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Comparing Proportions Between Two Independent Populations

John McGready

Johns Hopkins University

Lecture Topics

- CI's for difference in proportions between two independent populations
- Large sample methods for comparing proportions between two populations
  - Normal method
  - Chi-squared test
- Fisher's exact test
- Relative risk

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Section A

The Two Sample Z-Test for Comparing Proportions Between Two Independent Populations

Comparing Two Proportions

- We will motivate by using data from the Pediatric AIDS Clinical Trial Group (ACTG) Protocol 076 Study Group[1]

[1] *Conner, E., et al. Reduction of Maternal-Infant Transmission of Human Immunodeficiency Virus Type 1 with Zidovudine Treatment,* New England Journal of Medicine *331: 18*

Continued

Comparing Two Proportions

- Study Design
  - "We conducted a randomized, double-blinded, placebo-controlled trial of the efficacy and safety of zidovudine (AZT) in reducing the risk of maternal-infant HIV transmission"
  - 363 HIV infected pregnant women were randomized to AZT or placebo

Continued

Comparing Two Proportions

- Results
  - Of the 180 women randomized to AZT group, 13 gave birth to children who tested positive for HIV within 18 months of birth

Continued

Comparing Two Proportions

- Result
  - Of the 183 women randomized to the placebo group, 40 gave birth to children who tested positive for HIV within 18 months of birth

Notes on Design

- Random assignment of Tx
  - Helps insure two groups are comparable
  - Patient and physician could not request particular Tx

Continued

Notes on Design

- Double blind
  - Patient and physician did not know Tx assignment

HIV Transmission Rates

- AZT $\hat{p}_{AZT} = \frac{13}{180} = 0.072$

- Placebo $\hat{p}_{PLAC} = \frac{40}{183} = 0.219$

Continued

HIV Transmission Rates

- Note—these are NOT the true population parameters for the transmission rates, they are estimates based on our two samples

Continued

HIV Transmission Rates

- There is sampling variability
- 95% confidence intervals
  - AZT 95% CI .04 - .12
  - Placebo 95% CI .16 - .28

95% CIs for HIV Transmission Rates

- AZT $n_{AZT} \times \hat{p}_{AZT} \times (1 - \hat{p}_{AZT}) = 180 \times 0.072 \times .928 = 12$

- Placebo $n_{PLAC} \times \hat{p}_{PLAC} \times (1 - \hat{p}_{PLAC}) = 183 \times 0.22 \times .78 = 31$

HIV Transmission Rates

```
. cii 180 13

                                                    -- Binomial Exact --
    Variable |        Obs        Mean    Std. Err.       [95% Conf. Interval]
-------------+---------------------------------------------------------------
             |        180    .0722222     .019294        .0390137    .1203358

. cii 183 40

                                                    -- Binomial Exact --
    Variable |        Obs        Mean    Std. Err.       [95% Conf. Interval]
-------------+---------------------------------------------------------------
             |        183    .2185792    .0305507         .160984    .2855248
```

Notes on HIV Transmission Rates

- Is the difference significant, or can it be explained by chance?
- Since CI's do not overlap suggests significant difference
  - Can we compute a confidence interval on the difference in proportions?
  - Can we compute a p-value?

Sampling Distribution of the Difference in Sample Means

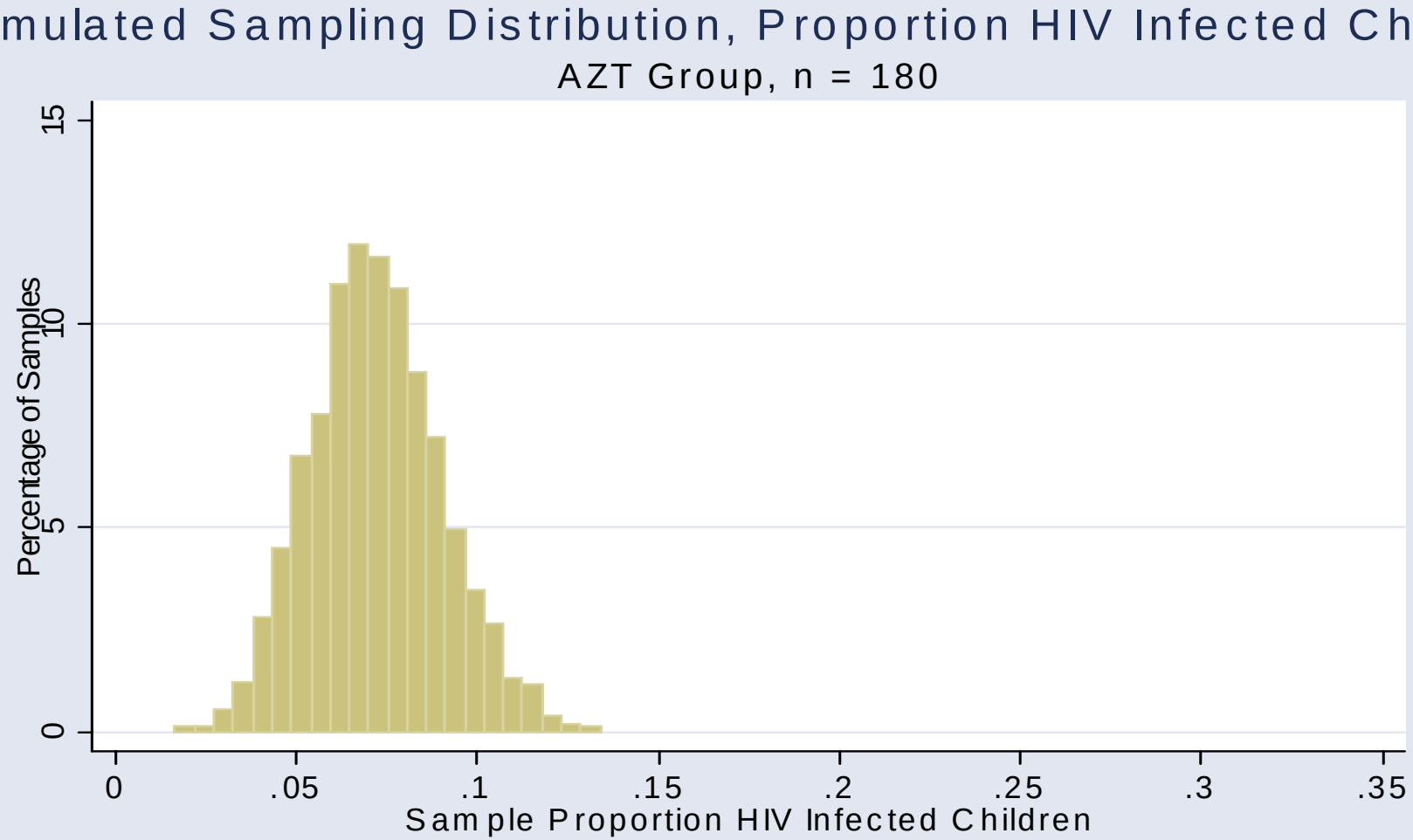
- Since we have large samples we know the sampling distributions of the sample proportions in both groups are approximately normal
- It turns out the difference of quantities, which are (approximately) normally distributed, are also normally distributed

Continued

Sampling Distribution of the Difference in Sample Means

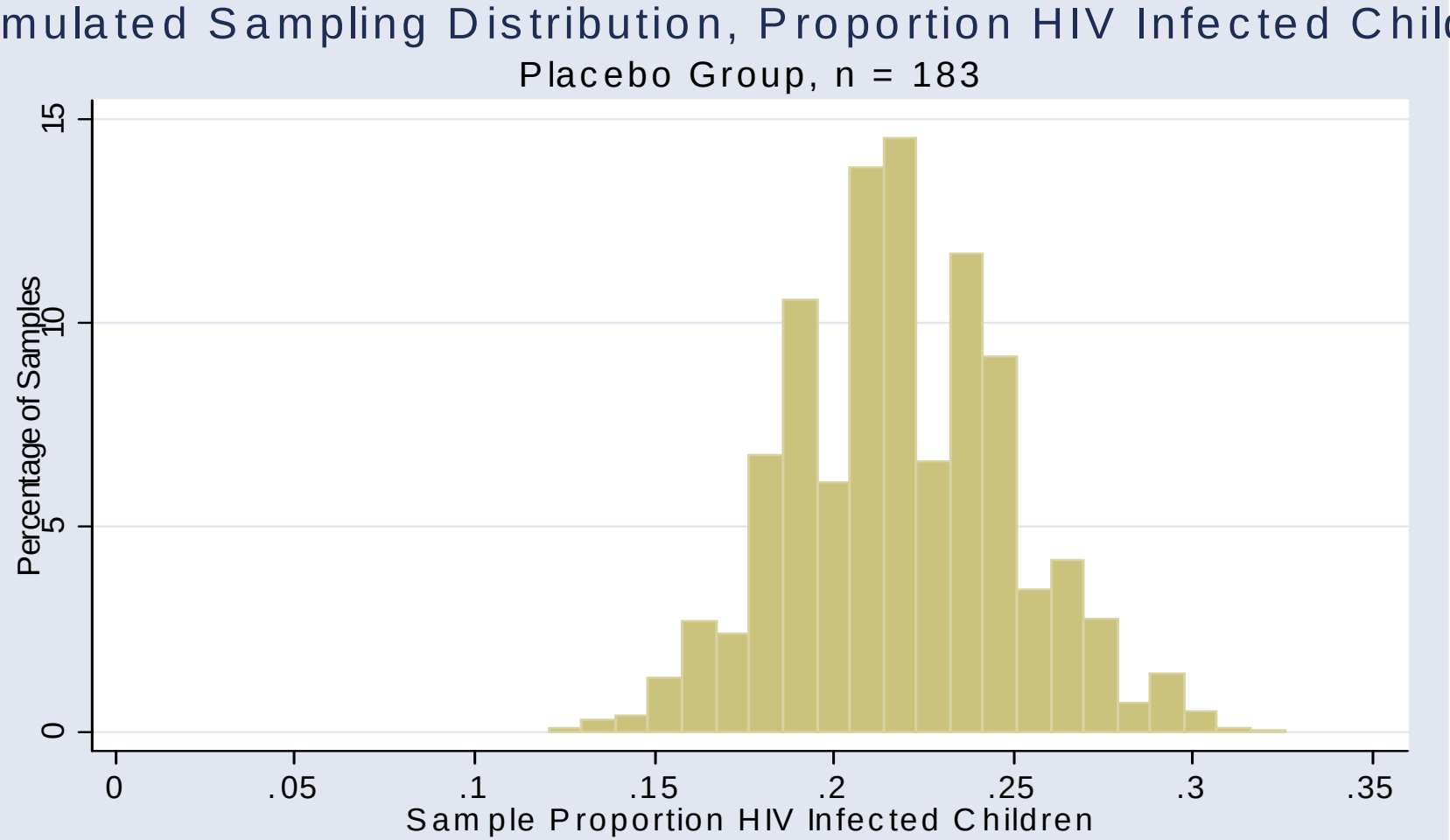
- So, the big news is . . .
  - The sampling distribution of the difference of two sample proportions, each based on large samples, approximates a normal distribution
  - This sampling distribution is centered at the true (population) difference, P1 - P2

