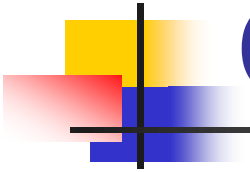
Statistics for Health Care

Unit 2:

Overview



Overview

- Basic study designs; measures of disease frequency and association

Teaser 1, Unit 2

2000 *NEJM* study on rofecoxib vs. naproxen, Randomized Trial

The New England Journal of Medicine

COMPARISON OF UPPER GASTROINTESTINAL TOXICITY OF ROFECOXIB AND NAPROXEN IN PATIENTS WITH RHEUMATOID ARTHRITIS

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ABSTRACT

Background Each year, clinical upper gastrointestinal events occur in 2 to 4 percent of patients who are taking nonselective nonsteroidal antiinflammatory drugs (NSAIDs). We assessed whether rofecoxib, a selective inhibitor of cyclooxygenase-2, would be as-

NONSTEROIDAL antiinflammatory drugs (NSAIDs) are among the most commonly used medications in the world.[1] A major factor limiting their use is gastrointestinal toxicity. Although endoscopic studies reveal that gastric or duodenal ulcers develop in 15 to 30 percent

Teaser 2, Unit 2

Results: "Myocardial infarctions were less common in the naproxen group than in the rofecoxib group (0.1 percent vs. 0.4 percent; 95 percent confidence interval for the difference, 0.1 to 0.6 percent; relative risk, 0.2; 95 percent confidence interval, 0.1 to 0.7)."

Teaser 1, Unit 2

Conclusion: "Thus, our results are consistent with the theory that naproxen has a coronary protective effect and highlight the fact that rofecoxib does not provide this type of protection...The finding that naproxen therapy was associated with a lower rate of myocardial infarction needs further confirmation in larger studies."

Teaser 2, study of caloric labeling

- Researchers studied the beverage purchases of teenagers at 4 stores; each store was measured at baseline and under 3 "caloric conditions" (signs posted outside the store):
  - Absolute calories: "Did you know that a bottle of soda or fruit juice has about 250 calories?"
  - Relative calories: "Did you know that a bottle of soda or fruit juice has about 10% of your daily calories?"
  - Exercise equivalents: "Did you know that working off a bottle of soda or fruit juice takes about 50 minutes of running?"

Bleich SN, Herring BJ, Flagg DD, Gary-Webb TL. Reduction in purchases of sugar-sweetened beverages among low-income black adolescents after exposure to caloric information. *Am J Public Health*. February 2012, Vol. 102, No. 2, pp. 329-335.

The Results…

Condition	What percent of drinks purchased were sugary beverages?
Pre-intervention (no information)	93.3%
Absolute calories	87.5%
Relative calories	86.5%
Exercise equivalent	86.0%

What conclusions would you draw from the data?

Headlines…

- ’Exercise labels’ beat out calorie counts in steering consumers away from junk food
- Exercise labels are better at keeping teens away from junk food, researchers say

Media coverage…

- The researcher said: "*The results are really encouraging. We found that providing any information (via the three signs) relative to none,* ***reduced the likelihood that they would buy a sugary beverage by 40 per cent.***
- *"Of those three signs,* ***the one that was most effective was the physical activity equivalent****.*
- *"We found that when that sign was posted,* ***the likelihood that they would buy a sugary beverage reduced by around 50 per cent****."*

Statistics for Health Care

Module 1:

Quick review of study designs

Types of studies

- Observational
  - Descriptive
  - Cross-sectional
  - Case-control/nested case-control
  - Prospective or retrospective cohort
- Experimental
  - Randomized controlled trial

Increasing level of evidence.

Limitation of observational research: confounding

- Confounding: risk factors don't happen in isolation, except in a controlled experiment.
  - Example: Alcohol and lung cancer are correlated, but this is only because drinkers also tend to be smokers.

Risk factors cluster!

