JOHNS HOPKINS
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Section D

Another Non-Randomized Study Design: The Case-Control Design

Case-Control Study

- Researchers were interested in studying the association between alcohol consumption and esophageal cancer

- Esophageal cancer is a rare condition—a prospective study would require a huge number of subjects

- Another approach—choose subjects whose cancer status is known at the time of recruitment into the study
  - In this scenario, researchers chose 200 cases and 775 controls and asked about alcohol consumption

Case-Control Study

- Study results: case/control status by alcohol consumption per day

	> 80 gm/day	≤ 80 gm/day	Totals
Case	96	104	200
Control	109	666	775
Totals	205	770	975

Alcohol/Esophageal Cancer

- Important questions
  - Can we estimate the prevalence of esophageal cancer based on the results for this study?
  - Can we calculate the probability of cancer if you drink more than 80 grams of alcohol per day using this case-control study?
  - Can we compute the relative risk of cancer for those who drink > 80 grams of alcohol per day as compared to those who drink ≤ 80 grams per day?

Important Caveat in Case-Control Studies

- In case-control studies, the individuals with the disease (the cases) have been over-sampled

- The percentage of subjects in your study who have disease are greater than in the population: hence the prevalence/risk in the sample is an overestimate of actual prevalence/risk, usually by a large factor

- "Prevalence" in the sample is a function of the design of the study: in this example researchers set prevalence (risk) at . . .

$$\frac{200}{200+775} = \frac{200}{975} \approx .21$$

Important Caveat in Case-Control Studies

- The percentage of the population who have disease from a case-control study (i.e., the risk/prevalence of disease) cannot be correctly estimated from a case-control study
- Hence, you cannot estimate relative risk (RR) relating disease to exposure of interest
- CANNOT compute relative risk from case-control study
- CAN compute odds ratio from case-control study

Odds Ratios in Case-Control Studies

- Recall, the estimated odds ratio of an outcome compares the observed odds of the outcome for two groups of individuals and is a function of the risk for each group

$$\hat{OR} = \frac{\hat{p}_1 / 1 - \hat{p}_1}{\hat{p}_2 / 1 - \hat{p}_2}$$

Case-Control Study

- Quick approach to computing odds ratio from a 2x2 table: diagonal cross products!

	> 80 gm/day	≤ 80 gm/day	Totals
Case	96	104	200
Control	109	666	775
Totals	205	770	975

$$Odds\ Ratio\ Estimate\ (\hat{OR}) = \frac{96 \times 666}{109 \times 104} \approx 5.60$$

Alcohol and Esophageal Cancer

- Interpretation
  - Individuals with high alcohol consumption (> 80 grams/day) are over five times the odds of esophageal cancer compared to individuals with low alcohol consumption

Important Caveat in Case-Control Studies

- The odds ratio is very close to what the relative risk would be if you had performed a cohort study (provided the disease was rare, say < 1/100)

- If the disease is not rare, OR still follows same direction as RR, but may not be a very accurate estimate of RR

Odds Ratios

- In the alcohol-esophageal cancer example, 5.64 is an estimate of the odds ratio based on a limited sample of data
- It is not the population parameter odds ratio
- Confidence intervals can be calculated that give the range of plausible values for the population odds ratio
- If the 95% confidence interval for the odds ratio does not include one, it suggests that there is a significant association ($p < .05$)

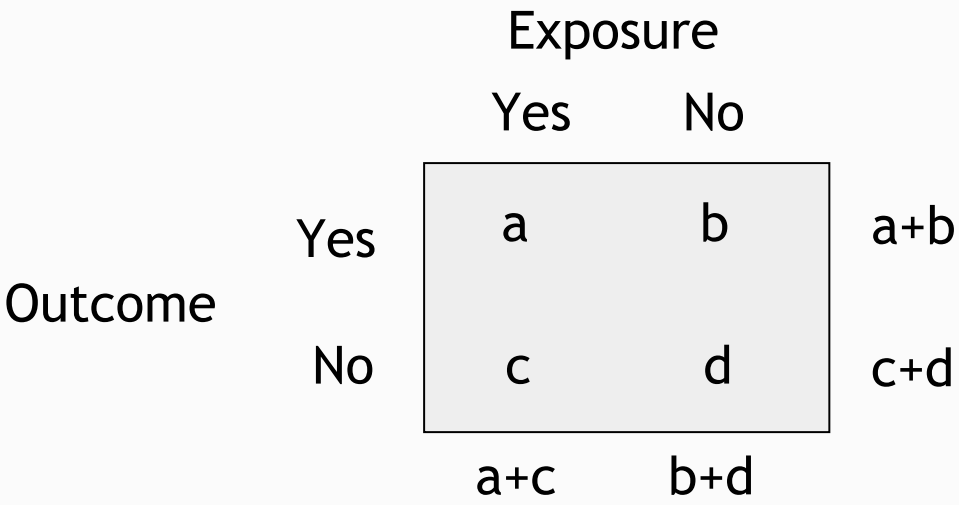
Odds Ratios

- How can you test if the population odds ratio is one or not?
  - Fisher's exact test
  - Chi- square test (approximation)

Using Stata

- "cci" command syntax—same setup as "csi" command that we saw in SR1
  - cci a b c d

- Where a, b, c, d from appropriate 2x2 table:



Using Stata

- Alcohol/esophageal cancer example
  - cci 96 105 109 666

- Recall the 2x2 table:

		Exposure: Yes	Exposure: No	
Outcome	Yes	96	104	200
	No	109	666	775
		205	770	

Using Stata

- Results from Stata

```
. cci 96 104 109 666

                                                        Proportion
                 |   Exposed   Unexposed  |      Total     Exposed
-----------------+------------------------+------------------------
           Cases |        96         104  |        200      0.4800
        Controls |       109         666  |        775      0.1406
-----------------+------------------------+------------------------
           Total |       205         770  |        975      0.2103
                 |                        |
                 |      Point estimate    |    [95% Conf. Interval]
                 |------------------------+------------------------
      Odds ratio |         5.640085       |    3.937435    8.061794 (exact)
 Attr. frac. ex. |         .8226977       |    .7460276    .8759581 (exact)
 Attr. frac. pop |         .3948949       |
                 +-----------------------------------------------
                              chi2(1) =   110.26  Pr>chi2 = 0.0000
```

Using Stata

- Results from Stata

```
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                                                        Proportion
                |   Exposed   Unexposed  |      Total     Exposed
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Using Stata

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                +-------------------------------------------------
                           chi2(1) =   110.26  Pr>chi2 = 0.0000
```

Using Stata

- The 95% CI for the OR of esophageal cancer for those consuming > 80 grams of alcohol per day compared to those consuming 80 grams or less is 4.0 to 8.0

Odds Ratio and Case-Control Studies

- Why would we even bother calculating the odds ratio when we can calculate relative risk?
  - The odds ratio turns out to be important because you can calculate it either in cohort studies or case-control studies
  - The relative risk can only be calculated from cohort studies

- Luckily, as we saw in SR1, the odds ratio informs us about risk

- If the outcome of interest is rare overall then the odds ratio is a good estimate for the relative risk

Odds Ratio and Case-Control Studies

- Recall:

$$H_o: p_1 = p_2 \quad \Rightarrow \quad H_o: RR = 1 \quad \Rightarrow \quad H_o: OR = 1$$

$$H_a: p_1 \neq p_2 \qquad H_a: RR \neq 1 \qquad H_a: OR \neq 1$$

- All three hypotheses testing for disease exposure relationship