Causality in Biomedicine Lecture Series: Lecture 5

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20 Nov, 2020

Causal Inference

- **Model** a causal inference problem with assumptions manifest in Causal Graphical Models **[Pearl]**

- **Identify** an expression for the causal effect under these assumptions (“causal estimand”), [**Pearl**]

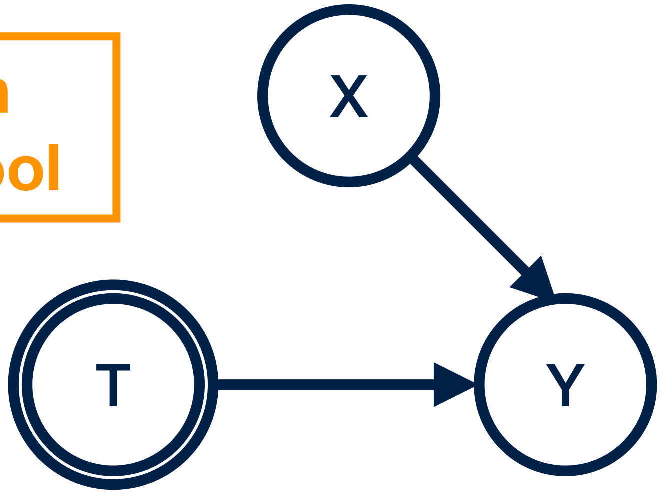
- **Estimate** the expression using statistical methods such as matching or instrumental variables, [**Rubin**’s Potential Outcomes]

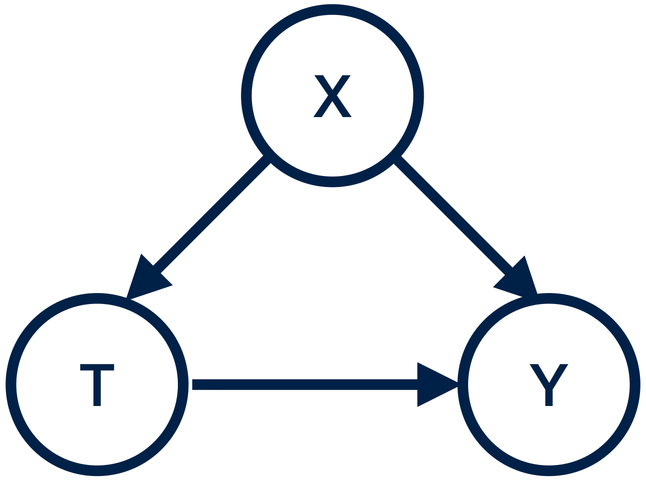
- **Verify** the validity of the estimate using a variety of robustness checks.

The adjustment formula

T: Drug usage
X: Gender
Y: Recovery

Use Pm as an intermediate tool





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(T=1) **vs**
(ii) complement, i.e., everyone is prevented from taking the drug do(T=0)

Aim: Estimate the difference (**Average Causal Effect ACE**)

$$\boxed{p(Y=1|do(T=1)) - p(Y=1|do(T=0))}$$

Pearl, Causal Inference in Statistics (2016)

The Backdoor Criterion

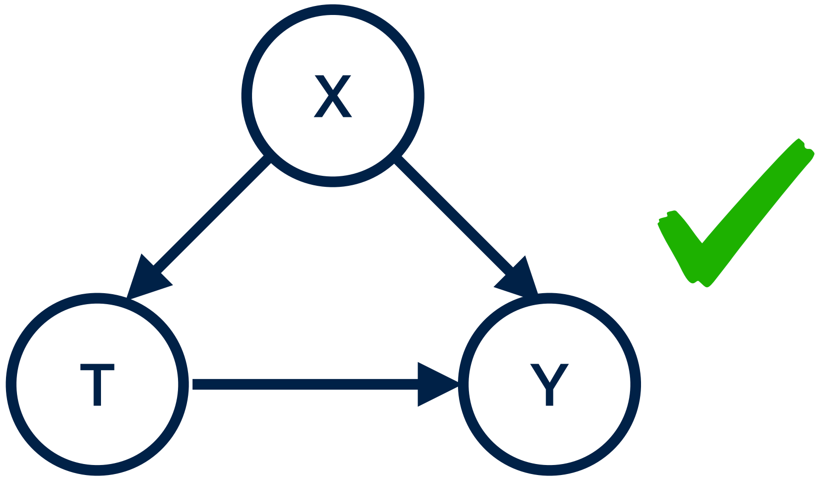
Under what conditions does a causal model permit computing the causal effect of one variable on another, from **data** obtained from **passive observations**, with **no intervention**?
i.e.,
Under what conditions is the structure of a causal graph sufficient of computing a causal effect from a given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

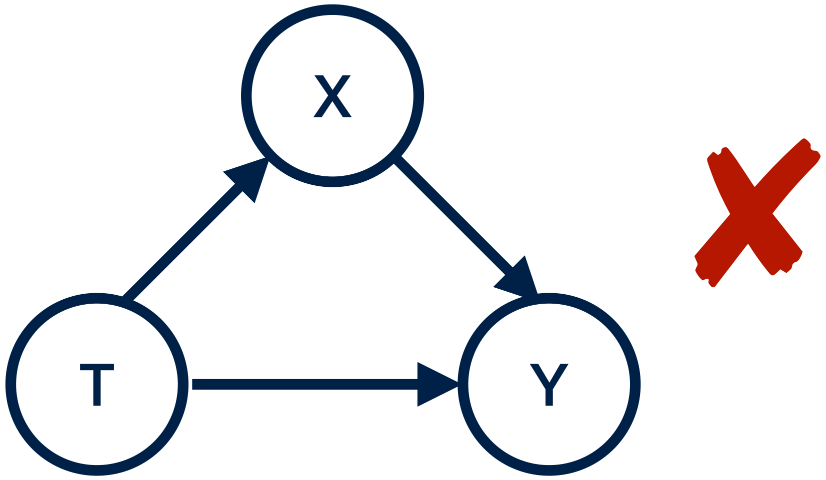
Backdoor Criterion: Given an ordered pair of variables (T,Y) in a DAG G, a set of variables X satisfies the backdoor criterion relative to (T,Y) if:

