

STAT 226 Lecture 4

Difference of Proportions, Relative Risk, Odds Ratio

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This set of slides covers Section 2.2-2.3 of the textbook.

- Difference of Proportions
- Relative Risk (Ratio of Proportions)
- Odds & Odds Ratio

Two Sample Problems for Proportions

Choose an SRS of size n_1 from a large population having proportion π_1 of successes and an independent SRS of size n_2 from another population having proportion π_2 of successes.

Population	Population proportion	Sample size	Count of successes	Estimate of π_i
1	π_1	n_1	y_1	$\widehat{\pi}_1 = y_1/n_1$
2	π_2	n_2	y_2	$\widehat{\pi}_2 = y_2/n_2$

Example: Physician's Health Study on Aspirin & Heart Attack

Physician's Health Study was a 5-year randomized study published testing whether regular intake of aspirin reduces mortality from cardiovascular disease¹.

- Participants were male physicians 40-84 years old in 1982 with no prior history of heart attack, stroke, and cancer, no current liver or renal disease, no contraindication of aspirin, no current use of aspirin
- Every other day, the male physicians participating in the study took either one aspirin tablet or a placebo.
- Response: whether the participant had a heart attack (including fatal or non-fatal) during the 5 year period.

¹ Source: Preliminary Report: Findings from the Aspirin Component of the Ongoing Physician's Health Study. *New Engl. J. Med.*, **318**: 262-64, 1988.

Data: Physician's Health Study (Aspirin & Heart Attack) (p.30)

Myocardial Infarction (MI) = heart attack. 2×2 table.

Group	MI	
	Yes	No
Placebo	189	10845
Aspirin	104	10933

Still 2×2 :

Group	MI		Total
	Yes	No	
Placebo	189	10845	11034
Aspirin	104	10933	11037
Total	293	21778	22071

Difference of Proportions

Wald CI for Diff. of Proportions

Wald CI for $\pi_1 - \pi_2$ is

$$\widehat{\pi}_1 - \widehat{\pi}_2 \pm z_{\alpha/2} \sqrt{\frac{\widehat{\pi}_1(1 - \widehat{\pi}_1)}{n_1} + \frac{\widehat{\pi}_2(1 - \widehat{\pi}_2)}{n_2}}$$

Example: Aspirin & Heart Attack (p. 30)

Group	MI		Total	
	Yes	No		
Placebo	189	10845	11034	$\Rightarrow \widehat{\pi}_1 = 189/11034 \approx 0.0171$
Aspirin	104	10933	11037	$\Rightarrow \widehat{\pi}_2 = 104/11037 \approx 0.0094$

95% CI for $\pi_1 - \pi_2$:

$$\begin{aligned} & 0.0171 - 0.0094 \pm 1.96 \sqrt{\frac{0.0171 \times 0.9829}{11034} + \frac{0.009 \times 0.9906}{11037}} \\ & = 0.0077 \pm 1.96(0.00154) = 0.0077 \pm 0.0030 = (0.0047, 0.0107) \end{aligned}$$

Example: Aspirin & Heart Attack — Conclusion

- As the 95% CI does not contain 0, the incidence rate of heart attack was significantly lower in aspirin group than in the placebo group
- Can we claim that taking aspirin every other day is effective in reducing the chance of heart attack?

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- As the 95% CI does not contain 0, the incidence rate of heart attack was significantly lower in aspirin group than in the placebo group
- Can we claim that taking aspirin every other day is effective in reducing the chance of heart attack?

Yes, because it was a randomized, double-blind, placebo-controlled experiment.

Agresti-Caffo Confidence Interval for $\pi_1 - \pi_2$

For small samples, Wald CI for $\pi_1 - \pi_2$ suffers from similar problem with achieving the nominal of confidence level as Wald CI for a single proportion.