Simulated Sampling Distribution of Sample Proportion

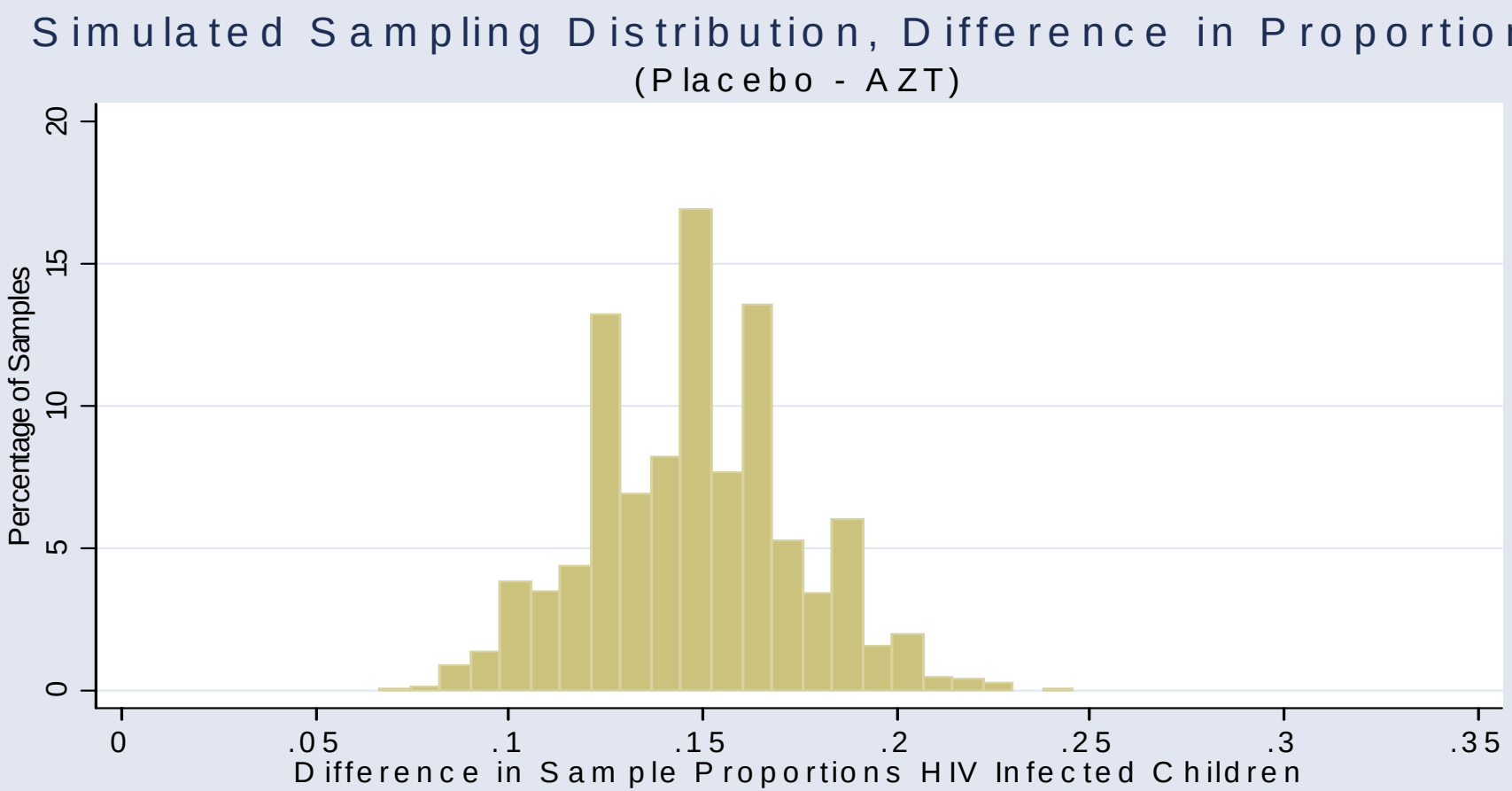


Continued

Simulated Sampling Distribution of Sample Proportion



Simulated Sampling Distribution Difference in Sample Proportions



95% Confidence Interval for Difference in Proportions

- Our most general formula:

(our best estimate) ± 2*(SE of our best estimate)

95% Confidence Interval for Difference in Means

- Well, our best estimate for the mean difference would be :

$$\hat{p}_1 - \hat{p}_2$$

- Where . . .
  - $\hat{p}_1$= proportion HIV infected children in AZT group
  - $\hat{p}_2$= proportion HIV infected children in placebo group

Continued

95% Confidence Interval for Difference in Means

- Since $\hat{p}_1 - \hat{p}_2 = 0.07 - .22 = -0.15$, our formula is . . .

$$-.15 \pm 2 \; SE\,(\hat{p}_1 - \hat{p}_2)$$

- $SE(\hat{p}_1 - \hat{p}_2)$ = standard error of the difference of two sample means

Two Independent Groups

- Statisticians have developed formulas for the standard error of the difference
  - These formulas depend on sample sizes in both groups and sample proportion in both groups

Continued

Two Independent Groups

- The $SE(\hat{p}_1 - \hat{p}_2)$ is greater than either the $SE(\hat{p}_1)$ or $SE(\hat{p}_2)$
- Why do you think this is?

Continued

Two Independent Groups

- In the example . . .

$$SE(\hat{p}_1 - \hat{p}_2) = .036$$

$$SE(\hat{p}_1) = .019$$

$$SE(\hat{p}_2) = .031$$

Example

- 95% confidence interval for difference in proportions $SE\ (\hat{p}_1 - \hat{p}_2)$
  - $.15 \pm 2$
  - $.15 \pm 2 * .036$
  - $.15 \pm .07$

  - 0.22 to - 0.08

Note

- The confidence interval does not include 0

The SE of the Difference in Sample Proportions

- Variation from independent sources can be added

$$Variance(\hat{p}_1 - \hat{p}_2) = [SE(\hat{p}_1)]^2 + [SE(\hat{p}_2)]^2$$

$$Variance(\hat{p}_1 - \hat{p}_2) = \frac{\hat{p}_1(1-\hat{p}_1)}{n_1} + \frac{\hat{p}_2(1-\hat{p}_2)}{n_2}$$

- Why do you think we add?

Continued

The SE of the Difference in Sample Proportions

- Variation from independent sources can be added

$$SE(\hat{p}_1 - \hat{p}_2) = \sqrt{\frac{\hat{p}_1(1-\hat{p}_1)}{n_1} + \frac{\hat{p}_2(1-\hat{p}_2)}{n_2}}$$

Principle

- Formula depends on n_1, n_2, $\hat{p}_1$, $\hat{p}_2$
- There are other slightly different equations for (e.g. Altman, p.234) $SE\,(\hat{p}_1 - \hat{p}_2)$
- But they all give similar answers

Simple Approximation Method to Compare Proportions

- Hypotheses

$$H_0: P_1 = P_2$$

$$H_a: P_1 \neq P_2$$

Continued

Simple Approximation Method to Compare Proportions

- Hypotheses

$$H_0: P_1 - P_2 = 0$$

$$H_a: P_1 - P_2 \neq 0$$

Continued

Simple Approximation Method to Compare Proportions

- Recall the general "recipe" for hypothesis testing:

1. State null and alternative hypotheses
2. Calculate test statistic based on sample
3. Compare test statistic to appropriate distribution to get p-value

Continued

Simple Approximation Method to Compare Proportions

- Principle
  - General formula for test statistic . . .

$$test = \frac{\textbf{(observed diff) - (null diff)}}{\textbf{SE of the difference}}$$

Comparing Proportions

- But since null difference is zero, this reduces to . . .

$$test = \frac{\text{(observed diff)}}{\text{SE of the difference}}$$

Continued

Comparing Proportions

- Principle
  - Estimate parameter (the difference) divide by SE of estimate

$$Z = \frac{\hat{p}_1 - \hat{p}_2}{SE(\hat{p}_1 - \hat{p}_2)}$$

Two-Sample z-test for Comparing Proportions

- Which is just . . .

$$Z = \frac{\hat{p}_1 - \hat{p}_2}{SE(\hat{p}_1 - \hat{p}_2)}$$

$$z = \frac{.07 - (.22)}{.036} = \frac{-.15}{.036} = -4.2$$

Note

- This is a two sample z-test for comparing two proportions
  - The value z = - 4.2 is the test statistic
- We calculate a p-value which is the probability of obtaining a test statistic as extreme as we did if H_0 was true

How Are p-values Calculated?

