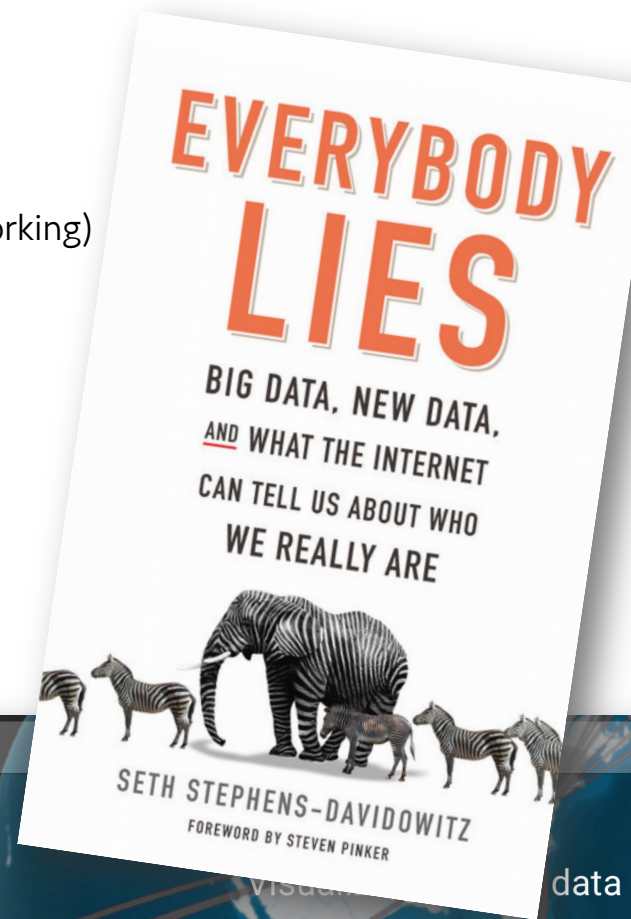
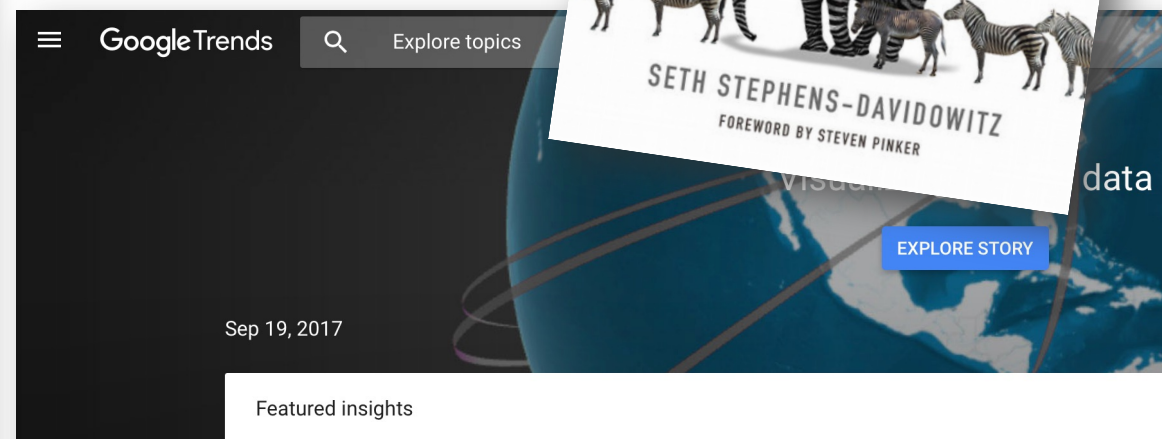
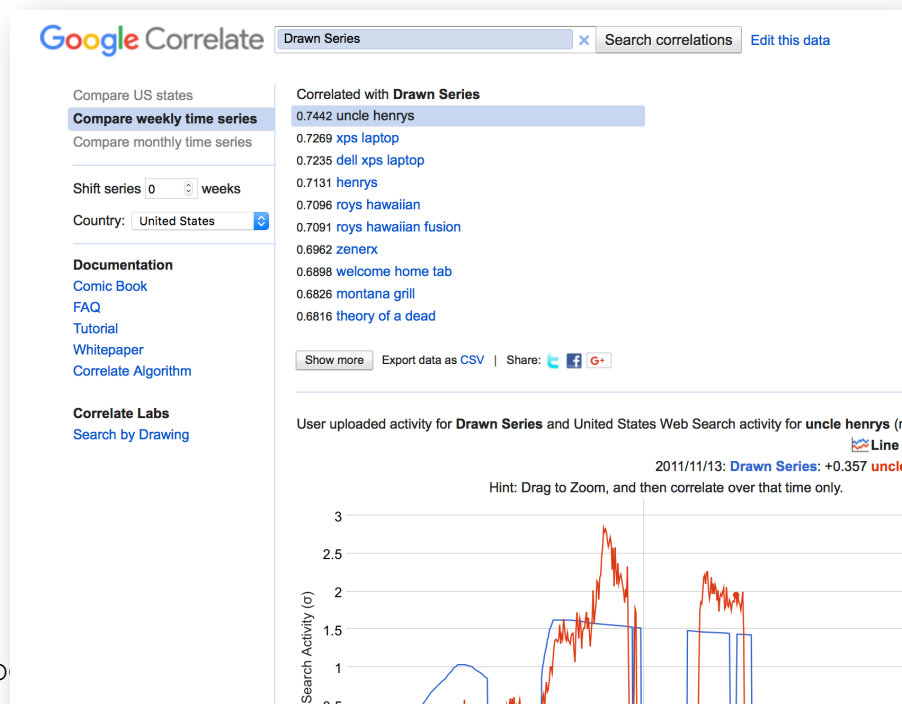


