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Comparing Proportions between Two Independent Populations

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Johns Hopkins University
Lecture Topics

- Using CIs 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
Section A

The Two Sample z-Test for Comparing Proportions between Two Independent Populations: The Confidence Interval Approach
Comparing Two Proportions

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

- 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

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.
  - 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 treatment

- Double blind
  - Patient and physician did not know treatment assignment
Observed HIV Transmission Proportions

- AZT
  \[ \hat{p}_{AZT} = \frac{13}{180} = 0.07 = 7\% \]

- Placebo
  \[ \hat{p}_{PLAC} = \frac{40}{183} = 0.22 = 22\% \]
HIV Transmission Proportions: 95% CIs

```
ci 180 13

<table>
<thead>
<tr>
<th>Variable</th>
<th>Obs</th>
<th>Mean</th>
<th>Std. Err.</th>
<th>[95% Conf. Interval]</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>180</td>
<td>.0722222</td>
<td>.019294</td>
<td>.0390137 .1203358</td>
</tr>
</tbody>
</table>

ci 183 40

<table>
<thead>
<tr>
<th>Variable</th>
<th>Obs</th>
<th>Mean</th>
<th>Std. Err.</th>
<th>[95% Conf. Interval]</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>183</td>
<td>.2185792</td>
<td>.0305507</td>
<td>.160984 .2855248</td>
</tr>
</tbody>
</table>
```
Notes on HIV Transmission Proportions

- Is the difference significant, or can it be explained by chance?

- Since CIs 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: Difference in Sample Proportions

- 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.
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, \( p_1 - p_2 \).
Simulated sampling distribution of sample proportion: AZT group
Sampling Distribution: Difference in Sample Proportions

- Simulated sampling distribution of sample proportion: placebo group

![Simulated Sampling Distribution: Proportion HIV+](image-url)

- 5,000 Random Samples: Placebo Group (n=183)
Sampling Distribution: Difference in Sample Proportions

- Simulated sampling distribution of difference in sample proportions: AZT - placebo

Simulated Sampling Distribution: Proportion HIV+
5,000 Random Samples: AZT (n=180) - Placebo (n=183)
Our most general formula

\[ \text{best estimate from sample } \pm 2 \times SE(\text{best estimate from sample}) \]

The best estimate of a population difference based on sample proportions:

\[ \hat{p}_1 - \hat{p}_2 \]

Here, \( \hat{p}_1 \) may represent the sample proportion of infants HIV positive (within 18 months of birth) for 180 infants in the AZT group, and \( \hat{p}_2 \) may represent the sample proportion of infants HIV positive (within 18 months of birth) for 183 infants in the AZT group.
95% CI for Difference in Proportions: AZT Study

- So, \( \hat{p}_1 - \hat{p}_2 = 0.07 - 0.22 = -0.15 \): hence the formula for the 95% CI for \( p_1 - p_2 \) is:

\[
-0.15 \pm 2 \times SE(\hat{p}_1 - \hat{p}_2)
\]

- Where \( SE(\hat{p}_1 - \hat{p}_2) \) = standard error of the difference of two sample proportions
Statisticians have developed formulas for the standard error of the difference.

These formulas depend on sample sizes in both groups and sample proportions in both groups.

The $SE(\hat{p}_1 - \hat{p}_2)$ is greater than either $SE(\hat{p}_1)$ or $SE(\hat{p}_2)$.

Why do you think this is?
Variation from independent sources can be added

Why do you think this is additive?

$$SE(\hat{p}_1 - \hat{p}_2) = \sqrt{\frac{p_1 \times (1 - p_1)}{n_1} + \frac{p_2 \times (1 - p_2)}{n_2}}$$

Of course, we don’t know $p_1$ and $p_2$: so we estimate with $\hat{p}_1$ and $\hat{p}_2$ to get an estimated standard error:

$$SE(\hat{p}_1 - \hat{p}_2) = \sqrt{\frac{\hat{p}_1 \times (1 - \hat{p}_1)}{n_1} + \frac{\hat{p}_2 \times (1 - \hat{p}_2)}{n_2}}$$
Comparing Two Independent Groups: HIV/AZT Study

- Recall the data from the Infant HIV/ AZT study

<table>
<thead>
<tr>
<th>Group</th>
<th>AZT</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of subjects (n)</td>
<td>64</td>
<td>68</td>
</tr>
<tr>
<td>Proportion Infants HIV+</td>
<td>0.07</td>
<td>0.22</td>
</tr>
<tr>
<td>Within 18 Months</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\[
SE(\hat{p}_1 - \hat{p}_2) = \sqrt{\frac{.07 \times .93}{180} + \frac{.22 \times .78}{183}} \approx .36
\]
So in this example, the estimated 95% for the true difference in proportions of infants contracting HIV between the AZT and placebo groups:

\[-0.15 \pm 2 \times \hat{SE}(\hat{p}_1 - \hat{p}_2)\]

\[-0.15 \pm 2 \times 0.036\]

\[-0.15 \pm 0.072\]

\[-0.222 \text{ to } 0.078 \approx\]

\[-22\% \text{ to } -8\%\]
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%)

- The study results estimate the absolute decrease in the proportion of HIV positive infants born to HIV positive mothers associated with AZT to be as low as 8% and as high as 22%
Section B

Two Sample z-test: Getting a p-value
Hypothesis Test to Compare Two Proportions

- Two sample z-test

- Are the proportions of infants contracting HIV within 18 months-of-birth equivalent at the population level for those whose mothers are treated with AZT versus untreated (placebo)?
  - \( H_0: p_1 = p_2 \)
  - \( H_A: p_1 \neq p_2 \)

- In other words, is the expected difference in proportions zero?
  - \( H_0: p_1 - p_2 = 0 \)
  - \( H_A: p_1 - p_2 \neq 0 \)
Recall, general “recipe” for hypothesis testing . . .