Table 1. Selected Age-Adjusted Characteristics of the National Institutes of Health–AARP Cohort by Red Meat Quintile Category[a]

Characteristic	Red Meat Intake Quintile, g/1000 kcal				
	Q1	Q2	Q3	Q4	Q5
	Men (n=322 263)				
Meat intake					
Red meat, g/1000 kcal	9.3	21.4	31.5	43.1	68.1
White meat, g/1000 kcal	36.6	32.2	30.7	30.4	30.9
Processed meat, g/1000 kcal	5.1	7.8	10.3	13.3	19.4
Age, y	62.8	62.8	62.5	62.3	61.7
Race, %					
Non-Hispanic white	88.6	91.8	93.1	94.0	94.1
Non-Hispanic black	4.2	3.2	2.7	2.2	1.9
Hispanic/Asian/Pacific Islander/American Indian/Alaskan native/unknown	7.2	5.0	4.2	3.8	4.0
Positive family history of cancer,%	47.0	47.7	48.4	48.6	47.8
Currently married, %	80.8	84.4	86.1	86.7	85.6
BMI	25.9	26.7	27.1	27.6	28.3
Smoking history, %[b]					
Never smoker	34.4	30.5	28.8	27.6	25.4
Former smoker	56.5	58.1	57.5	57.1	55.8
Current smoker or having quit <1 y prior	4.9	7.6	9.9	11.4	14.8
Education, college graduate or postgraduate, %	53.0	47.3	45.1	42.3	39.1
Vigorous physical activity ≥5 times/wk, %	30.7	23.6	20.5	18.6	16.3
Dietary intake					
Energy, kcal/d	1899	1955	1998	2038	2116
Fruit, servings/1000 kcal	2.3	1.8	1.6	1.4	1.1
Vegetables, servings/1000 kcal	2.4	2.1	2.0	2.0	1.9

Reproduced with permission from Table 1 of: Sinha R, Cross AJ, Graubard BI, Leitzmann MF, Schatzkin A. Meat intake and mortality: a prospective study of over half a million people. *Arch Intern Med* 2009;169:562-71.

Ways to avoid or control for confounding

- During the design phase: randomize or match
- In the analysis phase: use multivariate regression to statistically "adjust for" confounders
  - Statistical adjustment is not a panacea; you cannot control for all confounders and there is always "residual" confounding

Cross-sectional (prevalence) studies

- Measure prevalence of disease and exposure on a random sample of the population of interest at one time point.

- Advantages:
  - Cheap and easy!

- Limitations:
  - Correlation does not imply causation
  - Cannot determine what came first
  - Confounding

Example: cross-sectional study

- Relationship between atherosclerosis and late-life depression (Tiemeier et al. *Arch Gen Psychiatry*, 2004).
- Methods: Researchers measured the prevalence of coronary artery calcification (atherosclerosis) and the prevalence of depressive symptoms in a large cohort of elderly men and women in Rotterdam (n=1920).

Case-Control Studies

- Sample on disease status and ask retrospectively about exposures

- Advantages:
  - Efficient for rare diseases and outbreak situations
- Limitations:
  - Getting appropriate controls is tricky.
  - Recall bias
  - Confounding
  - The risk factor may have come after the disease.

Example: case-control study

- Early case-control studies among AIDS cases and matched controls indicated that AIDS was transmitted by sexual contact or blood products.
- In 1982, an early case-control study matched AIDS cases to controls and found a large, positive association between amyl nitrites ("poppers") and AIDS (Marmor et al. *NEJM*, 1982). This is an example of confounding.

Prospective cohort study

- Measure risk factors on people who are disease-free at baseline; then follow them over time and calculate risks or rates of developing disease.

- Advantages:
  - Exposures are measured prior to outcomes!
  - Can study multiple outcomes
- Limitations:
  - Time and money!
  - Confounding
  - Loss to follow-up

Example: cohort study

- The Framingham Heart Study enrolled 5209 residents of Framingham, MA, aged 28 to 62 years, in 1948. Researchers measured their health and lifestyle factors (blood pressure, weight, exercise, etc.). Then they followed them for decades to determine the occurrence of heart disease. The study continues today, tracking the kids and grandkids of the original cohort.

