Stat 13, Intro. to Statistical Methods for the Life and Health Sciences.

1. Some recommended book problems.
2. Aspirin example.
3. The big idea of chapter 4, experiments and causation.
4. Random sampling, random assignment, and blocking.
5. Blinding.
6. Portacaval shunt example.
7. Coverage, adherer bias and clofibrate example.
8. More about confounding factors.
9. Confounding and lefties example.
10. Comparing two proportions using numerical and visual summaries, good or bad year example.
11. Comparing 2 proportions with CIs + testing using simulation, dolphin example.

Read ch5 and 6. The midterm will be on ch 1-6.
Midterm is Wed Jul16, 11am-12:50pm.
A practice midterm is on the course website,
http://www.stat.ucla.edu/~frederic/13/sum25 .
We will discuss it Monday July 14 and do review as well.
HW2 is due Fri Jul11, 10pm. 2.3.15, 3.3.18, and 4.1.23.
HW3 is due Fri Jul18, 10pm. 4.CE.10, 5.3.28, 6.1.17, and 6.3.14. In 5.3.28d, use the theory-based formula. You do not need to use an applet.

1. Some good hw problems from the book.

1.2.18, 1.2.19, 1.2.20, 1.3.17, 1.5.18, 2.1.38, 2.2.6, 2.2.24, 2.3.3, 2.3.25, 3.2.11, 3.2.12, 3.3.8, 3.3.19, 3.3.22, 3.5.23, 4.1.14, 4.1.18, 5.2.2, 5.2.10, 5.2.24, 5.3.11, 5.3.21, 5.3.24, 6.2.23, 6.3.1, 6.3.12, 6.3.22, 6.3.23.

2. Experiments and aspirin example.

Physicians’ Health Study I (study aspirin’s affect on reducing heart attacks.

- Started in 1982 with 22,071 male physicians.
- The physicians were **randomly assigned** into one of two groups.
  - Half took a 325mg aspirin every other day and half took a placebo.

Results

- Intended to go until 1995, the aspirin study was stopped in 1988 after finding significant results.
- 189 (1.7%) heart attacks occurred in the placebo group and 104 (0.9%) in the aspirin group. This is a 45% reduction in heart attacks for the aspirin group.
- What about confounding variables? Could the aspirin group be different than the placebo group in some other ways?
  - Did they have a better diet?
  - Did they exercise more?
  - Were they genetically less likely to have heart attacks?
  - Were they younger?

3. The Big Idea

- Confounding variables are often circumvented in experiments due to the **random assignment** of subjects to treatment groups.
- Randomly assigning people to groups tends to balance out all other variables between the groups.
- So confounding variables, including ones the researchers didn't anticipate, should be roughly equalized between the two groups and therefore should not be confounding.
- **Thus, cause and effect conclusions are sometimes possible in experiments through random assignment.** It must be a well run experiment though.

4. Random sampling, random assignment, and blocking.

- With observational studies, **random sampling** is often done. This possibly allows us to make inferences from the sample to the population where the sample was drawn.
- With experiments, **random assignment** is done. This might allows us to conclude causation.

- The Physician’s Health Study used random assignment. Did it also use random sampling?
- No, hardly any experiments use random sampling, but get their subjects in other ways.
- The Physician’s Health Study sent out invitation letters and questionnaires to all 261,248 male physicians between 40 and 84 years of age who lived in the United States.
- Of the 59,285 who were willing to participate in the trial, 26,062 were told they could not because of some medical condition or current medical treatment.

- So to what group can we generalize the results that taking aspirin can reduce heart attacks?
  - Just physicians in the study?
  - All male physicians between 40-84 years old?
  - All males physicians?
  - All males between 40-84 years olds?
  - All males?
  - Everyone between 40-84 years old?
  - Everyone?

Article Baseline Demographics After Random Assignment

Parameter	Placebo (n=129)	Uceris (n=128)
Mean age, years (range)	39.9 (12–68)	37.6 (13–66)
Men	77 (59.7)	70 (54.7)
Women	52 (40.3)	58 (45.3)
Mean disease duration (yrs)	6.3	5.5
Duration ≤1 year, n (%)	23 (17.8)	28 (21.9)
Duration >5 years, n (%)	51 (39.5)	44 (34.4)
Proctosigmoiditis	64 (49.6)	58 (45.3)
Left-sided colitis	44 (34.1)	37 (28.9)
Mean baseline UCDAI score	6.2	6.5
Mean baseline EI score	6.6	6.5
Prior mesalazine use	75 (58.1)	66 (51.6)
Prior sulfasalazine use	28 (21.7)	33 (25.8)

Sandborn WJ, Travis S, Moro L, Jones R, Gautille T, Bagin R, Huang M, Yeung P, Ballard ED 2nd Once-daily budesonide MMX® extended-release tablets induce remission in patients with mild to moderate ulcerative colitis: results from the CORE I study. *Gastroenterology* 2012 Nov;143(5):1218-26

Blocking and Random Assignment

- The goal in random assignment is to make the two groups as similar as possible in all ways other than the treatment.
- Sometime there are known confounders and you can block on (control for) these variables.
- For example, if our subjects consist of 60% females and 40% males, we can force each group to be 60% female and 40% male, using a matched pair design.
- Blocking makes sense when there are known confounders you want to control for. But randomly assigning subjects to groups makes them as similar as possible in terms of unknown confounders.

