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SCHOOL of PUBLIC HEALTH

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

                 |   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
```

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

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

- 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

                 |   Exposed   Unexposed  |      Total
-----------------+------------------------+----------
           Cases |          40          13  |         53
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-----------------+------------------------+----------
           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
```

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_o: $p_1 = p_2$ H_o: $p_1 - p_2 = 0$ $H_o : \frac{p_1}{p_2} = 1$
  - H_a: $p_1 \neq p_2$ H_A: $p_1 - p_2 \neq 0$ $H_A : \frac{p_1}{p_2} \neq 1$

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: .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

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

Example

- In the AZT example, the estimated 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 as follows:

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

AZT/Mother-Infant Transmission Example

- The estimated odds ratio of an HIV birth with AZT relative to placebo

$$\hat{OR} = \frac{\hat{p}_1 / 1 - \hat{p}_1}{\hat{p}_2 / 1 - \hat{p}_2} = \frac{.08}{.28} \approx .28$$

  - 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

                 |   Exposed   Unexposed  |     Total
-----------------+------------------------+----------
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 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 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

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

Odds Ratio

- Hence we need to test
  - H_o: OR = 1
  - H_A: OR ≠ 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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Hypothesis of Equal Proportions Expressed by RR

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

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

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

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

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

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