- Is a result 4.2 standard errors below 0 unusual?
  - It depends on what kind of distribution we are dealing with

Continued

How Are p-values Calculated?

- The p-value is the probability of getting a test statistic as or more extreme than what you observed (- 4.2) by chance if H_0 was true
- The p-value comes from the sampling distribution of *the difference in two sample proportions*

Sampling Distribution

- What is sampling distribution of the difference in sample proportions?
  - If both groups are large then this distribution is approximately normal

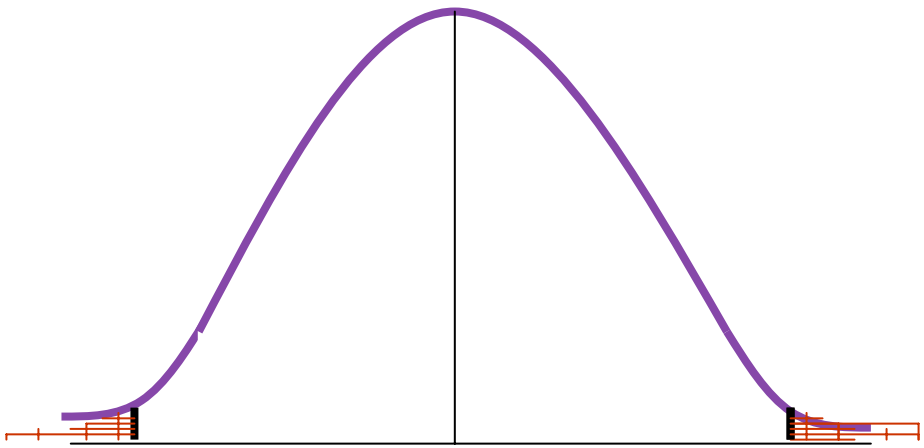
AZT Study

- So, since both our samples are large our sampling distribution will be approximately normal
  - This sampling distribution will be centered at true difference, $P_1 - P_2$
  - Under null hypothesis, this true difference is 0

Continued

AZT Study

- To compute a p-value, we would need to compute the probability of being 4.2 or more standard errors away from 0 on a standard normal curve



Continued

AZT Study

- If we were to look this up on a normal table, we would find a very low p-value ($p < .001$)

Notes

- This method is also essentially equivalent to the chi-square (χ^2) method
  - Gives about the same answer
  - (p-value)
  - We will discuss chi-square method next

Display Data in a 2x2 Table

- Two rows and two columns
- Contingency table

HIV Transmission	Drug Group: AZT	Drug Group: Placebo	
Yes	13	40	53
No	167	143	310
	180	183	363

Continued

Display Data in a 2x2 Table

- Grand total

HIV Transmission	Drug Group: AZT	Drug Group: Placebo	
Yes	13	40	53
No	167	143	310
	180	183	363

Continued

Display Data in a 2x2 Table

- Column totals

HIV Transmission	Drug Group: AZT	Drug Group: Placebo	
Yes	13	40	53
No	167	143	310
	180	183	363

Continued

Display Data in a 2x2 Table

- Row totals

HIV Transmission	Drug Group: AZT	Drug Group: Placebo	Row Total
Yes	13	40	53
No	167	143	310
	180	183	363

Continued

Display Data in a 2x2 Table

- Cell counts

HIV Transmission	Drug Group: AZT	Drug Group: Placebo	
Yes	13	40	53
No	167	143	310
	180	183	363

Using Stata

- We can get Stata to give us a 95% CI for the difference in proportions, and a p-value by using the csi command

Continued

Using Stata

- Syntax—if we create a 2x2 table using our sample results as such

		Exposure: Yes	Exposure: No
Outcome	Yes	a	b
	No	c	d

Continued

Using Stata

- Syntax:
  - csi a b c d

Continued

Using Stata

- 2x2 table formed using results from a Maternal-Infant Transmission Study

HIV Transmission	Drug Group: AZT	Drug Group: Placebo	
Yes	13	40	53
No	167	143	210
	180	183	263

Continued

Using Stata

```
.   csi 13 40 167 143

                 |   Exposed   Unexposed  |     Total
-----------------+------------------------+----------
           Cases |        13          40  |        53
        Noncases |       167         143  |       310
-----------------+------------------------+----------
           Total |       180         183  |       363
                 |                        |
            Risk |   .0722222    .2185792  |   .1460055
                 |                        |
                 |      Point estimate    |  [95% Conf. Interval]
                 |------------------------+----------------------
 Risk difference |         -.146357       | -.2171766   -.0755374
      Risk ratio |         .3304167       |  .1829884    .5966235
 Prev. frac. ex. |         .6695833       |  .4033765    .8170116
 Prev. frac. pop |         .3320248       |
                 +-------------------------------------------------
                           chi2(1) =    15.59  Pr>chi2 = 0.0001
```

Continued

Using Stata

```
.   csi 13 40 167 143

                 |   Exposed   Unexposed  |     Total
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Continued

Using Stata

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Continued

Using Stata

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                 +------------------------+----------------------
                           chi2(1) =    15.59  Pr>chi2 = 0.0001
```

Summary: AZT Study

- **Statistical Method**
  - "We conducted a randomized, double-blind, placebo-controlled trial of the efficacy and safety of zidovudine (AZT) in reducing the risk of maternal-infant HIV transmission"

Continued

Summary: AZT Study

- **Statistical Method**
  - The proportion of infants diagnosed as HIV positive within 18 months of birth was compared between the AZT and placebo groups using a two-sample z-test of proportions
  - 95% confidence intervals were computed for the 18-month infection proportion in each group, and for the difference in proportions between both groups

Continued

Summary: AZT Study

- **Results**
  - The proportion of infants who tested positive for HIV within 18 months of birth was seven percent (95% CI 4 -12%) in the AZT group and twenty-two percent in the placebo group (95% CI 16 - 28%)
  - This difference is statistically significant ($p < .001$)

Continued

Summary: AZT Study

- **Results**
  - The study results estimate the decrease in the proportion of HIV positive infants born to HIV positive mothers attributable to AZT to possibly be as low as 8% and as high as 22%

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Section A

Practice Problems

Practice Problems

- A study was performed on a representative sample of 258 intravenous drug users (IVDUs)
- Of particular interest to the researchers were factors which may influence the risk of contracting tuberculosis amongst IVDUs[1]

Source: [1] Based on data reported in: Graham, N., et al. Prevalence of Tuberculin Positivity and Skin Test Anergy in HIV-1-Seropisitive and Seronegative Intravenous Drug Users, Journal of the American Medical Association *267: 3.*

Continued

Practice Problems

- Ninety seven of the study subjects admitted to sharing needles to shoot drugs
- Of these 97, 24 had a positive tuberculin test result
- The other 161 subjects denied having shared needles—of these 161 subjects, 28 had a positive tuberculin test result

Continued

Practice Problems

a) Using the study results, construct a 95% confidence interval for the difference in the proportion of tuberculosis infected IVDUS who shared needles as compared to IVDUS who did not share needles

Continued

Practice Problems

b) What is the p-value for testing the null hypothesis that the proportions of individuals testing positive for tuberculosis are the same between the two groups of IVDUs?

Continued

Practice Problems

c) Does this study suggest a relationship between tuberculosis infection and needle sharing in IVDUs?

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Section A

Practice Problems Solutions

Practice Problems

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Continued

Practice Problems

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Continued

Practice Problems

a) Using the study results, construct a 95% confidence interval for the difference in the proportion of tuberculosis infected IVDUS who shared needles as compared to IVDUS who did not share needles

Continued

Practice Problems

- First, it may prove helpful to arrange the study results in a 2x2 contingency table

		Share Needles?		
		Yes	No	
TB Positive?	Yes	24	28	52
	No	73	133	206
		97	161	258

Continued

Practice Problems

```
. csi 24 28 73 133

                 |   Exposed   Unexposed  |     Total
-----------------+------------------------+----------
           Cases |        24          28  |        52
        Noncases |        73         133  |       206
-----------------+------------------------+----------
           Total |        97         161  |       258
                 |                        |
            Risk |  .2474227     .173913  |  .2015504
                 |                        |
                 |      Point estimate    |  [95% Conf. Interval]
                 |------------------------+----------------------
 Risk difference |         .0735096       | -.0304235    .1774428
      Risk ratio |          1.42268       |  .8772363    2.307268
 Attr. frac. ex. |         .2971014       | -.1399437     .566587
 Attr. frac. pop |         .1371237       |
                 +-----------------------------------------------
                           chi2(1) =     2.03  Pr>chi2 = 0.1540
```

Continued

Practice Problems

b) What is the p-value for testing the null hypothesis that the proportions of individuals testing positive for tuberculosis are the same between the two groups of IVDUs?