5. Blinding.

Even in experiments, the treatment and control groups can be different in ways other than the explanatory variable. This is especially true when the response variable is somewhat subjective.

Pain is an example. One study found that 1/4 of patients suffering from post-operative pain, when given a placebo (just a pill of sugar and water) claimed they experienced "significant prompt pain relief".

Blinding.

People might not be able to judge their own levels of pain very well, and may be influenced by the belief that they have taken an effective treatment.

Thus in an experiment with such a response variable, researchers should ensure the subject does not know whether he or she received the treatment or the control. This is called blinding.

In a *double-blind* experiment, neither the subject nor the researcher recording the response variable knows the level of the explanatory variable for each subject, i.e. treatment or control.

6. Portacaval shunt example.

The following example shows the importance of doing a randomized controlled experiment.

The portacaval shunt is a medical procedure aimed at curbing bleeding to death in patients with cirrhosis of the liver.

The following table summarizes 51 studies on the portacaval shunt. The poorly designed studies were very enthusiastic about the surgery, while the carefully designed studies prove that the surgery is largely ineffective.

	Degree of enthusiasm		
Design	High	Moderate	None
No controls	24	7	1
Controls, but not randomized	10	3	2
Randomized controlled	0	1	3

Portacaval shunt example.

Why did the poorly designed studies come to the wrong conclusion?

A likely explanation is that in the studies where patients were not randomly assigned to the treatment or control group, by and large the healthier patients were given the surgery.

This alone could explain why the treatment group outlived the control group in these studies.

	Degree of enthusiasm		
Design	High	Moderate	None
No controls	24	7	1
Controls, but not randomized	10	3	2
Randomized controlled	0	1	3

7. Coverage, adherer bias and Clofibrate example.

Surveys are observational.

- Coverage is a common issue. Coverage is the extent to which the people you sampled from represent the overall population. A survey at a fancy research hospital in a wealthy neighborhood may yield patients with higher incomes, higher education, etc.
- Non-response bias is another common problem. Poor coverage means the people getting the survey do not represent the general population. Non-response bias means that out of the people you gave the survey to, the people actually filling it out and submitting it are different from the people who did not.
- Same exact issues in web surveys.

Coverage, adherer bias, and Clofibrate example.

Non-response bias is similar to adherer bias, in experiments.
A drug called clofibrate was tested on 3,892 middle-aged men with heart trouble. It was supposed to prevent heart attacks.

1,103 assigned at random to take clofibrate,

2,789 to placebo (lactose) group.

Subjects were followed for 5 years.

Is this an experiment or an observational study?

Clofibrate	patients who died during followup
adherers	15%
non-adherers	25%
total	20%

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Is this an experiment or an observational study?

It is an experiment. Does Clofibrate work?

Clofibrate	patients who died during followup
adherers	**15%**
non-adherers	**25%**
total	20%

Clofibrate	patients who died during followup
adherers	**15%**
non-adherers	**25%**
total	20%

Placebo	
adherers	15%
nonadherers	28%
total	21%

Those who took clofibrate did much better than those who didn't keep taking clofibrate. Does this mean clofibrate works?

Clofibrate	patients who died during followup
adherers	15%
non-adherers	25%
total	20%

Placebo	
adherers	**15%**
nonadherers	**28%**
total	21%

Those who adhered to placebo also did much better than those who stopped adhering.

Clofibrate	patients who died during followup
adherers	15%
non-adherers	25%
total	**20%**

Placebo	
adherers	15%
nonadherers	28%
total	**21%**

All in all there was little difference between the two groups.

Clofibrate	patients who died during followup
adherers	15%
non-adherers	25%
total	**20%**

Placebo	
adherers	15%
nonadherers	28%
total	**21%**

Adherers did better than non-adherers, not because of clofibrate, but because they were healthier in general. Why?

Clofibrate	patients who died during followup
adherers	15%
non-adherers	25%
total	**20%**

Placebo	
adherers	15%
nonadherers	28%
total	**21%**

Adherers did better than non-adherers, not because of clofibrate, but because they were healthier in general. Why?