Retrospective cohort study

- Conceptually similar to a prospective cohort study, but the cohort is assembled after outcomes have occurred using stored data.

- Advantages:
  - Exposure data were collected before outcomes occurred.
  - Cheaper and faster than prospective designs
- Limitations:
  - Data quality may be limited.

Example: retrospective cohort study

- **Mortality in former Olympic athletes: retrospective cohort analysis** (*BMJ* 2012; 345: e7456.)
- Methods: Using the Sports Reference database, researchers identified a cohort of 9889 athletes who participated in the Olympic Games between 1896 and 1936 and were born before 1910. They used the database to find dates of death for these athletes. Then they compared the mortality rates of athletes in different types of sports.

Nested Case-Control Studies

- A case-control study in which cases and controls are drawn from within a prospective cohort study. Cases who develop the outcome during follow-up are compared with matched controls, selected from those in the cohort who did not develop the outcome.

- Advantages:
  - Efficient for "expensive" measurements such as blood markers and gene assays.
  - Biomarkers are collected prior to the development of disease, which avoids reverse causality.

- Limitations:
  - Similar to cohort studies.

Example: Nested case-control

- Antenatal HIV-1 RNA load and timing of mother to child transmission; a nested case-control study in a resource poor setting. (Duri et al. *Virology Journal* 2010, 7:176.)
- **Methods:** The study enrolled 177 pregnant women in Zimbabwe who were HIV-1 positive at enrollment; women and infants were followed until six weeks after birth. Cases were mothers who transmitted HIV to their infants (n=29). Each case was matched to one control mother who did not transmit HIV to her infant (n=29). The researchers measured HIV RNA load from blood samples taken during pregnancy.

Randomized clinical trials

Considered the gold standard of study design.

- Advantages:
  - Randomization minimizes confounding.
  - Blinding minimizes bias.
- Limitations:
  - Expensive
  - Can only look at short-term outcomes.
  - Not always ethical to randomize
  - Results may not be generalizable.

Example: double-blind RCT

Comparison of upper gastrointestinal toxicity of rofecoxib and naproxen in patients with rheumatoid arthritis. (Bombardier et al. *N Engl J Med* 2000; 343: 1520-8).

Methods: Researchers randomly assigned 8076 patients with rheumatoid arthritis to receive either rofecoxib (Vioxx) or naproxen (non-steroidal anti-inflammatory) twice daily. The study was double blind. The primary end point was confirmed clinical upper gastrointestinal events (such as ulcers and bleeding).

Statistics for Health Care

Module 2:

Measures of disease frequency

Measures of disease frequency

- Incidence
- Cumulative risk (cumulative incidence)
- Prevalence

Measures of disease frequency

- Incidence
  - The **rate (involves time!)** at which people are developing a disease (new cases).
  - Example: there are 20 new cases of heart disease per 1000 men per year.

Measures of disease frequency

- Cumulative risk (cumulative incidence)
  - The **proportion (percentage)** of people who develop a disease in a specified time period (new cases).
  - Example: During a two-year study, 1% of smokers developed heart disease.

Measures of disease frequency

- Prevalence
  - The **proportion (percentage)** of people who have a disease at a given point in time; **includes old and new cases.**
  - For example, 10% of men over 70 have heart disease.

Example RCT data: rofecoxib vs. Naproxen

Comparison of upper gastrointestinal toxicity of rofecoxib and naproxen in patients with rheumatoid arthritis. (Bombardier et al. *N Engl J Med* 2000; 343: 1520-8).

Methods: Researchers randomly assigned 8076 patients with rheumatoid arthritis to receive either rofecoxib (Vioxx) or naproxen (non-steroidal anti-inflammatory) twice daily. The study was double blind. The primary end point was confirmed clinical upper gastrointestinal events (such as ulcers and bleeding).