Continued

Practice Problems

```
. csi 24 28 73 133

                 |   Exposed   Unexposed  |     Total
-----------------+------------------------+----------
           Cases |        24          28  |        52
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 Attr. frac. pop |         .1371237       |
                 +-----------------------------------------------
                           chi2(1) =     2.03  Pr>chi2 = 0.1540
```

Continued

Practice Problems

c) Does this study suggest a relationship between tuberculosis infection and needle sharing in IVDUs?

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Section B

The Chi-Squared Test

Hypothesis Testing Problem

- H_0: $P_1 = P_2$ $\quad (P_1 - P_2 = 0)$
- H_a: $P_1 \neq P_2$ $\quad (P_1 - P_2 \neq 0)$
  - In the context of the 2x2 table, this is testing whether there is a relationship between the rows (HIV status) and columns (treatment type)

Statistical Test Procedures

- **(Pearson's) Chi-Square Test (χ^2)**
  - Calculation is easy (can be done by hand)
- Works well for big sample sizes

The Chi-Square Approximate Method

- Gives (essentially) same p-value as z-test for comparing two proportions
- Can be extended to compare proportions between more than two independent groups in one test

Continued

The Chi-Square Approximate Method

- Looks at discrepancies between observed and expected cell counts

  0 = observed

  $$E = \text{expected} = \frac{\text{row total} \times \text{column total}}{\text{grand total}}$$

Continued

The Chi-Square Approximate Method

- Expected refers to the values for the cell counts that would be expected if the null hypothesis is true
  - The expected values if the proportions are equal

Continued

The Chi-Square Approximate Method

- Test statistic

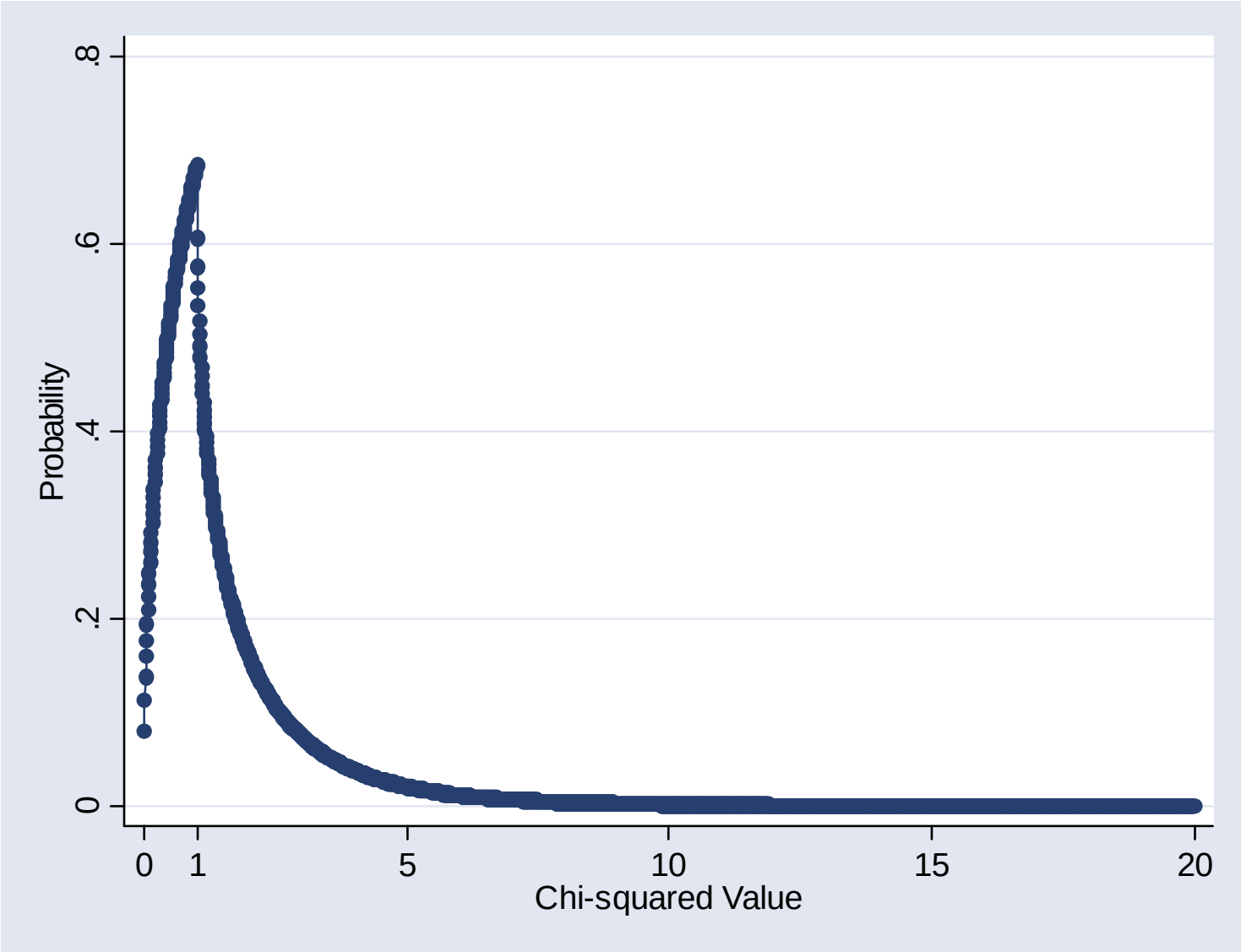
$$\chi^2 = \sum_{4 \text{ cells}} \frac{(0 - E)^2}{E}$$

Continued

The Chi-Square Approximate Method

- The sampling distribution of this statistic when the null is a chi-square distribution with one degree of freedom
- We can use this to determine how likely it was to get such a big discrepancy between the observed and expected by chance alone

Sampling Distribution: Chi-Square with One Degree of Freedom



Display Data in a 2x2 Table

HIV Transmission	Drug Group: AZT	Drug Group: Placebo	
Yes	13	40	53
No	167	143	310
	180	183	363

- The observed value for cell one is 13
- Let's calculate its expected value

Example of Calculations of Chi-Square 2x2 Contingency Table

HIV Transmission	Drug Group: AZT	Drug Group: Placebo	
Yes	13	40	53
No	167	143	310
	180	183	363

- Take row one total

Continued

Example of Calculations of Chi-Square 2x2 Contingency Table

HIV Transmission	Drug Group: AZT	Drug Group: Placebo	
Yes	13	40	53
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- Take row one total, multiply by column one total

Continued

Example of Calculations of Chi-Square 2x2 Contingency Table

HIV Transmission	Drug Group: AZT	Drug Group: Placebo	
Yes	13	40	53
No	167	143	310
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- Take row one total, multiply by column one total, and divide by grand total

Continued

Example of Calculations of Chi-Square 2x2 Contingency Table

HIV Transmission	Drug Group: AZT	Drug Group: Placebo	
Yes	13	40	53
No	167	143	310
	180	183	363

- Expected = $\frac{53*180}{363} = 26.3$

Continued

Example of Calculations of Chi-Square 2x2 Contingency Table

HIV Transmission	Drug Group: AZT	Drug Group: Placebo	
Yes	13	40	53
No	167	143	310
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- We could do the same for the other three cells; the above table has expected counts

Continued

Example of Calculations of Chi-Square 2x2 Contingency Table

- Test statistic

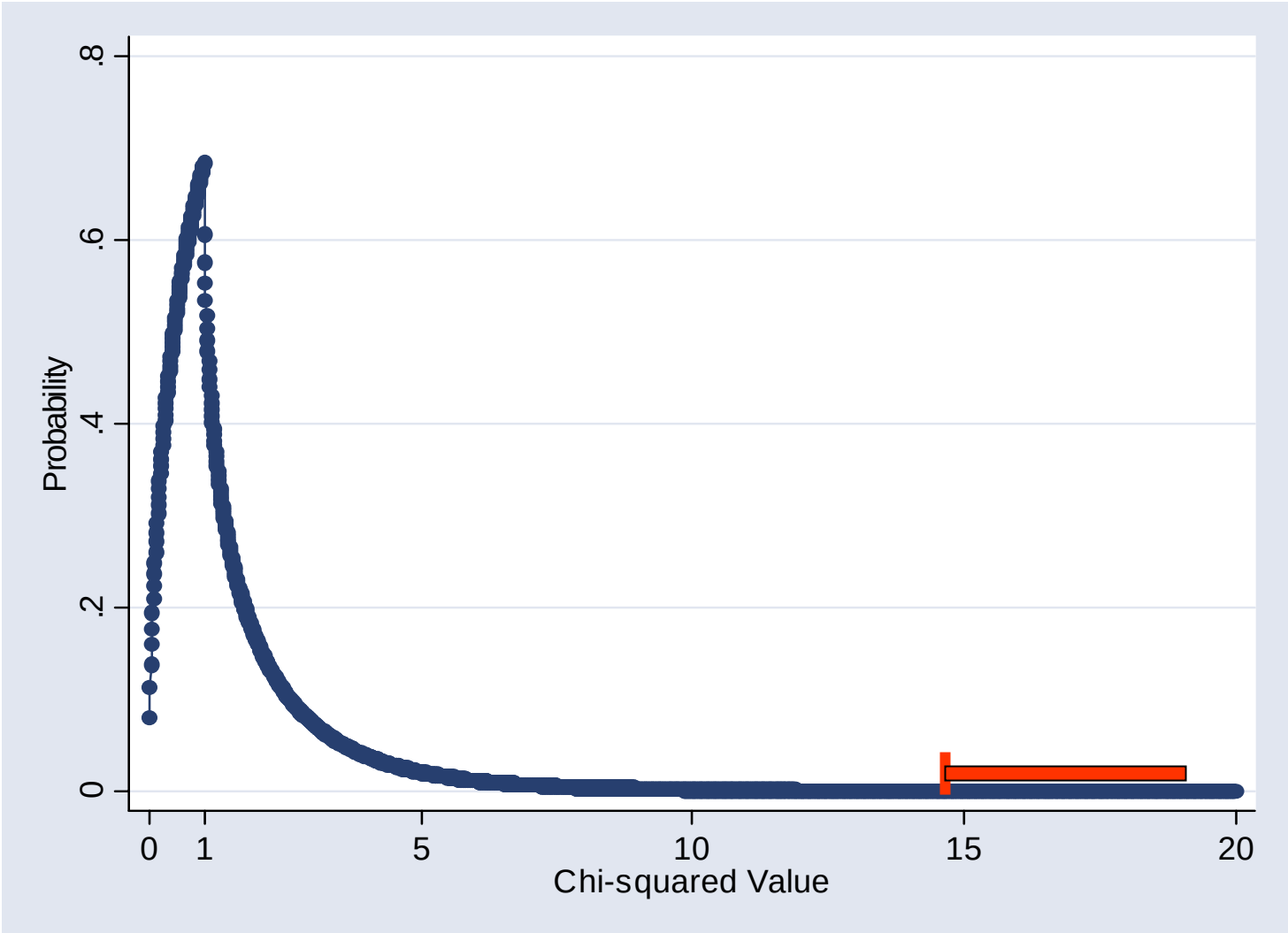
$$\chi^2 = \sum_{4 \text{ cells}} \frac{(0 - E)^2}{E}$$