1. Start by assuming $H_0$ true
2. Measure distance of sample result from $\mu_0$ (here again its 0)
3. Compare test statistic (distance) to appropriate distribution to get p-value

\[ z = \frac{(\text{observed dif f}) - (\text{null dif f})}{\text{SE of observed difference}} \]

\[ z = \frac{\hat{p}_1 - \hat{p}_2}{SE(\hat{p}_1 - \hat{p}_2)} = \frac{\hat{p}_1 - \hat{p}_2}{\sqrt{\frac{\hat{p}_1 \times (1 - \hat{p}_1)}{n_1} + \frac{\hat{p}_2 \times (1 - \hat{p}_2)}{n_2}}} \]
In the infant HIV/AZT study, recall:

\[
\hat{p}_1 - \hat{p}_2 = -0.15
\]

\[
SE(\hat{p}_1 - \hat{p}_2) = 0.036
\]

So in this study:

\[
z = \frac{-0.15}{0.36} \approx -4.2
\]

So this study result was 4.2 standard errors below the null mean of 0 (i.e., 4.2 standard errors from the difference in the proportion of HIV+ infants between the AZT and placebo groups expected if null 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

- The p-value is the probability of getting a test statistic as (or more extreme than) what you observed (-4.2) by chance

- The p-value comes from the sampling distribution of the difference in two sample proportions

- What is the sampling distribution of the difference in sample means?
  - If both groups are large then this distribution is approximately normal
  - This sampling distribution will be centered at true difference,
  - Under null hypothesis, this true difference is 0
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.
If we were to look this up on a normal table, we would find a very low p-value \( (p < .001) \)

This method is also essentially equivalent to the chi-square \( (\chi^2) \) method
  - Gives about the same answer \( (p\text{-value}) \)
  - This is how Stata approaches it
  - We will discuss chi-square method in more detail shortly: for now, just “take on faith” that it is equivalent so we can show you how to get the p-value, 95% CI \( (\text{etc.}) \) using Stata
To Do in Stata: Display Data in a 2x2 Table

- Stata “thinks” of data in a 2x2 (contingency) table
- Two rows and two columns

<table>
<thead>
<tr>
<th>HIV Transmission</th>
<th>Drug Group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>AZT</td>
</tr>
<tr>
<td>Yes</td>
<td>13</td>
</tr>
<tr>
<td>No</td>
<td>167</td>
</tr>
</tbody>
</table>

Total: 180 (AZT) + 183 (Placebo) = 363
We can get Stata to give us a 95% CI for the difference in proportions, and a p-value by using the csi command.

Syntax `csi a b c d`

Based on a 2x2 table using our sample results as such:

<table>
<thead>
<tr>
<th>Exposure</th>
<th>Outcome</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>Yes</td>
<td>a</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>b</td>
</tr>
<tr>
<td>No</td>
<td>Yes</td>
<td>c</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>d</td>
</tr>
</tbody>
</table>
Using Stata: AZT/HIV Example

- `csi 13 40 167 143`

<table>
<thead>
<tr>
<th>HIV Transmission</th>
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<th></th>
<th></th>
<th></th>
</tr>
</thead>
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<td></td>
</tr>
<tr>
<td></td>
<td>180</td>
<td>183</td>
<td>363</td>
<td></td>
</tr>
</tbody>
</table>
## Using Stata: AZT/HIV Example

### Results from `csi` command

```
csi 13 40 167 143
```

<table>
<thead>
<tr>
<th></th>
<th>Exposed</th>
<th>Unexposed</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases</td>
<td>13</td>
<td>40</td>
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</tr>
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</tr>
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<td>363</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Risk</th>
<th>.0722222</th>
<th>.2185792</th>
<th>.1460055</th>
</tr>
</thead>
<tbody>
<tr>
<td>Point estimate</td>
<td>[95% Conf. Interval]</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| 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
```
### Results from `csi` command

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csi 13 40 167 143
```

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| Risk   | .0722222 | .2185792 | .1460055 |

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</tr>
<tr>
<td>Risk ratio</td>
<td>.3304167</td>
</tr>
<tr>
<td>Prev. frac. ex.</td>
<td>.6695833</td>
</tr>
<tr>
<td>Prev. frac. pop</td>
<td>.3320248</td>
</tr>
</tbody>
</table>

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


### Results from `csi` command

```stata
. csi 13 40 167 143
```

<table>
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<td>167</td>
<td>143</td>
<td>310</td>
</tr>
</tbody>
</table>

<p>| | | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>180</td>
<td>183</td>
<td>363</td>
</tr>
<tr>
<td>Risk</td>
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</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
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</tr>
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<tbody>
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<td>- .146357</td>
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<tr>
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<td>.6695833</td>
</tr>
<tr>
<td>Prev. frac. pop</td>
<td>.3320248</td>
</tr>
</tbody>
</table>

chi²(1) = 15.59  Pr>chi² = 0.0001
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”
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.
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)
Results

The study results estimate the decrease in the proportion of HIV positive infants born to HIV positive mothers associated with AZT to be as low as 8% and as high as 22%
Section C

The Chi-Square Test: Mechanics
Hypothesis Testing Problem

- Testing equality of two population proportions using data from two samples
  - $H_0: p_1 = p_2$      $H_0: p_1 - p_2 = 0$
  - $H_a: p_1 \neq p_2$    $H_A: p_1 - p_2 \neq 0$

- In the context of the 2x2 table, this is testing whether there is a relationship between the rows (HIV status) and columns (treatment type)
(Pearson’s) Chi-Square Test ($\chi^2$)
- Calculation is easy (can be done by hand)

Works well for “big” sample sizes

Gives (essentially) the same p-value as z-test for comparing two proportions

Unlike z-test, can be extended to compare proportions between more than two independent groups in one test
The Chi-Square Approximate Method

- Looks at discrepancies between observed and expected cell counts in a 2x2 table
  - \( O = \text{observed} \)
  - \( E = \text{expected} = \frac{\text{row total} \times \text{column total}}{\text{grand total}} \)

- Expected refers to the values for the cell counts that would be expected if the null hypothesis is true
  - The expected cell proportions if the underlying population proportions are equal
Recall, general “recipe” for hypothesis testing . . .