(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:

$$p(Y=y|do(T=t)) = \sum_x p(Y=y|T=t,X=x)p(X=x)$$

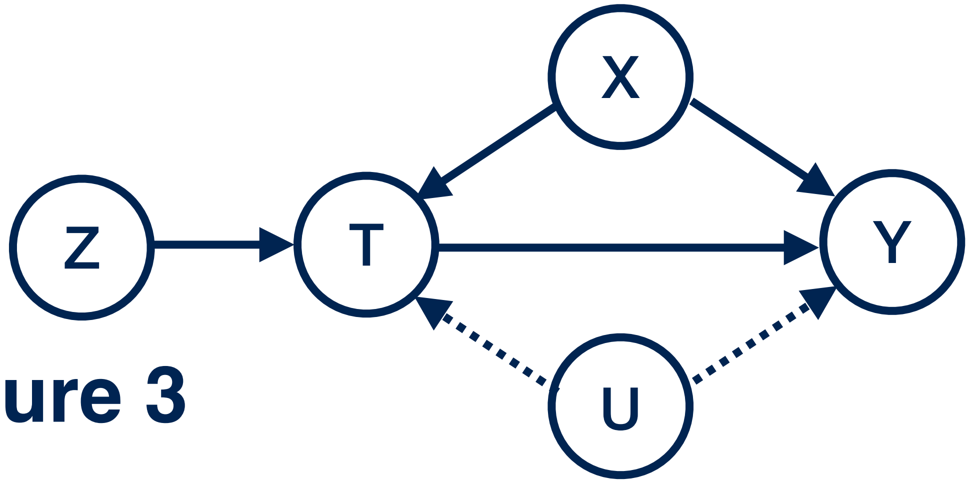




Pearl, Causal Inference in Statistics (2016)

Pearl’s Front-Door Criterion

- Backdoor does not exhaust all ways of estimating causal effects from a graph
- Front-door criterion can still be used for patterns that do not satisfy the backdoor criterion
- Example: Smoking and lung cancer (1970), industry argued to prevent antismoking regulation by suggesting that the correlation could be explained by a carcinogenic genotype that induces a craving for nicotine
- Recall sensitivity analysis in **Lecture 2**
- Recall instrumental variable approach in **Lecture 3**



Pearl, Causal Inference in Statistics (2016)

Instrumental Variable assumptions

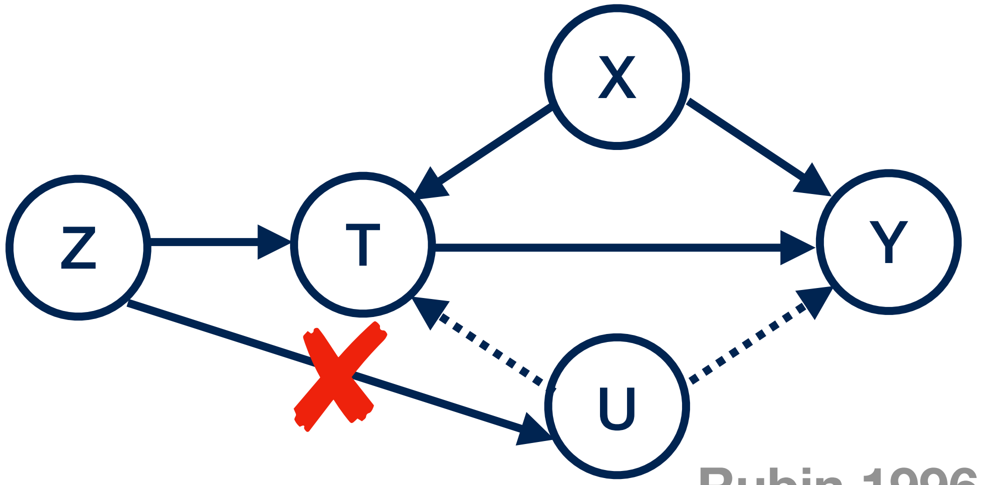
- Treatment assignment Z (**associated** with the treatment) is **random,** i.e., not affect by confounders (observed or unobserved)

- **Exclusion Restriction**: Any effect of Z on Y is via an effect of Z on T, i.e., Z should not affect Y when T is held constant $\left(Y^{(i)}|z=1,t\right) = \left(Y^{(i)}|z=0,t\right)$

- **Non-zero Average:** $\mathbb{E}\left[\left(T^{(i)}|z=1\right) - \left(T^{(i)}|z=0\right)\right]$

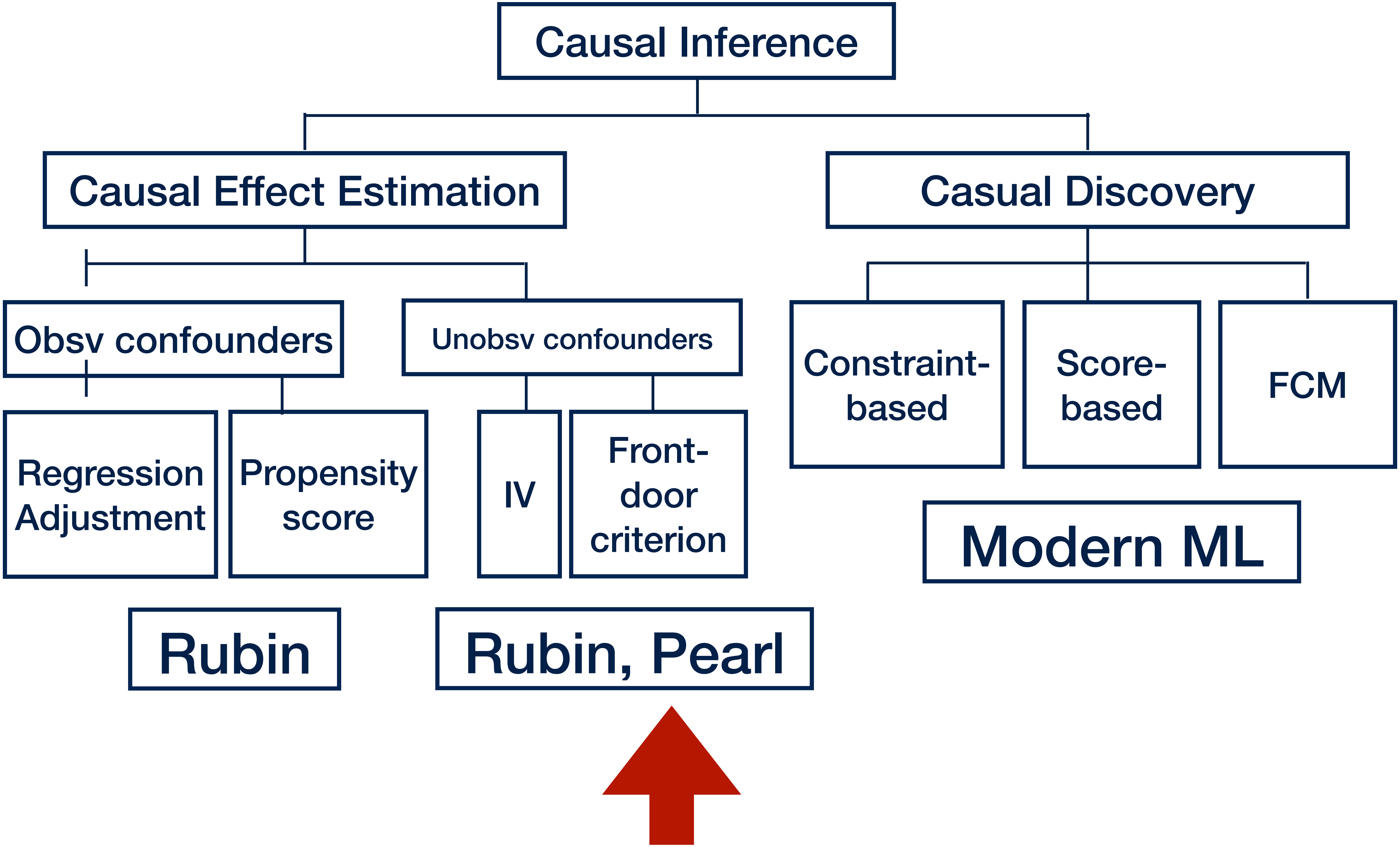
- **Monotonicity** (increasing encouragement “dose”

