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

1. Some good hw problems from the book.
2. Observational studies and experiments. Nightlights example.
3. Experiments and aspirin example.
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. Lefties example.
10. Formula for CIs for one variable.
11. Comparing two proportions, and good year example.

Read chapter 4.
Midterm is Tue May5 in class.
HW2, due Fri, May8, 1159pm. 2.3.15, 3.3.18, and 4.1.23.
The course website is http://www.stat.ucla.edu/~frederic/13/S26 .

1. Some good optional hw problems from the book, that you might want to look at on your own.

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. Nightlights and Nearsightedness

Example 4.1

Nightlights and nearsightedness

- Near-sightedness often develops in childhood
- Recent studies looked to see if there is an association between near-sightedness and night light use with infants
- Researchers interviewed parents of 479 children who were outpatients in a pediatric ophthalmology clinic
- Asked whether the child slept with the room light on, with a night light on, or in darkness before age 2
- Children were also separated into two groups: near-sighted or not near-sighted based on the child's recent eye examination

Night-lights and near-sightedness

	Darkness	Night Light	Room Light	Total
Near-sighted	18	78	41	137
Not near-sighted	154	154	34	342
Total	172	232	75	479

The largest group of near-sighted kids slept in rooms with night lights. It might be better to look at the data in terms of proportions.

Conditional proportions

18/172 ≈ 0.105   78/232 ≈ 0.336   41/75 ≈ 0.547

Night lights and near-sightedness

	Darkness	Night Light	Room Light	Total
Near-sighted	**10.5%** 18/172	**33.6%** 78/232	**54.7%** 41/75	137
Not near-sighted	154	154	34	342
Total	172	232	75	479

- Notice that as the light level increases, the percentage of near-sighted children also increases.
- We say there is an **association** between near-sightedness and night lights.
- Two variables are **associated** if the values of one variable provide information (help you predict) the values of the other variable.

Night lights and near-sightedness

- While there is an association between the lighting condition and nearsightedness, can we claim that night lights and room lights *caused* the increase in near-sightedness?
- Might there be other reasons for this association?

Night lights and near-sightedness

- Could parents' eyesight be another explanation?
  - Maybe parents with poor eyesight tend to use more light to make it easier to navigate the room at night and parents with poor eyesight also tend to have children with poor eyesight.
  - Now we have a third variable of *parents' eyesight*
  - *Parents' eyesight* is considered a ***confounding variable.***
  - Other possible confounders? Wealth? Books? Computers?

Confounding Variables

- A **confounding variable** is associated with both the explanatory variable and the response variable.
- We say it is confounding because its effects on the response cannot be separated from those of the explanatory variable.
- Because of this, we can't draw cause and effect conclusions when confounding variables are present.

Confounding Variables

- Since confounding variables can be present in observational studies, we can’t conclude causation from these kinds of studies.
- This doesn’t mean the explanatory variable isn’t influencing the response variable. **Association may not imply causation, but can be a pretty big hint.**

Observational studies versus Experiments

Section 4.2

Observational Studies vs. Experiments

- In an **observational study**, the researchers do not set the level of the explanatory variable for each subject. Typically each subject herself decides her level of the explanatory variable. Sometimes nature decides.
- For example, the researchers didn't control which children slept with a night light on or not.
- Observational studies always have potential confounding variables present and these may prevent us from determining cause and effect.

Observational Studies vs. Experiments

- In an **experiment**, the researchers set the level of the explanatory variable for each subject.
- These levels may correspond to a treatment and control.
- Well designed experiments can control for confounding variables by making the treatment and control groups very similar except for what the experimenter manipulates.

3. 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?

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 and random assignment.

- 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. Most 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%

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?

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

U.S.

WORLD | U.S. | N.Y. / REGION | BUSINESS | TECHNOLOGY | SCIENCE | HEALTH | SPORTS | OPINION

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?

