LECTURE 08

Causal Inference

November 13, 2023

PBHLTH 198, Fall 2023 @ UC Berkeley

Andrew O'Connor

Measures of Mortality

Overview of measures

Measures of Mortality: Overview

Measure	Numerator	Denominator	Type
Mortality rate	# of deaths from all causes	Total population	Proportion
Cause-specific mortality rate	# of deaths from a specific disease/condition	Total population	Proportion
Proportionate mortality	# of deaths from a specific disease/condition	Total number of deaths	Proportion
Case-fatality rate	# of deaths from a specific disease/condition	Total number of persons with specific disease/condition	Proportion

These measures can be considered a type of incidence but instead of the occurrence of new cases of disease or morbidity**, it is the occurrence of new cases of death.** Incidence measures the risk of morbidity and mortality measures the risk of death.

Study Designs

Hierarchy of Epidemiology Studies

Components of Studies

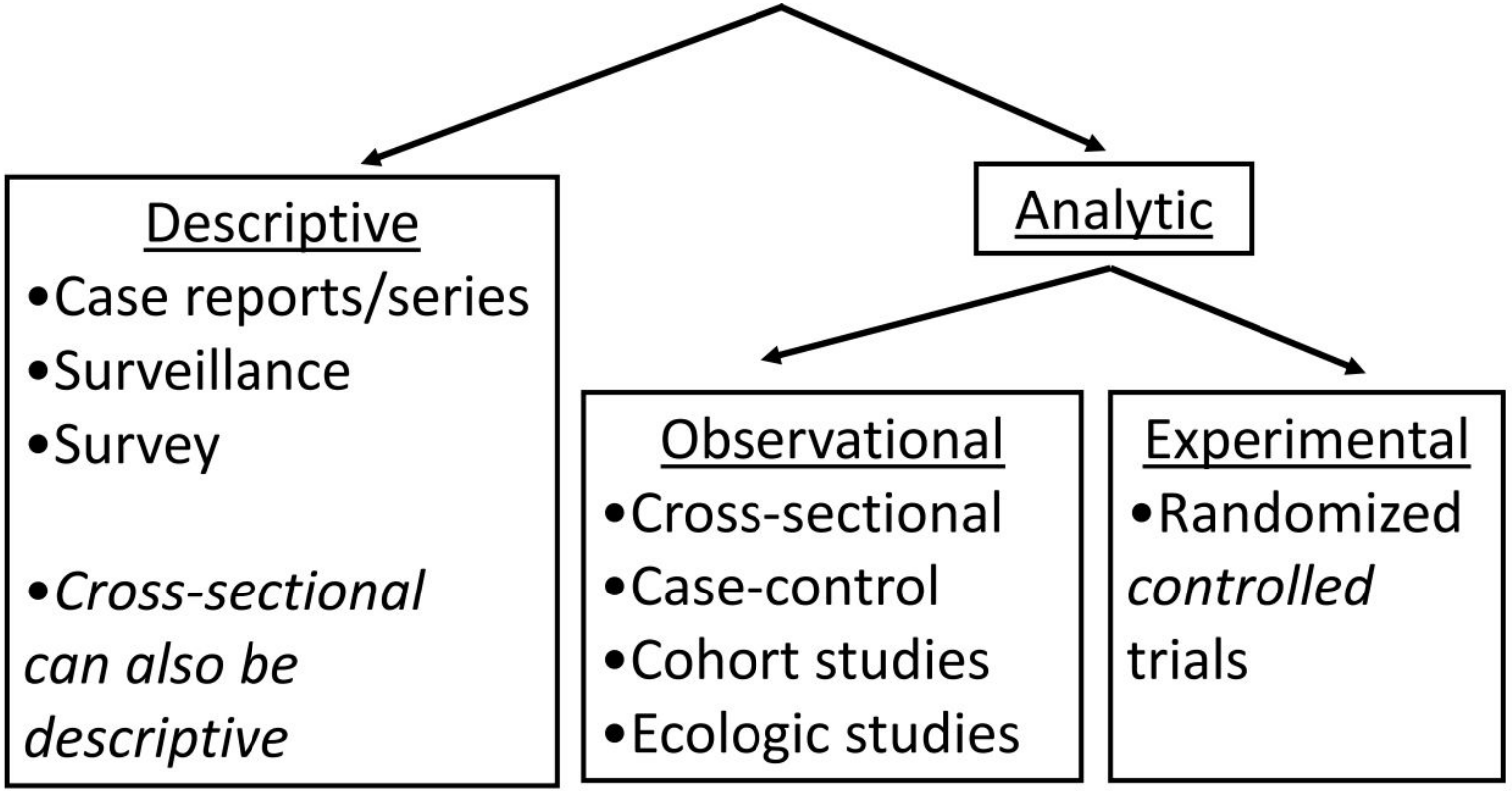
Ecological

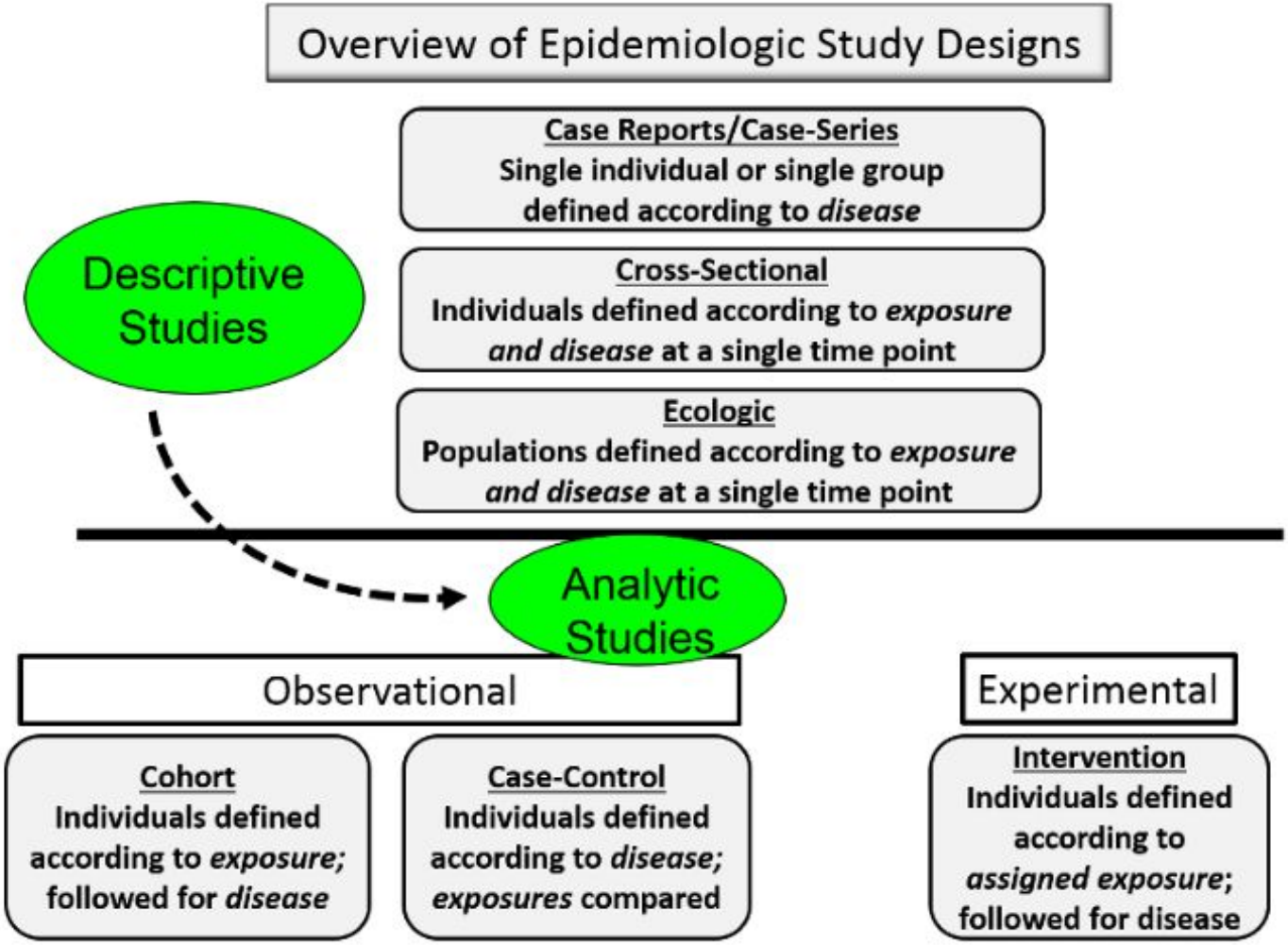
Cross-Sectional (Prevalence)

Cohort

Case-Control

Hierarchy of Epidemiological Studies




Overview of Epidemiologic Study Designs
Case Reports/Case-Series
Single individual or single group defined according to *disease*
Descriptive Studies
Cross-Sectional
Individuals defined according to *exposure and disease* at a single time point
Ecologic
Populations defined according to *exposure and disease* at a single time point
Analytic Studies
Observational
Experimental
Cohort
Individuals defined according to *exposure;* followed for *disease*
Case-Control
Individuals defined according to *disease; exposures* compared
Intervention
Individuals defined according to *assigned exposure*; followed for disease

Measures of Risk and Association

Risk

Risk

- **Risk**: The probability of an event occurring (such as development of disease or death over a specified observation window)
- Studies seek to determine whether there is a greater risk of the disease in persons who have been exposed to certain agent than persons not exposed

Measures of Risk

Incidence density ratio (IDR) = Relative rate;

Rate ratio = ID exposed/ID nonexposed

Cumulative incidence ratio (CIR) = Relative Risk;

Risk ratio = CI exposed/CI nonexposed

Odds ratio (OR) = Odds exposure diseased/

Odds exposure not diseased

Measures of Risk

DISEASE			
EXPOSED	**Yes**	**No**	**Total**
Yes	**a**	**b**	
No	**c**	**d**	
	a+c		**a+b+c+d**

Among those who have the disease, the **risk** of having been **exposed** to [specific factor] is...

