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Binary Data

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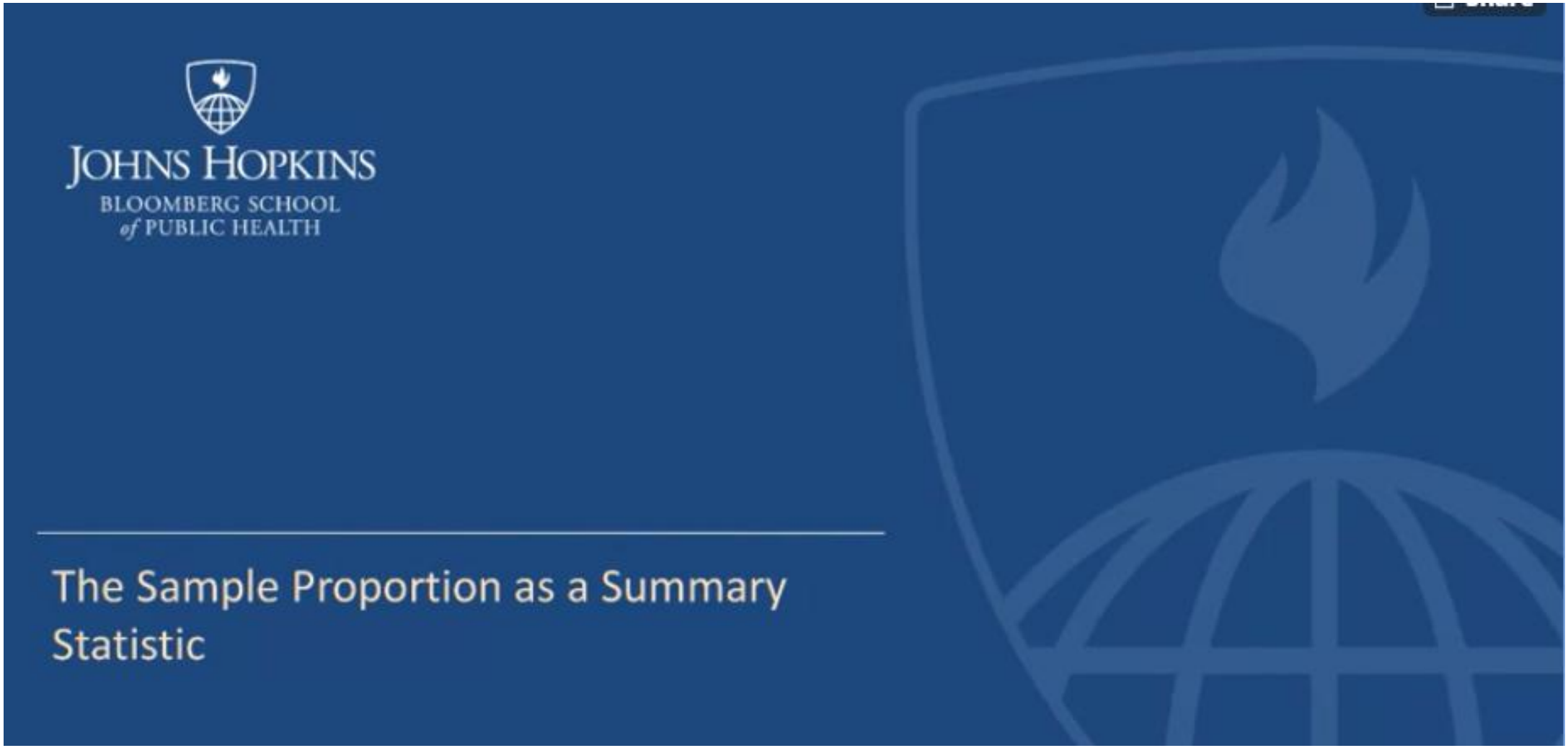
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The Sample Proportion as a Summary Statistic

Learning Objectives

- Upon completion of this lecture section, you will be able to:
  - Summarize a binary outcome across a group of individual observations via the sample proportion
  - Explain why, with binary data, the sample proportion is the only summary statistic (besides sample size n) necessary to describe characteristics of the sample
  - Compute the sample proportion based on the results of a study

Example: Treatment Response to ART, HIV+ Individuals—1

- Response to therapy in a random sample of 1,000 HIV-positive patients from a citywide clinical population
- 206 of the 1,000 patients responded. The summary measure used for binary outcomes is the sample proportion $\hat{p}$ (pronounced p-hat!), given by

$$\hat{p} = \frac{\#\ of\ responders}{total\ \#\ in\ sample} = \frac{206}{1{,}000} = 0.206\ or\ 20.6\%$$

- Why the hat? To distinguish $\hat{p}$, the sample estimate, from the underlying true (population) proportion p (which can only be estimated)

p-hat, Generally Speaking

- Response to therapy in a random sample of 1,000 HIV-positive patients from a citywide clinical population
- The sample proportion $\hat{p}$ is just a sample mean of data that takes on two values, 0 and 1
- Generally, binary data values are given a value of x=1 for observations that have the outcome, and x=0 for observations that do not have the outcome

Standard Deviation of Binary Data

- There is a formula for the standard deviation of binary data:

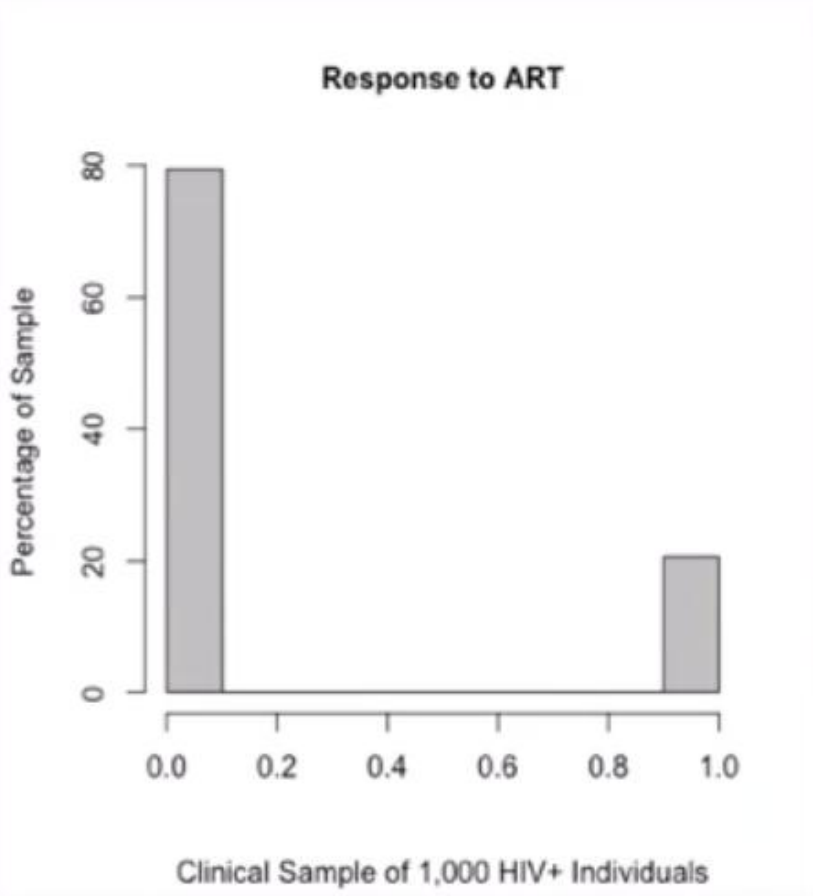
$$s = \sqrt{n\hat{p}(1-\hat{p})}$$

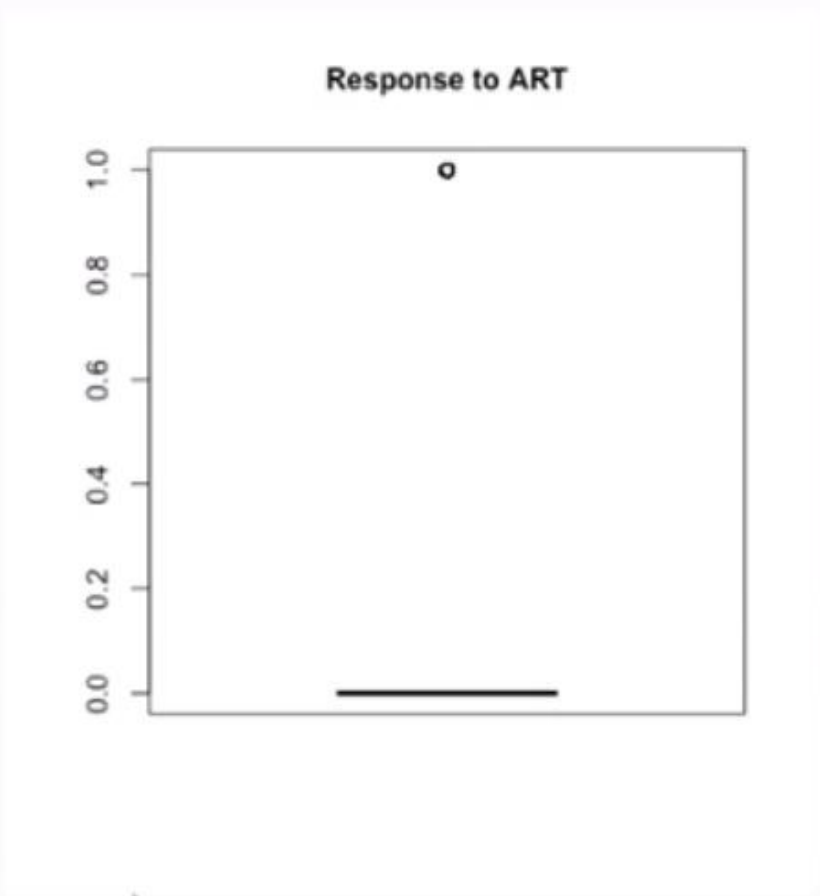
- Unlike with continuous sample values, this quantity is not particularly useful in understanding the distribution; however, it is relevant to note that the variability of the sample values is dependent on the value of the summary statistic, $\hat{p}$

Percentiles of Binary Data

- If we know the value of $\hat{p}$, we have have information regarding the sample percentile values
- For example, with the sample of 1,000 HIV+ clinic patients, the proportion responding was $\hat{p} = 0.206$
- However, as with *s* (sample *sd*), the sample percentile values for binary data are not particularly useful in characterizing the sample distribution

Visual Displays of Binary Data (Not So Useful)





Summary

- For quantifying the distribution of binary outcomes in a sample (and hence estimating the distribution in the population from which the sample was taken), the sample proportion $\hat{p}$ is paramount
  - $\hat{p}$ not only summarizes the percentage (probability, risk) of outcomes among a sample, it also gives information about the variability of individual sample observations and the sample percentiles
  - $\hat{p}$ is the sample mean of sample observations that take on the value of 1 for observations with the outcome and 0 for observations without the outcome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Comparing Binary Outcomes Between Two (or More) Populations Using Sample Results: Risk Difference and Relative Risk

Learning Objectives

- Upon completion of this lecture section, you will be able to:
  - Compute the risk difference and relative risk for comparing binary outcomes between two samples
  - Interpret the risk difference and relative risk in a public health/personal health context
  - Understand that the risk difference and relative risk will always agree in terms of direction but can differ greatly in magnitude
  - Understand that neither the risk difference alone nor the relative risk alone is sufficient to quantify the association of interest

Example: Treatment Response to ART, HIV+ Individuals—1

- Response to therapy in a random sample of 1,000 HIV-positive patients from a citywide clinical population
- 206 of the 1,000 patients responded. The overall response to treatment in this sample was:

$$\hat{p} = \frac{\#\ of\ responders}{total\ \#\ in\ sample} = \frac{206}{1{,}000} = 0.206\ or\ 20.6\%$$

Example: Treatment Response to ART, HIV+ Individuals—2

- Among the 1,000 subjects in the sample:
  - 497 had CD4 counts ≥ 250 at start of therapy, and 79 responded to therapy
  - 503 had CD4 counts < 250 at start of therapy, and 127 responded to therapy

- 2x2 table representation

	CD4<250	**CD4≥250**	
Responded	127	79	206
Did not respond	376	418	794
	503	497	1,000

Example: Treatment Response to ART, HIV+ Individuals: Summary Measure 1

- Summary measure 1: the difference in proportions (also called *risk difference* or *attributable risk*)

$$\hat{p}_{CD4<250} - \hat{p}_{CD4\geq250} = 0.25 - 0.16 = 0.09\ (9\%)$$

- Interpretation(s):
  - 9% greater (absolute) response to therapy in CD4<250 group as compared to CD4≥250 group
  - 9% greater absolute "risk" of response to therapy in CD4<250 group as compared to CD4≥250 group

Example: Treatment Response to ART, HIV+ Individuals: Summary Measure 2

- Summary measure 2: the relative risk (also called the *risk ratio* or *ratio of proportions*)

$$\frac{\hat{p}_{CD4<250}}{\hat{p}_{CD4\geq250}} = \frac{0.25}{0.16} = 1.56$$

- Interpretation(s):
  - Those in the CD4<250 group have 1.56 times the chances (risk) of responding to therapy as compared to CD4≥250 group
  - 56% greater relative "risk" of response to therapy in CD4<250 group as compared to CD4≥250 group

Example: Maternal/Infant HIV Transmission: Results in a 2x2 Table

	AZT	PLACEBO	
HIV+	13	40	53
HIV-	167	143	310
	180	183	363

$$\hat{p}_{AZT} = \frac{13}{180} \approx 0.07\ (7\%), \qquad \hat{p}_{Placebo} = \frac{40}{183} \approx 0.22\ (22\%)$$

Example: Maternal/Infant HIV Transmission: Summary Measure 1

- Summary measure 1: the difference in proportions (also called *risk difference* or *attributable risk*)

$$\hat{p}_{AZT} - \hat{p}_{PLACEBO} = 0.07 - 0.22 = -0.15\ (15\%)$$

- Interpretation(s):
  - 15% (absolute) reduction in HIV+ transmission to children born to mothers given AZT, as compared to children born to mothers given placebo
  - 15% lower absolute "risk" of HIV+ transmission to children born to mothers given AZT

