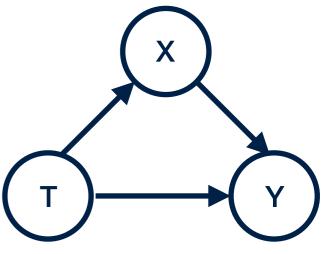
The previous example may give the impression that X-specific analysis, as compared to nonspecific, is the correct way forward. This is not the case. For example, let T=drug, Y=recovery, X= blood pressure **post-treatment**, i.e., important to take into account **how** the data is generated. Here, we know:

- (i) the drug affects recovery by lowering the blood pressure
- (ii) but it has a toxic effect for those who take it

NB: Data (numbers) in this table are identical to those in Table 1.1.

Table 1.2 Results of a study into a new drug, with posttreatment blood pressure taken into account

	No drug	Drug
Low BP	81 out of 87 recovered (93%)	234 out of 270 recovered (87%)
High BP	192 out of 263 recovered (73%) 55 out of 80 recovered (69%)	
Combined data	273 out of 350 recovered (78%)	289 out of 350 recovered (83%)



Pearl: To adjust or not to adjust

For general population, the drug might improve recovery rates because of its effect on blood pressure. But in low BP/high BP **post-treatment** subpopulations, we only observe the toxic effect of the drug.

Aim, as before, to gauge the overall causal effect of the drug on recovery.

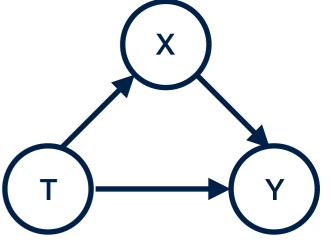
Unlike before, it does **not** make sense to separate results by blood pressure as treatment affect recovery via reducing BP.

Contrast this with the a situation per BP is measure **before** treatment and direction of arrow from T to X is reversed.

Therefore, we **should** recommend treatment in this case.

Table 1.2 Results of a study into a new drug, with posttreatment blood pressure taken into account

	No drug	Drug
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Pearl: To adjust or not to adjust

Pearls algorithmic approach tells us to adjust or not. Starting with: p(Y=1|do(T=1)), intervene on T. But since no arrow is entering T, there will be no change in the graph: p(Y=1|do(T=1))=p(Y=1|T=1)

Table 1.2 Results of a study into a new drug, with posttreatment blood pressure taken into account			(x)
	No drug	Drug	
Low BP	81 out of 87 recovered (93%)	234 out of 270 recovered (87%)	
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The Causal Effect Rule: Given a graph G in which a set of variables PA are designated as the parents of T, the causal effect of T on Y is given by:

$$p(Y = y|do(T = t)) = \sum_{x} p(Y = y|T = t, PA = X)p(PA = X)$$

The Backdoor Criterion

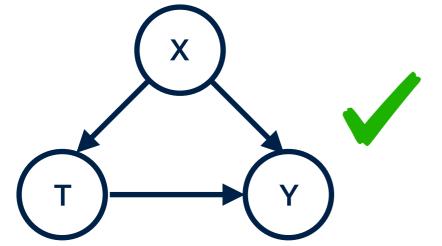
Under what conditions does a causal model permit computing the causal effect of one variable on another, from **data** obtained from **passive observations**, with **no intervention**? i.e.,

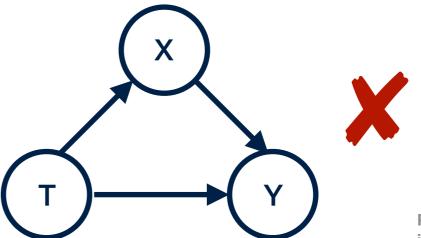
Under what conditions is the structure of a causal graph sufficient of computing a causal effect from a given data set?

Backdoor Criterion: Given an ordered pair of variables (T,Y) in a DAG G, a set of variables X satisfies the backdoor criterion relative to (T,Y) if:

- (i) no node in X is a descendent of T
- (ii) X block every path between T and Y that contains an arrow into T If X satisfies the backdoor criterion then the causal effect of T on Y is given by:

$$p(Y = y|do(T = t)) = \sum_{x} p(Y = y|T = t, X = x)p(X = x)$$





Rubin vs Pearl

Rubin	Pearl	
SUTVA	Implicit assumption of no interference between any pairs of individual	
Unconfoundedness (ignorability)	Back-door criterion satisfied	
Potential outcomes: $y_0^{(i)}$, $y_1^{(i)}$ Observed: $y_0^{(i)}$, Unobserved: $y^*_1^{(i)}$	Counterfactuals are equivalent to individual unobserved outcomes in Rubin (Hypothetical distributions that cannot be identified through interventions)	