- adherers are the type to engage in healthier behavior.
- sick patients are less likely to adhere.

8. More about confounding factors.

- By a confounding factor, we mean an alternative explanation that could explain the apparent relationship between the two variables, even if they are not causally related. Typically this is done by finding another difference between the treatment and control group. For instance, different studies have examined smokers and non-smokers and have found that smokers have higher rates of liver cancer. One explanation would be that smoking causes liver cancer. But is there any other, alternative explanation?
- One alternative would be that the smokers tend to drink more alcohol, and it is the alcohol, not the smoking, that causes liver cancer.

More about confounding factors.

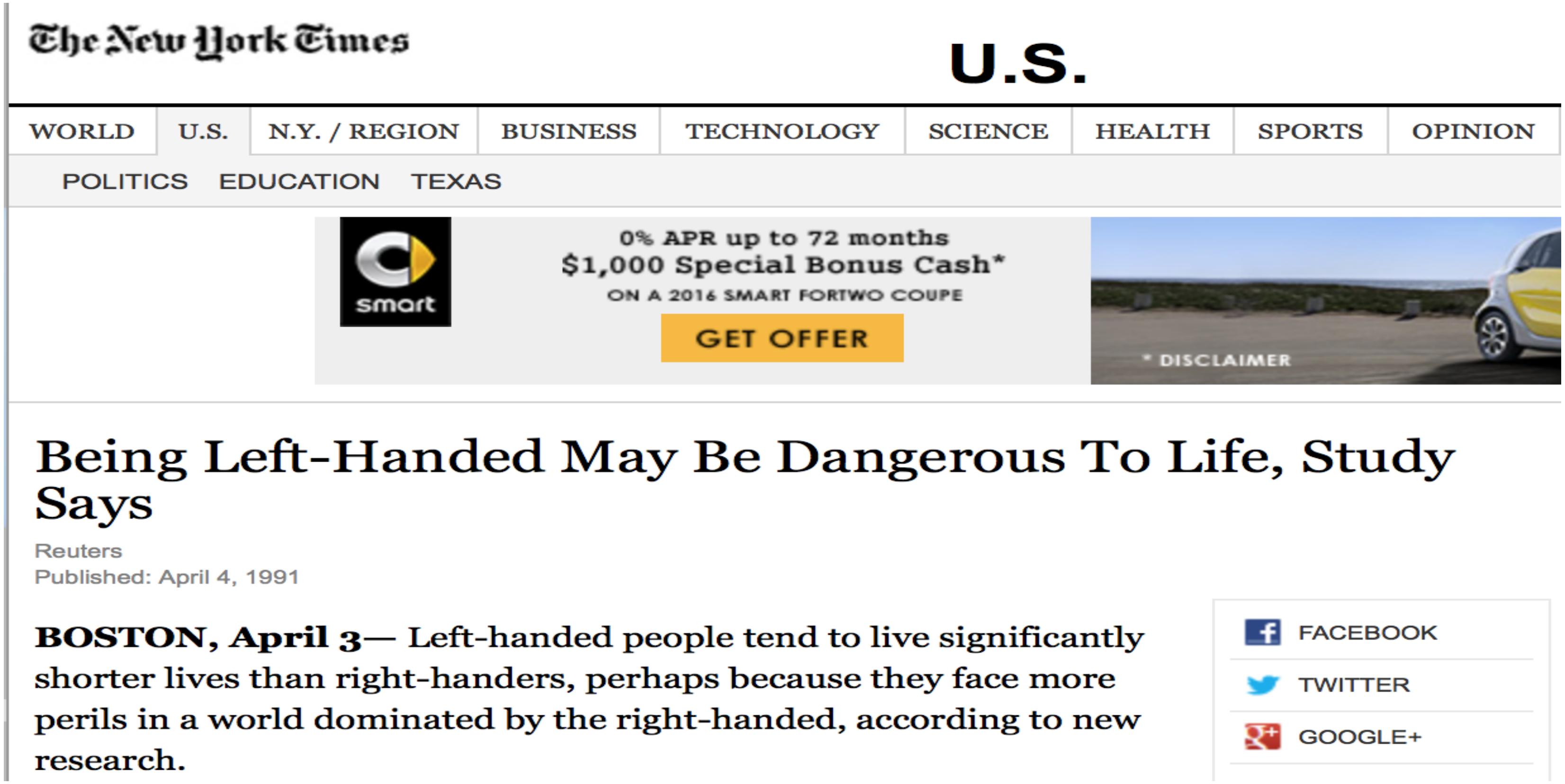
- Another plausible explanation is that the smokers are probably older on average than the non-smokers, and older people are more at risk for all sorts of cancer than younger people.
- Another might be that smokers engage in other unhealthy activities more than non-smokers.
- Note that if one said that “smoking makes you want to drink alcohol which causes liver cancer,” that would not be a valid confounding factor, since in that explanation, smoking effective is causally related to liver cancer risk.