- In our table

$$\chi^2 = 15.6$$

Continued

Sampling Distribution: Chi-Square with One Degree of Freedom



Using Stata to Compute Chi-Squared

```
.   csi 13 40 167 143

                 |   Exposed   Unexposed  |     Total
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                 +-------------------------------------------------
                           chi2(1) =    15.59  Pr>chi2 = 0.0001
```

Summary: Large Sample Procedures for Comparing Proportions Between Two Independent Populations

- To create a 95% confidence interval for the difference in two proportions

$$\hat{p}_1 - \hat{p}_2 \pm 2SE(\hat{p}_1 - \hat{p}_2)$$

Continued

Summary: Large Sample Procedures for Comparing Proportions Between Two Independent Populations

- To get a p-value for testing:
  - H_0: $P_1 = P_2$ vs.
  - H_a: $P_1 \neq P_2$

- Two sample z-test or Chi-Squared Test (give same p-value)

Extendability of Chi-Squared

- Chi-squared test can be extended to test for differences in proportions across more than two independent populations
  - Proportion analogue to ANOVA

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Section C

Fisher's Exact Test

Hypothesis Testing Problem

- H_0: $P_1 = P_2$
- H_a: $P_1 \neq P_2$
  - Where

    P_1 = Proportion infected on AZT

    P_2 = Proportion infected on placebo

Continued

Hypothesis Testing Problem

- H_0: $P_1 - P_2 = 0$
- H_a: $P_1 - P_2 \neq 0$
  - Where:

    P_1 = Proportion infected on AZT

    P_2 = Proportion infected on placebo

Continued

Hypothesis Testing Problem

- H_0: $P_1 = P_2$
- H_a: $P_1 \neq P_2$
  - In the context of the 2x2 table, this is testing whether there is a relationship between the rows (HIV status) and columns (treatment type)

Statistical Test Procedures

- **Fisher's Exact Test**
  - Calculations are difficult
  - Always appropriate to test equality of two proportions
  - Computers are usually used
  - Exact p-value (no approximations): no minimum sample size requirements

Continued

Statistical Test Procedures

- **(Pearson's) Chi-Square Test (χ^2)/ Two-sample z-test**
  - Both based on central limit theorem "kicking in"
  - Both results are "approximate," but are excellent approximations if sample sizes are large
  - These do not perform so well in smaller samples

Fisher's Exact Test

- **Rationale**
  - Suppose H_0 is true: AZT is not effective
  - Imagine putting 53 red balls (the infected) and 310 blue balls (non-infected) in a jar
  - Shake it up

Continued

Fisher's Exact Test

- Now choose 180 balls (that's AZT group)
  - The remaining balls are the placebo group
- We calculate the probability you get 13 or fewer red balls among the 180
  - That is the one-sided p-value

Continued

Fisher's Exact Test

- The two-sided p-value is just about (but not exactly) twice the one-sided
- P-value
  - It accounts for the probability of getting either extremely few red balls or a lot of red balls in the AZT group

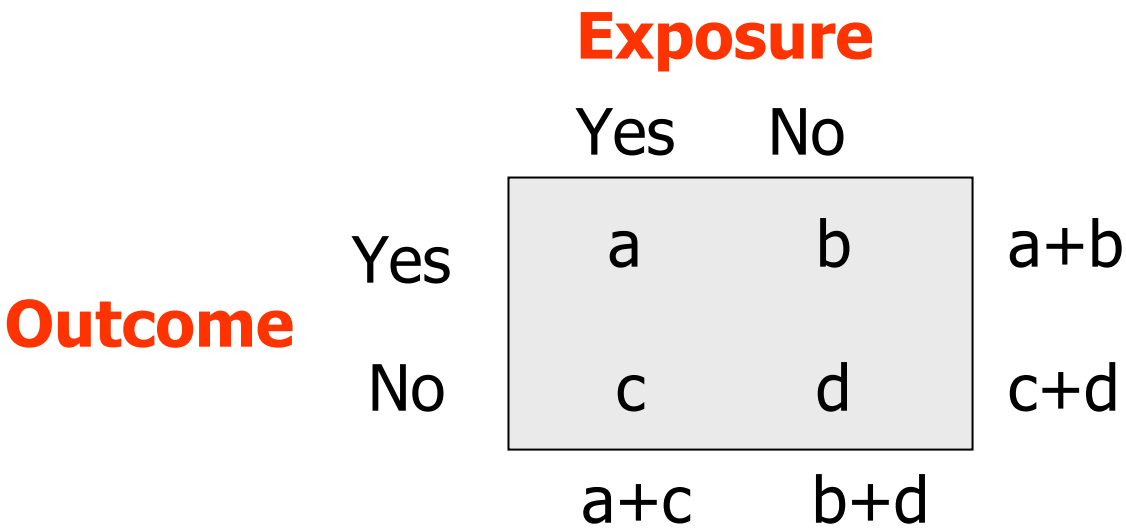
Continued

Fisher's Exact Test

- The p-value is the probability of obtaining a result as or more extreme (more imbalance) than you did by chance alone

How to Use STATA to Calculate Fisher's Exact Test

- **Command syntax**
  - tabi a b \ c d



Continued

How to Use STATA to Calculate Fisher's Exact Test

- **With HIV example**
  - tabi 13 40 \ 167 143

HIV Transmission	Drug Group: Placebo	Drug Group: AZT	
Yes	13	40	53
No	167	143	310
	180	183	363

Continued

How to Use STATA to Calculate Fisher's Exact Test

```
tabi 13 40 \ 167 143

           |          col
       row |         1           2 |     Total
-----------+----------------------+----------
         1 |        13          40 |        53
         2 |       167         143 |       310
-----------+----------------------+----------
     Total |       180         183 |       363

          Fisher's exact =                 0.000
  1-sided Fisher's exact =                 0.000
```

Continued

How to Use STATA to Calculate Fisher's Exact Test

```
tabi 13 40 \ 167 143

           |          col
       row |         1          2 |     Total
-----------+----------------------+----------
         1 |        13         40 |        53
         2 |       167        143 |       310
-----------+----------------------+----------
     Total |       180        183 |       363

          Fisher's exact =                 0.000
  1-sided Fisher's exact =                 0.000
```

- (p-value not really 0, just < .001)

Continued

How to Use STATA to Calculate Fisher's Exact Test

- However, the tabi command did not give a confidence interval for the difference in proportions!
- Can also use csi command with "exact" option

Continued

How to Use STATA to Calculate Fisher's Exact Test

```
. csi 13 40 167 143, exact

                 |   Exposed   Unexposed  |     Total
-----------------+------------------------+----------
           Cases |        13          40  |        53
        Noncases |       167         143  |       310
-----------------+------------------------+----------
           Total |       180         183  |       363
                 |                        |
            Risk |  .0722222    .2185792  |  .1460055
                 |                        |
                 |      Point estimate    |  [95% Conf. Interval]
                 |------------------------+----------------------
 Risk difference |         -.146357       | -.2171766   -.0755374
      Risk ratio |         .3304167       |  .1829884    .5966235
 Prev. frac. ex. |         .6695833       |  .4033765    .8170116
 Prev. frac. pop |         .3320248       |
                 +-----------------------------------------------
                               1-sided Fisher's exact P = 0.0001
                               2-sided Fisher's exact P = 0.0001
```

Continued

How to Use STATA to Calculate Fisher's Exact Test

```
. csi 13 40 167 143, exact

                 |   Exposed   Unexposed  |     Total
-----------------+------------------------+----------
           Cases |        13          40  |        53
        Noncases |       167         143  |       310
-----------------+------------------------+----------
           Total |       180         183  |       363
                 |                        |
            Risk |  .0722222    .2185792  |  .1460055
                 |                        |
                 |      Point estimate    |  [95% Conf. Interval]
                 |------------------------+----------------------
 Risk difference |         -.146357       | -.2171766   -.0755374
      Risk ratio |         .3304167       |  .1829884    .5966235
 Prev. frac. ex. |         .6695833       |  .4033765    .8170116
 Prev. frac. pop |         .3320248       |
                 +-----------------------------------------------
                                  1-sided Fisher's exact P = 0.0001
                                  2-sided Fisher's exact P = 0.0001
```