increases probability of treatment, no defiers)**:** $\left(T^{(i)}|z=1\right) \geq \left(T^{(i)}|z=0\right)$



Rubin 1996

Overview of the course



Causal Inference

Causal Effect Estimation

Casual Discovery

Obsv confounders

Unobsv confounders

Regression Adjustment

Propensity score

IV

Front-door criterion

Constraint-based

Score-based

FCM

Modern ML

Rubin

Rubin, Pearl

Pearl’s Front-Door Criterion: An example

- Fig (a): The graph does not satisfy the backdoor, since the quantity we need to condition on to block the path, i.e. the genotype, is unobserved
- Fig (b): Additional measurement available: tar deposits in patients lungs
- Fig (b) still does not satisfy the backdoor criterion but we can determine the causal effect:

$$p(Y = y|do(X = x))$$

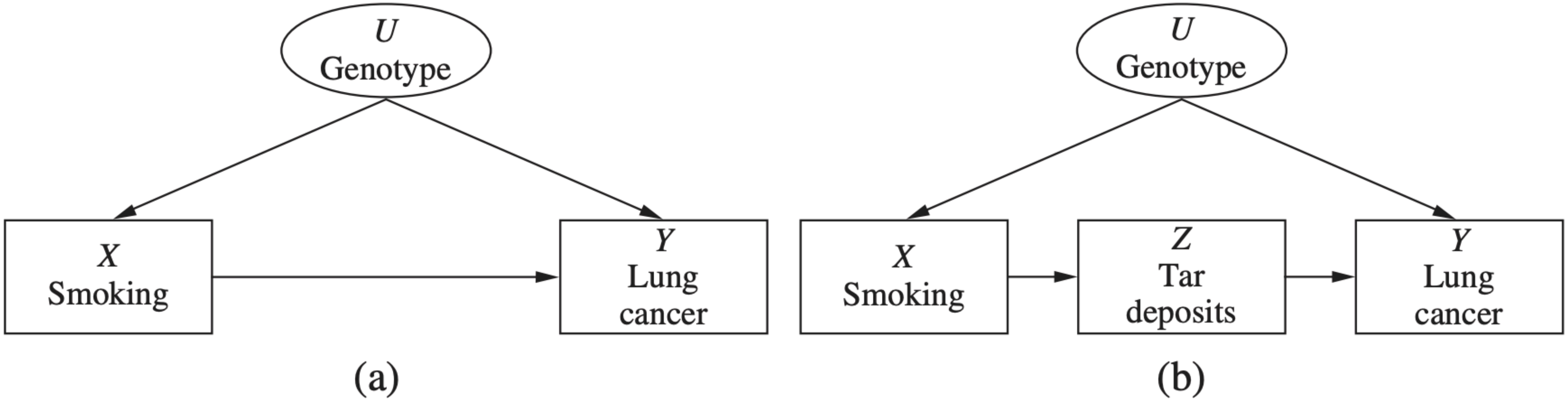


Figure 3.10 A graphical model representing the relationships between smoking (X) and lung cancer (Y), with unobserved confounder (U) and a mediating variable Z

Pearl, Causal Inference in Statistics (2016)

Pearl’s Front-Door Criterion: A crafted example

Interpretation 1: Tobacco industry

Beneficial effect of smoking:

15% of smokers have developed lung cancer vs 90.25% of non-smokers

within tar and non-tar subgroups, smokers have a much lower percentage of cancer than non-smokers (numbers in the table are engineered to illustrate the point that observations are not to be trusted)