1. Start by assuming $H_0$ true
2. Measure distance of sample result from $H_0$
3. Compare test statistic (distance) to appropriate distribution to get p-value

$$
\chi^2 = \sum_{4 \text{ cells}} \frac{(0 - E)^2}{E}
$$
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
Chi-Square with One Degree of Freedom
Display Data in a 2x2 Table

- 2x2 table setup

<table>
<thead>
<tr>
<th>HIV Transmission</th>
<th>Drug Group</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>AZT</td>
<td>Placebo</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>13</td>
<td>40</td>
<td>53</td>
</tr>
<tr>
<td>No</td>
<td>167</td>
<td>143</td>
<td>310</td>
</tr>
</tbody>
</table>

- The observed value for cell one is 13

- Let’s calculate its expected value
Display Data in a 2x2 Table

- Expected value computation: \( \frac{\text{row total} \times \text{column total}}{\text{grand total}} \)

<table>
<thead>
<tr>
<th>HIV Transmission</th>
<th>Drug Group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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<tr>
<td>Yes</td>
<td>13</td>
</tr>
<tr>
<td>No</td>
<td>167</td>
</tr>
<tr>
<td></td>
<td>180</td>
</tr>
</tbody>
</table>

\[
\frac{53 \times 180}{363} = 26.3
\]
We could do the same for the other three cells; the below table has expected counts.

<table>
<thead>
<tr>
<th>HIV Transmission</th>
<th>Drug Group</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>AZT</td>
<td>26.3</td>
<td>153.7</td>
<td>180</td>
</tr>
<tr>
<td></td>
<td>Placebo</td>
<td>26.7</td>
<td>156.3</td>
<td>183</td>
</tr>
<tr>
<td>Yes</td>
<td></td>
<td></td>
<td></td>
<td>53</td>
</tr>
<tr>
<td>No</td>
<td></td>
<td>310</td>
<td></td>
<td>363</td>
</tr>
</tbody>
</table>
Example of Calculations: Chi-Square

- Test statistic (“distance”)

\[ \chi^2 = \sum_{4 \text{ cells}} \frac{(O - E)^2}{E} \]

- In our example

\[ \chi^2 = 15.6 \]
Sampling Dist’n: Chi-Square w/1 Degree of Freedom
Using Stata: AZT/HIV Example

- Results from csi command

```
. csi 13 40 167 143

<table>
<thead>
<tr>
<th></th>
<th>Exposed</th>
<th>Unexposed</th>
<th>Total</th>
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</thead>
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<td>183</td>
<td>363</td>
</tr>
<tr>
<td>Risk</td>
<td>0.0722222</td>
<td>0.2185792</td>
<td>0.1460055</td>
</tr>
<tr>
<td></td>
<td>Point estimate</td>
<td>[95% Conf. Interval]</td>
<td></td>
</tr>
<tr>
<td>Risk difference</td>
<td>-0.146357</td>
<td>-0.2171766</td>
<td>-0.0755374</td>
</tr>
<tr>
<td>Risk ratio</td>
<td>0.3304167</td>
<td>0.1829884</td>
<td>0.5966235</td>
</tr>
<tr>
<td>Prev. frac. ex.</td>
<td>0.6695833</td>
<td>0.4033765</td>
<td>0.8170116</td>
</tr>
<tr>
<td>Prev. frac. pop</td>
<td>0.3320248</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
```

\[\text{chisq}(1) = 15.59 \quad \text{Pr}>\text{chisq} = 0.0001\]
Comparing Proportions between Two Populations

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

\[ \hat{p}_1 - \hat{p}_2 \pm 2 \times SE(\hat{p}_1 - \hat{p}_2) \]

- To get a p-value for testing:
  - \( H_0: p_1 = p_2 \) \( H_0: p_1 - p_2 = 0 \)
  - \( H_a: p_1 \neq p_2 \) \( H_A: p_1 - p_2 \neq 0 \)

- Two sample z-test or chi-squared test (give same p-value)
Extendibility of Chi-Squared

- Chi-squared test can be extended to test for differences in proportions across more than two independent populations
  - Analogue to ANOVA with binary outcomes
Extendibility of Chi-Squared

Example: health care indicators by immigrant status*

<table>
<thead>
<tr>
<th>TABLE 2—Health Status, Health Care Access, and Health Care Use, by Immigrant Status: National Survey of America’s Families, 1999</th>
</tr>
</thead>
<tbody>
<tr>
<td>Citizenship</td>
</tr>
<tr>
<td>US Born</td>
</tr>
<tr>
<td>Citizen Parents</td>
</tr>
<tr>
<td>Health and well-being</td>
</tr>
<tr>
<td>Fair/poor current health status</td>
</tr>
<tr>
<td>Negative behavior at ages 6–11 y</td>
</tr>
<tr>
<td>Negative behavior at ages 12–17 y</td>
</tr>
<tr>
<td>No involvement in activities at ages 6–17 y</td>
</tr>
<tr>
<td>Health insurance covaries and health care use and access</td>
</tr>
<tr>
<td>Lack of medical insurance at any time in past 12 mo</td>
</tr>
<tr>
<td>No usual source of care other than ER</td>
</tr>
<tr>
<td>At least one doctor visit in past year</td>
</tr>
<tr>
<td>ER visit in past year</td>
</tr>
<tr>
<td>At least one visit to dentist in past year (≥3 y old)</td>
</tr>
<tr>
<td>Visit to mental health specialist in past year (≥3 y old)</td>
</tr>
<tr>
<td>Subset of items targeted specifically to families with incomes at or below 200% of FPL</td>
</tr>
<tr>
<td>Lack of medical insurance at any time in past 12 mo</td>
</tr>
<tr>
<td>Current Medicaid/SCHIP/state coverage</td>
</tr>
<tr>
<td>Aware of separate SCHIP program</td>
</tr>
<tr>
<td>Aware of Medicaid program</td>
</tr>
</tbody>
</table>

Note: ER = emergency room; FPL = federal poverty level; SCHIP = State Child Health Insurance Program. All χ² P values were less than .05.