9. Lefties example.

- A confounding factor must be plausibly linked to both the explanatory and response variables. So for instance saying “perhaps a higher proportion of the smokers are men” would not be a very convincing confounding factor, unless you have some reason to think gender is strongly linked to liver cancer.
- Another example: left-handedness and age at death. Psychologists Diane Halpern and Stanley Coren looked at 1,000 death records of those who died in Southern California in the late 1980s and early 1990s and contacted relatives to see if the deceased were righthanded or lefthanded. They found that the average ages at death of the lefthanded was 66, and for the righthanded it was 75. Their results were published in prestigious scientific journals, Nature and the New England Journal of Medicine.

Lefties example.

All sorts of causal conclusions were made about how this shows that the stress of being lefthanded in our righthanded world leads to premature death.



The New York Times

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POLITICS EDUCATION TEXAS

Being Left-Handed May Be Dangerous To Life, Study Says

Reuters
Published: April 4, 1991

BOSTON, April 3— Left-handed people tend to live significantly shorter lives than right-handers, perhaps because they face more perils in a world dominated by the right-handed, according to new research.

FACEBOOK
TWITTER
GOOGLE+

Lefties example.

- Is this an observational study or an experiment?

Lefties example.

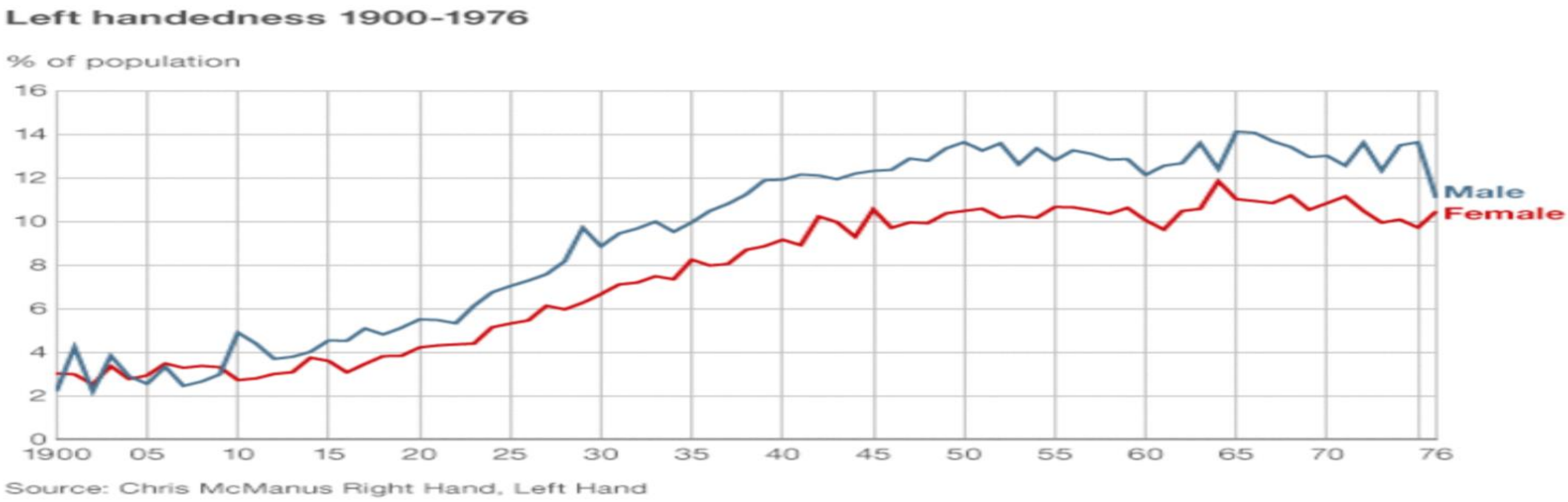
- Is this an observational study or an experiment?

It is an observational study.

- Are there plausible confounding factors you can think of?

Lefties example.

- A confounding factor is the age of the two populations in general. Lefties in the 1980s were on average younger than righties. Many old lefties were converted to righties at infancy, in the early 20th century, but this practice has subsided. Thus in the 1980s and 1990s, there were relatively few old lefties but many young lefties in the overall population. This alone explains the discrepancy.



Unit 2. Comparing Two Groups

- In Unit 1, we learned the basic process of statistical inference using tests and confidence intervals. We did all this by focusing on a single proportion.
- In Unit 2, we will take these ideas and extend them to comparing two groups. We will compare two proportions, two independent means, and paired data.