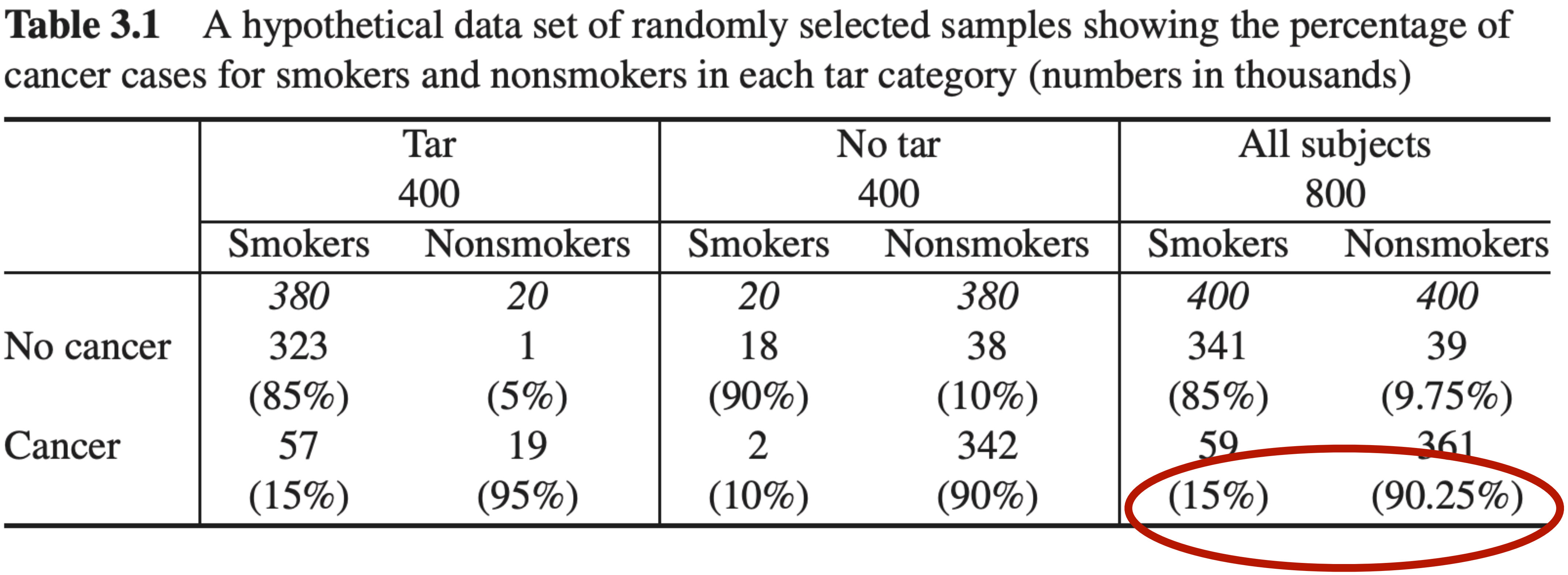


Table 3.1 A hypothetical data set of randomly selected samples showing the percentage of cancer cases for smokers and nonsmokers in each tar category (numbers in thousands)

	Tar 400		No tar 400		All subjects 800	
	Smokers	Nonsmokers	Smokers	Nonsmokers	Smokers	Nonsmokers
	380	*20*	*20*	*380*	*400*	*400*
No cancer	323	1	18	38	341	39
	(85%)	(5%)	(90%)	(10%)	(85%)	(9.75%)
Cancer	57	19	2	342	59	361
	(15%)	(95%)	(10%)	(90%)	(15%)	(90.25%)

Pearl, Causal Inference in Statistics (2016)

Pearl’s Front-Door Criterion: A crafted example

Interpretation 2: Anti-smoking lobbyists

Smoking **increases** the risk of lung cancer

If one chooses to smoke, then one’s chances of building tar deposits are 95% (380/400) vs 5% (20/400) for the non-smokers.

To evaluate effect of tar, look at **smokers and non-smokers separately**. Tar has harmful effects in both groups: in smokers it increases risk of cancer from 10% to 15% and in non-smokers 90% to 95%. Therefore: Smoking -> tar -> cancer.

Regardless of any natural craving, avoid harmful tar by not smoking.

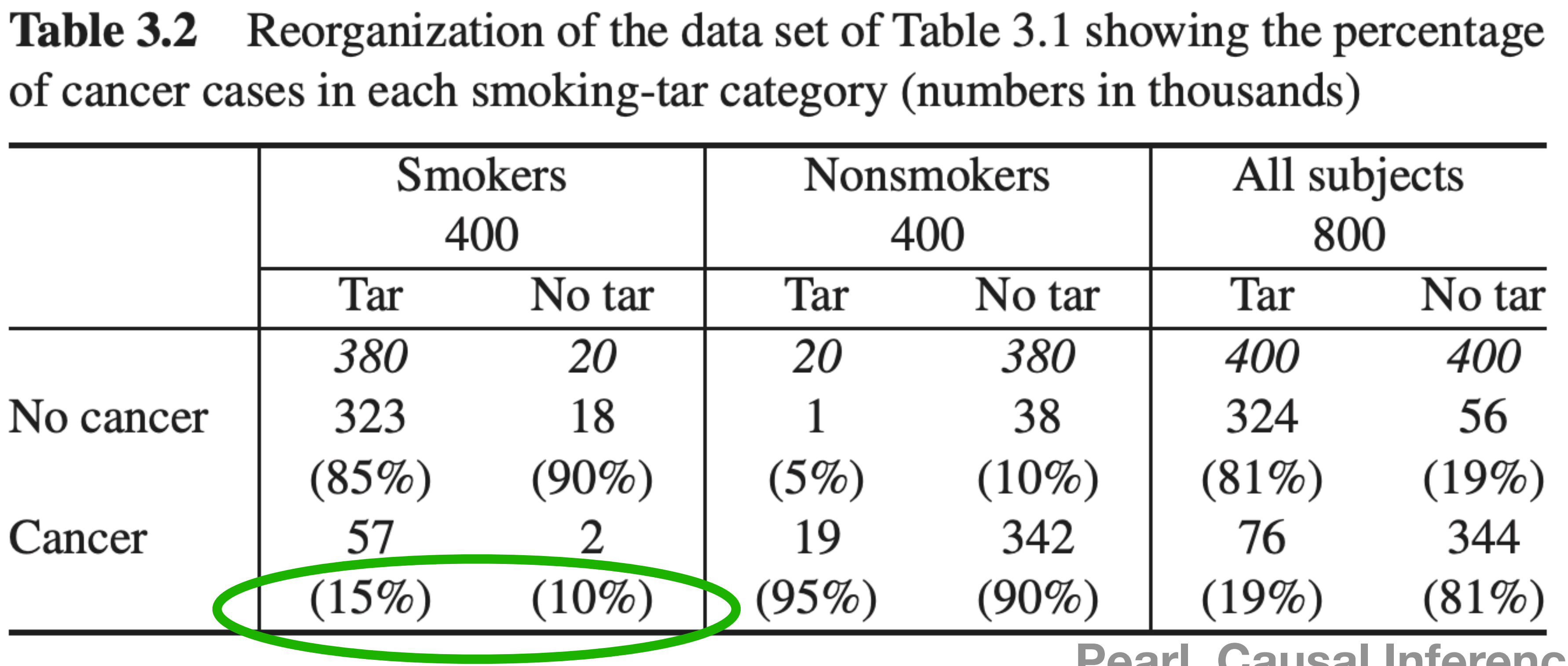


Table 3.2 Reorganization of the data set of Table 3.1 showing the percentage of cancer cases in each smoking-tar category (numbers in thousands)

	Smokers 400		Nonsmokers 400		All subjects 800	
	Tar	No tar	Tar	No tar	Tar	No tar
	380	*20*	*20*	*380*	*400*	*400*
No cancer	323 (85%)	18 (90%)	1 (5%)	38 (10%)	324 (81%)	56 (19%)
Cancer	57 (15%)	2 (10%)	19 (95%)	342 (90%)	76 (19%)	344 (81%)

Pearl, Causal Inference in Statistics (2016)