Extendibility of Chi-Squared

- Zoom in

<table>
<thead>
<tr>
<th>Table 2—Health Status, Health Care Access, and Health Care Use, by Immigrant Status: National Survey of America’s Families, 1999</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td>US Born, % (SE)</td>
</tr>
<tr>
<td>Citizen Parents</td>
</tr>
<tr>
<td>------------------</td>
</tr>
<tr>
<td>Lack of medical insurance at any time in past 12 mo</td>
</tr>
<tr>
<td>No usual source of care other than ER</td>
</tr>
<tr>
<td>At least one doctor visit in past year</td>
</tr>
<tr>
<td>ER visit in past year</td>
</tr>
<tr>
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</tr>
<tr>
<td>Visit to mental health specialist in past year (≥3 y old)</td>
</tr>
</tbody>
</table>

Note. ER = emergency room; FPL = federal poverty level; SCHIP = State Child Health Insurance Program. All \( \chi^2 \) Ps were less than .05.
## Extendibility of Chi-Squared

- **Zoom in**

### TABLE 2—Health Status, Health Care Access, and Health Care Use, by Immigrant Status:
National Survey of America’s Families, 1999

<table>
<thead>
<tr>
<th></th>
<th>US Born, % (SE)</th>
<th>Foreign Born, % (SE)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Citizen Parents</td>
<td>Noncitizen Parents</td>
</tr>
<tr>
<td>Lack of medical insurance at any time in past 12 mo</td>
<td>15.34 (0.55)</td>
<td>34.37 (2.62)</td>
</tr>
<tr>
<td>No usual source of care other than ER</td>
<td>5.78 (0.27)</td>
<td>18.21 (1.93)</td>
</tr>
<tr>
<td>At least one doctor visit in past year</td>
<td>77.03 (0.54)</td>
<td>65.43 (2.28)</td>
</tr>
<tr>
<td>ER visit in past year</td>
<td>25.43 (0.47)</td>
<td>23.47 (1.96)</td>
</tr>
<tr>
<td>At least one visit to dentist in past year (≥3 y old)</td>
<td>80.47 (0.44)</td>
<td>62.73 (2.81)</td>
</tr>
<tr>
<td>Visit to mental health specialist in past year (≥3 y old)</td>
<td>7.17 (0.32)</td>
<td>2.83 (0.89)</td>
</tr>
</tbody>
</table>

*Note. ER = emergency room; FPL = federal poverty level; SCHIP = State Child Health Insurance Program. All χ² Ps were less than .05.*
## Extendibility of Chi-Squared

- Zoom in

### TABLE 2—Health Status, Health Care Access, and Health Care Use, by Immigrant Status:
National Survey of America’s Families, 1999

<table>
<thead>
<tr>
<th></th>
<th>US Born, % (SE)</th>
<th>Foreign Born, % (SE)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Citizen Parents</td>
<td>Noncitizen Parents</td>
</tr>
<tr>
<td>Lack of medical insurance at any time in past 12 mo</td>
<td>15.34 (0.55)</td>
<td>34.37 (2.62)</td>
</tr>
<tr>
<td>No usual source of care other than ER</td>
<td>5.78 (0.27)</td>
<td>18.21 (1.93)</td>
</tr>
<tr>
<td>At least one doctor visit in past year</td>
<td>77.03 (0.54)</td>
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<td>25.43 (0.47)</td>
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</tr>
<tr>
<td>At least one visit to dentist in past year (≥3 y old)</td>
<td>80.47 (0.44)</td>
<td>62.73 (2.81)</td>
</tr>
<tr>
<td>Visit to mental health specialist in past year (≥3 y old)</td>
<td>7.17 (0.32)</td>
<td>2.83 (0.89)</td>
</tr>
<tr>
<td></td>
<td>Citizen (Naturalized)</td>
<td>Noncitizen</td>
</tr>
<tr>
<td></td>
<td>12.86 (3.68)</td>
<td>52.3 (2.77)</td>
</tr>
<tr>
<td></td>
<td>12.19 (4.18)</td>
<td>27.93 (2.63)</td>
</tr>
<tr>
<td></td>
<td>77.04 (5.36)</td>
<td>51.75 (2.48)</td>
</tr>
<tr>
<td></td>
<td>11.59 (3.62)</td>
<td>12.45 (1.72)</td>
</tr>
<tr>
<td></td>
<td>84.65 (3.42)</td>
<td>55.59 (2.81)</td>
</tr>
<tr>
<td></td>
<td>5.55 (1.86)</td>
<td>1.77 (0.46)</td>
</tr>
</tbody>
</table>

Note. ER = emergency room; FPL = federal poverty level; SCHIP = State Child Health Insurance Program. All $\chi^2$ Ps were less than .05.
Section D

More Examples of Comparing Two Proportions
Example: GI Outbreak in Maryland

- Outbreak of Gastroenteritis in Maryland high school
- Sample of 263 students who bought lunch on single day: some ate sandwiches, others ate other meals

<table>
<thead>
<tr>
<th>Ate Sandwich</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sick Yes</td>
<td>109</td>
<td>4</td>
</tr>
<tr>
<td>Sick No</td>
<td>116</td>
<td>34</td>
</tr>
<tr>
<td></td>
<td>225</td>
<td>38</td>
</tr>
</tbody>
</table>
Example: GI Outbreak in Maryland