Example Data: rofecoxib vs. Naproxen RCT

Gastrointestinal events in the rofecoxib and naproxen groups:

	Number per group	Person-years of follow-up	Number of GI events
rofecoxib group	4047	2666	56
Naproxen group	4029	2688	121

Bombardier C, Laine L, Reicin A, et al. *N Engl J Med* 2000; 343: 1520-8.

Incidence Rates, GI events:

	Number of GI events	Person-years of follow-up	Calculation	Incidence Rate
rofecoxib group	56	2666	56/2666 person-years=.021	**2.1 events per 100 person-years**
Naproxen group	121	2688	121/2688 person-years=.045	**4.5 events per 100 person-years**

Cumulative Risks, GI events:

	Number per group	Number of GI events	Calculation	Cumulative risk
rofecoxib group	4047	56	56/4047=	**1.38%**
Naproxen group	4029	121	121/4029=	**3.00%**

Note: cumulative risk depends on the duration of follow-up.

- In this study, the average follow-up time was 8 months (median = 9 months)
- If follow-up had been 1 year, we'd expect the cumulative risks to be about 2.1% in the rofecoxib group and 4.5% in the Naproxen group.

Example: cross-sectional study

- Relationship between atherosclerosis and late-life depression (Tiemeier et al. *Arch Gen Psychiatry*, 2004).
- Methods: Researchers measured the prevalence of coronary artery calcification (atherosclerosis) and the prevalence of depressive symptoms in a large cohort of elderly men and women in Rotterdam (n=1920).

Example data, cross-sectional study

Depressive disorders by coronary calcification level:

Coronary calcification level	Total number	Number with depressive disorders
0-100	894	9
101-500	487	11
>500	539	16

Tiemeier et al. *Arch Gen Psychiatry*, 2004

Prevalence of depressive disorders

Prevalence of depressive disorders by coronary calcification level:

Coronary calcification level	Total number	Number with dep. disorders	Prevalence of depressive disorders
0-100	894	9	9/894=0.9%
101-500	487	11	11/487=2.3%
>500	539	16	16/539=3.0%

Tiemeier et al. *Arch Gen Psychiatry*, 2004

Statistics for Health Care

Module 3:

Measures of association: absolute differences in risks or rates

Measures of absolute risk differences:

- Difference in rates
- Difference in risks (proportions/percentages)
  - Difference in cumulative risk
  - Difference in prevalence
- Number needed to treat/number needed to harm
  - 1/(rate difference)

Difference in rates, GI events:

	Number of heart attacks	Person-years of follow-up	Incidence Rate
rofecoxib group	56	2666	**2.1 events per 100 person-years**
Naproxen group	121	2688	**4.5 events per 100 person-years**

4.5 – 2.1 = 2.4 fewer GI events in the rofecoxib group per 100 person-years

Difference in cumulative risk, GI events:

	Number per group	Number of GI events	Cumulative risk
rofecoxib group	4047	56	**1.38%**
Naproxen group	4029	121	**3.00%**

1.38% – 3% = 1.62% decrease in the risk of GI events in the rofecoxib group.

Note that the rate difference is a better measure *when it's available!*

From the paper's abstract:

- "2.1 confirmed gastrointestinal events per 100 patient-years occurred with rofecoxib, as compared with 4.5 per 100 patient-years with naproxen."

Bombardier C, Laine L, Reicin A, et al. *N Engl J Med* 2000; 343: 1520-8.

Number needed to treat (NNT)…

- Number needed to treat falls right out of the rate difference!
- You prevent 2.4 GI events when you treat 100 people with rofecoxib for a year. So you need to treat 100/2.4 = 42 people to prevent 1 GI event.
- NNT = 42 (people needed to be treated with rofecoxib to prevent 1 event)

Heart attack data, rofecoxib vs. Naproxen

Heart attacks in the rofecoxib and naproxen groups:

	Number per group	Person-years of follow-up	Number of heart attacks
rofecoxib group	4047	2315 (6.8 months)	17
Naproxen group	4029	2316 (6.8 months)	4

Bombardier C, Laine L, Reicin A, et al. *N Engl J Med* 2000; 343: 1520-8.
Curfman GD, Morrissey S, Drazen JM. *N Engl J Med* 2005; 353:2813-4.