Continued

How to Use STATA to Calculate Fisher's Exact Test

```
. csi 13 40 167 143, exact

                 |   Exposed   Unexposed  |     Total
-----------------+------------------------+----------
           Cases |        13          40  |        53
        Noncases |       167         143  |       310
-----------------+------------------------+----------
           Total |       180         183  |       363
                 |                        |
            Risk |  .0722222    .2185792  |  .1460055
                 |                        |
                 |      Point estimate    |  [95% Conf. Interval]
                 |------------------------+
 Risk difference |         -.146357       | -.2171766   -.0755374
      Risk ratio |         .3304167       |  .1829884    .5966235
 Prev. frac. ex. |         .6695833       |  .4033765    .8170116
 Prev. frac. pop |         .3320248       |
                 +-----------------------------------------------

                      1-sided Fisher's exact P = 0.0001
                      2-sided Fisher's exact P = 0.0001
```

Small Sample Application

- Sixty-five pregnant women, all who were classified as having a high risk of pregnancy induced hypertension, were recruited to participate in a study of the effects of aspirin on hypertension
- The women were randomized to receive either 100 mg of aspirin daily, or a placebo during the third trimester of pregnancy

1. Schiff, E. et al; The use of aspirin to prevent pregnancy-induced hypertension and lower the ratio of thromboxane A2 to prostacyclin in relatively high risk pregnancies, New England Journal of Medicine *321;6*

Continued

Small Sample Application

- Results

Hypertension	Aspirin	Placebo	
	Drug Group		
Yes	4	11	15
No	30	20	50
	34	31	65

Sample Proportions

$$\hat{p}_{aspirin} = \frac{4}{34} = .12$$

$$\hat{p}_{placebo} = \frac{11}{31} = .35$$

Smaller Sample

- In this example:

$$n_{aspirin} * \hat{p}_{aspirin} * (1 - \hat{p}_{aspirin}) = 34 * .12 * .88 = 3.6$$

$$n_{placebo} * \hat{p}_{placebo} * (1 - \hat{p}_{placebo}) = 31 * .35 * 65 = 7.1$$

Fisher's Exact Test

```
. csi 4 11  30 20, exact

                 |   Exposed   Unexposed  |     Total
-----------------+------------------------+----------
           Cases |         4          11  |        15
        Noncases |        30          20  |        50
-----------------+------------------------+----------
           Total |        34          31  |        65
                 |                        |
            Risk |  .1176471    .3548387  |  .2307692
                 |                        |
                 |      Point estimate    |  [95% Conf. Interval]
                 |------------------------+----------------------
 Risk difference |        -.2371917       | -.4374335   -.0369498
      Risk ratio |         .3315508       |  .1176925    .9340096
 Prev. frac. ex. |         .6684492       |  .0659904    .8823075
 Prev. frac. pop |         .3496503       |
                 +-----------------------------------------------
                   1-sided Fisher's exact P = 0.0236
                   2-sided Fisher's exact P = 0.0378
```

Chi-Squared Test

```
. csi 4 11  30 20

                 |   Exposed   Unexposed  |     Total
-----------------+------------------------+----------
           Cases |         4          11  |        15
        Noncases |        30          20  |        50
-----------------+------------------------+----------
           Total |        34          31  |        65
                 |                        |
            Risk |  .1176471    .3548387  |  .2307692
                 |                        |
                 |      Point estimate    |  [95% Conf. Interval]
                 |------------------------+----------------------
 Risk difference |        -.2371917       | -.4374335   -.0369498
      Risk ratio |         .3315508       |  .1176925    .9340096
 Prev. frac. ex. |         .6684492       |  .0659904    .8823075
 Prev. frac. pop |         .3496503       |
                 +------------------------+

                           chi2(1) =    5.14  Pr>chi2 = 0.0234
```

95% Confidence Interval (not quite correct)

```
. csi 4 11  30 20

                 |   Exposed   Unexposed  |     Total
-----------------+------------------------+----------
           Cases |         4           11 |        15
        Noncases |        30           20 |        50
-----------------+------------------------+----------
           Total |        34           31 |        65
                 |                        |
            Risk |  .1176471    .3548387  |  .2307692
                 |                        |
                 |      Point estimate    |  [95% Conf. Interval]
                 |------------------------+----------------------
 Risk difference |        -.2371917       | -.4374335   -.0369498
      Risk ratio |         .3315508       |  .1176925    .9340096
 Prev. frac. ex. |         .6684492       |  .0659904    .8823075
 Prev. frac. pop |         .3496503       |
                 +-------------------------------------------------
                           chi2(1) =     5.14  Pr>chi2 = 0.0234
```

Summary: Large Sample Procedures for Comparing Proportions between Two Independent Populations

- To create a 95% confidence interval for the difference in two proportions

$$\hat{p}_1 - \hat{p}_2 \pm 2SE(\hat{p}_1 - \hat{p}_2)$$

Continued

Summary: Large Sample Procedures for Comparing Proportions Between Two Independent Populations

- To get a p-value for testing:
  - H_0: $P_1 = P_2$ vs.
  - H_a: $P_1 \neq P_2$
- Two Sample z-test or Chi-Squared Test (give same p-value)
- Fisher's exact

Small Sample Procedures for Comparing Proportions Between Two Independent Populations

- To create a 95% confidence interval for the difference in two proportions, can use this result as a guideline:

$$\hat{p}_1 - \hat{p}_2 \pm 2SE(\hat{p}_1 - \hat{p}_2)$$

- Not quite correct but will give you a good sense of width/range of CI

Summary: Large Sample Procedures for Comparing Proportions Between Two Independent Populations

- To get a p-value for testing:
  - H_0: $P_1 = P_2$ vs.
  - H_a: $P_1 \neq P_2$

- Fisher's exact test

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Section C

Practice Problems

Practice Problems

- Researchers are interested in studying the relationship between salt in a diet and high blood pressure in men in their early 50s
- A random sample is taken of 58 men between the ages of 50–54
- Each subject keeps a food diary for a one-month period, and is evaluated for high blood pressure

Continued

Practice Problems

- Seven of the 58 men have high salt diets
  - Of these seven men, one had high blood pressure at the time of the study
- 51 of the 58 men have low salt diets
  - Of these 58 men, 28 have high blood pressure at the time of the study

Continued

Practice Problems

1. Construct a 2x2 contingency table which summarizes the study data
2. Estimate a 95% confidence interval for the difference in the proportion of men with high blood pressure in the two diet groups (use the large sample approach, even if not appropriate)

Continued

Practice Problems

3. Perform (using computer) both a Fisher's exact test and a chi-squared test
   - If you were using a strict .05 level cutoff for statistical significance, how would your conclusions from each of the two tests compare?

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Section C

Practice Problem Solutions

Practice Problems

- Researchers are interested in studying the relationship between salt in a diet and high blood pressure in men in their early 50s
- A random sample is taken of 58 men between the ages of 50–54
- Each subject keeps a food diary for a one-month period and is evaluated for high blood pressure

Continued

Practice Problems

- Seven of the 58 men have high salt diets
  - Of these seven men, one had high blood pressure at the time of the study
- 51 of the 58 men have low salt diets
  - Of these 58 men, 28 have high blood pressure at the time of the study

Continued

Practice Problems

1. Construct a 2x2 contingency table which summarizes the study data

		High Salt Diet? Yes	No	
High Blood Pressure?	Yes	1	28	29
	No	6	23	29
		7	51	

Continued

Practice Problems

2. Estimate a 95% confidence interval for the difference in the proportion of men with high blood pressure in the two diet groups (use the large sample approach, even if not appropriate)

Continued

Practice Problems

- 95% confidence interval

```
. csi 1 28 6 23

                 |   Exposed   Unexposed  |     Total
-----------------+------------------------+----------
           Cases |         1          28  |        29
        Noncases |         6          23  |        29
-----------------+------------------------+----------
           Total |         7          51  |        58
                 |                        |
            Risk |  .1428571    .5490196  |        .5
                 |                        |
                 |      Point estimate    |  [95% Conf. Interval]
                 |------------------------+----------------------
 Risk difference |        -.4061625       | -.6991594   -.1131655
      Risk ratio |         .2602041       |  .0416759    1.624588
 Prev. frac. ex. |         .7397959       | -.6245882    .9583241
 Prev. frac. pop |         .0892857       |
                 +-------------------------------------------------
                           chi2(1) =     4.06  Pr>chi2 = 0.0439
```

Continued

Practice Problems

3. Perform (using computer) both a Fisher's exact test and a chi-squared test
   - If you were using a strict .05 level cutoff for statistical significances, how would your conclusions from each of the two tests compare?