Among those who are exposed, the **risk** of **developing** disease X is …

Video: Relative Risk

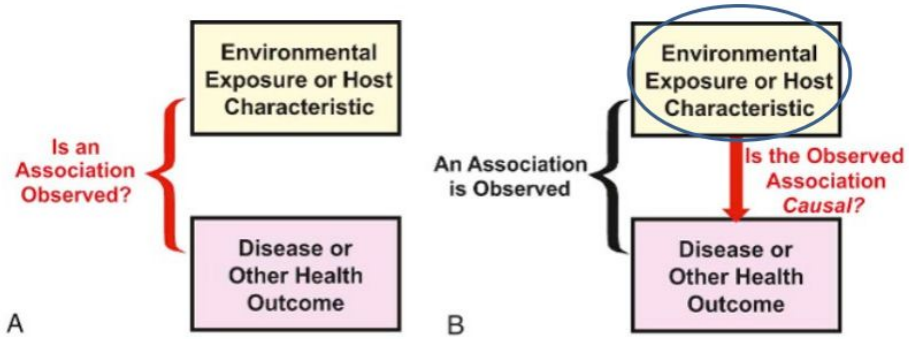
Causal Inference

Definitions

Causal Relationships

Inference in Epidemiology

- Studies ultimately answer 2 main questions
  - Is an association observed between exposure and outcome?
    - **statistical inference**
  - How meaningful are the study findings?
    - **causal inference**



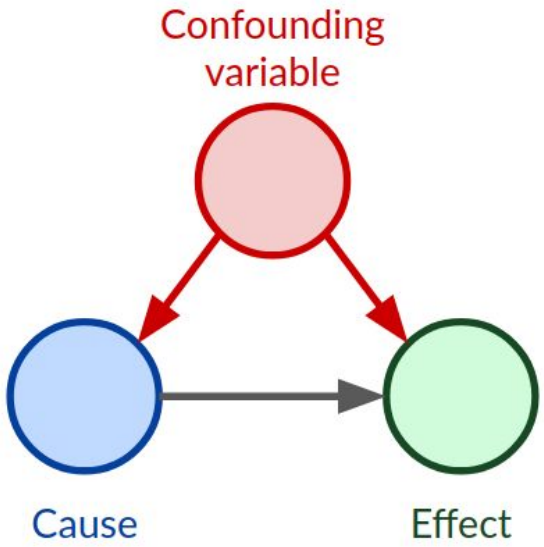
Definitions

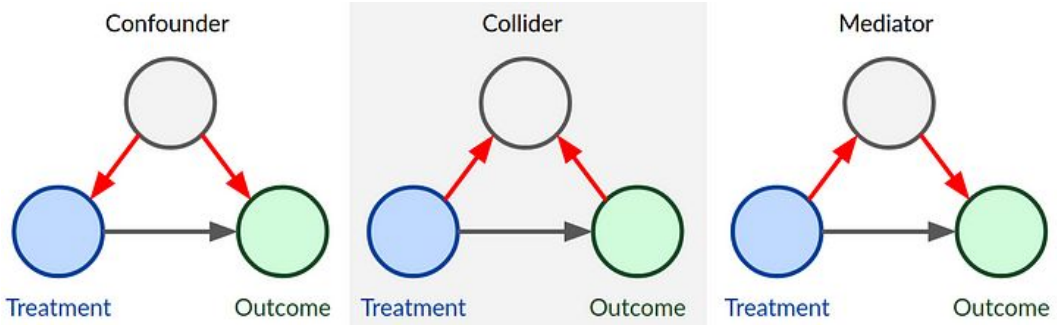
- **Cause**: An event, condition, or characteristic that preceded the disease event and without which the disease event either would not have occurred at all or would not have occurred until some later time
- **Causal inference**: process of evaluating all available knowledge of the association between a particular exposure and an outcome

Causal Relationships

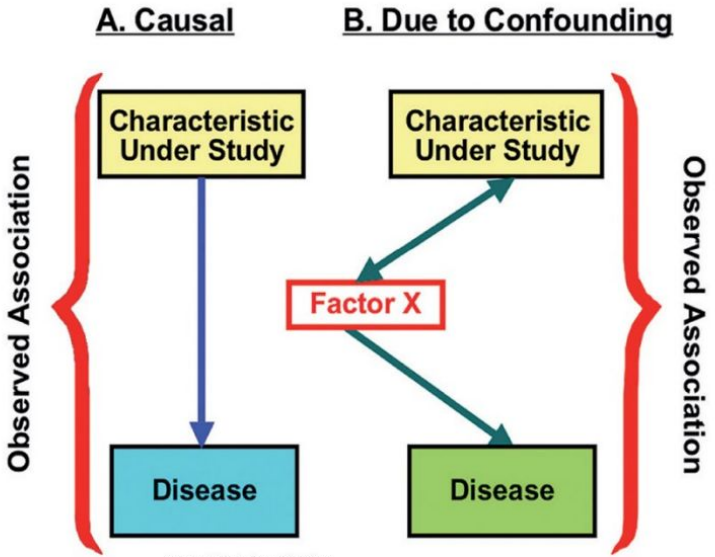
- Causal relationships can formally be visualized **directed acyclic diagrams** (DAGs)
- Must consider
  - **Bias**: any systematic error in the design, conduct and analysis of a study that distorts the results of the study
  - **Confounding**: Situation where exposure and disease appear to be associated because they are both linked to a third factor
  - **Random error**

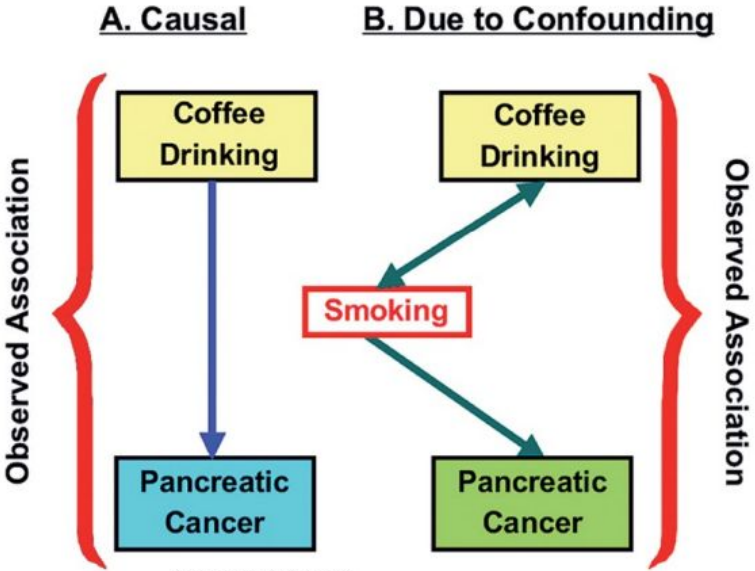
Directed Acyclic Graphs (DAGs)