Agresti and Caffo (2000) suggested adding *one success* and *one failure* in each of the two samples.

$$\tilde{\pi}_1 = \frac{y_1+1}{n_1+2}, \quad \tilde{\pi}_2 = \frac{y_2+1}{n_2+2}$$

Agresti-Caffo CI for $\pi_1 - \pi_2$ is given by

$$(\tilde{\pi}_1 - \tilde{\pi}_2) \pm z_{\alpha/2} \sqrt{\frac{\tilde{\pi}_1(1 - \tilde{\pi}_1)}{n_1+2} + \frac{\tilde{\pi}_2(1 - \tilde{\pi}_2)}{n_2+2}}$$

Note we still estimate π_1 and π_2 by $\hat{\pi}_1 = y_1/n_1$ and $\hat{\pi}_2 = y_2/n_2$, not by $\tilde{\pi}_1$ and $\tilde{\pi}_2$.

The true confidence level of the Agresti-Caffo CI is closer to the nominal level than the Wald CI and hence is recommended.

Testing the Equality of Two Proportions

The z -statistic for testing $H_0: \pi_1 = \pi_2$ is

$$z = \frac{\widehat{\pi}_1 - \widehat{\pi}_2}{\sqrt{\widehat{\pi}(1 - \widehat{\pi})\left(\frac{1}{n_1} + \frac{1}{n_2}\right)}}, \quad \text{where } \widehat{\pi} = \frac{y_1 + y_2}{n_1 + n_2}$$

Under H_0 , z is approx. $N(0, 1)$.

Example: Aspirin & Heart Attack (p. 30)

Group	MI		Total	
	Yes	No		
Placebo	189	10845	11034	$\Rightarrow \widehat{\pi}_1 = 189/11034 \approx 0.0171$
Aspirin	104	10933	11037	$\Rightarrow \widehat{\pi}_2 = 104/11037 \approx 0.0094$

For testing $H_0: \pi_1 = \pi_2$, $\widehat{\pi} = \frac{189+104}{11034+11037} \approx 0.0132$

$$z = \frac{0.0171 - 0.0094}{\sqrt{0.0132(1 - 0.0132)\left(\frac{1}{11034} + \frac{1}{11037}\right)}} \approx \frac{0.0077}{0.00154} \approx 5.001$$

2-sided P -value = 0.00000057, strong evidence against H_0 .

Small Sample Tests for 2×2 Tables

Note the test on the previous slide works for large sample only. Use it only when the numbers of successes and failures are both at least 5 in both samples (i.e., all n_{ij} 's are ≥ 5 .)

		Success	Failure
Sample	1	n_{11}	n_{12}
	2	n_{21}	n_{22}

A small sample test for $H_0: \pi_1 = \pi_2$ (Fisher's exact test) will be introduced in Section 2.6.

Relative Risk

Why Ratio of Porportions?

E.g., consider the probability of a certain disease for smokers (π_1) and for nonsmokers (π_2):

- Case 1: $\pi_1 = 0.51$ and $\pi_2 = 0.50$
- Case 2: $\pi_1 = 0.011$ and $\pi_2 = 0.001$.

In both cases $\pi_1 - \pi_2 = 0.01$.

However, in Case 1, an increase of 0.01 due to smoking is small relative to the already sizable risk of disease in the nonsmoking population.

Case 2 has smokers with 11 times the chance of disease than nonsmokers.

When π_1 and π_2 are both small, the ratio π_1/π_2 might be a more relevant measure of the smoking effect than the difference $\pi_1 - \pi_2$.

Relative Risk (RR) = Ratio of Proportions

Relative Risk (RR) = $\frac{\pi_1}{\pi_2}$, estimated by = $\frac{\widehat{\pi}_1}{\widehat{\pi}_2}$.

Example: Aspirin & Heart Attack (p. 30)

Sample relative risk in the Physicians Health Study is

$$\frac{\widehat{\pi}_{placebo}}{\widehat{\pi}_{aspirin}} = \frac{0.0171}{0.0094} = 1.82$$

The risk (probability) of heart attacks was estimated to be 82% higher (or 1.82 times as high as) in placebo group than in the Aspirin group.