Example: Maternal/Infant HIV Transmission: Summary Measure 2

- Summary measure 2: the relative risk (also called the *risk ratio* or *ratio of proportions*)

$$\frac{\hat{p}_{AZT}}{\hat{p}_{PLACEBO}} = \frac{0.07}{0.22} \approx 0.32$$

- Interpretation(s):
  - Risk of mother/child HIV transmission for mothers given AZT is 0.32 times the chances (risk) of mother/child HIV transmission for mothers given placebo
  - 68% lower relative risk of mother/child HIV transmission for mothers given AZT

Comparing and Contrasting Risk Difference and Relative Risk—1

- Risk difference versus relative risk: Substantive interpretations
- Both measures use exact same information but give seemingly different results:
  - (Risk difference) 15% reduction in HIV transmission
  - (Relative risk) 68% reduction in HIV transmission
- Notice, both agree in terms of direction of association

Comparing and Contrasting Risk Difference and Relative Risk—2

- Risk difference: Substantive interpretation
  - Can be interpreted as impact (assuming causation) on a fixed number of persons

- For example, with this risk difference of -15%:
  - In a group of 1,000 HIV+ pregnant women, we'd expect to see 150 (15%) fewer mother/child transmissions if the 1,000 women were given AZT during pregnancy
  - In a group 50,000 HIV+ pregnant women, we'd expect to see 7,500 (15%) fewer mother/child transmissions if the 50,000 women were given AZT during pregnancy

Comparing and Contrasting Risk Difference and Relative Risk—3

- Relative risk : Substantive interpretation
  - Can be interpreted as impact (assuming causation) at the "individual level"

- For example, with this relative risk of 0.32:
  - The risk that a HIV+ mother who takes AZT during pregnancy transmits HIV to her child is 0.32 times her risk if she did not take AZT
  - The risk that a HIV+ mother transmits HIV to her child is 68% lower if she takes AZT during pregnancy (as compared to if she were not taking AZT)

Estimating Percentiles Based on Normality Assumption with Skewed Data (Length of Stay)—1

- Using only the sample mean and standard deviation, and assuming normality, let's estimate the 2.5th and 97.5th percentiles for length of stay in this population

$$2.5^{th}\ \%\text{ile: } \bar{x} - 2s = 4.4 - 2\times 4.7 = -5 \text{ days}$$

$$97.5^{th}\ \%\text{ile: } \bar{x} + 2s = 4.4 + (2\times 4.7) = 13.8 \text{ days}$$

- Based on this sample data, we estimate that *most (95%)* of the persons making claims in this health care population had length of stays between *-5.5 and 14.1 days* in 2011 (???????)

(1, 14.1)

- Note: the empirical 2.5th and 97.5th percentile of the 12,298 sample values are *1 day and 21 days*, respectively

Comparing and Contrasting Risk Difference and Relative Risk—4

- The risk difference and relative risk will always agree in terms of the direction of estimated association

$$\text{If } \hat{p}_1 < \hat{p}_2 \text{ then } \hat{p}_1 - \hat{p}_2 < 0 \text{ and } 0 < \frac{\hat{p}_1}{\hat{p}_2} < 1.$$

$$\text{If } \hat{p}_1 > \hat{p}_2 \text{ then } \hat{p}_1 - \hat{p}_2 > 0 \text{ and } \frac{\hat{p}_1}{\hat{p}_2} > 1.$$

$$\text{If } \hat{p}_1 = \hat{p}_2 \text{ then } \hat{p}_1 - \hat{p}_2 = 0 \text{ and } \frac{\hat{p}_1}{\hat{p}_2} = 1.$$

- However, the two quantities can appear different in terms of magnitude

- It is possible to see a "large" effect with one measure and a "small" effect with the other
- For example:

  If $\hat{p}_1 = 0.001$ and $\hat{p}_2 = 0.004$ then $\hat{p}_1 - \hat{p}_2$ $= -0.003\ (-0.3\%)$, *an absolute decrease of* 0.3%. However, $\frac{\hat{p}_1}{\hat{p}_2} = \frac{0.001}{0.004}$ $= 0.25$, *a relative decrease of* 75%!

Example: Hormone Replacement Therapy—1

- Marilyn Vos Savant takes on a serious question

PARADE October

BY MARILYN VOS SAVANT

Ask Marilyn

I'm a middle-aged woman on hormone replacement therapy (HRT), and the news about HRT is very confusing. For example, I read that heart disease increased by almost a third as a result of the medication. Yet I also read that the increase was slight. Which is it? Now I read that the use of HRT is being questioned for this and other serious findings. What do the numbers really mean?
—Jeannie R., St. Louis, Mo.

A study that followed 16,608 women for 5.2 years—sending 8506 with HRT and 8102 with a placebo—reported a total of 286 cases of heart disease among them all. The incidence was 29% higher in the HRT group (164 cases) than in the placebo group (122 cases). (The percentage of increase is calculated with additional factors, so the numbers don't quite match.)

The incidence of heart disease in two groups of similar women will vary from group to group, so we asked Jacques Rossouw, director of the study, how many cases it took for the difference to be significant. He replied that it took few, so most of the difference in cases would be counted. "Leaving little doubt that the effect on cardiovascular disease is real." Note that this effect is still statistical. As yet, we know no cause-and-effect relationship.

And is the effect large? Not really. The lower the incidence of problems, the larger the percentage of change. For example: If only one woman in the placebo group had a problem, and two women in the HRT group had problems, the increase would be a shocking 100%, even though the actual risk would be minute.

The data on hormone replacement therapy show that the results are far from black and white.