- Sample proportions and 95% CIs of proportions with illness for sandwich and non-sandwich group (Stata)

```
. cii 225 109

<table>
<thead>
<tr>
<th>Variable</th>
<th>Obs</th>
<th>Mean</th>
<th>Std. Err.</th>
<th>[95% Conf. Interval]</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>225</td>
<td>.4844444</td>
<td>.0333172</td>
<td>.4175076 .5517965</td>
</tr>
</tbody>
</table>

. cii 38 4

<table>
<thead>
<tr>
<th>Variable</th>
<th>Obs</th>
<th>Mean</th>
<th>Std. Err.</th>
<th>[95% Conf. Interval]</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>38</td>
<td>.1052632</td>
<td>.0497845</td>
<td>.0294345 .2480494</td>
</tr>
</tbody>
</table>
```
Example: GI Outbreak in Maryland

- Results from comparison of proportions

```
csi 109 4 116 34

<table>
<thead>
<tr>
<th></th>
<th>Exposed</th>
<th>Unexposed</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases</td>
<td>109</td>
<td>4</td>
<td>113</td>
</tr>
<tr>
<td>Noncases</td>
<td>116</td>
<td>34</td>
<td>150</td>
</tr>
<tr>
<td>Total</td>
<td>225</td>
<td>38</td>
<td>263</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>.4844444</th>
<th>.1052632</th>
<th>.4296578</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk</td>
<td>Point estimate</td>
<td>[95% Conf. Interval]</td>
<td></td>
</tr>
</tbody>
</table>

| Risk difference | .3791813 | .2617709 | .4965917 |
| Risk ratio     | 4.602222 | 1.803663 | 11.74302 |
| Attr. frac. ex. | .7827137 | .4455728 | .914843 |
| Attr. frac. pop | .755007  |          |          |
```

```
chi2 (1) = 19.07  Pr>chi2 = 0.0000
```
Insurance Status, Dialysis Patients by Country

- Proportion of dialysis patients with national insurance in 12 countries (only six shown)

EXHIBIT 1
Descriptive Measures Of The Prevalent Cross-Sectional Patient Sample, Dialysis Patients In Twelve Countries, 2002–2004

<table>
<thead>
<tr>
<th></th>
<th>A/NZ (n = 561)</th>
<th>BEL (n = 468)</th>
<th>CAN (n = 503)</th>
<th>FRA (n = 481)</th>
<th>GER (n = 524)</th>
<th>ITA (n = 540)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mean age (years)</strong></td>
<td>59.9 (14.7)</td>
<td>66.2 (13.4)</td>
<td>62.1 (14.7)</td>
<td>64.1 (14.5)</td>
<td>61.7 (14.1)</td>
<td>64 (13.7)</td>
</tr>
<tr>
<td><strong>Minoritya</strong></td>
<td>21.5%</td>
<td>5.3%</td>
<td>18.7%</td>
<td>7.1%</td>
<td>0.4%</td>
<td>0.4%</td>
</tr>
<tr>
<td><strong>Income ($US)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;$20,000</td>
<td>85.0%</td>
<td>73.4%</td>
<td>71.8%</td>
<td>67.0%</td>
<td>59.7%</td>
<td>78.3%</td>
</tr>
<tr>
<td>$20,000–$39,000</td>
<td>9.1%</td>
<td>17.5%</td>
<td>20.8%</td>
<td>21.8%</td>
<td>27.1%</td>
<td>17.4%</td>
</tr>
<tr>
<td>≥$40,000</td>
<td>5.9%</td>
<td>9.1%</td>
<td>7.4%</td>
<td>11.2%</td>
<td>13.1%</td>
<td>4.2%</td>
</tr>
<tr>
<td><strong>Insurance type</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>National only</td>
<td>69.8%</td>
<td>74.1%</td>
<td>79.6%</td>
<td>45.5%</td>
<td>95.4%</td>
<td>99.6%</td>
</tr>
<tr>
<td>Private only</td>
<td>5.4%</td>
<td>0.4%</td>
<td>0.2%</td>
<td>0.2%</td>
<td>2.9%</td>
<td>0.0%</td>
</tr>
<tr>
<td><strong>Mean number of comorbid conditionsb</strong></td>
<td>3.7 (2)</td>
<td>3.9 (2.1)</td>
<td>4.1 (2.1)</td>
<td>3.1 (1.9)</td>
<td>3.4 (2.1)</td>
<td>2.7 (1.9)</td>
</tr>
<tr>
<td><strong>Mean number of prescribed medications</strong></td>
<td>8.7 (3.6)</td>
<td>9.9 (4.1)</td>
<td>12.6 (4.8)</td>
<td>7.7 (3.5)</td>
<td>9.7 (3.5)</td>
<td>6.4 (3.6)</td>
</tr>
</tbody>
</table>
Insurance Status, Dialysis Patients by Country

- Observed proportions and 95% CI for Canada and France, respectively
  - Canada

  . cii 503 361

<table>
<thead>
<tr>
<th>Variable</th>
<th>Obs</th>
<th>Mean</th>
<th>Std. Err.</th>
<th>95% Conf. Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>503</td>
<td>0.7176938</td>
<td>0.0200699</td>
<td>0.6761616 - 0.7566455</td>
</tr>
</tbody>
</table>

- France

  . cii 481 219

<table>
<thead>
<tr>
<th>Variable</th>
<th>Obs</th>
<th>Mean</th>
<th>Std. Err.</th>
<th>95% Conf. Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>481</td>
<td>0.4553015</td>
<td>0.0227068</td>
<td>0.4101514 - 0.5010042</td>
</tr>
</tbody>
</table>
## Insurance Status, Dialysis Patients by Country

- **2x2 table setup**

<table>
<thead>
<tr>
<th>Insurance</th>
<th>CAN</th>
<th>FR</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>361</td>
<td>219</td>
<td>503</td>
</tr>
<tr>
<td>No</td>
<td>142</td>
<td>262</td>
<td>481</td>
</tr>
<tr>
<td>Total</td>
<td>503</td>
<td>481</td>
<td>984</td>
</tr>
</tbody>
</table>
Insurance Status, Dialysis Patients by Country