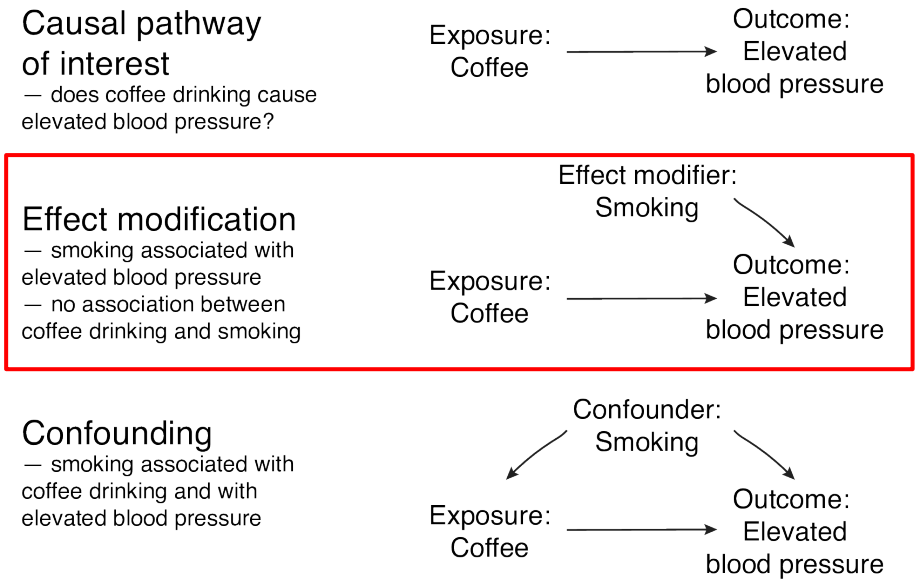
Example: Causal vs. Confounded





Effect Measure Modification

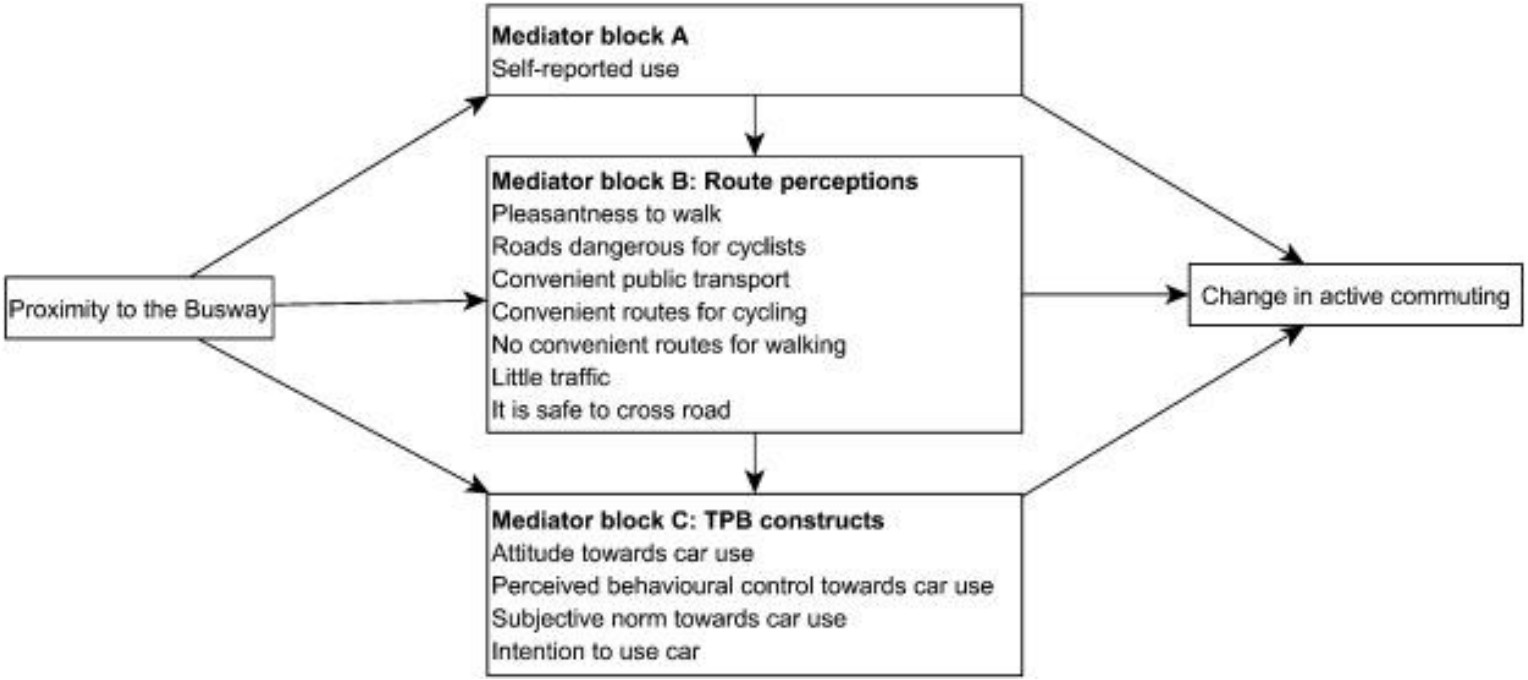
- Strength or direction of association between the exposure and the outcome is modified according to subgroups of a third factor
- Third factor is referred to as an **effect modifier**