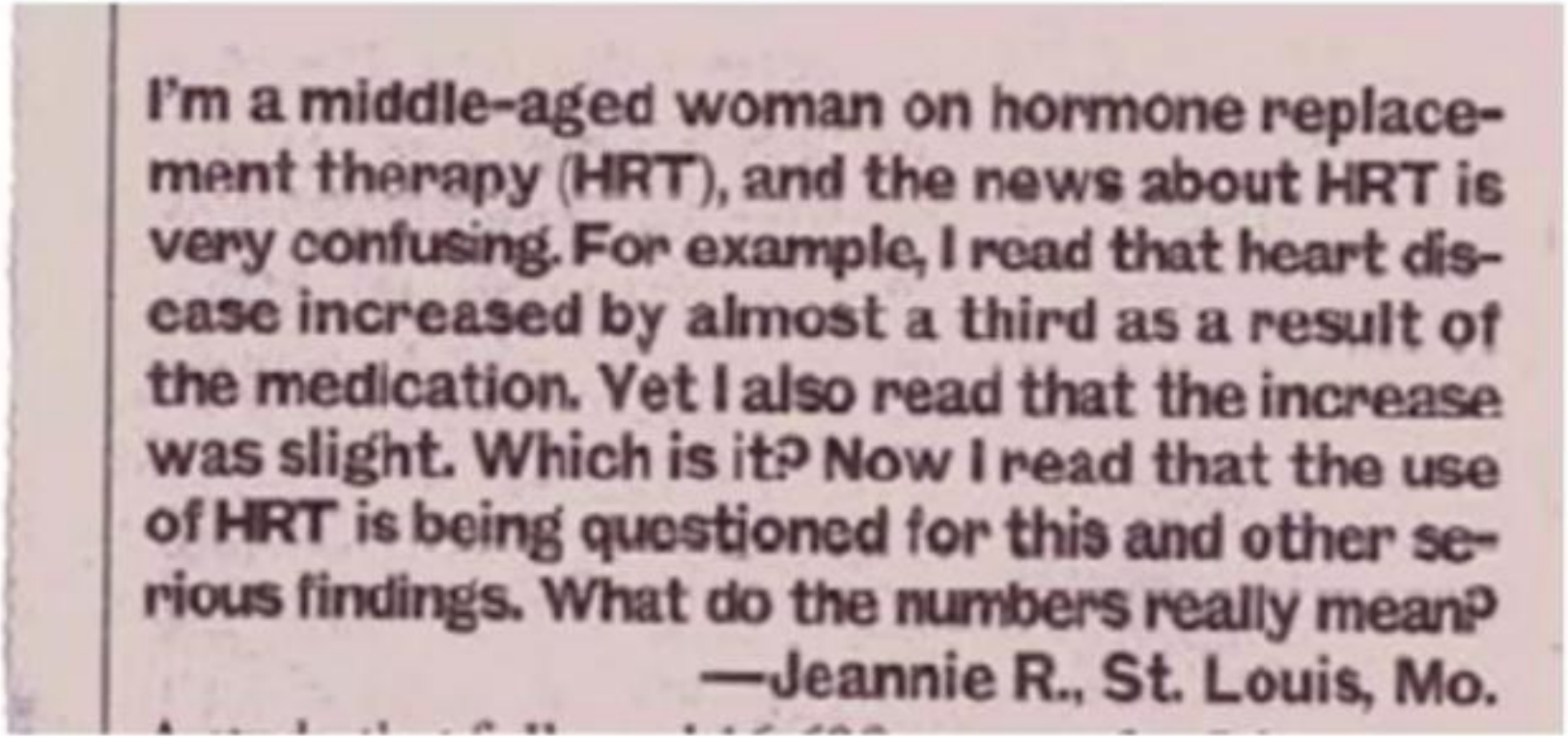
So, although we should not minimize the recent findings, we should not maximize them either. Interested readers should look at the actual study, available online at www.jama.com, site of *The Journal of the American Medical Association*. (Click on "Past Issues," then on "July 17, 2002.") You'll see that the results are not nearly as black and white as published reports indicate.

Perhaps as important, the quality-of-life data (energy level, sexual interest, skin tone, hair quality and so on) from the study have not yet been analyzed. When this information is released, we surely will see more front-page news.

Whose The Phleben?!

Example: Hormone Replacement Therapy—2

- Marilyn Vos Savant takes on a serious question



I'm a middle-aged woman on hormone replacement therapy (HRT), and the news about HRT is very confusing. For example, I read that heart disease increased by almost a third as a result of the medication. Yet I also read that the increase was slight. Which is it? Now I read that the use of HRT is being questioned for this and other serious findings. What do the numbers really mean?

—Jeannie R., St. Louis, Mo.

Example: Hormone Replacement Therapy: Proportion of Women Developing CHD (Incidence), in a 2x2 Table

	HRT	PLACEBO	
CHD	163	122	285
No CHD	8,345	7,980	16,325
	8,508	8,102	16,610

$$\hat{p}_{HRT} = \frac{163}{8{,}508} \approx 0.019\ (1.9\%), \qquad \hat{p}_{PLACEBO} = \frac{122}{8{,}102} \approx 0.015\ (1.5\%)$$

Example: Hormone Replacement Therapy—3

- Results: Risk difference and relative risk
- Which value do you think was most quoted in the press?

$$\widehat{RD} = \hat{p}_{HRT} - \hat{p}_{PLACEBO} = 0.019 - 0.015 = 0.004\ (0.4\%)$$

$$\widehat{RR} = \frac{\hat{p}_{HRT}}{\hat{p}_{PLACEBO}} = \frac{0.019}{0.014} = 1.27$$

Example: Comparing More than Two Groups: Colon Cancer Screening—1

Background: Screening decreases colorectal cancer (CRC) incidence and mortality, yet almost half of age-eligible patients are not screened at recommended intervals.

Objective: To determine whether interventions using electronic health records (EHRs), automated mailings, and stepped increases in support improve CRC screening adherence over 2 years.

Design: 4-group, parallel-design, randomized, controlled comparative effectiveness trial with concealed allocation and blinded outcome assessments. (ClinicalTrials.gov: NCT00697047)

Setting: 21 primary care medical centers.

Patients: 4675 adults aged 50 to 73 years not current for CRC screening.

Intervention: Usual care, EHR-linked mailings ("automated"), automated plus telephone assistance ("assisted"), or automated and assisted plus nurse navigation to testing completion or refusal ("navigated"). Interventions were repeated in year 2.

Measurements: The proportion of participants current for screening in both years, defined as colonoscopy or sigmoidoscopy (year 1) or fecal occult blood testing (FOBT) in year 1 and FOBT, colonoscopy, or sigmoidoscopy (year 2).

Results: Compared with those in the usual care group, participants in the intervention groups were more likely to be current for CRC screening for both years with significant increases by intensity (usual care, 26.3% [95% CI, 23.4% to 29.2%]; automated, 50.8% [CI, 47.3% to 54.4%]; assisted, 57.5% [CI, 54.5% to 60.6%]; and navigated, 64.7% [CI, 62.5% to 67.0%]; $P < 0.001$ for all pairwise comparisons). Increases in screening were primarily due to increased uptake of FOBT being completed in both years (usual care, 3.9% [CI, 2.8% to 5.1%]; automated, 27.5% [CI, 24.9% to 30.0%]; assisted, 30.5% [CI, 27.9% to 33.2%]; and navigated, 35.8% [CI, 33.1% to 38.6%]).

Example: Comparing More than Two Groups: Colon Cancer Screening—2

screening for both years with significant increases by intensity (usual care, 26.3% [95% CI, 23.4% to 29.2%]; automated, 50.8% [CI, 47.3% to 54.4%]; assisted, 57.5% [CI, 54.5% to 60.6%]; and navigated, 64.7% [CI, 62.5% to 67.0%]; $P < 0.001$ for all pair-wise comparisons). Increases in screening were primarily due to increased uptake of FOBT being completed in both years (usual care, 3.9% [CI, 2.8% to 5.1%]; automated, 27.5% [CI, 24.9% to 30.0%]; assisted, 30.5% [CI, 27.9% to 33.2%]; and navigated, 35.8% [CI, 33.1% to 38.6%]).