Continued

Practice Problems

- Chi-Squared

```
. csi 1 28 6 23

                 |   Exposed   Unexposed  |     Total
-----------------+------------------------+----------
           Cases |         1          28  |        29
        Noncases |         6          23  |        29
-----------------+------------------------+----------
           Total |         7          51  |        58
                 |                        |
            Risk |  .1428571    .5490196  |        .5
                 |                        |
                 |      Point estimate    |  [95% Conf. Interval]
                 |------------------------+----------------------
 Risk difference |        -.4061625       | -.6991594   -.1131655
      Risk ratio |         .2602041       |  .0416759    1.624588
 Prev. frac. ex. |         .7397959       | -.6245882    .9583241
 Prev. frac. pop |         .0892857       |
                 +-------------------------------------------------
                           chi2(1) =     4.06  Pr>chi2 = 0.0439
```

Continued

Practice Problems

- Fisher's Exact

```
. csi 1 28 6 23, exact

                 |   Exposed   Unexposed  |     Total
-----------------+------------------------+----------
           Cases |         1          28  |        29
        Noncases |         6          23  |        29
-----------------+------------------------+----------
           Total |         7          51  |        58
                 |                        |
            Risk |  .1428571    .5490196  |        .5
                 |                        |
                 |      Point estimate    |  [95% Conf. Interval]
                 |------------------------+----------------------
 Risk difference |        -.4061625       | -.6991594   -.1131655
      Risk ratio |         .2602041       |  .0416759    1.624588
 Prev. frac. ex. |         .7397959       | -.6245882    .9583241
 Prev. frac. pop |         .0892857       |
                 +-----------------------------------------------
                           1-sided Fisher's exact P = 0.0510
                           2-sided Fisher's exact P = 0.1020
```

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Section D

Measures of Association: Risk Difference, Relative Risk and the Odds Ratio

Risk Difference

- Risk difference (attributable risk)—difference in proportions
  - Sample (estimated) risk difference

$$\hat{p}_1 - \hat{p}_2$$

Continued

Risk Difference

- The difference in risk of HIV for children born to HIV+ mothers taking AZT relative to HIV+ mothers taking placebo

$$\hat{p}_1 - \hat{p}_2 = .07 - .22 = -.15$$

Continued

Risk Difference

- Interpretation
  - If AZT was given to 1,000 HIV infected pregnant women, this would reduce the number of HIV positive infants by 150 relative the number of HIV positive infants born to 1,000 women not treated with AZT

Continued

Risk Difference

```
.   csi 13 40 167 143

                 |   Exposed   Unexposed  |     Total
-----------------+------------------------+----------
           Cases |        13          40  |        53
        Noncases |       167         143  |       310
-----------------+------------------------+----------
           Total |       180         183  |       363
                 |                        |
            Risk |   .0722222    .2185792  |   .1460055
                 |                        |
                 |      Point estimate    |  [95% Conf. Interval]
                 |------------------------+----------------------
 Risk difference |         -.146357       | -.2171766   -.0755374
      Risk ratio |         .3304167       |  .1829884    .5966235
 Prev. frac. ex. |         .6695833       |  .4033765    .8170116
 Prev. frac. pop |         .3320248       |
                 +-------------------------------------------------
                           chi2(1) =    15.59  Pr>chi2 = 0.0001
```

Continued

Risk Difference

- Interpretation
  - Study results suggest that the reduction in HIV positive births from 1,000 HIV positive pregnant women treated with AZT could range from 75 to 220 fewer than the number occurring if the 1,000 women were not treated

Measures of Association

- Relative risk (risk ratio)—ratio of proportions
  - Sample (estimated) relative risk

$$\frac{\hat{p}_1}{\hat{p}_2}$$

AZT/Mother-Infant Transmission Example

- The risk of HIV with AZT relative to placebo
  - Relative risk = $\frac{\hat{p}_1}{\hat{p}_2} = \frac{.07}{.22} = .32$
  - The risk of HIV transmission with AZT is about 1/3 the risk of transmission with placebo

Relative Risk

- Interpretation
  - An HIV positive pregnant woman could reduce her personal risk of giving birth to an HIV positive child by nearly 70% if she takes AZT during her pregnancy

Continued

Relative Risk

```
.   csi 13 40 167 143

                 |   Exposed   Unexposed  |     Total
-----------------+------------------------+----------
           Cases |        13          40  |        53
        Noncases |       167         143  |       310
-----------------+------------------------+----------
           Total |       180         183  |       363
                 |                        |
            Risk |   .0722222    .2185792  |   .1460055
                 |                        |
                 |      Point estimate    |  [95% Conf. Interval]
                 |------------------------+----------------------
 Risk difference |         -.146357       | -.2171766   -.0755374
      Risk ratio |         .3304167       |  .1829884    .5966235
 Prev. frac. ex. |         .6695833       |  .4033765    .8170116
 Prev. frac. pop |         .3320248       |
                 +-----------------------------------------------
                           chi2(1) =    15.59  Pr>chi2 = 0.0001
```

Continued

Relative Risk

- Interpretation
  - Study results suggest that this reduction in risk could be as small as 40% and as large as 82%

Note about Relative Risk

- The RR could be computed in the other direction as well
- (ie: RR of transmission for placebo compared to AZT group)

$$= \frac{\hat{p}_2}{\hat{p}_1} = \frac{.22}{.07} = 3.1$$

Relative Risk

- Interpretation
  - An HIV positive pregnant woman increases her personal risk of giving birth to an HIV positive child by slightly more than 3 times if she does not take AZT during her pregnancy

Continued

Relative Risk

```
. csi 40 13 143 167

                 |   Exposed   Unexposed  |     Total
-----------------+------------------------+----------
           Cases |        40          13  |        53
        Noncases |       143         167  |       310
-----------------+------------------------+----------
           Total |       183         180  |       363
                 |                        |
            Risk |   .2185792    .0722222  |   .1460055
                 |                        |
                 |      Point estimate    |  [95% Conf. Interval]
                 |------------------------+----------------------
 Risk difference |          .146357       |  .0755374    .2171766
      Risk ratio |         3.026482       |  1.676099    5.464827
 Attr. frac. ex. |         .6695833       |  .4033765    .8170116
 Attr. frac. pop |         .5053459       |
                 +-----------------------------------------------
                           chi2(1) =    15.59  Pr>chi2 = 0.0001
```

Continued

Relative Risk

- Interpretation
  - Study results suggest that this increase in risk could be as small as 1.7 times and as large as 5.5 times

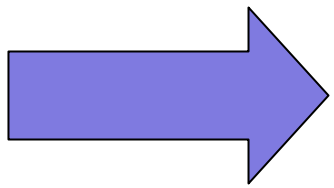
Relative Risk

- Direction of comparison is somewhat arbitrary
- Does not affect results as long as interpreted correctly!!

Hypothesis of Equal Proportions Expressed by RR

$H_0: P_1 - P_2 = 0$

$H_a: P_1 - P_2 \neq 0$



$H_0: \frac{P_1}{P_2} = 1$

$H_a: \frac{P_1}{P_2} \neq 1$

The Risk Difference vs. Relative Risk

- The **risk difference** (attributable) risk provides a measure of the public health impact of an exposure (assuming causality)
- The **relative risk** provides a measure of the magnitude of the disease-exposure association for an individual

Continued

The Risk Difference vs. Relative Risk

- AZT example—in this study 22% of the untreated mothers gave birth to children with HIV
  - Relative Risk : .32
  - Risk Difference : -15%

Continued

The Risk Difference vs. Relative Risk

- Suppose that only 2% of the children born to untreated HIV positive women became HIV positive
- Suppose the percentage in AZT treated women is .6%
  - Relative Risk : .32
  - Risk Difference : -1.4 %

Continued

The Risk Difference vs. Relative Risk

- Suppose that 90% of the children born to untreated HIV positive women became HIV positive
- Suppose this percentage was 75% for mothers taking AZT treatment during pregnancy
  - Risk Difference : 15%
  - Relative Risk : .83

The Odds Ratio

- Like the relative risk, the odds ratio provides a measure of association in a ratio (as opposed to difference)

What is an Odds?

- Odds is a function of risk (prevalence).
- Odds is the ratio of risk of having an outcome to risk of not having an outcome.
  - If *p* represents risk of an outcome, then the odds is given by:

$$Odds = \frac{p}{1-p}$$

Example

- In the AZT example, the estimate risk of giving birth to an HIV infected child among mothers treated with AZT was

$$\hat{p}_1 = .07.$$

- The corresponding odds estimate is

$$\hat{Odds} = \frac{\hat{p}_1}{1-\hat{p}_1} = \frac{.07}{1-.07} = \frac{.07}{.93} \approx .08$$

Example

- In the AZT example, the estimate risk of giving birth to an HIV infected child among mothers not treated (on the placebo) was $\hat{p}_2 = .22$.
- The corresponding odds estimate is

$$\hat{Odds} = \frac{\hat{p}_2}{1-\hat{p}_2} = \frac{.22}{1-.22} = \frac{.22}{.78} \approx .28$$

AZT/Mother-Infant Transmission Example

- The estimated odds ratio of an HIV birth with AZT relative to placebo
  - Odds Ratio = $\hat{OR} = \dfrac{\hat{p}_1 / 1-\hat{p}_1}{\hat{p}_2 / 1-\hat{p}_2} = \dfrac{.08}{.28} = .29$
  - The odds of HIV transmission with AZT is .29 (about 1/3) the odds of transmission with placebo

Estimating Odds Ratio With Stata

```
. csi 13 40 167 143, or

                 |   Exposed   Unexposed  |     Total
-----------------+------------------------+----------
           Cases |        13          40  |        53
        Noncases |       167         143  |       310
-----------------+------------------------+----------
           Total |       180         183  |       363
                 |                        |
            Risk |   .0722222    .2185792  |   .1460055
                 |                        |
                 |      Point estimate    |  [95% Conf. Interval]
                 |------------------------+----------------------
 Risk difference |         -.146357       | -.2171766   -.0755374
      Risk ratio |         .3304167       |  .1829884    .5966235
 Prev. frac. ex. |         .6695833       |  .4033765    .8170116
 Prev. frac. pop |         .3320248       |
      Odds ratio |         .2782934       |  .1445784    .5363045  (Cornfield)
                 +-------------------------------------------------
                           chi2(1) =    15.59  Pr>chi2 = 0.0001
```

Odds Ratio

- Interpretation
  - AZT is associated with an estimated 71% (estimated OR = .29) reduction in odds of giving birth to an HIV infected child among HIV infected pregnant women
  - Study results suggest that this reduction in odds could be as small as 46% and as large as 86% (95% CI on odds ratio, .14-.54)

Continued

Odds Ratio

- What about a p-value?
- What value of odds ratio indicates no difference in risk?
  - If $p_1 = p_2$, then

$$OR = \frac{p_1 / 1 - p_1}{p_2 / 1 - p_2} = 1$$

Odds Ratio

- Hence we need to test

H_o: OR=1

vs. H_a: OR ≠1

But, from previous slide OR = 1 only if $p_1=p_2$: so same test from before applies!