- Independence $\iff \pi_1 = \pi_2 \iff RR = \frac{\pi_1}{\pi_2} = 1$

Inference of Relative Risk (RR) π_1/π_2 (1)

- Sampling distribution for sample RR ($\widehat{\pi}_1/\widehat{\pi}_2$) is highly skewed. The large sample normal approximation is NOT good.
- Sampling distribution of $\log(\widehat{\pi}_1/\widehat{\pi}_2)$ is closer to normal.
- It can be shown (by delta method in Stat 244) that

$$\text{Var}\left(\log\left(\frac{\widehat{\pi}_1}{\widehat{\pi}_2}\right)\right) \approx \frac{1 - \pi_1}{n_1\pi_1} + \frac{1 - \pi_2}{n_2\pi_2}.$$

The SE of $\log(\widehat{\pi}_1/\widehat{\pi}_2)$ is thus

$$\begin{aligned}\text{SE} &= \sqrt{\widehat{\text{Var}}\left(\log\left(\frac{\widehat{\pi}_1}{\widehat{\pi}_2}\right)\right)} = \sqrt{\frac{1 - \widehat{\pi}_1}{n_1\widehat{\pi}_1} + \frac{1 - \widehat{\pi}_2}{n_2\widehat{\pi}_2}} \\ &= \sqrt{\frac{1}{y_1} - \frac{1}{n_1} + \frac{1}{y_2} - \frac{1}{n_2}}\end{aligned}$$

Confidence Interval for Relative Risk (RR)

CI for $\log(\text{RR})$:

$$\begin{aligned}\log\left(\frac{\widehat{\pi}_1}{\widehat{\pi}_2}\right) \pm z_{\alpha/2}\text{SE} &= \log\left(\frac{\widehat{\pi}_1}{\widehat{\pi}_2}\right) \pm z_{\alpha/2} \sqrt{\frac{1}{y_1} - \frac{1}{n_1} + \frac{1}{y_2} - \frac{1}{n_2}} \\ &= (L, U)\end{aligned}$$

CI for RR:

$$(e^L, e^U)$$

Example: Aspirin & Heart Attack (p. 30)

Group	MI		Total	
	Yes	No		
Placebo	189	10845	11034	$\Rightarrow \hat{\pi}_1 = 189/11034 \approx 0.0171$
Aspirin	104	10933	11037	$\Rightarrow \hat{\pi}_2 = 104/11037 \approx 0.0094$

SE for $\log(\text{RR})$ is

$$\sqrt{\frac{1}{y_1} - \frac{1}{n_1} + \frac{1}{y_2} - \frac{1}{n_2}} = \sqrt{\frac{1}{189} - \frac{1}{11034} + \frac{1}{104} - \frac{1}{11037}} \approx 0.1213$$

95% CI for $\log(\text{RR})$ is

$$\log(\hat{\pi}_1/\hat{\pi}_2) \pm z_{\alpha/2}\text{SE} = \log\left(\frac{0.0171}{0.0094}\right) \pm 1.96(0.1213) = 0.5984 \pm 0.2378 \\ \approx (0.3606, 0.8362).$$

95% CI for RR is $(e^{0.3606}, e^{0.8362}) = (1.4342, 2.3076)$.

Interpretation. With 95% confidence, the risk of MI with 5 years for male physicians taking placebo is 1.43 to 2.30 times as high (or 43% to 130% higher) compared to those taking Aspirin.

Interpretation of Relative Risk

		<i>Response (Y)</i>	
		Success	Failure
<i>Explanatory Variable (X)</i>	Group 1	π_1	$1 - \pi_1$
	Group 2	π_2	$1 - \pi_2$

Interpretation of the Relative Risk (RR) = π_1/π_2 :

The probability (or risk) of success is RR times as large in group 1 as in group 2.

Interpretation of a 95% CI (L, U) for the RR :

With 95% confidence, the probability (or risk) of success is L to U times as large in group 1 as in group 2.

Here, “success”, “group 1”, and “group 2” would be replaced with meaningful terms in context.

Example (Problem 2.9 in ICDA3ed)

A 20-year study of British male physicians noted that the proportion who died from heart disease was

- $\widehat{\pi}_1 = 0.00669$ for smokers and
- $\widehat{\pi}_2 = 0.00413$ for nonsmokers.