$$\hat{p}_{USUAL\ CARE} = 0.263\ (26.3\%)$$

$$\hat{p}_{AUTOMATED} = 0.508\ (50.8\%)$$

$$\hat{p}_{ASSISTED} = 0.575\ (57.5\%)$$

$$\hat{p}_{NAVIGATED} = 0.647\ (64.37\%)$$

Example: Comparing More than Two Groups: Colon Cancer Screening—3

- For both risk difference and relative risk comparisons, designate one of the four groups as a reference (arbitrary: I will make "usual care" the reference here)

$$\hat{p}_{AUTOMATED} - \hat{p}_{USUAL\,CARE} = 0.508 - 0.263 = 0.245\ (24.5\%)$$

$$\hat{p}_{ASSISTED} - \hat{p}_{USUAL\,CARE} = 0.575 - 0.263 = 0.312\ (31.2\%)$$

$$\hat{p}_{NAVIGATED} - \hat{p}_{USUAL\,CARE} = 0.647 - 0.263 = 0.384\ (38.4\%)$$

$$\frac{\hat{p}_{AUTOMATED}}{\hat{p}_{USUAL\,CARE}} = \frac{0.508}{0.263} \approx 1.93$$

$$\frac{\hat{p}_{ASSISTED}}{\hat{p}_{USUAL\,CARE}} = \frac{0.575}{0.263} \approx 2.19$$

$$\frac{\hat{p}_{NAVIGATED}}{\hat{p}_{USUAL\,CARE}} = \frac{0.647}{0.263} \approx 2.46$$

Summary

- Risk difference $(\hat{p}_1 - \hat{p}_2)$ and relative risk $\left(\frac{\hat{p}_1}{\hat{p}_2}\right)$ are two different estimates of the magnitude and direction of association for binary outcomes (between groups)
  - These two estimates are based on the exact same inputs and will always agree in terms of the direction of association, but not necessarily magnitude
- The *risk difference* helps to quantify the potential impact of a treatment or exposure for a group of individuals
- The *relative risk* helps quantify the potential impact of a treatment or exposure for an individual
- Neither estimate alone is sufficient to tell the whole "story"

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Comparing Binary Outcomes Between Two (or More) Populations Using Sample Results: The Odds Ratio

Learning Objectives

- Upon completion of this lecture section, you will be able to:
  - Quantify the association between a binary outcome variable and two (and more than two) groups as a ratio of odds (odds ratio)
  - Interpret the risk difference, relative risk, and odds ratio in a substantive public health context
  - Compare and contrast the three estimates (risk difference, relative risk, and odds ratio)

Example: Treatment Response to ART, HIV+ Individuals: How to Summarize Difference in Response between the CD4 Count Groups

	CD4<250	CD4≥250	
Responded	127	79	206
Did not respond	376	418	794
	503	497	1,000

- Sample proportions

$$\hat{p}_{CD4<250} = \frac{127}{503} = 0.25\ (25\%), \qquad \hat{p}_{CD4\geq250} = \frac{79}{497} = 0.16\ (16\%)$$

Example: Treatment Response to ART, HIV+ Individuals: Summary Measures

- Summary measure 1: the risk difference (also called *difference in proportions* or *attributable risk*)

$$\hat{p}_{CD4<250} - \hat{p}_{CD4\geq250} = 0.25 - 0.16 = 0.09\ (9\%)$$

- Summary measure 2: relative risk (also called the ratio of proportions, or *risk ratio*)

$$\frac{\hat{p}_{CD4<250}}{\hat{p}_{CD4\geq250}} = \frac{0.25}{0.16} = 1.56$$

- Summary measure 3: the odds ratio (also called *relative odds*)

Odds

- What is odds? The (estimated) odds of an event for any group is the (estimated) probability of the event occurring, divided by the (estimated) probability of it not occurring:

$$\widehat{ODDS} = \frac{\hat{p}}{1-\hat{p}}$$

- As $\hat{p}$ increases , $\widehat{ODDS}$ increases

$\hat{p}$	$\widehat{ODDS}$
0	$\frac{0}{1} = 0$
.1	$\frac{.1}{.9} = \frac{1}{9}$
.3	$\frac{.3}{.7} = \frac{3}{7}$
.5	$\frac{.5}{.5} = 1$
.6	$\frac{.6}{.4} = 1.5$
.75	$\frac{.75}{.25} = 4$

Odds for Each Group: Treatment Response to ART, HIV+ Individuals—1

- In this example, the odds of response for each of the two CD4 count groups are:

$$\hat{p}_{CD4<250} = 0.25\ (25\%):\ \widehat{ODDS}_{CD4<250} = \frac{0.25}{1-0.25} = \frac{0.25}{0.75}$$

$$\hat{p}_{CD4\geq250} = 0.16\ (16\%):\ \widehat{ODDS}_{CD4\geq250} = \frac{0.16}{1-0.16} = \frac{0.16}{0.84}$$

Odds For Each Group: Treatment Response to ART, HIV+ Individuals—2

- In this example, the odds of response for each of the two CD4 count groups are:

$$OR = \frac{\widehat{ODDS}_{CD4<250}}{\widehat{ODDS}_{CD4\geq 250}} = \frac{\left(\frac{0.25}{0.75}\right)}{\left(\frac{0.16}{0.84}\right)} \approx \frac{0.33}{0.19} = 1.75$$

- Interpretation
  - The <250 CD4 count group has 1.75 times the odds of responding to therapy as the ≥250 CD4 count group
  - The <250 CD4 count group has 75% greater odds of responding to therapy than the ≥250 CD4 count group

Odds Ratio Value Compared to Relative Risk Value

- Recall, that the relative risk comparing the proportions responding between the two CD4 groups is 1.56
- The odds ratio is 1.75
- In general, the relative risk and odds ratio estimates based on the same data will agree in terms of the direction of comparison but may differ in magnitude

Example: Maternal/Infant HIV Transmission: Results in a 2x2 Table

	AZT	PLACEBO	
HIV+	13	40	53
HIV-	167	143	310
	180	183	363

$$\hat{p}_{AZT} = \frac{13}{180} \approx 0.07\ (7\%), \qquad \hat{p}_{CD4\geq 250} = \frac{40}{183} \approx 0.22\ (22\%)$$

Example: Maternal/Infant HIV Transmission—1

- Risk difference $\widehat{RD} = 0.07 - 0.22 = -0.15$
- Relative risk $\widehat{RR} = \frac{0.07}{0.22} \approx 0.32$
- Odds ratio $\widehat{OR} = \frac{\left\{\frac{0.07}{0.93}\right\}}{\left(\frac{0.22}{0.78}\right)} \approx 0.27$

Example: Maternal/Infant HIV Transmission—1

- Risk difference $\widehat{RD} = 0.07 - 0.22 = -0.15$ (-15 %)
- Relative risk $\widehat{RR} = \frac{0.07}{0.22} \approx 0.32$ (68% reduction)
- Odds ratio $\widehat{OR} = \frac{\left\{\frac{0.07}{0.93}\right\}}{\left(\frac{0.22}{0.78}\right)} \approx 0.27$

Example: Maternal/Infant HIV Transmission—2

- Odds ratio: Interpretation
  - The AZT group has 0.27 times the odds (of HIV transmission to child) of the placebo group
  - The AZT group has 73% lower odds of HIV transmission to child than the placebo group

- Relative risk versus odds ratio: in this example, the relative risk and odds ratio are 0.32 and 0.27, respectively

Relative Risk Versus Odds Ratio, In General

- Both are relative measures of comparison, and neither imparts information about the absolute magnitude of the risk/odds in the groups being compared
- Both measures use exact same information but can give numerically different results: both will always agree in terms of direction of association

$$\text{If } \widehat{RR} > 1, \text{then } \widehat{OR} > 1.$$
$$\text{If } \widehat{RR} < 1, \text{then } \widehat{OR} < 1.$$
$$\text{If } \widehat{RR} = 1, \text{then } \widehat{OR} = 1.$$

- The smaller $\hat{p}_1$ and $\hat{p}_2$ are in value, the closer $\widehat{RR}$ and $\widehat{OR}$ will be in value

Why Even Bother with Odds Ratio?