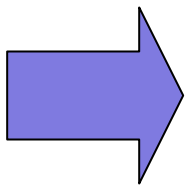
Hypothesis Testing with Odds Ratio

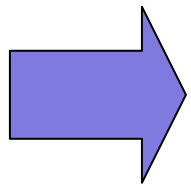
```
. csi 13 40 167 143, or

                 |   Exposed   Unexposed  |     Total
-----------------+------------------------+----------
           Cases |        13          40  |        53
        Noncases |       167         143  |       310
-----------------+------------------------+----------
           Total |       180         183  |       363
                 |                        |
            Risk |   .0722222    .2185792  |   .1460055
                 |                        |
                 |      Point estimate    |  [95% Conf. Interval]
                 |------------------------+----------------------
 Risk difference |         -.146357       | -.2171766   -.0755374
      Risk ratio |         .3304167       |  .1829884    .5966235
 Prev. frac. ex. |         .6695833       |  .4033765    .8170116
 Prev. frac. pop |         .3320248       |
      Odds ratio |         .2782934       |  .1445784    .5363045  (Cornfield)
                 +-------------------------------------------------
                             chi2(1) =    15.59  Pr>chi2 = 0.0001
```

Hypothesis of Equal Proportions Expressed by RR or OR

$H_0: P_1 - P_2 = 0$ $\quad$ $H_0: RR=1$ $\quad$ $H_0: OR=1$





$H_a: P_1 - P_2 \neq 0$ $\quad$ $H_a: RR=1$ $\quad$ $H_a: OR \neq 1$

How Does OR Compare to RR?

- Always will estimate same direction of association

$$\hat{OR} < 1 \Leftrightarrow \hat{RR} < 1$$

$$\hat{OR} > 1 \Leftrightarrow \hat{RR} > 1$$

$$\hat{OR} = 1 \Leftrightarrow \hat{RR} = 1$$

How Does OR Compare to RR?

- If CI for OR does not include 1, CI for RR will not include 1
- If CI for OR includes 1, CI for RR will include 1

$$OR < 1 \Leftrightarrow RR < 1$$

$$OR > 1 \Leftrightarrow RR > 1$$

$$OR = 1 \Leftrightarrow RR = 1$$

How Does OR Compare to RR?

- The lower the risk in both groups being compared, the more similar the *OR* and *RR* will be in magnitude

The Odds Ratio vs. Relative Risk

- AZT example—in this study 7% of AZT treated mothers and 22% of the untreated mothers gave birth to children with HIV
  - Relative Risk : .32
  - Odds Ratio : .28

Continued

The Risk Difference vs. Relative Risk

- Suppose that only 2% of the children born to untreated HIV positive women became HIV positive
- Suppose the percentage in AZT treated women is .6%
  - Relative Risk : .32
  - Odds Ratio : .30

Continued

The Risk Difference vs. Relative Risk

- Suppose that 90% of the children born to untreated HIV positive women became HIV positive
- Suppose this percentage was 75% for mothers taking AZT treatment during pregnancy
  - Relative Risk : .83
  - Odds Ratio : .33

Why Even Bother With Odds Ratio?

- It is less "intuitively intepretable" than relative risk
- However, we will see in SR2 that with certain types of non-randomized study designs we can not get a valid estimate of *RR* but can still get a valid estimate of *OR*

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Section D

Practice Problems

Practice Problems

1. Define relative risk for an outcome when comparing two groups. Why is the p-value for testing the equality of the proportion of subjects with the outcome across the two groups equivalent to the p-value for testing:

$$H_o: RR = 1$$
$$\text{vs.} \quad H_a: RR \neq 1,$$

Where RR = relative risk?

Continued

Practice Problems

2. What can one conclude about the 95% confidence interval for a relative risk if the p-value for the test described in question one is less than .05?

Continued

Practice Problems

3. In the maternal HIV transmission example, the relative risk of transmission for mothers on AZT as compared with mothers on placebo is about .30. This estimate was statistically and significantly different than one. How can this estimate be interpreted scientifically? What would the estimate be for the relative risk of transmission for mothers on placebo as compared to mothers on AZT?

Continued

Practice Problems

4. What is the relationship between a relative risk and an odds ratio? Why do we even bother with odds ratios?

Continued

Practice Problems

5. In the maternal/child HIV transmission example, the estimated odds ratio of HIV transmission for mothers on AZT compared to mothers in the placebo group is .28, with 95% CI of .14 – .54. Suppose we wanted to estimate the odds ratio in the other direction, i.e.: odds for mothers on placebo to mothers on AZT? Based on the given information can you provide an odds ratio estimate and 95% CI for this comparison?

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Section D

Practice Problem Solutions

Question

1. Define relative risk for an outcome when comparing two groups. Why is the p-value for testing the equality of the proportion of subjects with the outcome across the two groups equivalent to the p-value for testing:

$$H_o: RR = 1$$
$$\text{vs.} \quad H_a: RR \neq 1,$$

Where RR = relative risk?

Answer

- The relative risk is P_1/P_2, where P_1 = proportion of subjects in group one with the outcome and P_2 = proportion of subjects in group two with the outcome.
- This ratio, the relative risk, would be statistically different than one if P_1 is statistically different from P_2.
- Therefore, testing the equality of P_1 and P_2 is equivalent to testing RR =1.

Continued

Answer

2. What can one conclude about the 95% confidence interval for a relative risk, if the p-value for the test described in question one is less than .05?
   - 95% CI would not include one.

Question

3. In the maternal HIV transmission example, the relative risk of transmission for mothers on AZT as compared with mothers on placebo is about .30. This estimate was statistically and significantly different than one. How can this estimate be interpreted scientifically? What would the estimate be for the relative risk of transmission for mothers on placebo as compared to mothers on AZT?

Answer

- A relative risk of .30 indicates that in this sample, mothers on AZT have .30 times the risk of transmission that mothers on placebo have (30% of the risk)
- Because this number is statistically significant (different than one), researchers could conclude that mothers on AZT have less risk of transmitting the virus to their children

Continued

Answer

- If, instead, the relative risk of transmission for mothers on placebo, as compared to mothers on AZT was computed, this estimate would be 3.3, indicating that mother's on placebo have over three times the risk of transmission as compared to mothers on AZT
- This can be easily computed by taking the reciprocal of .30 (1/.30 = 3.3)
- The p-value for testing the significance of this estimate would be exactly the same as computing the relative risk in the other direction

Question

4. What is the relationship between a relative risk and an odds ratio? Why do we even bother with odds ratios?

Answer

- The relative risk and odds ratio both provide a measure of association between an outcome and a predictor: the two measures will always concur on the direction and statistical significance of the association, but the estimates and confidence limits of the two may differ.

Continued

Answer

- While odds ratio are less easily interpreted than relative risk, they can be estimated in situations where a valid estimate of the relative risk cannot be obtained. This will be explored further in 612.

Question

5. In the maternal/child HIV transmission example, the estimated odds ratio of HIV transmission for mothers on AZT compared to mothers in the placebo group is .28, with 95% CI of .15 – .54. Suppose we wanted to estimate the odds ratio in the other direction, i.e.: odds for mothers on placebo to mothers on AZT? Based on the given information can you provide an odds ratio estimate and 95% CI for this comparison?

Answer

- To get the odds ratio estimate, all we need to do is take the reciprocal of the results, $1/.28 \approx 3.6$. In other words, mother's in the placebo have odds of giving birth to an HIV infected child of 3.6 times the odds of mothers taking AZT.

Continued

Answer

- To get the endpoints for the 95% CI, we could take the reciprocal of the endpoints for the OR comparing mothers on AZT to placebo. This would yield a 95% CI for the true odds ratio of 1.9–6.7.

Continued

Answer

- Here's the result using Stata (results slightly different because I rounded)

```
csi 40 13 143 167, or
```

```
                 |   Exposed   Unexposed  |     Total
-----------------+------------------------+----------
           Cases |        40          13  |        53
        Noncases |       143         167  |       310
-----------------+------------------------+----------
           Total |       183         180  |       363
                 |                        |
            Risk |  .2185792    .0722222  |  .1460055
                 |                        |
                 |      Point estimate    |  [95% Conf. Interval]
                 |------------------------+----------------------
 Risk difference |          .146357       |  .0755374    .2171766
      Risk ratio |         3.026482       |  1.676099    5.464827
 Attr. frac. ex. |         .6695833       |  .4033765    .8170116
 Attr. frac. pop |         .5053459       |
      Odds ratio |          3.59333       |  1.864612    6.916661  (Cornfield)
                 +-----------------------------------------------
                              chi2(1) =    15.59  Pr>chi2 = 0.0001
```