Interpretation of (estimated) Relative Risk (RR) = $\widehat{\pi}_1/\widehat{\pi}_2 = 1.62$:

The estimated probability (or risk) of dying from heart disease for cigarette smokers was 1.62 times as large compared to nonsmokers.

or

Cigarette smokers were estimated to be 1.62 times as likely as (or 62% more likely than) nonsmokers to die from heart disease

Interpretation of Relative Risk

- If $RR < 1$, it might be more appealing to say
The probability/risk of success is $1/RR$ times as large in group 2 as in group 1.

than to say

The probability/risk of success is RR times as large in group 1 as in group 2.

since “11 times as large” might sound more striking than
“ $1/11 = 0.091$ times as large.”

- However, it might be okay to keep $RR < 1$ if Group 1 is some treatment and Group 2 is a placebo since in that case $RR < 1$ means reduction of risk.
- To sum up, we may, but not always have to, make $RR > 1$

Side Notes: Vaccine Efficacy & Relative Risk

Vaccine efficacy/effectiveness is defined to be

$$1 - RR = 1 - \frac{\pi_{vaccinated}}{\pi_{unvaccinated}}.$$

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e.g., 2 dose of Pfizer vaccine + booster had 70% efficacy immediately after the third dose

- 70% efficacy doesn't mean you have a 30% chance of getting sick
- 70% efficacy \Rightarrow $RR = 0.3$, the chance of getting sick for vaccinated people is only 30% of the chance for unvaccinated people

Odds & Odds Ratio

Odds

Consider a variable with binary outcome {Success, Failure}={S, F} (or {Yes, No})

	Outcome	
	Success	Failure
probability	π	$1 - \pi$

The odds of outcome S (instead of F) is

$$\text{odds}(S) = \frac{P(S)}{P(F)} = \frac{\pi}{1 - \pi}.$$

- if odds = 3, then S is three times as likely as F ;
- if odds = $1/3$, then F is three times as likely as S .

$$P(S) = \pi = \frac{\text{odds}(S)}{1 + \text{odds}(S)}$$

$$\text{odds}(S) = 3 \implies P(S) = \frac{3}{1 + 3} = \frac{3}{4}, \quad P(F) = \frac{1}{4}$$

$$\text{odds}(S) = \frac{1}{3} \implies P(S) = \frac{1/3}{1 + 1/3} = \frac{1}{4}, \quad P(F) = \frac{3}{4}$$

Odds Ratio (OR) = Ratio of Odds

Population	Population proportion	Sample size	Count of successes	Estimate of π_i
1	π_1	n_1	y_1	$\widehat{\pi}_1 = y_1/n_1$
2	π_2	n_2	y_2	$\widehat{\pi}_2 = y_2/n_2$

$$odds(\text{Success}) = \begin{cases} \frac{\pi_1}{1 - \pi_1} & \text{in population 1} \\ \frac{\pi_2}{1 - \pi_2} & \text{in population 2} \end{cases}$$

Definition (Odds Ratio)

$$\text{Odds Ratio : } \theta = \frac{odds_1}{odds_2} = \frac{\pi_1/(1 - \pi_1)}{\pi_2/(1 - \pi_2)}$$

Relative Risk (RR) v.s. Odds Ratio (OR)

$$\text{Odds Ratio} = \text{Relative Risk} \times \frac{1 - \pi_2}{1 - \pi_1}$$

When $\pi_1 \approx 0$ and $\pi_2 \approx 0$,

Odds Ratio \approx Relative Risk

Odds ratio is more further away from 1 than relative risk (RR)

- If $\pi_1 > \pi_2$, then Odds Ratio $>$ RR $>$ 1.
- If $\pi_1 < \pi_2$, then Odds Ratio $<$ RR $<$ 1.