10. Comparing two proportions using numerical and visual summaries, and the good or bad year example.

Section 5.1

Example 5.1: Positive and Negative Perceptions

- Consider these two questions:
  - Are you having a good year?
  - Are you having a bad year?

- Do people answer each question in such a way that would indicate the same answer? (e.g. Yes for the first one and No for the second.)

Positive and Negative Perceptions

- Researchers questioned 30 students (randomly giving them one of the two questions).
- They then recorded if a positive or negative response was given.
- They wanted to see if the wording of the question influenced the answers.

Positive and negative perceptions

- Observational units
  - The 30 students
- Variables
  - Question wording (good year or bad year)
  - Perception of their year (positive or negative)
- Which is the explanatory variable and which is the response variable?
- Is this an observational study or experiment?

Raw Data in a Spreadsheet

Individual	Type of Question	Response
1	Good Year	Positive
2	Good Year	Negative
3	Bad Year	Positive
4	Good Year	Positive
5	Good Year	Negative
6	Bad Year	Positive
7	Good Year	Positive
8	Good Year	Positive
9	Good Year	Positive
10	Bad Year	Negative
11	Good Year	Negative
12	Bad Year	Negative
13	Good Year	Positive
14	Bad Year	Negative
15	Good Year	Positive

Individual	Type of Question	Response
16	Good Year	Positive
17	Bad Year	Positive
18	Good Year	Positive
19	Good Year	Positive
20	Good Year	Positive
21	Bad Year	Negative
22	Good Year	Positive
23	Bad Year	Negative
24	Good Year	Positive
25	Bad Year	Negative
26	Good Year	Positive
27	Bad Year	Negative
28	Good Year	Positive
29	Bad Year	Positive
30	Bad Year	Negative

Two-Way Tables

- A **two-way table** organizes data
  - Summarizes *two* categorical variables
  - Also called contingency table
- Are students more likely to give a positive response if they were given the good year question?

	Good Year	Bad Year	Total
Positive response	15	4	19
Negative response	3	8	11
Total	18	12	30

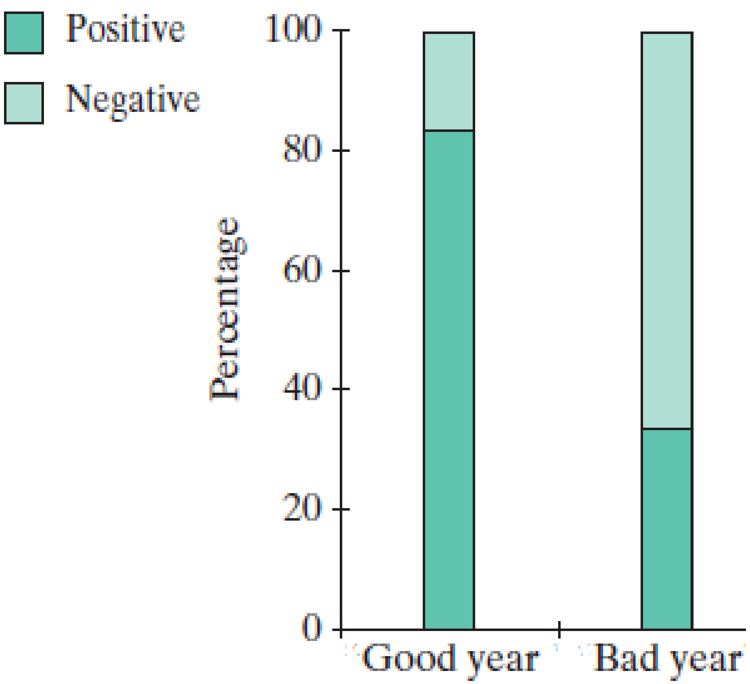
Two-Way Tables

- Conditional proportions will help us better determine if there is an association between the question asked and the type of response.
- We can see that the subjects with the positive question were ***more likely*** to respond positively.

	Good Year	Bad Year	Total
Positive response	$15/18 \approx 0.83$	$4/12 \approx 0.33$	19
Negative response	3	8	11
Total	18	12	30

Segmented Bar Graphs

- We can also use segmented bar graphs to see this association between the "good year" question and a positive response.



Statistic

- The statistic we will mainly use to summarize this table is the difference in proportions of positive responses is 0.83 – 0.33 = 0.50.

	Good Year	Bad Year	Total
Positive response	15 (83%)	4 (33%)	19
Negative response	3	8	11
Total	18	12	30

Another Statistic

- Another statistic that is often used, called **relative risk**, is the ratio of the proportions: 0.83/ 0.33 = 2.5.
- We can say that those who were given the good year question were 2.5 times as likely to give a positive response.