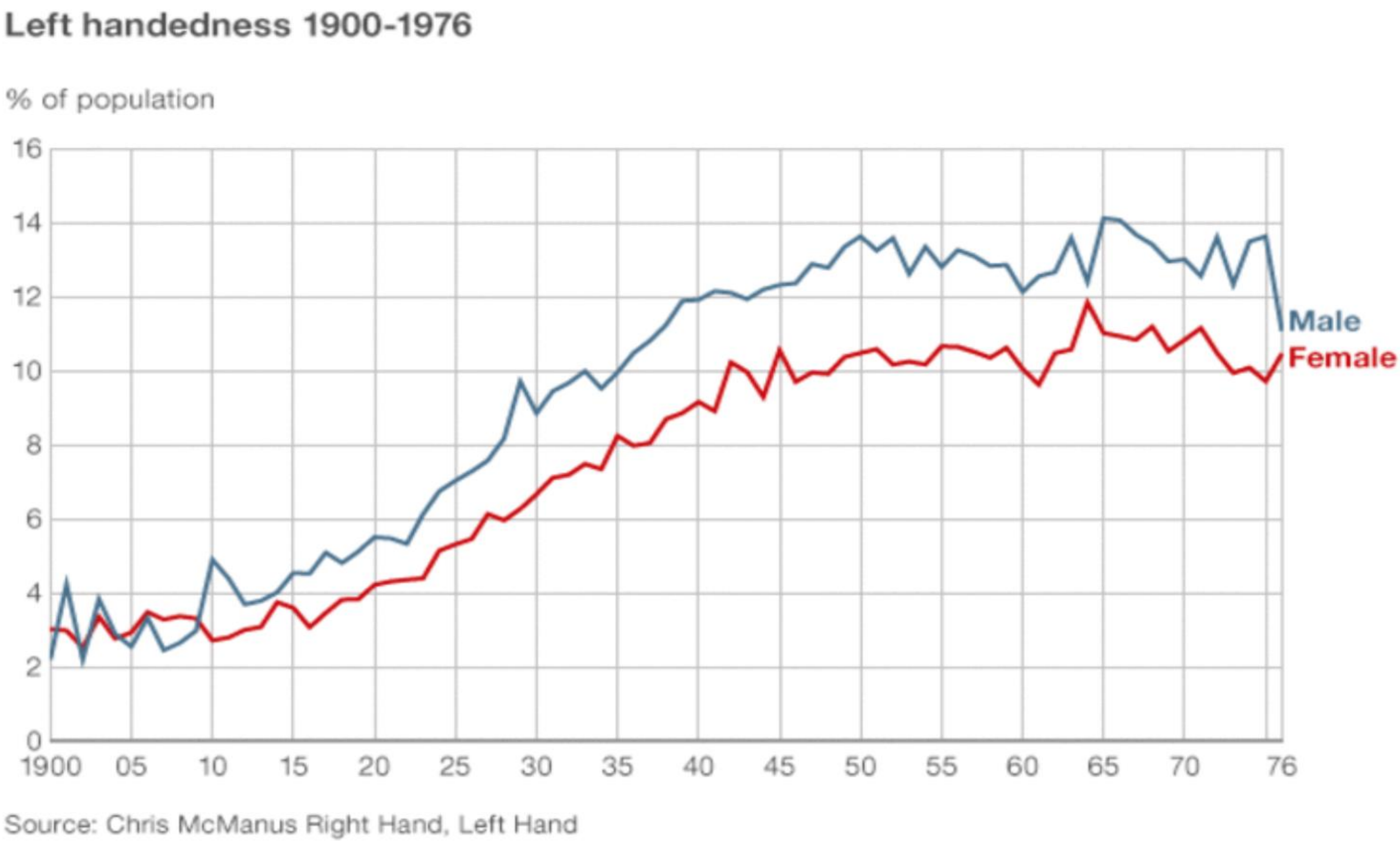
Lefties example.

- Is this an observational study or an experiment?

It is an observational study.

- Are there plausible confounding factors you can think of?

Lefties example.



10. Formulas for CIs for one variable, quantitative or categorical.

if the observations are iid and n is large, then

P(μ is in the range $\bar{x}$ +/- 1.96 $\sigma/\sqrt{n}$) ~ 95%.

and since s ~ σ when n is large, 95% CI is

$\bar{x}$ +/- 1.96 s/√n .