Incidence Rates, heart attacks:

	Number of heart attacks	Person-years of follow-up	Calculation	Incidence Rate
rofecoxib group	17	2315	17/2315 person-years=.0073	**7.3 events per 1000 person-years**
Naproxen group	4	2316	4/2316 person-years=.0017	**1.7 events per 1000 person-years**

What is the rate difference?

	Incidence Rate
rofecoxib group	**7.3 events per 1000 person-years**
Naproxen group	**1.7 events per 1000 person-years**

7.3 – 1.7 = 5.6 excess heart attacks in the rofecoxib group per 1000 person-years

Cumulative Risks of heart attack

	Number per group	Number of heart attacks	Calculation	Cumulative risk
rofecoxib group	4047	17	17/4047=	**0.42%**
Naproxen group	4029	4	4/4029=	**0.10%**

What is the cumulative risk difference?

	Cumulative risk
rofecoxib group	**0.42%**
Naproxen group	**0.10%**

0.42%-0.10% = 0.32% increase in the risk of heart attacks in the rofecoxib group.

From the paper's abstract:

- "The incidence of myocardial infarction was lower among patients in the naproxen group than among those in the rofecoxib group (0.1 percent vs. 0.4 percent)."

They've reported the cumulative risks not the incidences!

Bombardier C, Laine L, Reicin A, et al. *N Engl J Med* 2000; 343: 1520-8.

How would an alternate presentation change the message?

- The incidence of myocardial infarction was higher among patients in the rofecoxib group than among those in the naproxen group (7.3 events per 1000 person-years vs. 1.7 events per 1000 person-years).

Number needed to harm?

- NNH = 1000/5.6 = 179

179 people has to be treated with Rofecoxib (Vioxx) for a year to harm 1 additional person

Statistics for Health Care

Module 4:

Measures of association: relative risks

Measures of relative risk

- Rate ratio/hazard ratio
  - Ratio of incidence rates
  - Hazard ratio: ratio of hazard rates, which are instantaneous incidence rates; calculated using Cox regression.
- Risk ratio
  - Ratio of cumulative risks (proportions)
  - Ratio of prevalences (proportions)
- Odds ratio (also see: Module 5)
  - Odds ratios are the only valid measure of relative risk for case-control studies.
  - Odds ratios are calculated from logistic regression.

Interpretations:

- Rate ratio/hazard ratio
  - Percent increase (or decrease) in the rate of the outcome.
- Risk ratio
  - Percent increase (or decrease) in the risk (or prevalence) of the outcome.
- Odds ratio
  - Percent increase or decrease in the odds of the outcome.

Interpreting relative risks:

- 1.0 = null value (no difference)
- <1.0 = protective effect (decreased risk)
- >1.0 = harmful effect (increased risk)

Rate ratio, GI events:

	Incidence Rate
rofecoxib group	**2.1 events per 100 person-years**
Naproxen group	**4.5 events per 100 person-years**

$$\frac{2.1}{4.5} = 0.46$$

Interpretation: rofecoxib reduces the rate of GI events by 54%.

Risk ratio, GI events

	Cumulative risk
rofecoxib group	**1.38%**
Naproxen group	**3.00%**

$$\frac{1.38}{3.0} = 0.46$$

The risk ratio and rate ratio are identical here since the groups were followed for equal amounts of time.

From the paper's abstract…

- "During a median follow-up of 9.0 months, 2.1 confirmed gastrointestinal events per 100 patient-years occurred with rofecoxib, as compared with 4.5 per 100 patient-years with naproxen (**relative risk, 0.5; 95 percent confidence interval, 0.3 to 0.6; P<0.001**)."

Bombardier C, Laine L, Reicin A, et al. *N Engl J Med* 2000; 343: 1520-8.