	Good Year	Bad Year	Total
Positive response	15 (83%)	4 (33%)	19
Negative response	3	8	11
Total	18	12	30

11. Comparing two proportions with CIs and testing using simulation, dolphin example.

Section 5.2

Swimming with Dolphins

Example 5.2

Swimming with Dolphins

Is swimming with dolphins therapeutic for patients suffering from clinical depression?

- Researchers Antonioli and Reveley (2005), in British Medical Journal, recruited 30 subjects aged 18-65 with a clinical diagnosis of mild to moderate depression
- Discontinued antidepressants and psychotherapy 4 weeks prior to and throughout the experiment
- 30 subjects went to an island near Honduras where they were randomly assigned to two treatment groups

Swimming with Dolphins

- Both groups engaged in one hour of swimming and snorkeling each day
- One group swam in the presence of dolphins and the other group did not
- Participants in both groups had identical conditions except for the dolphins
- After two weeks, each subjects' level of depression was evaluated, as it had been at the beginning of the study
- The response variable is whether or not the subject achieved substantial reduction in depression

Swimming with Dolphins

Null hypothesis: Dolphins do not help.

– Swimming with dolphins is not associated with substantial improvement in depression

Alternative hypothesis: Dolphins help.

– Swimming with dolphins **increases** the probability of substantial improvement in depression symptoms

Swimming with Dolphins

- The parameter is the (long-run) difference between the probability of improving when receiving dolphin therapy and the prob. of improving with the control ($\pi_{\text{dolphins}} - \pi_{\text{control}}$)
- So we can write our hypotheses as:

H_0: $\pi_{\text{dolphins}} - \pi_{\text{control}} = 0.$

H_a: $\pi_{\text{dolphins}} - \pi_{\text{control}} > 0.$

or

H_0: $\pi_{\text{dolphins}} = \pi_{\text{control}}$

H_a: $\pi_{\text{dolphins}} > \pi_{\text{control}}$

(Note: we are not saying our parameters equal any certain number.)

Swimming with Dolphins

Results:

	Dolphin group	Control group	Total
Improved	10 (66.7%)	3 (20%)	13
Did Not Improve	5	12	17
Total	15	15	30

The difference in proportions of improvers is:

$\hat{p}_d - \hat{p}_c$ **= 0.667 – 0.20 = 0.467.**

Swimming with Dolphins

- There are two possible explanations for an observed difference of 0.467.
  - A tendency to be more likely to improve with dolphins (alternative hypothesis)
  - The 13 subjects were going to show improvement with or without dolphins and random chance assigned more improvers to the dolphins (null hypothesis)

Swimming with Dolphins

- If the null hypothesis is true (no association between dolphin therapy and improvement) we would have 13 improvers and 17 non-improvers regardless of the group to which they were assigned.
- Hence the assignment doesn't matter and we can just randomly assign the subjects' results to the two groups to see what would happen under a true null hypothesis.

Swimming with Dolphins

- We can simulate this with cards
  - 13 cards to represent the improvers
  - 17 cards represent the non-improvers
- Shuffle the cards
  - put 15 in one pile (dolphin therapy)
  - put 15 in another (control group)

Swimming with Dolphins

- Compute the proportion of improvers in the Dolphin Therapy group
- Compute the proportion of improvers in the Control group
- The difference in these two proportions is what could just as well have happened under the assumption there is no association between swimming with dolphins and substantial improvement in depression.

Dolphin Therapy

Non-improver	Improver	Improver
Non-improver	Improver	Improver
Non-improver	Improver	Improver
Non-improver	Improver	Improver
Non-improver	Improver	Improver

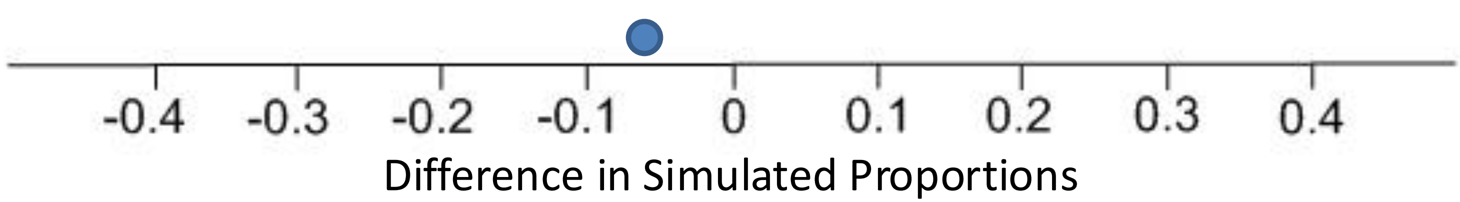
40.0% Improvers

Control

Non-improver	Non-improver	Non-improver
Non-improver	Non-improver	Non-improver
Non-improver	Non-improver	Improver
Non-improver	Non-improver	Improver
Non-improver	Non-improver	Improver