Lecture 09

Designing experiments!

Observational Studies

- Researchers do not assign choices, they simply observe them.
- An extreme case: <https://www.google.com/trends/correlate/draw?p=us> (not working)
- Also Google trends: <https://trends.google.com/trends/>



Observational Studies

- Valuable for discovering trends and possible relationships
- Widely used in public health and marketing
- Often retrospective (retrospective study <-> prospective study)
- Lots of lurking variables
- Noise, errors
- correlation \neq causation



©marketoonist.com

<https://twitter.com/tomfishburne/status/455486271339511808>

Randomized, Comparative Experiments

- Experiments require:
 - Random assignment of subjects to treatments
 - Manipulate **explanatory variables** (or factors)
 - Measure **response variables**
- **Four principles of experimental design**
 - Control
 - Randomize
 - Replicate
 - Block

Experimental design: Control

- Control sources of variation other than the factors we're manipulating
 - Making conditions as similar as possible for all treatment groups
 - To reduce the variability of the responses
- Bad for generalizability?
 - Consideration: generalizability and ecological validity

Experimental design: Randomize

- To equalize the effects of unknown or uncontrollable sources of variation
- **Not eliminating** the effects of these sources, but **distributing** them equally across treatment levels
- Protect against factors we might be missing
- “Control what you can, and randomize the rest”

Experimental design: Replicate

- Subject-level replication
 - Repeat treatments to many subjects
 - The outcome of an experiment on a single subject is an anecdote (not data)
- Study-level replication
 - The entire experiment is repeated on a different population of experimental units.
- Within-subject level replication
 - Repeated measures
 - Can measure the reliability of a measure
 - Increase signal-to-noise ratio

Experimental design: Block

- There are things that we are not studying, but we can't control (e.g., male, female).
- We can group similar individuals **together (block)**, and randomize within each of these blocks.
- This is a compromise between randomization and control, and this is not required, different than other three, Control, Randomize, Replicate.
- This is an idea similar to stratified random sampling.
- This design is called "**Randomized block design**"

Blinding

- Humans are susceptible to errors in judgement (e.g., preference in cola tasting)
- **Blinding** the participants to the treatment could prevent potential biases.
- **Experimenters** can subconsciously provide contextual cues related to treatment.
- **Two classes** of individuals who can affect the outcome of the experiment:
 - Those who could **influence** the results (e.g., subjects, treatment administrators, technicians, etc.)
 - Those who **evaluate** the results (e.g., judges, treating physicians, etc.)
- **Single-blind**: either one of these classes are blinded
- **Double-blind**: both classes are blinded

Placebos

- Simply applying any treatment can cause an improvement.
- **Placebo:** “fake” treatment that looks just like the real treatment
- Placebo effects tells us
 - The importance of effective blinding
 - The importance of comparing treatments with a proper control (e.g., active control)

Research Paper

PAIN

Increasing placebo responses over time in U.S. clinical trials of neuropathic pain

Alexander H. Tuttle^a, Sarasa Tohyama^a, Tim Ramsay^b, Jonathan Kimmelman^c, Petra Schweinhardt^d, Gary J. Bennett^e, Jeffrey S. Mogil^{a,*}

Abstract
Recent failures of clinical trials of novel analgesics designed to treat neuropathic pain have led to much speculation about the underlying reasons. One often discussed possibility is that the placebo response in these trials has increased in recent years, leading to lower separation between the drug and placebo arms. Whether this has indeed occurred has not yet been adequately addressed. Here, we extracted data from published randomized controlled trials (RCTs) of drugs for the treatment of chronic neuropathic pain over the years 1990 to 2013. We find that placebo responses have increased considerably over this period, but drug responses have remained stable, leading to diminished treatment advantage. This trend has been driven by studies conducted in the United States. Consideration of participant and study characteristics revealed that in the United States but not elsewhere, RCTs have increased in