95% Confidence interval, **0.3 to 0.6**

- Gives a plausible range of values for the true effect.
- We can be 95% confident that the true effect of rofecoxib (vs. naproxen) is between a 40% and 70% reduction in the rate of GI events.

Rate ratio, heart attacks

	Incidence Rate
rofecoxib group	**7.3 events per 1000 person-years**
Naproxen group	**1.7 events per 1000 person-years**

$$\frac{7.3}{1.7} = 4.2$$

Risk ratio, heart attacks:

	Cumulative risk
rofecoxib group	**0.42%**
Naproxen group	**0.10%**

$$\frac{0.42}{0.1} = 4.2$$

Interpretation: rofecoxib increases the rate/risk of heart attacks by 320 percent (4-fold).

From the paper's abstract…

"The incidence of myocardial infarction was lower among patients in the naproxen group than among those in the rofecoxib group (0.1 percent vs. 0.4 percent; **relative risk, 0.2; 95 percent confidence interval, 0.1 to 0.7).**"

They "flipped" the relative risk, implying that Naproxen is protective rather than that rofecoxib is harmful. (0.1/.42=0.24)

Paper's conclusion:

Conclusion: "Thus, our results are consistent with the theory that naproxen has a coronary protective effect and highlight the fact that rofecoxib does not provide this type of protection...

Introduction to hazard ratios

- A hazard ratio is similar to a rate ratio, but is the ratio of instantaneous incidence rates.
- Hazard ratios are calculated using Cox regression.
- More later in course.

Introduction to odds ratios

- Odds ratios are another measure of relative risk.
- For case-control studies, the odds ratio is the only valid measure of relative risk.

Risk vs. Odds

If the risk is…	Then the odds are…
½ (50%)	**1:1**
¾ (75%)	**3:1**
1/10 (10%)	**1:9**
1/100 (1%)	**1:99**

Note: An odds is always higher than its corresponding probability, unless the probability is 100%.

Risk (prevalence) ratios for depression and artery blockage data:

Coronary calcification level	Prevalence of depressive disorders	Risk ratio (compared with none/low group)
0-100	0.9%	reference
101-500	2.3%	2.3/0.9=2.56
>500	3.0%	3.0/0.9=3.33

Tiemeier et al. *Arch Gen Psychiatry*, 2004

Risk (prevalence) ratios for lockage data:

Interpretation: Those with moderate blockage have a 156% increased prevalence of depressive disorder compared with those with the least blockage.

Coronary calcification level	Prevalence of depressive symptoms	Risk ratio (compared with none/low group)
0-100	0.9%	reference
101-500	2.3%	2.3/0.9=2.56
>500	3.0%	3.0/0.9=3.33

Tiemeier et al. *Arch Gen Psychiatry*, 2004

Risk (prevalence) ratios for ry blockage data:

Interpretation: Those with severe blockage have a 233% increased prevalence of depressive disorder compared with those the least blockage.

Coronary calcification level	Prevalence of depressive symptoms	Risk ratio (compared with none/low group)
None/low	0.9%	reference
Moderate	2.3%	2.3/0.9=2.56
Severe	3.0%	3.0/0.9=3.33

Tiemeier et al. *Arch Gen Psychiatry*, 2004

From the paper…

Table 3. Relationship Between Coronary Calcifications and Depression Expressed as Odds Ratio*

Atherosclerosis Measure	Controls,† No.	Subthreshold Depressive Symptoms†			Depressive Disorders†		
		No.	Odds Ratio	95% CI	No.	Odds Ratio	95% CI
Coronary calcification							
0-100	865	20	1.0	Reference	9	1.0	Reference
101-500	463	13	1.10	0.53-2.30	11	2.45	0.98-6.13
>500	511	12	0.96	0.43-2.16	16	3.89	1.55-9.77

Abbreviation: CI, confidence interval.