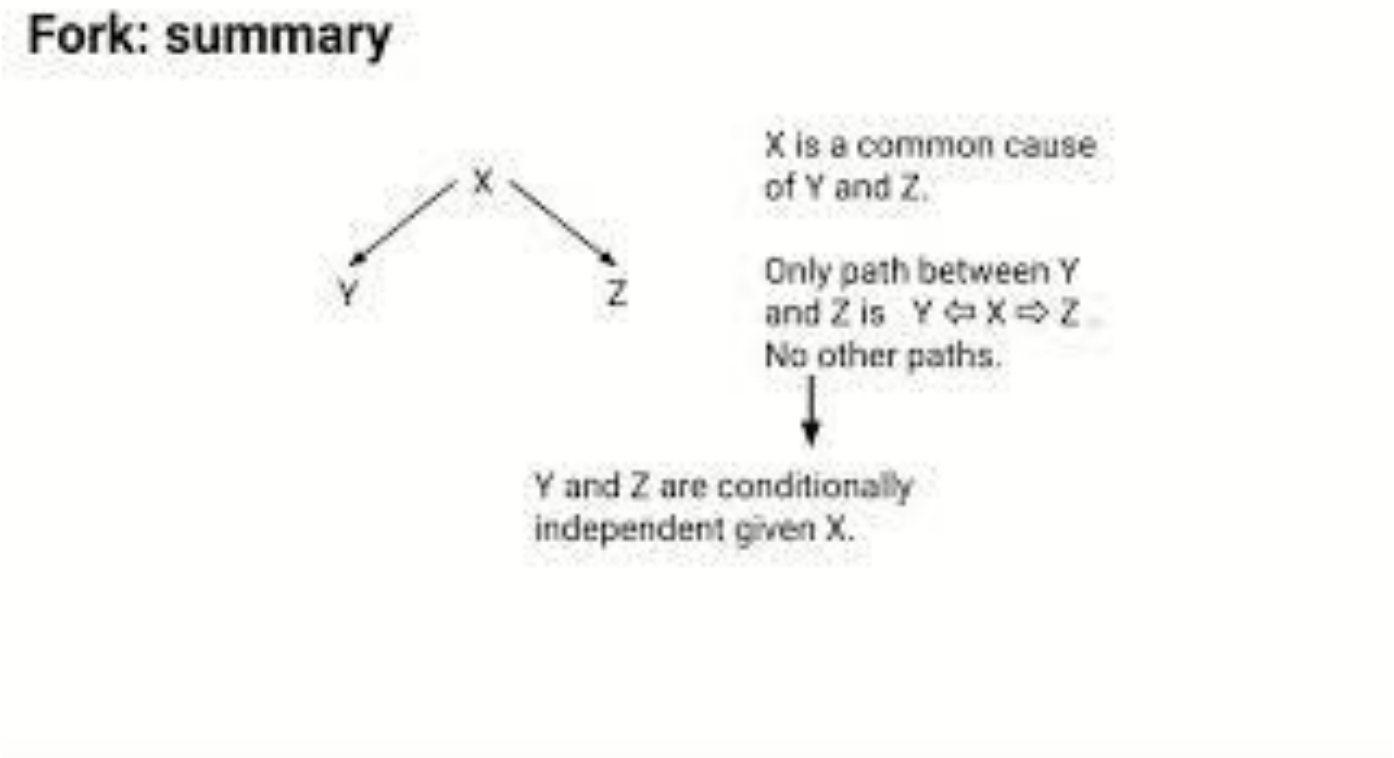
Summary: DAGs

- We want to examine
  - **cause → effect**
- If we're not careful, sometimes our "cause" is hiding behind a confounder
  - **cause → effect** is actually **cause ↔ confounder ↔ effect**
- If we observe a causal relationship, do we see any differences among subgroups? If so, the subgrouping category would be called an **effect modifier**
  - **cause → effect** breaks down into
    - **cause → Analyze effect in subgroup 1**
    - **cause → Analyze effect in subgroup 2**
- But what if we think there's multiple causes?

Example: Commuting



[Video] Causal Inference Structures



Exercise: DAGs

Consider the scenario

Concerned citizens have observed an unusual association between increased ice cream sales and higher rates of drowning incidents. Many believe that ice cream causes drowning.

1. Why do you think this is the case?
2. What variables are at play in this causal relationship?
3. Draw the DAG.

Exercise: DAGs

Draw the DAG corresponding to the scenario.

Label any confounders, colliders, mediators or effect modifiers.

Circle the causal pathway

Regular physical activity is believed to reduce the risk of heart disease. However, it's suggested that the effect of physical activity on heart disease is mediated by its impact on cholesterol levels

Exercise: DAGs

Draw the DAG corresponding to the scenario.

Label any confounders, colliders, mediators or effect modifiers.