Convolution of probability distributions

- C, E, N_C, N_E, are random variables and the above relation is NOT an algebraic equation (in general)
- Linear operations on random variables in Structural Causal
 Models (SCMs) can only be understood in terms of operations on their corresponding probability distributions, e.g., for Z = X + Y:

$$P_{X+Y}(Z=z) = \int P_{XY}(x, z-x) dx$$

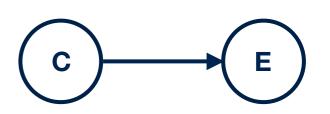
• Key independence statements, $\chi \perp \!\!\! \perp Y$ allow factorisation to the well-known convolution of probabilities:

$$P_{X+Y}(Z=z) = \int P_X(x)P_Y(z-x)dx$$

Intervention vs observation

Consider the following causal model with structure equations:

Random
$$C := N_C$$
 Variables $E := 4 \cdot C + N_E$



where, $N_C, N_E \sim \mathcal{N}(0, 1)$, are independent and iid. We expect:

- Apply do(C):
 - The new distribution $p(E|do(C)) \neq p(E)$



- Since there are no other confounders: p(E|do(C)) = p(E|C)
- Apply do(E):
 - The new distribution p(C|do(E)) = p(C)





Next Lectures

19 Feb (Lec 5):

- Observation vs Interventions in SCM
- CausalGraphical Models & DoWhy simulations (Microsoft packages)
- Intro to causal discovery methods
- Constrained-based method

26 Feb (Lec 6):

- Functional Causal Models (FCMs)
- Asymmetry & Heterogeneity in data
- The bivariate case
- Gene Network example

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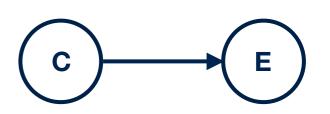
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- Since there are no other confounders: p(E|do(C)) = p(E|C)
- Apply do(E):
 - The new distribution p(C|do(E)) = p(C)





Intervention vs observation: Analytical computation

$$C:=N_C$$

$$E:=4\cdot C+N_E$$

$$N_C,N_E\sim\mathcal{N}(0,1),N_C\perp\!\!\!\perp N_E$$

Using $\operatorname{Var}[aX] = a^2 \operatorname{Var}[X]$, $4C \sim \mathcal{N}(0, 16)$.

Using, $4C \perp \!\!\! \perp N_E$, and the sum of two normally distributed random variables is another normally distributed random variable (by **convolution**):

$$E \sim \mathcal{N}\left(\mu_{4C} + \mu_{N_E}, \sigma_{4C}^2 + \sigma_{N_E}^2\right)$$

$$\Rightarrow E \sim \mathcal{N}\left(0, 17\right)$$
(do(c)

$$p(E) = \mathcal{N}(0, 17) \neq \mathcal{N}(8, 1) = p(E|do(C = 2)) = p(E|C = 2)$$
$$\neq \mathcal{N}(12, 1) = p(E|do(C = 3)) = p(E|C = 3)$$

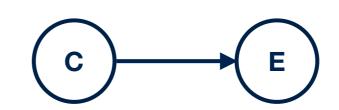
Jonas Peters et al, Elements of Causal Inference (2017)

Intervention vs observation: Analytical computation

$$C := N_C$$

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$$N_C, N_E \sim \mathcal{N}(0, 1), N_C \perp \!\!\! \perp N_E$$







$$p(C|do(E=2)) = \mathcal{N}(0,1) = p(C|do(E=\text{Any } r > 0)) = p(C)$$

eq p(C|E=2) in the original distribution above

Proof: Use Bayes' rule: $p(C|E) = \frac{p(C,E)}{p(E)}$

For a bivariate normal distribution (2 joint normal distributions), the marginal:

$$p(C|E) = \mathcal{N}(\tilde{\mu}, \tilde{\sigma}^2)$$
 s.t. $\tilde{\mu} = \mu_C + \rho \frac{\sigma_C}{\sigma_E} (E - \mu_E), \ \tilde{\sigma}^2 = \sigma_C^2 (1 - \rho^2)$

Intervention vs observation: Analytical computation

$$C:=N_C$$

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$$N_C,N_E\sim\mathcal{N}(0,1),N_C\perp\!\!\!\perp N_E$$

Proof (Cont.): Use Cov(aX, bY + cZ) = ab Cov(X, Y) + ac Cov(X, Z)

$$\Rightarrow \rho = \frac{\text{Cov}(C, E)}{\sigma_C \sigma_E} = \frac{4\text{Cov}(N_C, N_C) + \text{Cov}(N_C, N_E)}{\sigma_C \sigma_E} = \frac{4}{\sqrt{17}}$$

$$\Rightarrow p(C|E=2) = \mathcal{N}\left(\frac{8}{17}, \sigma^2 = \frac{1}{17}\right) \Rightarrow p(C|do(E)) \neq p(C|E)$$

Intervention vs observation: Numerical analysis

$$C:=N_C$$

$$E:=4\cdot C+N_E$$

$$N_C,N_E\sim\mathcal{N}(0,1),N_C\perp\!\!\!\perp N_E$$

Code Snippet

Causality in Biomedicine Lecture Series: Lecture 4

Ava Khamseh



12 Feb, 2020