- In many ways, the odds ratio is less intuitive and a less direct measure of association than the relative risk

- However:
  - In some types of studies (case control, more details coming in term 2), the odds ratio is the only measure of association that can be estimated
  - In logistic regression (also coming in term 2), the results are initially presented as odds ratios and, hence, frequently presented as odds ratios in publications

Example: Comparing More than Two Groups: Colon Cancer Screening

screening for both years with significant increases by intensity (usual care, 26.3% [95% CI, 23.4% to 29.2%]; automated, 50.8% [CI, 47.3% to 54.4%]; assisted, 57.5% [CI, 54.5% to 60.6%]; and navigated, 64.7% [CI, 62.5% to 67.0%]; $P < 0.001$ for all pair-wise comparisons). Increases in screening were primarily due to increased uptake of FOBT being completed in both years (usual care, 3.9% [CI, 2.8% to 5.1%]; automated, 27.5% [CI, 24.9% to 30.0%]; assisted, 30.5% [CI, 27.9% to 33.2%]; and navigated, 35.8% [CI, 33.1% to 38.6%]).

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Example, Comparing More than Two Groups: Colon Cancer Screening—3

- For both risk difference and relative risk comparisons, designate one of the four groups as a reference (arbitrary: I will make "usual care" the reference here)

$$\text{AUTOMATED to USUAL: } \widehat{RR} = 1.93;\ \widehat{OR} = 2.89$$

$$\text{ASSISTED to USUAL: } \widehat{RR} = 2.19;\ \widehat{OR} = 3.79$$

$$\text{NAVIGATED to USUAL: } \widehat{RR} = 2.46;\ \widehat{OR} = 5.14$$

Example: Comparing More than Two Groups: Colon Cancer Screening—2

- For both risk difference and relative risk comparisons, designate one of the four groups as a reference (arbitrary: I will make "usual care" the reference here)

$$\hat{p}_{AUTOMATED} - \hat{p}_{USUAL\ CARE} = 0.508 - 0.263 = 0.245\ (24.5\%)$$

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$$\frac{\hat{p}_{NAVIGATED}}{\hat{p}_{USUAL\ CARE}} = \frac{0.647}{0.263} \approx 2.46$$

Summary

- The odds ratio, $\widehat{OR}$, provides an alternative to the relative risk, $\widehat{RR}$, for quantifying the association between a binary outcome between groups
  - The odds ratio is ratio of odds between two groups: odds is related to risk (probability, proportion)

- The odds ratio and relative risk both estimate the association between a binary outcome between groups at the individual level
  - These two measures will agree in terms of direction but not always magnitude
  - The smaller the risk in the groups being compared, the more similar in value $\widehat{RR}$ and $\widehat{OR}$ are


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A Brief Note About Ratios (Will Also be Revisited Later in the Course)

Learning Objectives

- Upon completion of this lecture section, you will be able to:
  - Understand that the scaling of ratios is not symmetric around the value of 1 (which would indicate equal values in the numerator and denominator)
  - Consider the implications of the previous point when interpreting size of association
  - Understand that on the log scale (we'll use natural log, ln), the values of ln(ratios) are symmetric about the value 0

Example: Maternal/Infant HIV Transmission: Results in a 2x2 Table

	AZT	PLACEBO	
HIV+	13	40	53
HIV-	167	143	310
	180	183	363

$$\hat{p}_{AZT} = \frac{13}{180} \approx 0.07\ (7\%), \qquad \hat{p}_{Placebo} = \frac{40}{183} \approx 0.22\ (22\%)$$

Example: Maternal/Infant HIV Transmission: Summary Measures

- Summary measures (placebo compared to PAZT)
  - Risk difference: $\widehat{RD} = \hat{p}_{AZT} - \hat{p}_{PLACEBO} = 0.07 - 0.22 = -0.15\ (-15\%)$
  - Relative risk: $\widehat{RR} = \frac{\hat{p}_{AZT}}{\hat{p}_{PLACEBO}} = \frac{0.07}{0.22} \approx 0.32$
  - Odds ratio: $\widehat{OR} = \frac{\left(\frac{\hat{p}_{AZT}}{1-\hat{p}_{AZT}}\right)}{\left(\frac{\hat{p}_{PLACEBO}}{1-\hat{p}_{PLACEBO}}\right)} = \frac{\left(\frac{0.07}{0.93}\right)}{\left(\frac{0.22}{0.78}\right)} \approx 0.27$

Example: Maternal/Infant HIV Transmission: Interpretations

- Interpretations: AZT associated with (AZT as compared to placebo):
  - (Risk difference) 15% (absolute) decrease in HIV transmission risk
  - (Relative risk) 68% (relative) decrease in HIV transmission risk
  - (Odds ratio) 73% (relative) reduction in HIV transmission odds

Direction of Comparison is Arbitrary

- Summary measures (placebo compared to AZT)
  - Risk difference: $\widehat{RD} = \hat{p}_{PLACEBO} - \hat{p}_{AZT} = 0.22 - 0.07 = 0.15\ (15\%)$
  - Relative risk: $\widehat{RR} = \frac{\hat{p}_{PLACEBO}}{\hat{p}_{AZT}} = \frac{0.22}{0.07} = \frac{1}{0.32} \approx 3.1$
  - Odds ratio: $\widehat{OR} = \frac{\left(\frac{\hat{p}_{PLACEBO}}{1-\hat{p}_{PLACEBO}}\right)}{\left(\frac{\hat{p}_{AZT}}{1-\hat{p}_{AZT}}\right)} = \frac{\left(\frac{0.22}{0.78}\right)}{\left(\frac{0.07}{0.93}\right)} = \frac{1}{0.27} \approx 3.7$

Is This Saying the Same Thing as When AZT was Compared to Placebo?

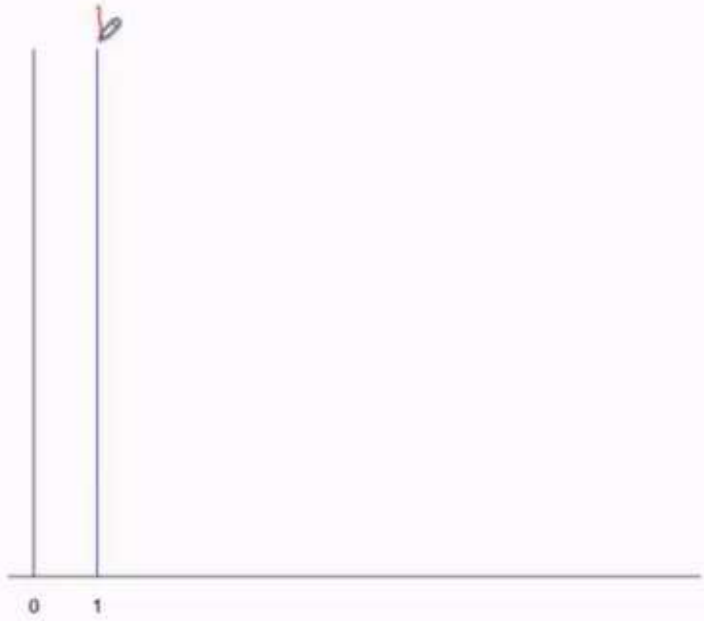
- Interpretations: Placebo associated with (placebo as compared to AZT):
  - (Risk difference) 15% (absolute) ***increase*** in HIV transmission risk
  - (Relative risk) 210% (relative) ***increase*** in HIV transmission risk
  - (Odds ratio) 270 % (relative) ***increase*** in HIV transmission odds