Circle the causal pathway

Regular consumption of fast food is believed to contribute to higher BMI. It's hypothesized that this relationship is influenced by a lack of physical activity acting as a potential confounder and the mediating effect of excessive calorie intake

Exercise: DAGs

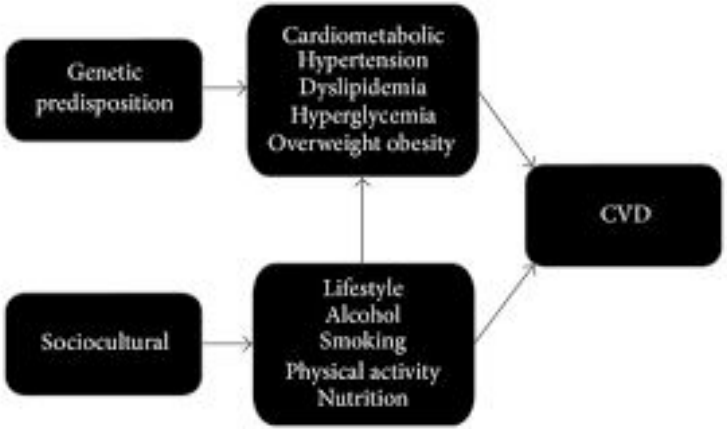
Draw the DAG corresponding to the scenario

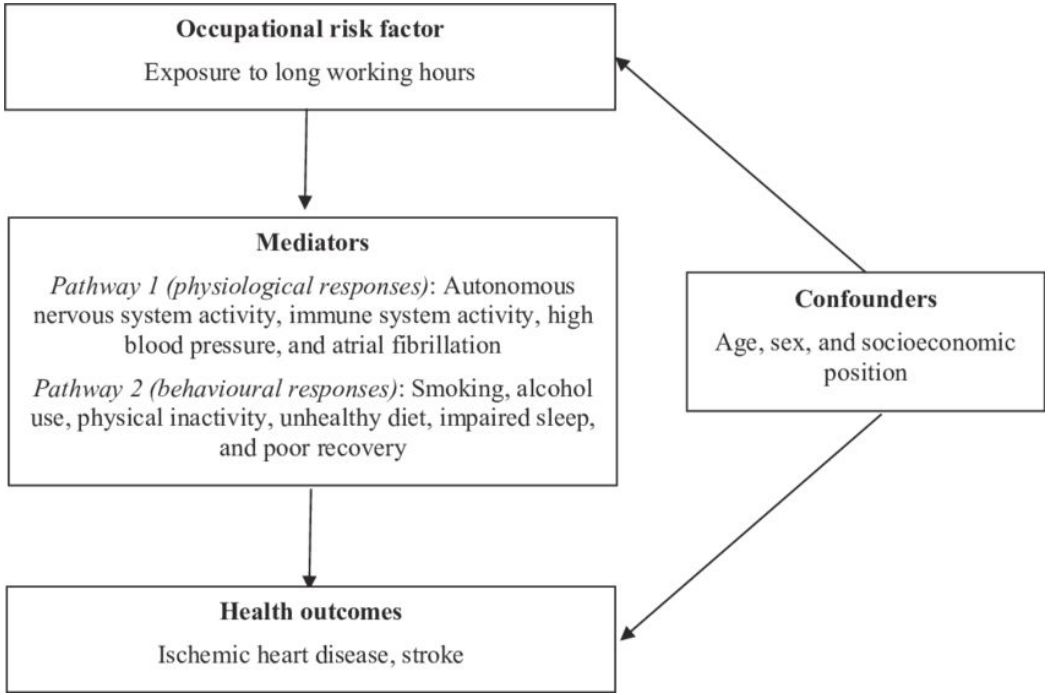
Label any confounders, colliders, mediators

Identify effect modifiers.

Heavy use of social media is associated with increased stress levels in UC Berkeley students. The relationship may be confounded by the presence of both academic workload and lack of face-to-face social interactions, and potentially mediated by the fear of missing out (FOMO). It was also noted that students of some majors (CS, EECS, Math, Physics) experienced significantly different levels than others (English, Psychology, Political Science).

More Examples





Types of Causal Relationships

4 Types

Exercises

Sufficient Cause Model

1964 Surgeon General's Report

Types of Causal Relationships

- 4 types
  - Necessary and sufficient
  - Necessary, not sufficient
  - Sufficient, not necessary
  - Neither necessary nor sufficient

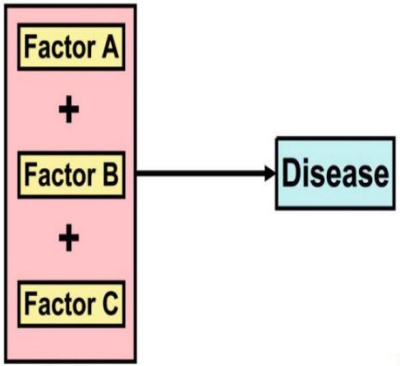
Types of Causal Relationships

(1) A factor is both necessary and sufficient. This relationship rarely if ever occurs.

Without the factor, the disease never develops and in the presence of that factor, the disease always develops

(2) <u>Each</u> factor is necessary, but not (in itself) sufficient to cause disease

Multiple factors are required, often in a specific temporal sequence.



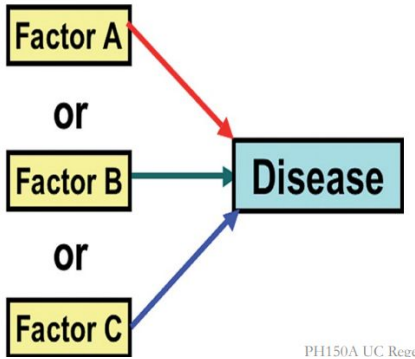
Examples:

-Cancer (multistage process) 'initiation and promotion'
-Tuberculosis (bacteria)
-AIDS (HIV)

Types of Causal Relationships

(3) Each factor is sufficient, but not necessary.