- Comparison of proportions

```
.csi 361 219 142 262
```

<table>
<thead>
<tr>
<th></th>
<th>Exposed</th>
<th>Unexposed</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases</td>
<td>361</td>
<td>219</td>
<td>580</td>
</tr>
<tr>
<td>Noncases</td>
<td>142</td>
<td>262</td>
<td>404</td>
</tr>
<tr>
<td>Total</td>
<td>503</td>
<td>481</td>
<td>984</td>
</tr>
</tbody>
</table>

```
Risk  .7176938  .4553015  .5894309

Point estimate [95% Conf. Interval]
```

| Risk difference | .2623924 | .2029955 | .3217893 |
| Risk ratio     | 1.576305 | 1.409195 | 1.763232 |
| Attr. frac. ex. | .3656049 | .2903748 | .4328596 |
| Attr. frac. pop | .2275575 |          |         |

```
chi2 (1) = 69.95  Pr>chi2 = 0.0000
```
Section E

Fisher’s Exact Test
Recall: HIV Transmission/AZT Example

- Recall 2X2 (contingency) table

<table>
<thead>
<tr>
<th>HIV Transmission</th>
<th>Drug Group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>AZT</td>
</tr>
<tr>
<td>Yes</td>
<td>13</td>
</tr>
<tr>
<td>No</td>
<td>167</td>
</tr>
<tr>
<td></td>
<td>180</td>
</tr>
</tbody>
</table>
Hypothesis Testing Problem: AZT and HIV Transmission

- Testing equality of two population proportions using data from two samples
  - $H_0: p_1 = p_2$  $H_0: p_1 - p_2 = 0$
  - $H_a: p_1 \neq p_2$  $H_A: p_1 - p_2 \neq 0$

- 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 ($\chi^2$)/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
- 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
Fisher’s Exact Test: HIV Transmission/AZT

- Rationale
  - Suppose $H_0$ is true—no association between AZT and maternal/infant HIV transmission
  - Imagine putting 53 red balls (the infected) and 310 blue balls (non-infected) in a jar
  - Shake it up
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

- 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
  - The p-value is the probability of obtaining a result as or more extreme (more imbalance) than you did by chance alone
Using Stata: AZT/HIV Example

- Results from `csi` command, with *exact* option

```
.csi 13 40 167 143, exact
```

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

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

Notes: *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.
### Results

<table>
<thead>
<tr>
<th>Hypertension</th>
<th>Aspirin</th>
<th>Placebo</th>
<th>Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>4</td>
<td>11</td>
<td>15</td>
</tr>
<tr>
<td>No</td>
<td>30</td>
<td>20</td>
<td>50</td>
</tr>
<tr>
<td></td>
<td>34</td>
<td>31</td>
<td>65</td>
</tr>
</tbody>
</table>
Display Data in a 2x2 Table

- Sample proportion of subjects with hypertension

\[
\hat{p}_{\text{aspirin}} = \frac{4}{34} = .12
\]

\[
\hat{p}_{\text{placebo}} = \frac{11}{31} = .35
\]
In this example . . . (just FYI)

\[ n_{\text{aspirin}} \cdot \hat{P}_{\text{aspirin}} \cdot (1 - \hat{P}_{\text{aspirin}}) = 34 \times 0.12 \times 0.88 = 3.6 \]

\[ n_{\text{placebo}} \cdot \hat{P}_{\text{placebo}} \cdot (1 - \hat{P}_{\text{placebo}}) = 31 \times 0.35 \times 0.65 = 7.1 \]
Fishers Exact

- Results from `csi` command, with *exact* option

```
csi 4 11 30 20, exact
```

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

1-sided Fisher's exact P = 0.0236
2-sided Fisher's exact P = 0.0378
### Chi Square

- Results from `csi` command, without *exact* option

```
csi 4 11 30 20
```

<table>
<thead>
<tr>
<th></th>
<th>Exposed</th>
<th>Unexposed</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases</td>
<td>4</td>
<td>11</td>
<td>15</td>
</tr>
<tr>
<td>Noncases</td>
<td>30</td>
<td>20</td>
<td>50</td>
</tr>
<tr>
<td>Total</td>
<td>34</td>
<td>31</td>
<td>65</td>
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</table>

| Risk          | .1176471 | .3548387 | .2307692 |

<table>
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<tr>
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<th>Point estimate</th>
<th>[95% Conf. Interval]</th>
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<tbody>
<tr>
<td>Risk difference</td>
<td>-.2371917</td>
<td>-.4374335  -.0369498</td>
</tr>
<tr>
<td>Risk ratio</td>
<td>.3315508</td>
<td>.1176925  .9340096</td>
</tr>
<tr>
<td>Prev. frac. ex.</td>
<td>.6684492</td>
<td>.0659904  .8823075</td>
</tr>
<tr>
<td>Prev. frac. pop</td>
<td>.3496503</td>
<td></td>
</tr>
</tbody>
</table>

```
chi2(1) = 5.14 Pr>chi2 = 0.0234
```
### Fishers Exact

- **95% CI:** not quite correct in smaller samples, but “good enough”

```
csi 4 11 30 20, exact
```

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<td>65</td>
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- **Risk:**
  - .1176471
  - .3548387
  - .2307692

- **Point estimate:**
  - [95% Conf. Interval]

<table>
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<td>.3496503</td>
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</table>

1-sided Fisher's exact P = 0.0236
2-sided Fisher's exact P = 0.0378
Comparing Proportions between Independent Populations

- To get a p-value for testing:
  - $H_0: p_1 = p_2$
  - $H_A: p_1 = p_2$

- Two sample z-test or chi-squared test (give same p-value): work better in “bigger” samples and will match results of Fishers Exact Test