Direction of Comparison is Arbitrary

- Summary measures (placebo compared to AZT)
  - Risk difference: $\widehat{RD} = \hat{p}_{PLACEBO} - \hat{p}_{AZT} = 0.22 - 0.07 = 0.15\ (15\%)$
  - Relative risk: $\widehat{RR} = \frac{\hat{p}_{PLACEBO}}{\hat{p}_{AZT}} = \frac{0.22}{0.07} = \frac{1}{0.32} \approx 3.1$
  - Odds ratio: $\widehat{OR} = \frac{\left(\frac{\hat{p}_{PLACEBO}}{1-\hat{p}_{PLACEBO}}\right)}{\left(\frac{\hat{p}_{AZT}}{1-\hat{p}_{AZT}}\right)} = \frac{\left(\frac{0.22}{0.78}\right)}{\left(\frac{0.07}{0.93}\right)} = \frac{1}{0.27} \approx 3.7$

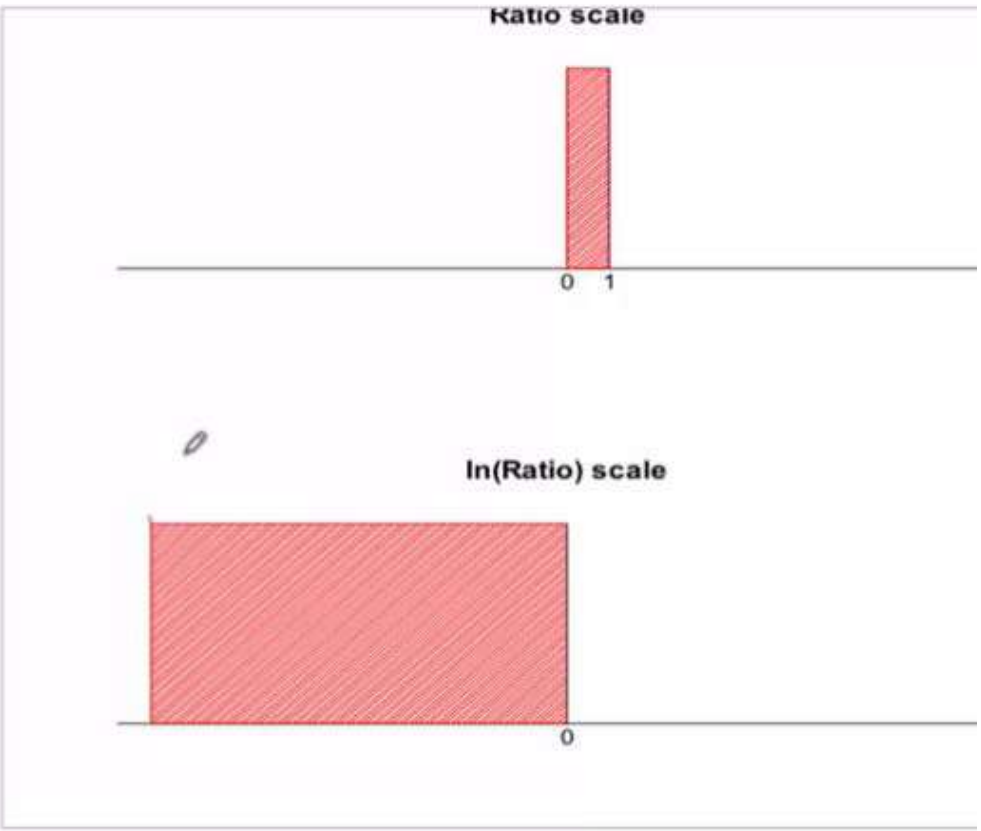
Scale of Ratios is Not Symmetric—1

- So why do these ratio-based associations seem to differ in magnitude if the direction of comparison is reversed??
- The range of possible values for "positive" and "negative" associations are very different for ratios



Scale of Ratios is Not Symmetric—2

- The ranges are equal on the ln(Ratio) scale



Example: Relative Risks (RRs) and ln(RRs) in Both Directions, Maternal Infant Transmission Study

- AZT to placebo

$$\widehat{RR}_{AZT\ vs\ P} = \frac{\hat{p}_{AZT}}{\hat{p}_{PLACEBO}} = \frac{0.07}{0.22} \approx 0.32$$

$$\ln\left(\widehat{RR}_{AZT\ vs\ P}\right)$$

$$\ln(\hat{p}_{AZT}) - \ln(\hat{p}_{PLACEBO}) =$$

$$\ln(0.07) - \ln(0.22) = -1.11$$

- Placebo to AZT

$$\widehat{RR}_{P\ vs\ PAZT} = \frac{\hat{p}_{PLACEBO}}{\hat{p}_{AZT}} = \frac{0.22}{0.07} \approx 3.1$$

$$\ln\left(\widehat{RR}_{P\ vs\ AZT}\right)$$

$$\ln(\hat{p}_{PLACEBO}) - \ln(\hat{p}_{AZT}) =$$

$$\ln(0.22) - \ln(0.07) = 1.11$$

Summary—1

- On the ratio scale (relative risk or odds ratio), the range of possible values is
  - *0 ≤ ratio < 1*: for "negative" associations, i.e., where the group in the numerator has lower risk (and hence odds) than the group in the denominator
  - 1 < ratio ≤ ∞ : for "positive" associations, i.e., where the group in the numerator has greater risk (and hence odds) than the group in the denominator

- On the ln(ratio) scale, the range of possible values is:
  - *−∞ < ln(ratio) < 0*: for "negative" associations, i.e. ,where the group in the numerator has lower risk (and hence odds) than the group in the denominator
  - 0 < ln(ratio) ≤ ∞ : for "positive" associations, i.e., where the group in the numerator has greater risk (and hence odds) than the group in the denominator

Summary—1

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- On the ln(ratio) scale, the range of possible values is:
  - $-\infty < ln(ratio) < 0$: for "negative" associations, i.e. ,where the group in the numerator has lower risk (and hence odds) than the group in the denominator
  - 0 < ln(ratio) ≤ ∞ : for "positive" associations, i.e., where the group in the numerator has greater risk (and hence odds) than the group in the denominator

Summary—2

- These properties of ratios and ln(ratios) have potential implications for:
  - Displaying associations for different group comparisons
  - Performing statistical inference on ratios
- STAY TUNED: more to come on these properties in both this class and the next

Example: Aspirin and CVD in Women—1

BACKGROUND

Randomized trials have shown that low-dose aspirin decreases the risk of a first myocardial infarction in men, with little effect on the risk of ischemic stroke. There are few similar data in women.