Pearl’s Front-Door Criterion

X -> Z is **identifiable**, since no back path from X and Z: $X \leftarrow U \rightarrow Y \leftarrow Z$

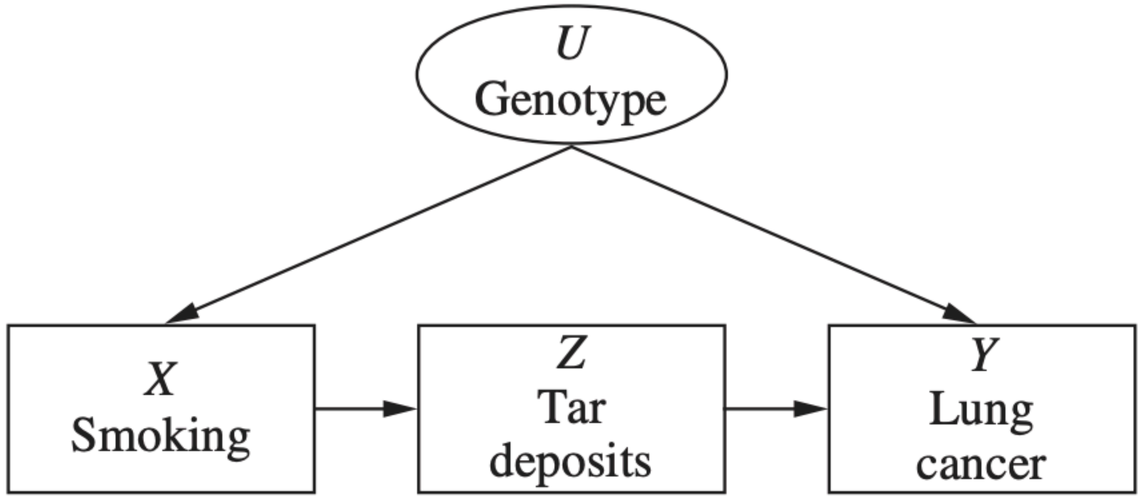
$$p(Z = z|do(X = x)) = p(Z = z|X = x) \qquad *$$

Z -> Y is **identifiable**, since backdoor from Z to Y:

$$Z \leftarrow X \leftarrow U \rightarrow Y$$

is **blocked** by conditioning on X:

$$p(Y = y|do(Z = z)) = \sum_x p(Y = y|Z = z, X = x)p(X = x) \qquad **$$



Pearl, Causal Inference in Statistics (2016)

Pearl’s Front-Door Criterion

Letting z be the value Z takes when setting X=x, from the graph, we have:

$$p(Y|do(X=x)) = p(Y|do(X=x),Z) = p(Y|do(Z=z))$$

Then summing over all states z of Z:

$$p(Y=y|do(X=x)) = \sum_z p(Y=y,z|do(X=x))$$

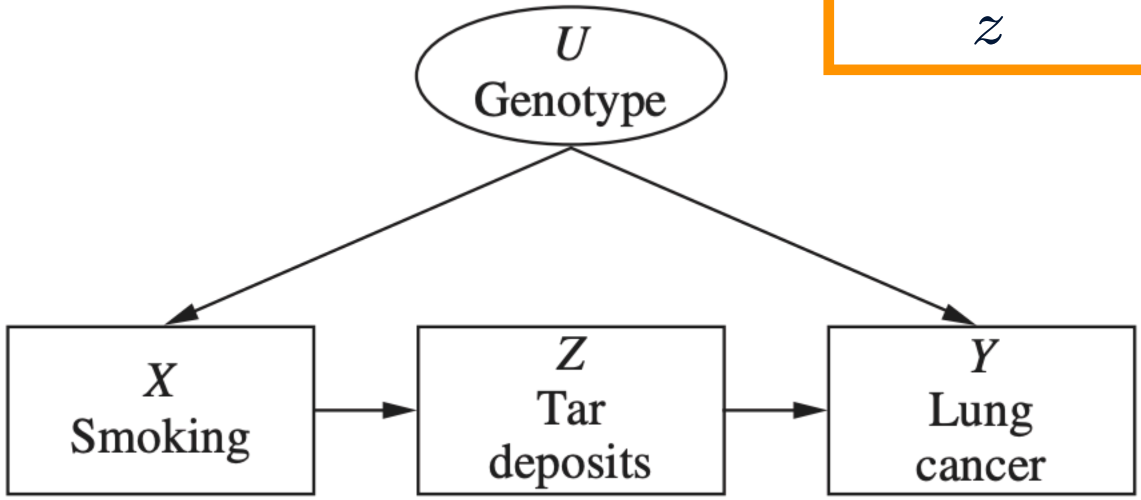
Total prob rule

Product rule:

$$= \sum_z p(Y=y|z,do(X=x))p(z|do(X=x))$$

Line 1

$$\boxed{= \sum_z p(Y=y|do(Z=z))p(z|do(X=x))}$$



Pearl, Causal Inference in Statistics (2016)

Pearl’s Front-Door Criterion

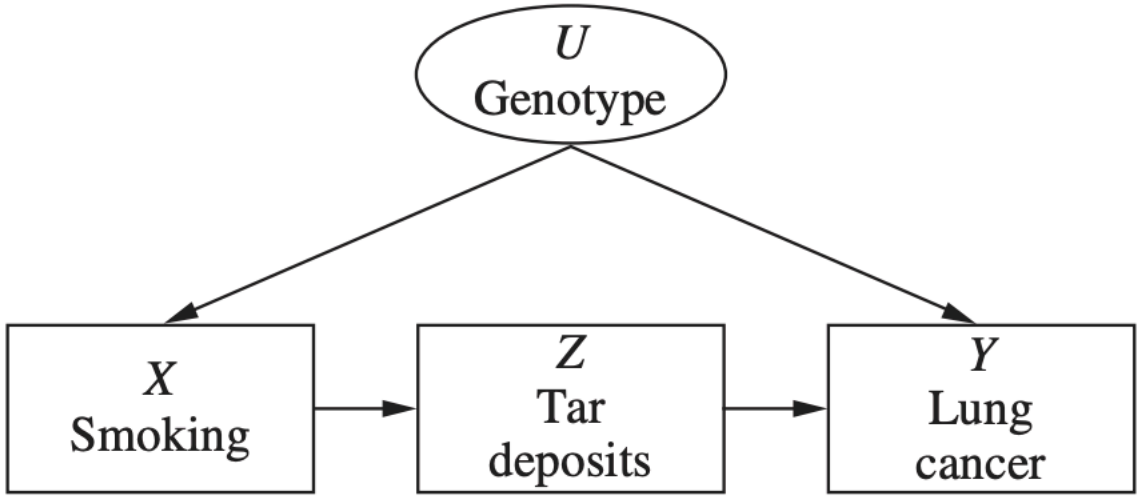
$$p(Z=z|do(X=x)) = p(Z=z|X=x) \qquad \star$$