nature International weekly

Home | News & Comment | Research | Careers

News & Comment | News | 2016 | October

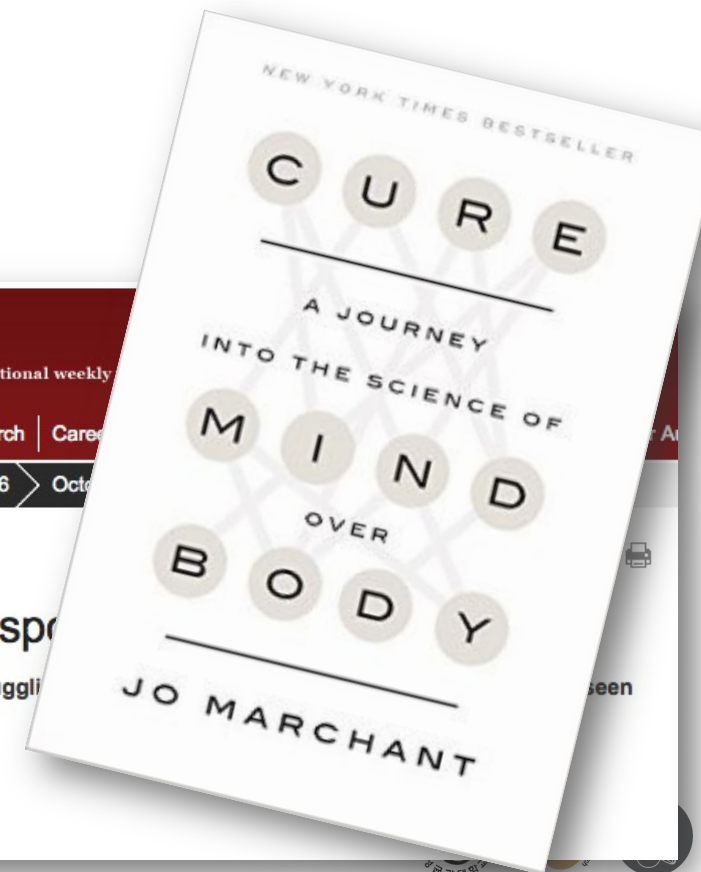
NATURE | NEWS

Strong placebo response

Potential pain treatments are struggling in US trials.

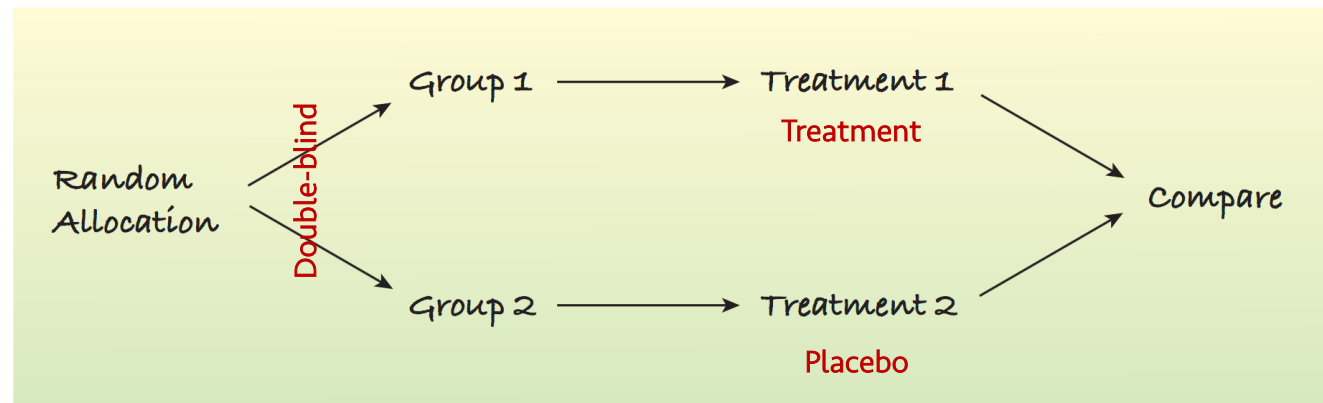
Jo Marchant

06 October 2015



Best experiments:

- Randomized
- Comparative
- Double-blind
- Placebo-controlled



Confounding

- Two factors are **confounded**: when the levels of one factor are associated with the level of another factor.
- No way to tease apart the two effects:
 - E.g., When examining the effects of different teaching styles, one class was during the fall semester, and the other class was spring. In this case, **different teaching style was confounded with the season**.
 - E.g., what if two different professors taught two different classes? **Different teaching styles was confounded with professors and the seasons**.
 - E.g., When examining the differences in brain signal for no pain and pain runs, and if no pain runs were always followed by pain runs, **the pain manipulation was confounded with the order effects**.
- It's super important to use the "control" and "randomize" strategies wisely.

Key Points

Chapter 13: Experiments and Observational Studies

- Observational studies: Valuable for discovering trends and relationships, but correlation \neq causation
- **Four principles of experimental design:** Control, Randomize, Replicate, Block
- Good experiments: Randomized, Comparative (control), Double-blind, Placebo-controlled
- Confounding