METHODS

We randomly assigned 39,876 initially healthy women 45 years of age or older to receive 100 mg of aspirin on alternate days or placebo and then monitored them for 10 years for a first major cardiovascular event (i.e., nonfatal myocardial infarction, nonfatal stroke, or death from cardiovascular causes).

RESULTS

During follow-up, 477 major cardiovascular events were confirmed in the aspirin group, as compared with 522 in the placebo group, for a nonsignificant reduction in risk with

Example: Aspiring and CVD in Women: Results in a 2x2 Table

	Aspirin	Placebo	
CVD	477	522	999
No CVD	19,457	19,420	38,887
	19,934	19,942	39,876

$$\hat{p}_{Aspirin} = \frac{477}{19{,}984} \approx 0.024\ (2.4\%), \qquad \hat{p}_{CD4 \geq Placebo} = \frac{522}{19{,}942} \approx 0.026\ (2.6\%)$$

Example: Aspiring and CVD in Women: Summary Measure 1

- Summary measure 1: the difference in proportions (also called *risk difference* or *attributable risk*)

$$\hat{p}_{Aspirin} - \hat{p}_{Placebo} = 0.024 - 0.026 = -0.002\ (0.2\%)$$

- Interpretation(s):
  - 0.2% (absolute) reduction in (10-year) risk of CVD for women on low-dose aspirin therapy compared to women not on low-dose therapy
  - In a population of 100,000 women, we would expect to see 0.002*100,000=200 fewer cases of CVD (developing within 10 years) if the women were given low-dose aspirin therapy

Example: Aspiring and CVD in Women: Summary Measure 2

- Summary measure 2: the relative risk (also called the *risk ratio* or *ratio of proportions*)

$$\frac{\hat{p}_{Aspirin}}{\hat{p}_{Placebo}} = \frac{0.024}{0.026} \approx 0.92$$

- Interpretation(s):
  - 10-year risk of CVD for women on low-dose aspirin regimen is 0.92 times the risk for women given placebo
  - A women can reduce her personal risk of CVD (developing within 10 years) by 8% if she takes a low dose of aspirin every other day

Example: Aspiring and CVD in Women: Summary Measure 3

- Summary measure 3: the odds ratio (also called the *relative odds*)

$$\frac{\left(\frac{\hat{p}_{Aspirin}}{1-\hat{p}_{Aspirin}}\right)}{\left(\frac{\hat{p}_{Placebo}}{1-\hat{p}_{Placebo}}\right)} = \frac{\left(\frac{0.024}{0.976}\right)}{\left(\frac{0.026}{0.974}\right)} \approx 0.92$$

- Interpretation(s):
  - 10-year odds of CVD for women on low-dose aspirin regimen is 0.92 times the odds for women given placebo
  - A women can reduce her personal odds of CVD (developing within 10 years) by 8% if she takes a low dose of aspirin every other day

RD, RR, and OR Compared—1

- Suppose we have study results comparing proportions for two groups, such that the risk difference $(\hat{p}_1 - \hat{p}_2) = 0.05$. Some possibilities for $\hat{p}_1 \; and \; \hat{p}_2$:

- $\hat{p}_1 = 0.06, \; \hat{p}_2 = 0.01$
- $\hat{p}_1 = 0.38, \; \hat{p}_2 = 0.33$
- $\hat{p}_1 = 0.99, \; \hat{p}_2 = 0.94$

1. When summarizing binary outcomes (a sample of 0 (Zeros) and 1 (Ones)), how is p-hat, the sample proportion, equivalent to a sample mean?

- (●) It is the sum of all values divided by the sample size.
- ( ) It informs you how skewed the dataset is.
- ( ) 50% of observations fall below that value.
- ( ) It measures the amount of variation in the data set.

2. If the sample proportion (p-hat) of a binary outcome is 0.35, which of the following is/are true: (check all responses that are true)

- [ ] The 75th percentile is 0
- [x] 35% of all observations were 1s ("yes" outcomes)
- [ ] The sample size was 100
- [x] The 50th percentile is 0

3. A study concludes that the estimate risk ratio of a new drug on cataract development compared to a placebo is 0.78. This means:

- ( ) The drug group has a 22% lower relative risk of developing cataracts compared to the placebo group.
- ( ) The risk of the developing cataracts in drug group is smaller than the risk of the placebo group.
- ( ) The absolute risk difference between the drug group compared to the placebo group is negative.
- (•) All of the above.

4. A study concludes that the relative risk of a certain cancer for persons with a genetic mutation compared to persons without this mutation is 3. The appropriate interpretation of this relative risk is:

- ○ There were 3 more cases of cancer in the group with the genetic mutation compared to the group without the mutation.
- ○ There were 3 percent more cases of cancer in the group with the genetic mutation compared to the group without the mutation.
- ○ There were 300 percent more cases of cancer in the group with the genetic mutation compared to the group without the mutation.
- ◉ Subjects with the mutation had 3 times the risk of the cancer compared to subjects without the mutation.

5. The absolute risk difference of developing cancer between the group with genetic mutation and the group without the mutation was 0.002 (Assuming causality). How would you interpret the absolute risk difference?

- ○ There were 20 more cancer cases amongst those in the sample with the genetic mutation (compared to those without).
- ○ Individuals with the mutation have .002 times the chance at getting cancer compared to individuals without the mutation.
- ○ In a population of 10,000 individuals, we'd expect to see 20 more cases of cancer if the individuals did not have the genetic mutation compared to if the 10,000 individuals had the mutation.
- ◉ In a population of 10,000 individuals, we'd expect to see 20 fewer cases of cancer if the individuals did not have the genetic mutation compared to if the 10,000 individuals had the mutation.

6. If the odds of an outcome occurring for a single group is equal to 1, this means:

- (●) The risk of the outcome within this group is 50%.
- ( ) The prevalence is the same between two comparison groups.
- ( ) The odds are the same between this group and another comparison group.
- ( ) The risk of the outcome within is 100%.

7. If the odds ratio comparing two groups is equal to 1, this means: (mark all that apply)

- [x] The odds of the outcome is the same between two comparison groups.
- [ ] The odds of an outcome within at least one of the groups is 50%.
- [ ] The risk of the outcome is 100%.
- [x] The risk of the outcome is the same between two comparison groups.

8. If the odds ratio between comparing two groups is less than 1, which of the following is true:

- The corresponding relative risk is greater than 1.
- The odds within each group is less than 1.
- The odds within each group is greater than 1.
- The corresponding relative risk is less than 1.

9. Why is the distribution of possible risk ratios (or odds ratios) not symmetric around 1?

- (●) When the risk of the numerator is less than the risk of the denominator, possible values fall between 0 and <1 and when the risk of the numerator is greater than the risk of the denominator, possible values fall between >1 and infinity.
- ( ) Relative risks are always structured such that the risk of the numerator is always greater than the risk of the denominator meaning values are greater than 1.
- ( ) The potential range of values less than 1 is much greater than the potential range of values greater than 1.
- ( ) The distribution of possible risk ratios (or odds ratios) is symmetric around 0.

10. Why would one transform the risk ratio or (odds ratio) using the log scale?

- ( ) To find the absolute risk difference between two groups.
- ( ) To calculate the risk ratio of two groups using the opposite reference group.
- (●) In order to have symmetric absolute differences between risk ratios of two groups on the log scale.
- ( ) No one would ever do that.