$$p(Y=y|do(Z=z)) = \sum_{x'} p(Y=y|Z=z, X=x')p(X=x') \qquad \star\star$$

$$p(Y=y|do(X=x)) = \boxed{\sum_{z} p(Y=y|do(Z=z))p(Z=z|do(X=x))}$$

Using $\star$ and $\star\star$ summing over all states z of Z:

$$p(Y=y|do(X=x)) = \sum_{z}\sum_{x'} p(Y=y|Z=z, X=x')p(X=x')p(Z=z|X=x)$$



Front-door formula

Pearl, Causal Inference in Statistics (2016)

Pearl's Front-Door Criterion: Which group is right?

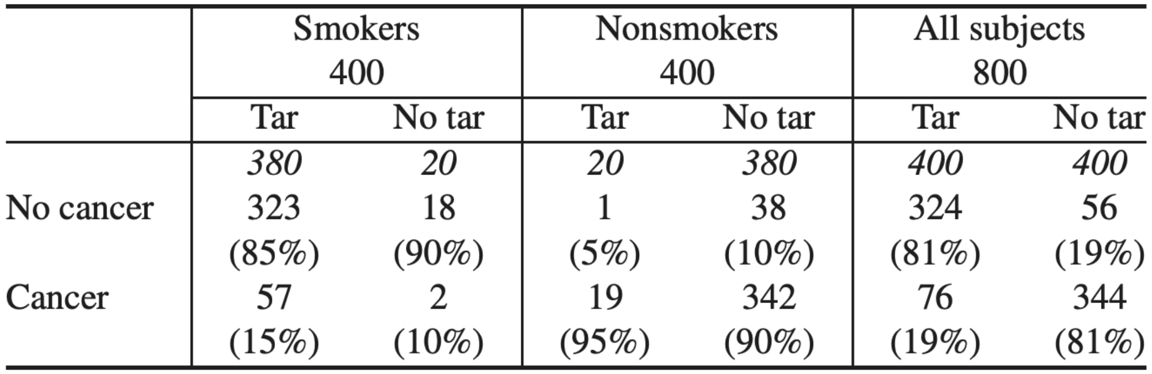
$$p(Y=y|do(X=x)) = \sum_{z}\sum_{x'} p(Y=y|Z=z, X=x')p(X=x')p(Z=z|X=x)$$

$$\begin{aligned}
p(Y=1|do(X=1)) &= \underbrace{p(Y=1|z=0,x'=0)}_{342/380}\,p(x'=0)\,\underbrace{p(z=0|x=1)}_{20/400} \\
&+ \underbrace{p(Y=1|z=0,x'=1)}_{2/20}\,p(x'=1)\,\underbrace{p(z=0|x=1)}_{20/400} \\
&+ \underbrace{p(Y=1|z=1,x'=0)}_{19/20}\,p(x'=0)\,\underbrace{p(z=1|x=1)}_{380/400} \\
&+ \underbrace{p(Y=1|z=1,x'=1)}_{57/380}\,\underbrace{p(x'=1)}_{0.5}\,\underbrace{p(z=1|x=1)}_{380/400} \\
&= 0.5475
\end{aligned}$$

$$p(Y=1|do(X=0)) = 0.5025$$

Average Causal Effect ACE: $p(Y=1|do(X=1)) - p(Y=1|do(X=0)) = 0.045$

Table 3.2 Reorganization of the data set of Table 3.1 showing the percentage of cancer cases in each smoking-tar category (numbers in thousands)



	Smokers 400		Nonsmokers 400		All subjects 800	
	Tar	No tar	Tar	No tar	Tar	No tar
	380	*20*	*20*	*380*	*400*	*400*
No cancer	323 (85%)	18 (90%)	1 (5%)	38 (10%)	324 (81%)	56 (19%)
Cancer	57 (15%)	2 (10%)	19 (95%)	342 (90%)	76 (19%)	344 (81%)

4.5% increase

Pearl, Causal Inference in Statistics (2016)

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$$\begin{aligned} p(Y=1|do(X=1)) = {} & \underbrace{p(Y=1|z=0,x'=0)}_{342/380}\boxed{p(x'=0)}\underbrace{p(z=0|x=1)}_{20/400} \\ & + \underbrace{p(Y=1|z=0,x'=1)}_{2/20}\boxed{p(x'=1)}\underbrace{p(z=0|x=1)}_{20/400} \\ & + \underbrace{p(Y=1|z=1,x'=0)}_{19/20}\boxed{p(x'=0)}\underbrace{p(z=1|x=1)}_{380/400} \\ & + \underbrace{p(Y=1|z=1,x'=1)}_{57/380}\underbrace{\boxed{p(x'=1)}}_{0.5}\underbrace{p(z=1|x=1)}_{380/400} \\ = {} & 0.5475 \end{aligned}$$

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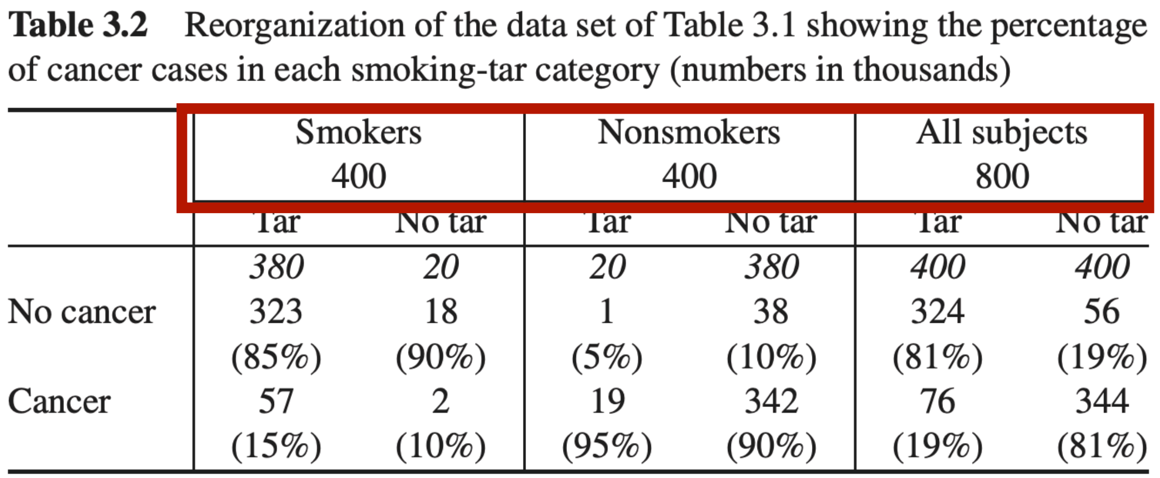

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Pearl’s Front-Door Criterion: Which group is right?

