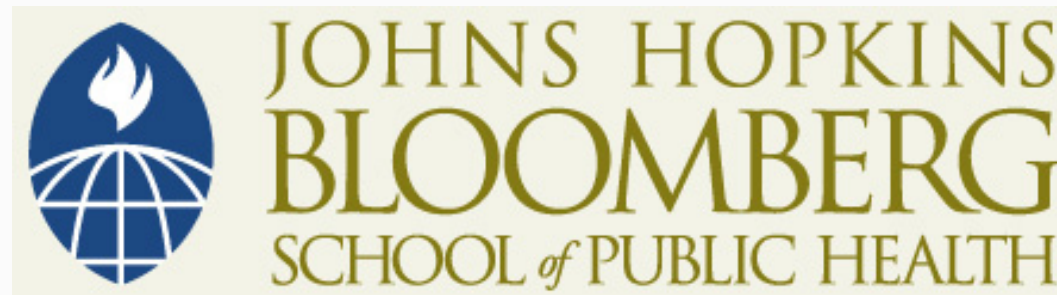


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Section E

Fisher's Exact Test

Recall: HIV Transmission/AZT Example

- Recall 2X2 (contingency) table

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

Hypothesis Testing Problem: AZT and HIV Transmission

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

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

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
```

	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

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.

Display Data in a 2x2 Table

- Results

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

Display Data in a 2x2 Table

- Sample proportion of subjects with hypertension

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

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

Smaller Sample

- In this example . . . (just FYI)

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

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

Fishers Exact

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

```
. 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 Square

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

```
. 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

Fishers Exact

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

```
. 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
```


Comparing Proportions between Independent Populations

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

Comparing Proportions between Independent Populations

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

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

- 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