Factor alone can produce the disease….but so can others that are acting alone

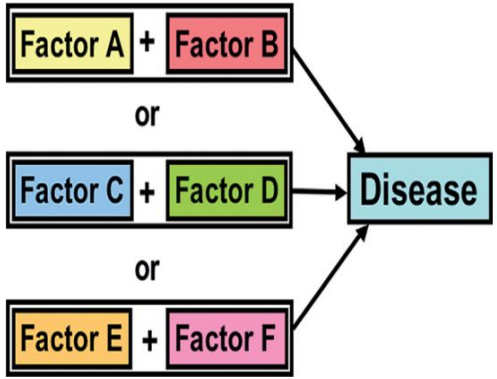


Examples: Benzene and leukemia; radiation and leukemia

Criterion of sufficient is rarely met by a single factor.

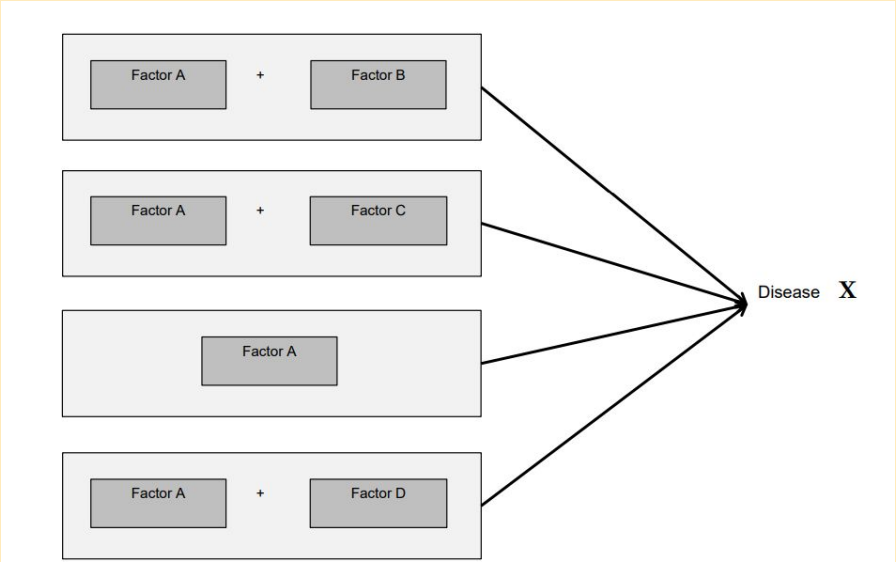
Better example: Decapitation causes death; but there are other causes of death.

(4) Each factor is neither sufficient nor necessary to produce disease (most chronic diseases) More complex model.



Example: Heart Disease (CVD)

-smoking
-diabetes
-low HDL
-physical inactivity
-hypertension
-more



Exercise: Sufficient Cause

Factor A is…

(necessary / not necessary)

and

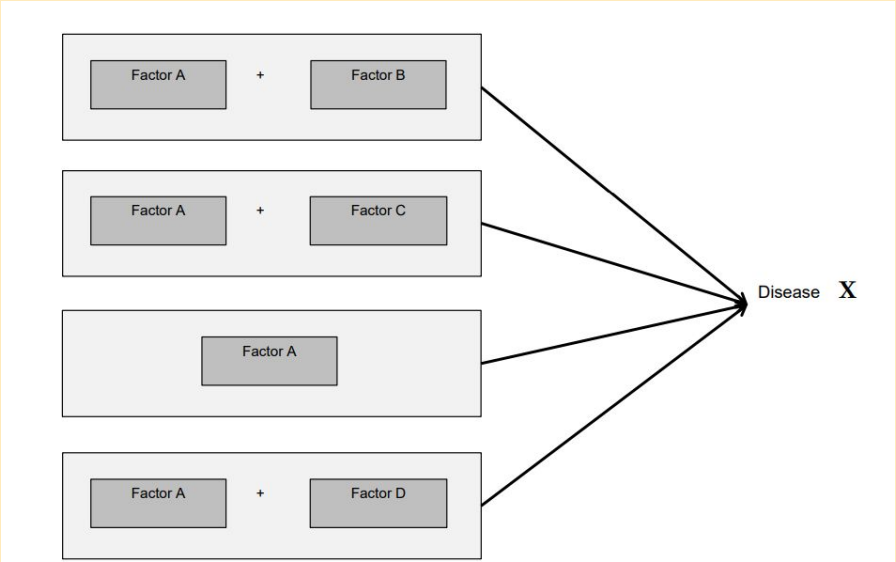
(sufficient / not sufficient)

Factor B is…

(necessary / not necessary)

and

(sufficient / not sufficient)



Exercise: Sufficient Cause

Factor A is…

(necessary / not necessary)

and

(sufficient / not sufficient)