46.7% Improvers

0.400 – 0.467 = -0.067



Dolphin Therapy

Non-improver	Non-improver	Non-improver
Non-improver	Improver	Improver
Improver	Non-improver	Improver
Non-improver	Non-improver	Improver
Non-improver	Non-improver	Improver

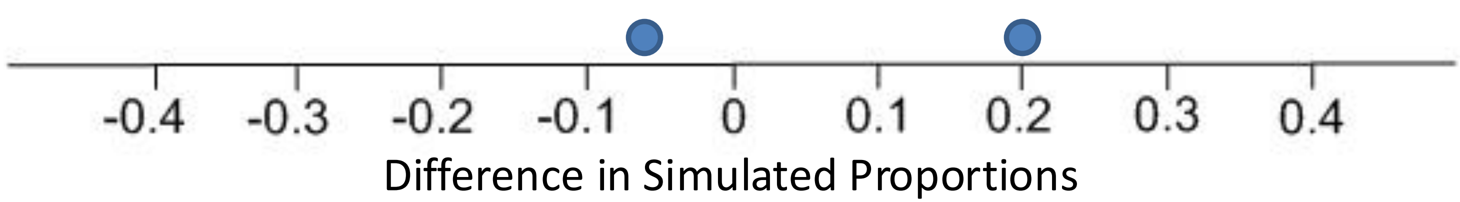
40.0% Improvers

Control

Non-improver	Improver	Non-improver
Non-improver	Non-improver	Improver
Non-improver	Non-improver	Improver
Improver	Non-improver	Improver
Improver	Improver	Non-improver

46.7% Improvers

0.533 – 0.333 = 0.200



Dolphin Therapy

Non-improver	Non-improver	Non-improver
Non-improver	Improver	Improver
Improver	Non-improver	Improver
Non-improver	Non-improver	Improver
Non-improver	Non-improver	Improver

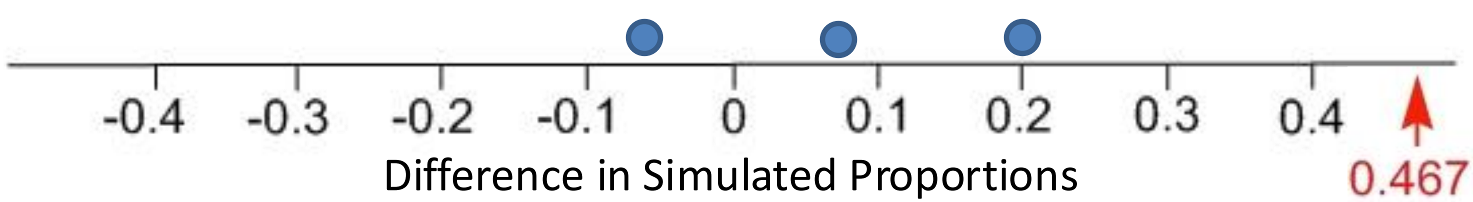
46.7% Improvers

Control

Non-improver	Improver	Non-improver
Non-improver	Non-improver	Improver
Non-improver	Non-improver	Improver
Improver	Non-improver	Improver
Improver	Improver	Non-improver