- Fisher’s exact test: always appropriate
To create a 95% confidence interval for the difference in two proportions:

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

- Fine for “bigger samples,” can be used as a “guideline” in smaller samples

- Not quite correct in “smaller samples” but will give you a good sense of width/range of CI
Section F

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

- Risk difference (attributable risk)—difference in proportions
  - Sample (estimated) risk difference
    \[ \hat{p}_1 - \hat{p}_2 \]
  - Example: the difference in risk of HIV for children born to HIV+ mothers taking AZT relative to HIV+ mothers taking placebo
    \[ \hat{p}_1 - \hat{p}_2 = .07 - .22 = -.15 \]
Risk Difference

- From *csi* command, with 95% CI

```
.  csi 13 40 167 143
```

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<tr>
<th></th>
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<th>Unexposed</th>
<th>Total</th>
</tr>
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<tbody>
<tr>
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<td>40</td>
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<tr>
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<td>167</td>
<td>143</td>
<td>310</td>
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<tr>
<td>Total</td>
<td>180</td>
<td>183</td>
<td>363</td>
</tr>
<tr>
<td>Risk</td>
<td>.0722222</td>
<td>.2185792</td>
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<td>.8170116</td>
</tr>
<tr>
<td>Prev. frac. pop</td>
<td>.3320248</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

```

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

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

- Interpretation 95% CI
  - 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

\[ R\hat{R} = \frac{\hat{p}_1}{\hat{p}_2} \]

- Ex: 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
Risk Ratio (Relative Risk)

- From *csi* command, with 95% CI

```
csi 13 40 167 143
```

<table>
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</table>

\[ \text{chi}^2(1) = 15.59 \quad \text{Pr}>\text{chi}^2 = 0.0001 \]
Relative Risk

- **Interpretation: sample estimate**
  - 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.

- **Interpretation: 95% CI**
  - 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
  - That is, RR of transmission for placebo compared to AZT group

\[
\frac{\hat{p}_2}{\hat{p}_1} = \frac{.22}{.07} = 3.1
\]
Risk Difference

- From *csi* command, with 95% CI