Factors B, C, D are…

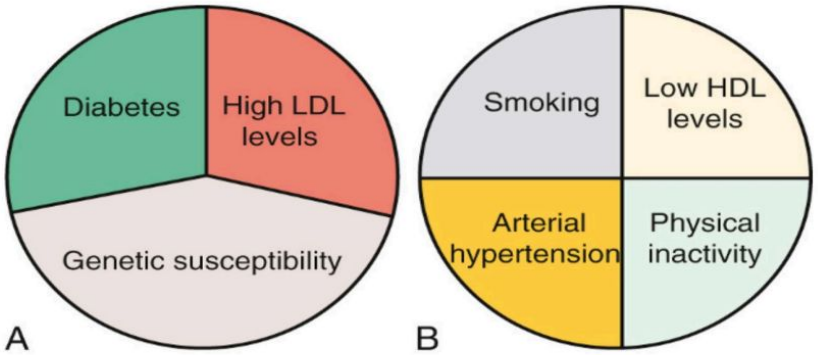
(necessary / not necessary)

and

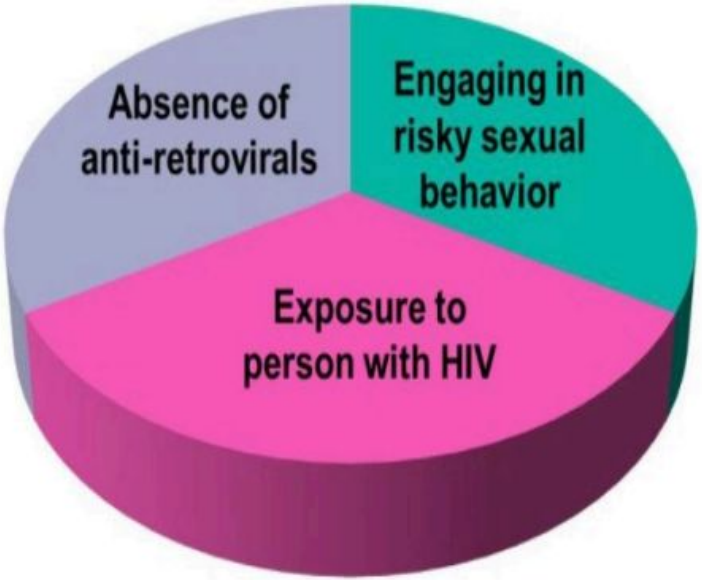
(sufficient / not sufficient)

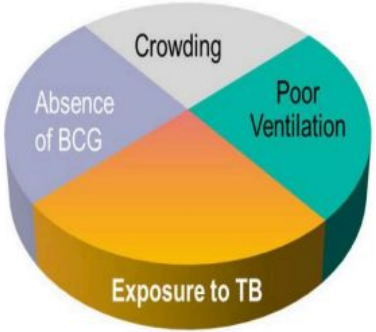
Rothman's Sufficient Cause Model

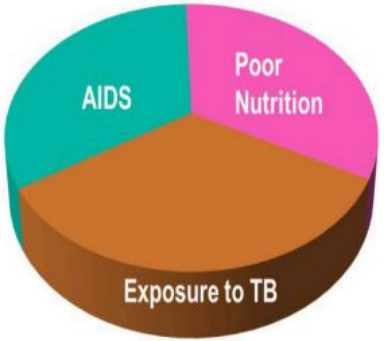
- A model showing the complete causal mechanism" that "inevitably produces disease
- A "sufficient cause" is not a single factor, but a minimum set of factors that will produce disease in an individual
- Example: Atherosclerotic disease



Sufficient Cause Models: AIDS, TB

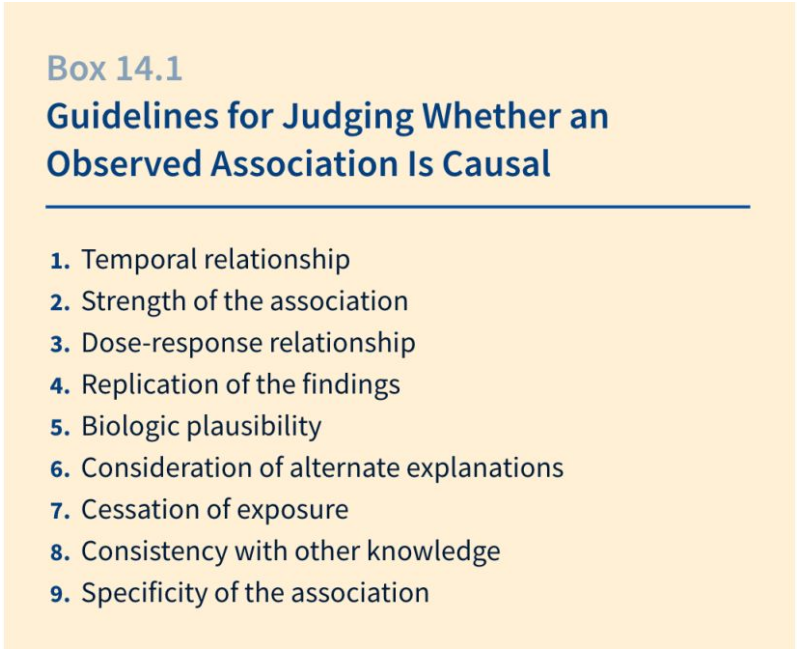






1964 Surgeon General's Report

- Highlighted the deleterious health consequences of tobacco use
- One of the first formal set of guidelines for determining causality



Box 14.1

Guidelines for Judging Whether an Observed Association Is Causal

1. Temporal relationship
2. Strength of the association
3. Dose-response relationship
4. Replication of the findings
5. Biologic plausibility
6. Consideration of alternate explanations
7. Cessation of exposure
8. Consistency with other knowledge
9. Specificity of the association

Any questions?