40.0% Improvers

0.467 – 0.400 = 0.067



More Simulations

0.067 -0.067 0.067 0.200 0.067

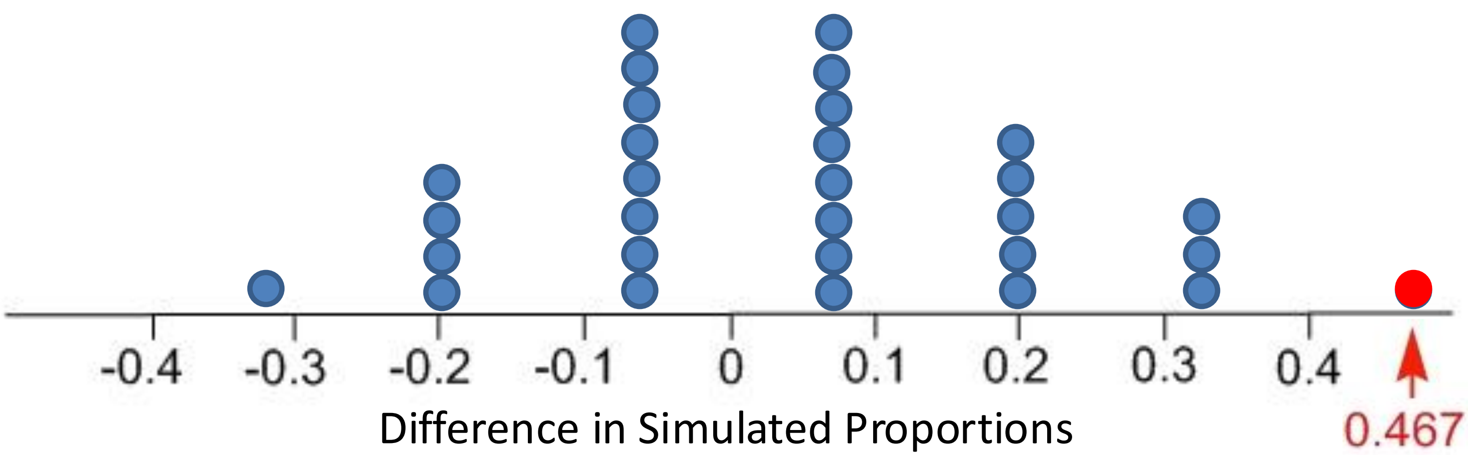
-0.067 0.067 -0.200 -0.200

-0.067 0.067 0.200

0.200

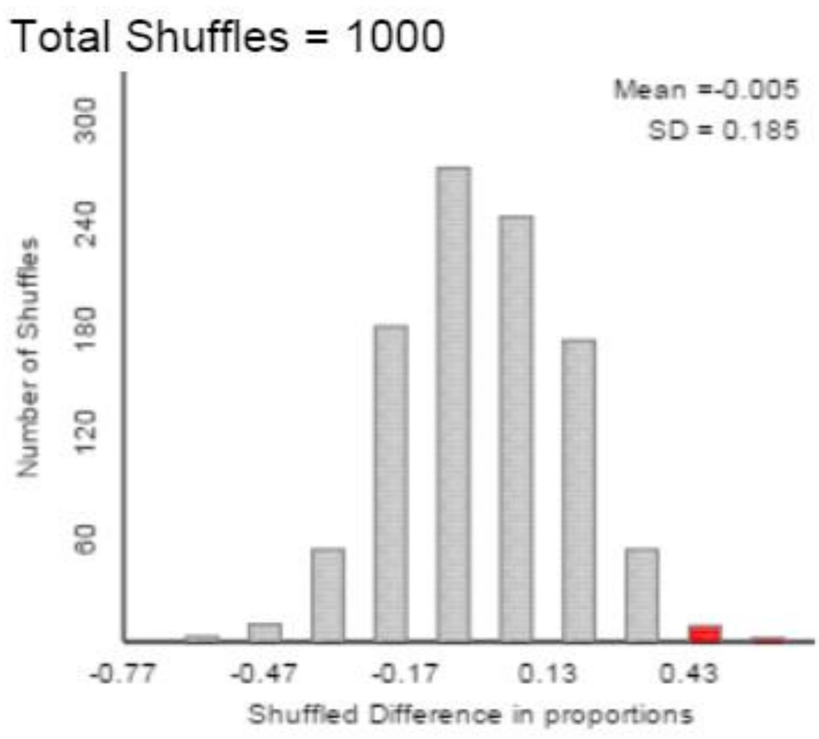
-0.200

Only one simulated statistics out of 30 was as large or larger than our observed difference in proportions of 0.467, hence our p-value for this null distribution is 1/30 ≈ 0.03.



Swimming with Dolphins

- We did 1000 repetitions to develop a null distribution.



Swimming with Dolphins

- 13 out of 1000 results had a difference of 0.467 or higher (p-value = 0.013).
- 0.467 is $\frac{0.467-0}{0.185} \approx 2.52$ SE above zero.
- Using either the p-value or standardized statistic, we have strong evidence against the null and can conclude that the improvement due to swimming with dolphins was statistically significant.

Swimming with Dolphins

- A 95% confidence interval for the difference in the probability using the standard error from the simulations is $0.467 \pm 1.96(0.185) = 0.467 \pm 0.363$, or (.104, .830).
- We are 95% confident that when allowed to swim with dolphins, the probability of improving is between 0.104 and 0.830 higher than when no dolphins are present.
- How does this interval back up our conclusion from the test of significance?

Swimming with Dolphins

- Can we say that the presence of dolphins *caused* this improvement?
  - Since this was a randomized experiment, and assuming everything was identical between the groups, we have strong evidence that dolphins were the cause
- Can we generalize to a larger population?
  - Maybe mild to moderately depressed 18-65 year old patients willing to volunteer for this study
  - We have no evidence that random selection was used to find the 30 subjects. "Outpatients, recruited through announcements on the internet, radio, newspapers, and hospitals."