

Lecture 2

Cause and Effect

Announcements

- Homework 1 out this afternoon, due Thursday 2/1
- All information on the <u>course website</u>

Causality

Really?



npr.org (report on a study in heart.bmj.com)

Observation

- individuals, study subjects, participants, units
 - European adults
- treatment
 - chocolate consumption
- outcome
 - heart disease

The first question

Is there any relation between chocolate consumption and heart disease?

association

"any relation"

An answer

Some data:

"Among those in the top tier of chocolate consumption, 12 percent developed or died of cardiovascular disease during the study, compared to 17.4 percent of those who didn't eat chocolate."

- Howard LeWine of Harvard Health Blog, reported by npr.org

Yes, this points to an association

The next question

Does chocolate consumption lead to a reduction in heart disease?

causality

This question is often harder to answer.

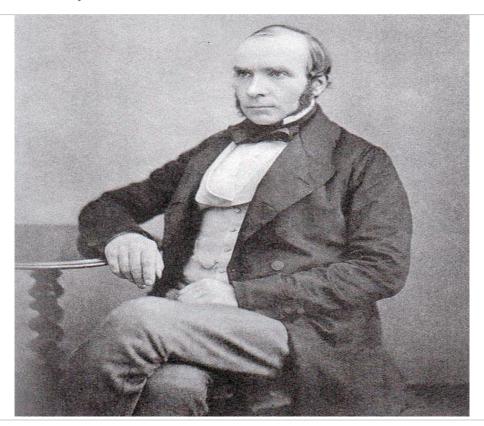
"[The study] doesn't prove a cause-and-effect relationship between chocolate and reduced risk of heart disease and stroke."

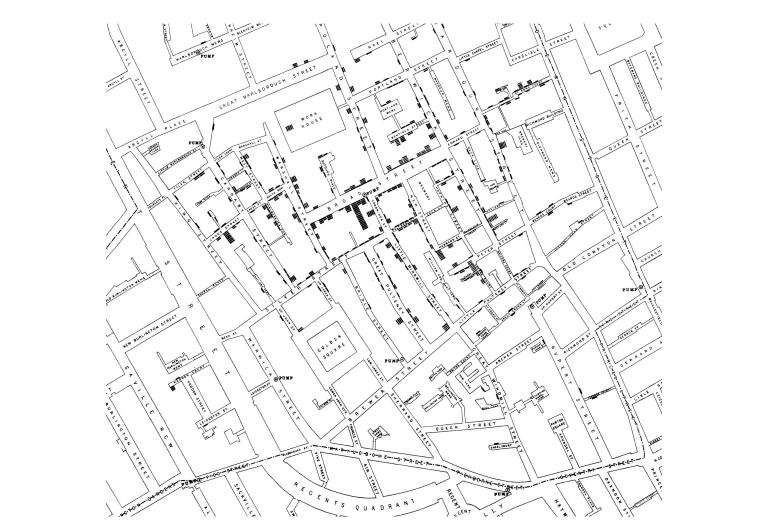
■ JoAnn Manson, chief of Preventive Medicine at Brigham and Women's Hospital, Boston

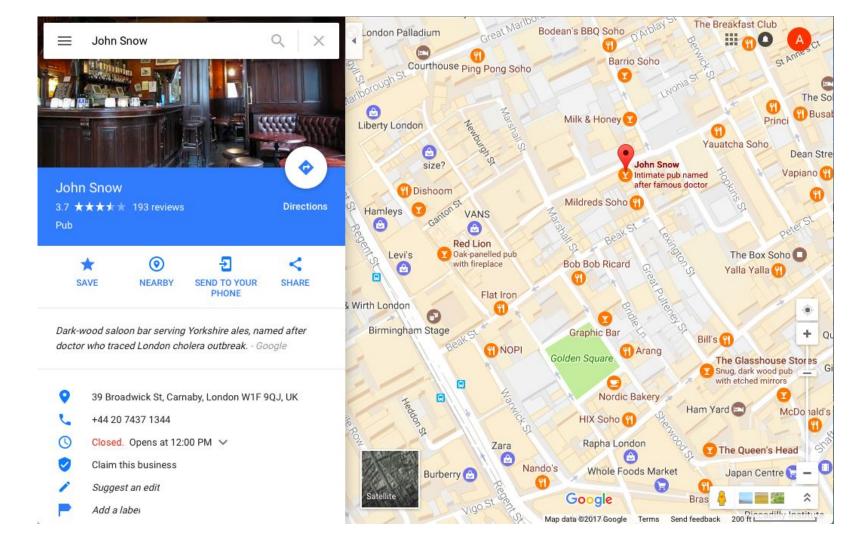
Miasmas, miasmatism, miasmatists

- Bad smells given off by waste and rotting matter
- Believed to be the main source of disease
- Suggested remedies:
 - "fly to clene air"
 - "a pocket full o'posies"
 - "fire off barrels of gunpowder"
- Staunch believers:
- Florence Nightingale
 Edwin Chadwick, Commissioner of the General Board of Health

