

## Causal inference in biomedical research

Two notions of causation:

- Causes of an effect/outcome
- Effects of a cause

Causes of an effect

- What were causes of World War II?
- What are causes of lung cancer?
- What was the cause of outbreak of food poisoning?
- Who is responsible for events of 9/11?

Historian's/detective's paradigm: explain the past, often complex chain of events that leads to outcome

Effects of a cause/intervention:

- Did contaminated water supply cause the cholera epidemic in London in the 1850s?
- Does aspirin prevent myocardial infarction?
- Does smoking cause lung cancer?
- How strong is the effect?

Experimental paradigm: learn about the effect of specified interventions

For this course, concentrate on effects of a cause/intervention

Fundamentally simpler question: search is for useful information rather than complete scientific understanding

Paradigm of experiment useful in elucidating causal ideas even when experiment cannot be performed

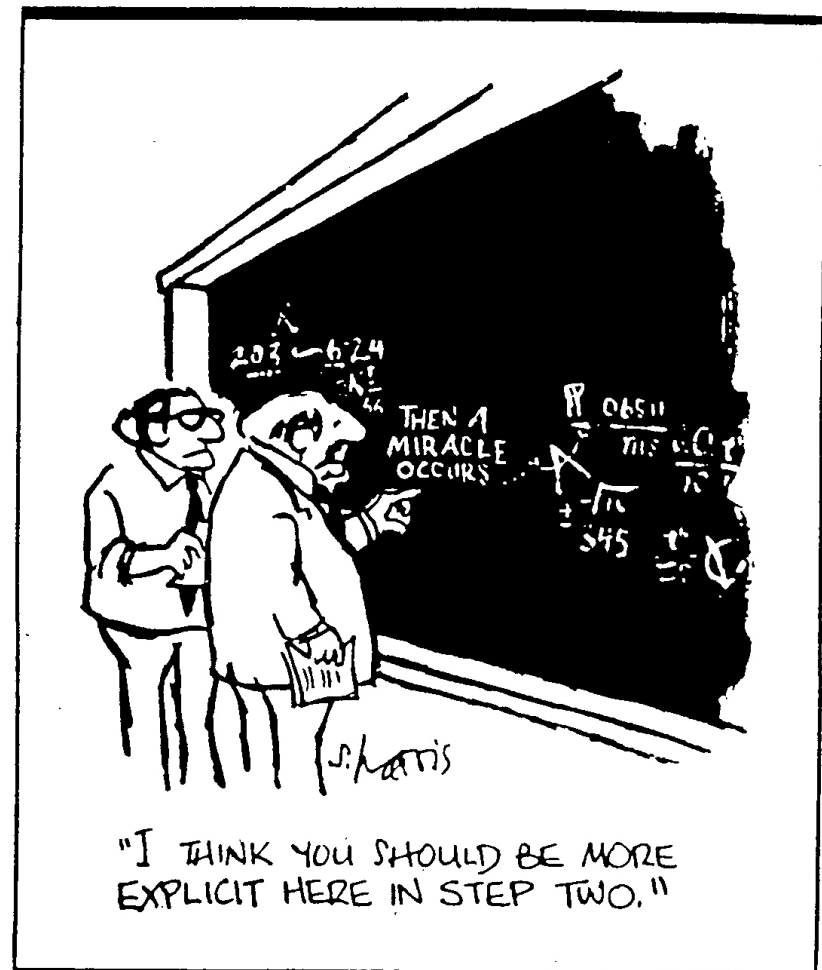
May also consider causes of an effect; not emphasized

Typical approach for determining whether an association is causal:

Observe treatments/exposures, outcomes, and other variables in population

Use standard statistical methods to derive inferences about associations between observable variables

Use series of *ad hoc* rules to determine whether associations have causal interpretation



Useful to have more precise definitions of causal effects:

- Demystifies the process of going from association to causation
- Allows explicit statements regarding what assumptions are necessary to justify causal inferences
- Allows for more critical, better informed evaluation of causal claims
- Helps determine when familiar methods useful or unfamiliar methods necessary
- Motivates derivation and use of unfamiliar methods

Paradigm:

1. Conceptual model for treatment effects; nonparametric ideas
2. Statistical/mathematical models and assumptions
3. Estimation/testing procedures

Useful to consider separately, in order

Steps often confused in vocabulary, thinking

Outline of course:

**Notions of causation: the potential outcomes model**

**Effects of point exposures:**

- Easier to understand
- Model, together with well-recognized assumptions, can justify familiar approaches

Consider randomized trials first, then observational studies

Alternative assumptions, models, methods of analysis (name some)

## **Joint effects of multiple treatments/exposures:**

- Problem ubiquitous in epidemiology/medicine
- Intuition from familiar methods often fails  
Understand why and when

### Problems include

- Direct and indirect effects
- Randomized trials with simple noncompliance

Some debate about appropriate estimands; will present various approaches

- Effects of time-varying exposures and treatments in randomized and observational studies

Other issues:

- Multivariate Outcomes

Principal stratification

Censoring by death

- Surrogate outcomes and exposures

Organization:

Lectures Tuesday and Thursday 10:30 AM - 12:00 PM

Office hour: time TBA

Assignments: weekly homework; final project; possibly final exam

Class participation requested, part of grade