Estimate of Odds Ratio

		Success	Failure	Total
Population	1	n_{11}	n_{12}	n_{1+}
	2	n_{21}	n_{22}	n_{2+}
	Total	n_{+1}	n_{+2}	n_{++}

$$\hat{\theta} = \frac{\hat{\pi}_1 / (1 - \hat{\pi}_1)}{\hat{\pi}_2 / (1 - \hat{\pi}_2)} = \frac{(n_{11}/n_{1+}) / (n_{12}/n_{1+})}{(n_{21}/n_{2+}) / (n_{22}/n_{2+})} = \frac{n_{11}n_{22}}{n_{12}n_{21}}$$

Odds ratio is thus called the **cross-product ratio**.

Properties of the Odds Ratio

- odds > 0 , $\theta > 0$
- $\theta = 1$ when $\pi_1 = \pi_2$; i.e., when X, Y are independent.
- The further θ is away from 1, the stronger the association.
e.g., For $Y =$ lung cancer, studies estimated that
 - $\theta \approx 10$ for $X =$ smoking,
 - $\theta \approx 2$ for $X =$ passive smoking.
- If rows are interchanged (or if columns are interchanged),

$$\theta \longrightarrow 1/\theta.$$

e.g., a value of $\theta = 1/5$ indicates the same strength of association as $\theta = 5$, but in the opposite direction.

Log Odds Ratio

- Sampling distribution of $\widehat{\theta}$ is skewed to the right.
Normal approximation for $\widehat{\theta}$ is NOT good.

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- Sampling distribution of $\log \widehat{\theta}$ is closer to normal.
- $\theta = 1 \iff \log \theta = 0$, when X, Y are independent
- If rows (or columns) are interchanged,

$$\log \theta \longrightarrow \log(1/\theta) = -\log \theta.$$

The log odds ratio ($\log \theta$) is symmetric about 0, e.g.,

$$\theta = 2 \iff \log \theta = 0.7$$

$$\theta = 1/2 \iff \log \theta = -0.7$$

The absolute value of $\log \theta$ indicates the strength of association

A Confidence Interval for the Odds Ratio

Large-sample (asymptotic) SE of $\log \hat{\theta}$ is

$$\text{SE}(\log \hat{\theta}) = \sqrt{\frac{1}{n_{11}} + \frac{1}{n_{12}} + \frac{1}{n_{21}} + \frac{1}{n_{22}}}$$

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CI for $\log \theta$:

$$(L, U) = \log \hat{\theta} \pm z_{\alpha/2} \times \text{SE}(\log \hat{\theta})$$

A Confidence Interval for the Odds Ratio

Large-sample (asymptotic) SE of $\log \hat{\theta}$ is

$$\text{SE}(\log \hat{\theta}) = \sqrt{\frac{1}{n_{11}} + \frac{1}{n_{12}} + \frac{1}{n_{21}} + \frac{1}{n_{22}}}$$

CI for $\log \theta$:

$$(L, U) = \log \hat{\theta} \pm z_{\alpha/2} \times \text{SE}(\log \hat{\theta})$$

CI for θ :

$$(e^L, e^U).$$

Example (Aspirin & Heart Attack)

Group	MI	
	Yes	No
Placebo	189	10845
Aspirin	104	10933

$$\widehat{\theta} = \frac{189 \times 10933}{104 \times 10845} = 1.83$$

$$\log \widehat{\theta} = \log(1.83) = 0.605$$

$$\text{SE}(\log \widehat{\theta}) = \sqrt{\frac{1}{189} + \frac{1}{10845} + \frac{1}{104} + \frac{1}{10933}} = 0.123$$

$$95\% \text{ CI for } \log \theta : 0.605 \pm 1.96(0.123) = (0.365, 0.846)$$

$$95\% \text{ CI for } \theta : (e^{0.365}, e^{0.846}) = (1.44, 2.33)$$

Interpretation: With 95% confidence, the odds of MI for the placebo group were 1.44 to 2.33 times the odds for the Aspirin group

- Apparently $\theta > 1$.
- $\widehat{\theta}$ is not at the midpoint of the CI
- Better estimate if we use $\{n_{ij} + 0.5\}$, especially if any $n_{ij} = 0$.