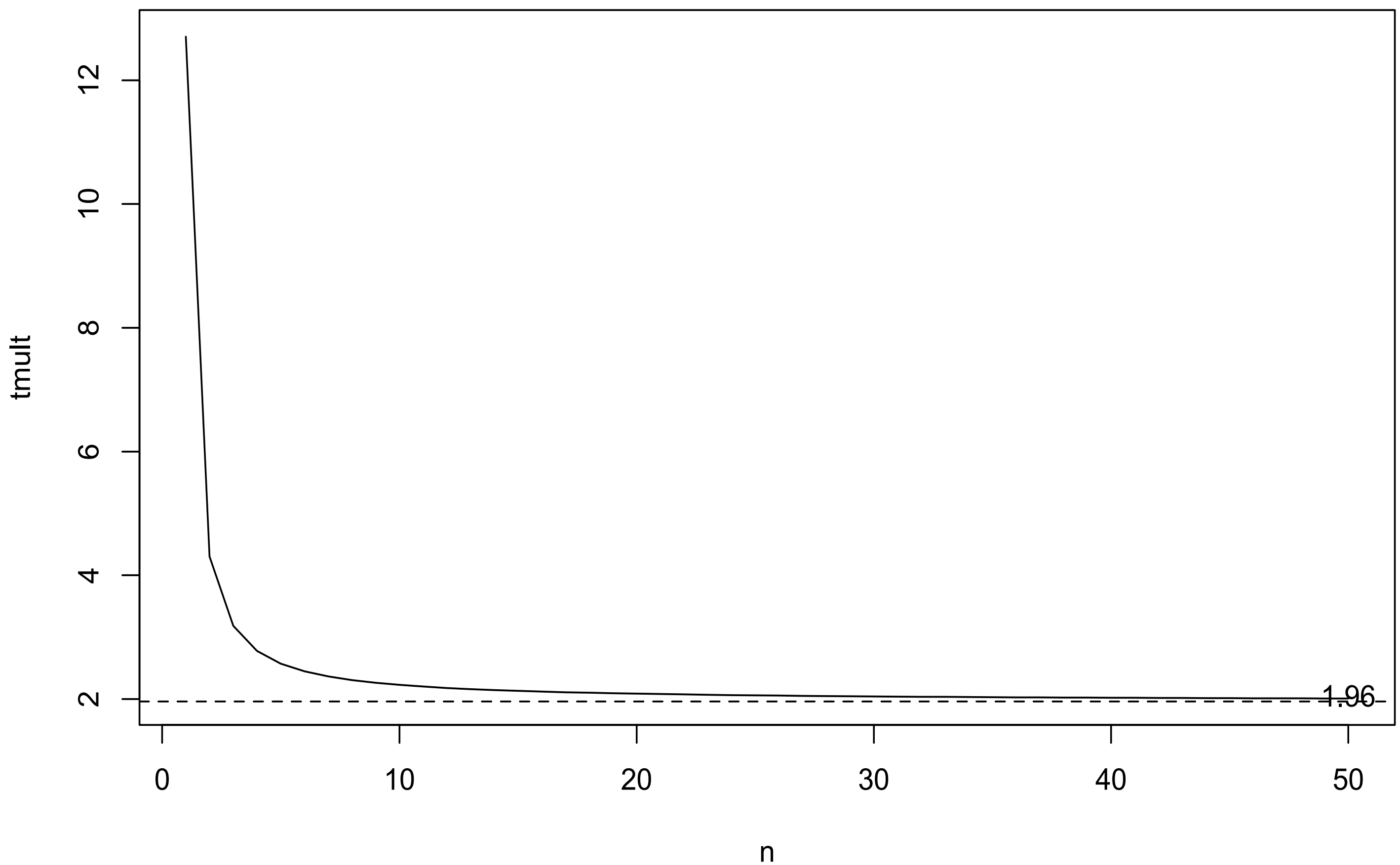
If the obs. are iid and normal and σ is unknown, then

even if n is small,

P(μ is in the range $\bar{x}$ +/- t_{mult} s/√n) ~ 95%.

where t_{mult} depends on n.

$\bar{x}$ +/- t_{mult} s/√n .



t_{mult} gets really close to 1.96 when n gets larger than about 30, so for this class we will use the rule of thumb

n ≥ 30 is large, for quantitative data. For categorical, at least 10 of each type in your sample will be the rule of thumb.

10. Formulas for CIs for one variable, quantitative or categorical.

Note that for quantitative variables, in the 95% CI formula

$\bar{x}$ **+/- 1.96 s/√n ,**

The quantity s / √n is called the SE for the mean.

For categorical data, the population is never normal!
View the values as 0 or 1. Then

$\hat{p} = \bar{x}$, and $s = \sqrt{\hat{p}(1-\hat{p})}$. So the formula for a 95% CI is

$$\hat{p} \pm 1.96 \sqrt{\hat{p}(1-\hat{p})/n}.$$

Here large n means ≥ 10 of each type in the sample.

11. 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
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

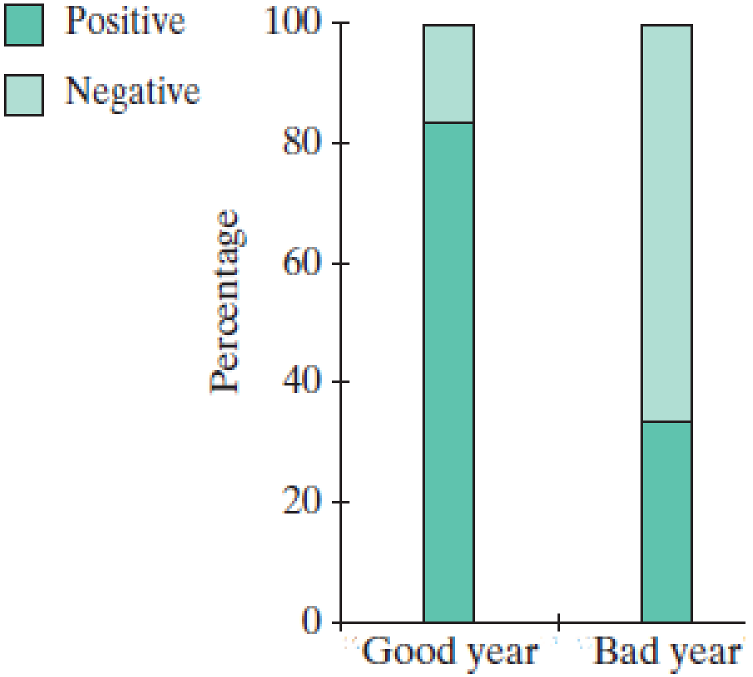
Two-Way Tables

- 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.



Difference in proportions

- 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

Relative risk

- 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