```
csi 40 13 143 167
```

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Risk

|               | .2185792 | .0722222 | .1460055 |

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```

\[
\text{chi2}(1) = 15.59 \quad \text{Pr}>\text{chi2} = 0.0001
\]
Relative Risk

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

- **Interpretation: 95% CI**
  - 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 it is interpreted correctly!
Hypothesis of Equal Proportions Expressed by RR

- Equivalent hypotheses sets

  - $H_0: p_1 = p_2$  \quad $H_0: p_1 - p_2 = 0$  \quad $H_0: \frac{p_1}{p_2} = 1$

  - $H_a: p_1 \neq p_2$  \quad $H_A: p_1 - p_2 \neq 0$  \quad $H_A: \frac{p_1}{p_2} \neq 1$
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

- Each provides a different piece of information about the “story”
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%
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%
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: 0.83
What Is an Odds?

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

- The odds ratio is a function of risk (prevalence).

- Odds is the ratio of the risk of having an outcome to the risk of not having an outcome.
  - If $p$ represents the risk of an outcome, then the odds are given by:

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

- In the AZT example, the estimated risk of giving birth to an HIV infected child among mothers treated with AZT was $\hat{p}_1 = .07$

- The corresponding odds estimate is

\[ \text{Odds} = \frac{\hat{p}_1}{1 - \hat{p}_1} = \frac{.07}{1 - .07} = \frac{.07}{.93} \approx .08 \]
Example

- In the AZT example, the estimated risk of giving birth to an HIV infected child among mothers not treated (on the placebo) was \( \hat{p}_2 = 0.22 \).

- The corresponding odds estimate is as follows:

\[
\text{Odds} = \frac{\hat{p}_2}{1 - \hat{p}_2} = \frac{0.22}{1 - 0.22} = \frac{0.22}{0.78} \approx 0.28
\]
The estimated odds ratio of an HIV birth with AZT relative to placebo

\[ \hat{OR} = \frac{\hat{p}_1}{1 - \hat{p}_1} \times \frac{1 - \hat{p}_2}{\hat{p}_2} = \frac{.08}{.28} \approx .28 \]

The odds of HIV transmission with AZT is .28 (about 1/3) the odds of transmission with placebo.
Odds Ratio with Stata

- From `csi` command, with `or` option

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

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<tr>
<td>Odds ratio</td>
<td>.2782934</td>
<td>.1445784</td>
<td>.5363045 (Cornfield)</td>
</tr>
</tbody>
</table>

\[ \text{chi}^2(1) = 15.59 \quad \text{Pr}>\chi^2 = 0.0001 \]
Odds Ratio

- Interpretation
  - AZT is associated with an estimated 72% (estimated OR = .28) 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).
Odds Ratio

- What about a p-value?

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

$$OR = \frac{\frac{p_1}{1 - p_1}}{\frac{p_2}{1 - p_2}} = 1$$
Hence we need to test

- $H_0$: OR = 1
- $H_A$: OR $\neq$ 1
- But, from previous slide OR = 1 only if $p_1 = p_2$
- So the same test from before applies!
Odds Ratio with Stata

- From `csi` command, with `or` option

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<p>| | | | |</p>
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Chi2(1) = 15.59  Prch2 = 0.0001
Hypothesis of Equal Proportions Expressed by RR

- Equivalent hypotheses sets
  - $H_0: p_1 = p_2$  $H_0: p_1 - p_2 = 0$  $H_o: \frac{p_1}{p_2} = 1$  $H_o: \frac{p_1 \times (1 - p_1)}{p_2 \times (1 - p_2)} = 1$

  - $H_a: p_1 \neq p_2$  $H_A: p_1 - p_2 \neq 0$  $H_A: \frac{p_1}{p_2} \neq 1$  $H_A: \frac{p_1 \times (1 - p_1)}{p_2 \times (1 - p_2)} \neq 1$
How Does OR Compare to RR?

- Always will estimate the same direction of association

\[
\hat{OR} < 1 \iff \hat{RR} < 1 \\
\hat{OR} > 1 \iff \hat{RR} > 1 \\
\hat{OR} = 1 \iff \hat{RR} = 1
\]
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

\[
\begin{align*}
OR < 1 & \iff RR < 1 \\
OR > 1 & \iff RR > 1 \\
OR = 1 & \iff RR = 1
\end{align*}
\]
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.
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
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
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 interpretable” 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
Section G

FYI: Sampling Behavior of Relative Risks/Odds Ratios
The sampling behavior of ratios (like the RR, OR) can be quite skewed
- The range of possible values for “positive” and “negative” associations are very different
The sampling behavior of ratios (like the RR, OR) can be quite skewed.
- The range of possible values for “negative” associations
The sampling behavior of ratios (like the RR, OR) can be quite skewed.
- The range of possible values for “positive” associations.
The ranges are equal on the ln(Ratio) scale
Sampling Behavior of Ratios is Not Normal

- The ranges are equal on the ln(Ratio) scale
### Sampling Behavior of Ratios is Not Normal

- Recall standard 2x2 table setup

<table>
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<th>Exposure</th>
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</tr>
<tr>
<td>No</td>
<td>c</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>Yes</td>
<td>b</td>
</tr>
<tr>
<td>No</td>
<td>d</td>
</tr>
</tbody>
</table>
Estimating CI for RR by Hand

- **ln ratios and standard errors**

\[
ln(\hat{RR}) = ln\left(\frac{\hat{p}_1}{\hat{p}_2}\right)
\]

- **Standard error, using counts from 2x2 table**

\[
SE(ln(\hat{RR})) = \sqrt{\frac{c}{a \times n_1} + \frac{d}{b \times n_2}}
\]

- **95% CI for \(ln(RR)\)**

\[
ln(\hat{RR}) \pm 2 \times SE(ln(\hat{RR}))
\]

- **To get 95% CI for RR, exponentiate endpoints of above**
## HIV/AIDS Example

- HIV/mother-infant transmission example

<table>
<thead>
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<th>Drug Group</th>
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<th></th>
<th></th>
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<td>167</td>
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<tr>
<td>Yes</td>
<td>Placebo</td>
<td>40</td>
<td>143</td>
<td>183</td>
</tr>
<tr>
<td>No</td>
<td></td>
<td></td>
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<td>363</td>
</tr>
</tbody>
</table>
Sampling Behavior of Ratios Is Not Normal

- ln ratios and standard errors
  
  \[ \ln(R\hat{R}) = \ln\left( \frac{\hat{p}_{AZT}}{\hat{p}_{Placebo}} \right) = \ln\left( \frac{0.07}{0.22} \right) = \ln(0.33) = -1.11 \]

- Standard error, using counts from 2x2 table
  
  \[ \hat{SE}(\ln(R\hat{R})) = \sqrt{\frac{167}{13 \times 180} + \frac{143}{40 \times 183}} \approx 0.30 \]

- 95% CI for \( \ln(RR) \)
  
  \[ -1.11 \pm 2 \times 0.30 \rightarrow (-1.71, -0.51) \]

- To get 95% CI for RR, exponentiate endpoints of above
  
  \[ (e^{-1.71}, e^{-0.51}) \approx (0.18, 0.60) \]
### HIV/AZT Example

- **95% CI from Stata**

  . csi 13 40 167 143, or

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  **Prev. frac. ex.** | .6695833 | .4033765 | .8170116
  **Prev. frac. pop** | .3320248 |        |        |
  **Odds ratio** | .2782934 | .1445784 | .5363045 (Cornfield)

  \[ \text{chi}^2(1) = 15.59 \quad \text{Pr}>\text{chi}^2 = 0.0001 \]
Sampling Behavior of Ratios Is Not Normal

- **ln ratios and standard errors**

\[
\ln(\hat{OR}) = \ln\left(\frac{\hat{p}_1/(1 - \hat{p}_1)}{\hat{p}_2/(1 - \hat{p}_2)}\right)
\]

- **Standard error, using counts from 2x2 table**

\[
SE(\ln(\hat{OR})) = \sqrt{\frac{1}{a} + \frac{1}{b} + \frac{1}{c} + \frac{1}{d}}
\]

- **95% CI for \( \ln(\hat{OR}) \)**

\[
\ln(\hat{OR}) \pm 2 \times SE(\ln(\hat{OR}))
\]

- **To get 95% CI for OR, exponentiate endpoints of above**
Sampling Behavior of Ratios is Not Normal

- HIV/AZT transmission example

\[ \ln(\hat{OR}) = \ln\left(\frac{0.07/0.93}{0.22/0.78}\right) \approx \ln(0.28) = -1.27 \]

- Standard error, using counts from 2x2 table

\[ \text{SE}(\ln(\hat{OR})) = \sqrt{\frac{1}{13} + \frac{1}{40} + \frac{1}{167} + \frac{1}{143}} \approx 0.34 \]

- 95% CI for \( \ln(\hat{OR}) \)

\[-1.27 \pm 2 \times 0.34 \rightarrow (-1.96, -0.60)\]

- To get 95% CI for OR, exponentiate endpoints of above

\[ (e^{-1.96}, e^{-0.60}) \approx (0.14, 0.55) \]
HIV/AZT Example

- 95% CI from Stata

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

<table>
<thead>
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<th></th>
<th>Exposed</th>
<th>Unexposed</th>
<th>Total</th>
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<td>40</td>
<td>53</td>
</tr>
<tr>
<td>Noncases</td>
<td>167</td>
<td>143</td>
<td>310</td>
</tr>
<tr>
<td>Total</td>
<td>180</td>
<td>183</td>
<td>363</td>
</tr>
</tbody>
</table>

| Risk        | .0722222 | .2185792  | .1460055 |

| 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`