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$342/380$

$2/20$

$19/20$

$57/380$

$20/400$

0.5

$380/400$

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\tfrac{342}{380} \longleftarrow \quad &+ \boxed{p(Y=1|z=0,x'=1)}p(x'=1)p(z=0|x=1) \longrightarrow \tfrac{20}{400} \\
\tfrac{2}{20} \longleftarrow \quad &+ p(Y=1|z=1,x'=0)p(x'=0)p(z=1|x=1) \\
\tfrac{19}{20} \longleftarrow \quad &+ p(Y=1|z=1,x'=1)\underset{\downarrow \atop 0.5}{p(x'=1)}p(z=1|x=1) \longrightarrow \tfrac{380}{400} \\
\tfrac{57}{380} \longleftarrow \quad &= 0.5475
\end{aligned}$$

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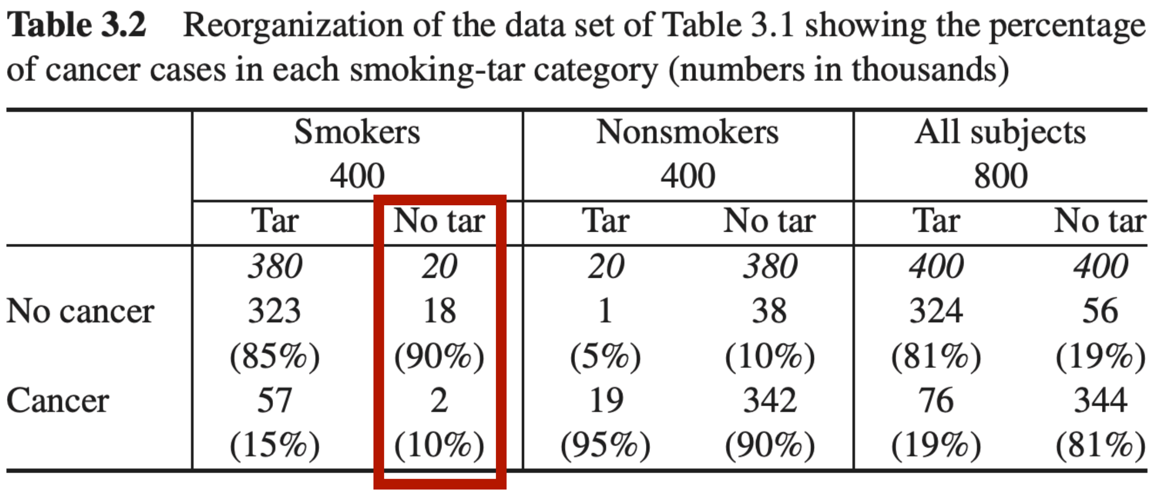

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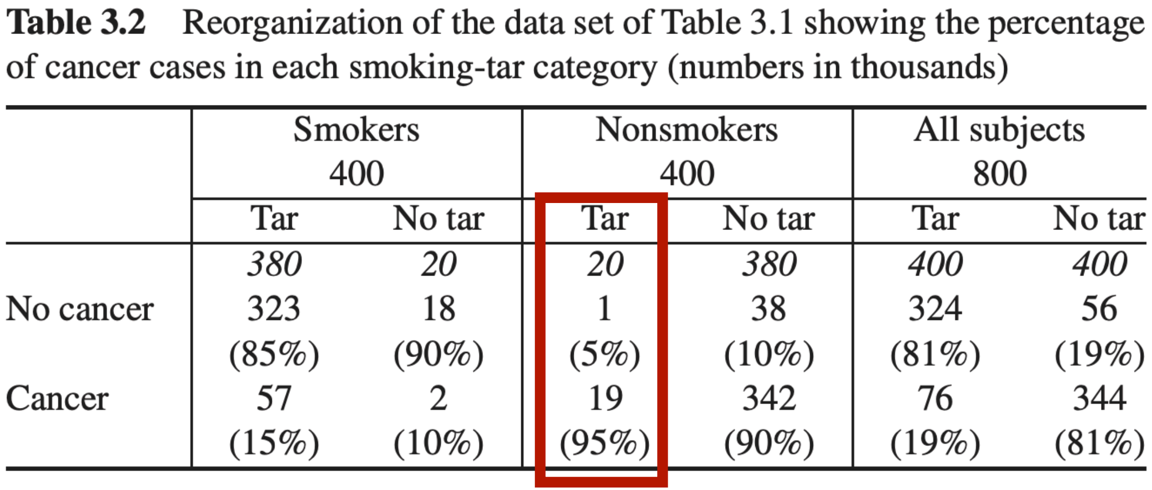

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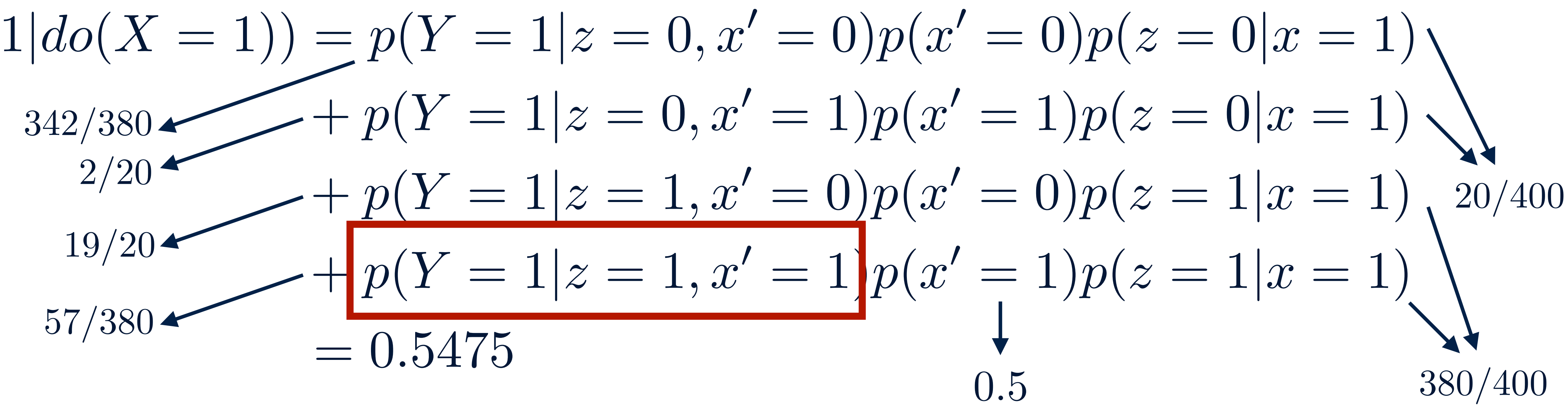