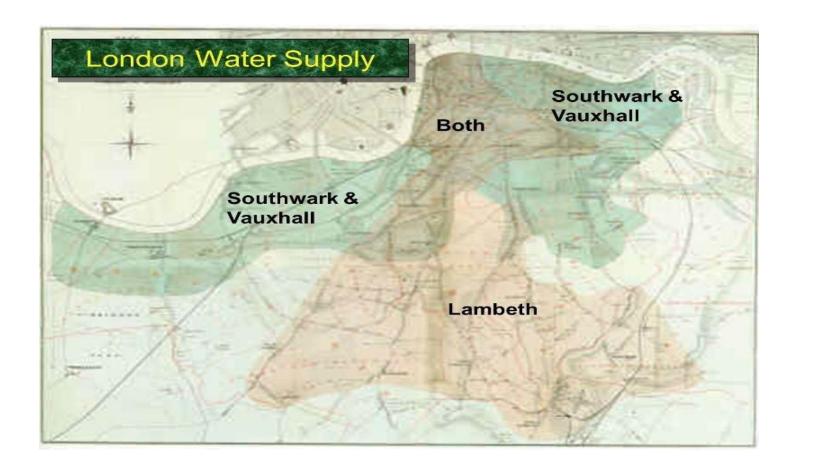
John Snow, 1813-1858











Comparison

- treatment group
- control group
 - does not receive the treatment

Snow's "Grand Experiment"

"... there is no difference whatever in the houses or the people receiving the supply of the two Water Companies, or in any of the physical conditions with which they are surrounded ..."

The two groups were similar except for the treatment.

Snow's table

| Supply Area | Number of houses | Cholera deaths | Deaths per 10,000 houses |
|----------------|------------------|----------------|--------------------------|
| S&V | 40,046 | 1,263 | 315 |
| Lambeth | 26,107 | 98 | 37 |
| Rest of London | 256,423 | 1,422 | 59 |

Key to establishing causality

If the treatment and control groups are *similar apart from the treatment*, then differences between the outcomes in the two groups can be ascribed to the treatment.

Trouble

If the treatment and control groups have systematic differences other than the treatment, then it might be difficult to identify causality.

Such differences are often present in **observational studies**.

When they lead researchers astray, they are called confounding factors.

Fluoride and Tooth Decay

There is no fluoride in the water in Ithaca; there is fluoride in the water in most other US cities. We want to know if fluoride prevents tooth decay.

- What observations will we need?
- What is the treatment group? What is the control group?
- What visualizations would you make?
- What confounding variables might you worry about?
- How to infer causality despite confounding variables?

Randomize!

- If you assign individuals to treatment and control at random, then the two groups are likely to be similar apart from the treatment.
- You can account mathematically for variability in the assignment.
- Randomized Controlled Experiment

Careful ...

Regardless of what the dictionary says, in probability theory

Random ≠ Haphazard

Parachute use to prevent death and major trauma related to gravitational challenge: systematic review of randomised controlled trials

Gordon C S Smith, Jill P Pell

Abstract

Objectives To determine whether parachutes are effective in preventing major trauma related to gravitational challenge.

Design Systematic review of randomised controlled trials.

Data sources: Medline, Web of Science, Embase, and the Cochrane Library databases; appropriate internet sites and citation lists.

Study selection: Studies showing the effects of using a parachute during free fall.

Main outcome measure Death or major trauma, defined as an injury severity score > 15.

Results We were unable to identify any randomised controlled trials of parachute intervention.

Conclusions As with many interventions intended to prevent ill health, the effectiveness of parachutes has not been subjected to rigorous evaluation by using randomised controlled trials. Advocates of evidence based medicine have criticised the adoption of interventions evaluated by using only observational data. We think that everyone might benefit if the most radical protagonists of evidence based medicine organised and participated in a double blind, randomised, placebo controlled, crossover trial of the parachute.

accepted intervention was a fabric device, secured by strings to a harness worn by the participant and released (either automatically or manually) during free fall with the purpose of limiting the rate of descent. We excluded studies that had no control group.

Definition of outcomes

The major outcomes studied were death or major trauma, defined as an injury severity score greater than 15.6

Meta-analysis

Our statistical apprach was to assess outcomes in parachute and control groups by odds ratios and quantified the precision of estimates by 95% confidence intervals. We chose the Mantel-Haenszel test to assess heterogeneity, and sensitivity and subgroup analyses and fixed effects weighted regression techniques to explore causes of heterogeneity. We selected a funnel plot to assess publication bias visually and Egger's and Begg's tests to test it quantitatively. Stata software, version 7.0, was the tool for all statistical analyses.

Results

Our search strategy did not find any randomised controlled trials of the parachute.

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Parachutes reduce the risk of injury after gravitational challenge, but their effectiveness has not been proved with randomised controlled trials

Why use observational data?

- Experiment is impractical
 - Does moving to Ithaca cause tooth decay?
- Experiment is unethical
 - Do parachutes prevent trauma?
- Use observational data to guide experiment design
 - Which genes cause cancer?