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$342/380$

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$19/20$

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$20/400$

$380/400$

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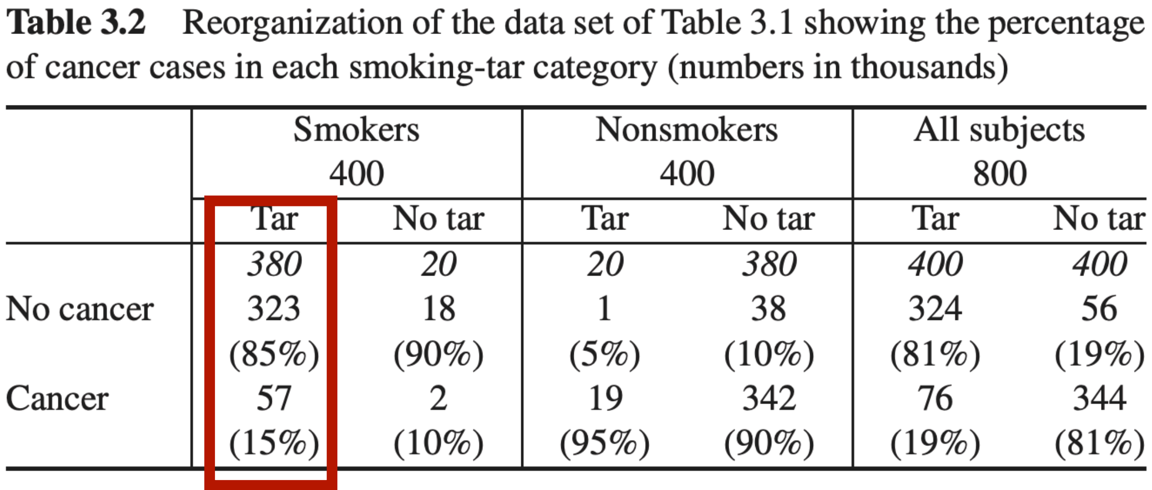

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	380	*20*	*20*	*380*	*400*	*400*
No cancer	323 (85%)	18 (90%)	1 (5%)	38 (10%)	324 (81%)	56 (19%)
Cancer	57 (15%)	2 (10%)	19 (95%)	342 (90%)	76 (19%)	344 (81%)

4.5% increase

Pearl, Causal Inference in Statistics (2016)

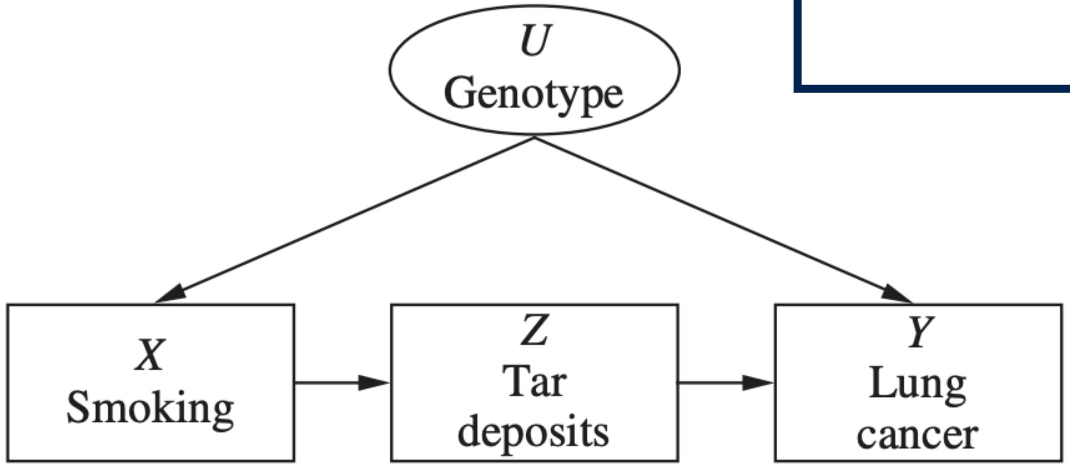
Pearl’s Front-Door Adjustment

Front-door criterion: A set of variables Z is said to satisfy the front-door criterion relative to (X,Y) if:

1. Z intercepts all directed paths from X to Y
2. There is no unblocked path from X to Z
3. All backdoor paths from Z to Y are blocked by X

Front-door adjustment: If Z satisfied the front-door criterion relative to (X,Y), and if p(x,z)>0, then the causal effect of X on Y is identifiable and is given by:

$$\boxed{p(y|do(x)) = \sum_{z} p(z|x) \sum_{x'} p(y|x', z)p(x')}$$



Pearl, Causal Inference in Statistics (2016)

Do Calculus

- Do-calculus: Contains, as subsets:
    - Backdoor criterion
    - Front-door criterion

- Allows analysis of more intricate structure beyond back- and front-door

- Uncovers **all** causal effects that can be identified from a given causal graph

- Power of causal graphs is not just representation but actually **discovery** of causal information

DoWhy Simulations

Simple DoWhy tutorials on my GitHub ‘Causality in Biomedicine’

DoWhy tutorials:
https://microsoft.github.io/dowhy/index.html

CausalGraphicalModels Tutorials:
https://github.com/ijmbarr/causalgraphicalmodels
Adjusting for the wrong variable: http://www.degeneratestate.org/posts/2018/Jul/10/causal-inference-with-python-part-2-causal-graphical-models/
Front-door: http://www.degeneratestate.org/posts/2018/Sep/03/causal-inference-with-python-part-3-frontdoor-adjustment/

Also see ML extensions to DoWhy, e.g. EconML:
https://github.com/microsoft/EconML

Causality in Biomedicine
Lecture Series: Lecture 5

Ava Khamseh (Biomedical AI Lab)

IGMM & School of Informatics

THE UNIVERSITY OF EDINBURGH

20 Nov, 2020