*Odds ratios were calculated with logistic regression adjusted for age, sex, total cholesterol level, cognitive score, blood pressure, diabetes mellitus, body mass index, smoking, antidepressant medication, history of stroke, and myocardial infarction. To test statistical significance of the association between coronary calcifications and depressive disorders, we calculated the overall *P* value with a test for trend; $P = .004$.

†See Table 2 for explanation.

The **ODDS** of depressive symptoms by coronary calcification level

Coronary calcification level	Prevalence of depressive symptoms	ODDS of depressive symptoms
0-100	0.9%	0.9%/99.1%
101-500	2.3%	2.3%/97.7%
>500	3.0%	3.0%/97.0%

Tiemeier et al. *Arch Gen Psychiatry*, 2004

Odds ratios for depressive symptoms

$$OR_{\text{moderate vs. low}} \frac{\frac{2.3\%}{97.7\%}}{\frac{.9\%}{99.1\%}} = 2.59$$

Interpretation: 159% increased ODDS of depressive disorder

$$OR_{\text{severe vs. low}} \frac{\frac{3.0\%}{97.0\%}}{\frac{.9\%}{99.1\%}} = 3.41$$

Interpretation: 241% increased ODDS of depressive disorder

Odds ratios and risk ratios are similar **for rare outcomes only**!

- When the outcome is rare, the odds ratio and risk ratio are very similar!
  - 2.56 vs. 2.59
  - 3.33 vs. 3.41
- When the outcome is common, this is not true and odds ratios can be misleading! (More in: Module 5!)

Why do we ever use an odds ratio??

- We cannot calculate risk or rate ratios from a case-control study (since we cannot calculate the risk or rate of developing the disease).
- **The multivariate regression model for binary outcomes (logistic regression) gives odds ratios, not risk ratios.

What is the odds ratio for the rofecoxib data?

	Cumulative risk
rofecoxib group	**0.42%**
Naproxen group	**0.10%**

What is the odds ratio for the rofecoxib data?

	Cumulative risk
rofecoxib group	**0.42%**
Naproxen group	**0.10%**

$$OR = \frac{\frac{0.42\%}{99.58\%}}{\frac{0.10\%}{99.9\%}} = 4.21$$

Odds ratios and risk ratios are similar when the outcome is rare!

Statistics for Health Care

Module 5:

Odds ratios can mislead

Odds ratios and risk ratios are similar for rare outcomes...

- Risk ratio: $\frac{3\%}{1\%} = 3.0$

- Corresponding Odds ratio: $\frac{\frac{3\%}{97\%}}{\frac{1\%}{99\%}} = 3.06$

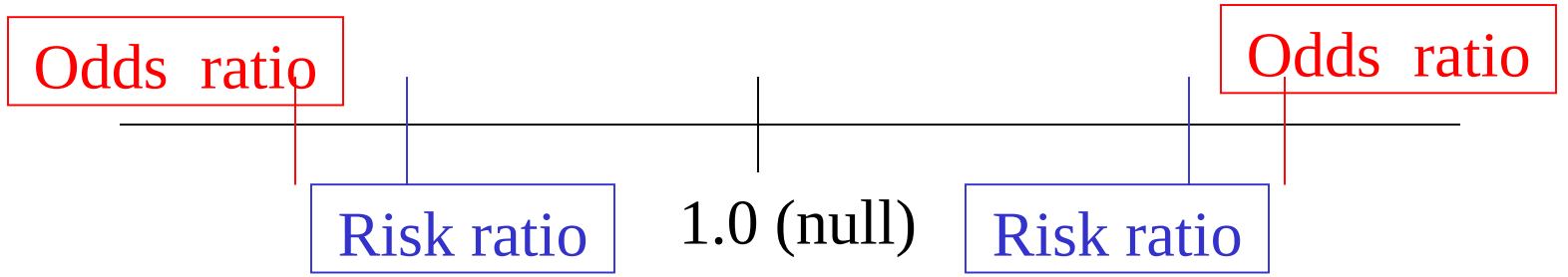
But odds ratios distort effects for common outcomes…

- Risk ratio: $\frac{60\%}{20\%} = 3.0$

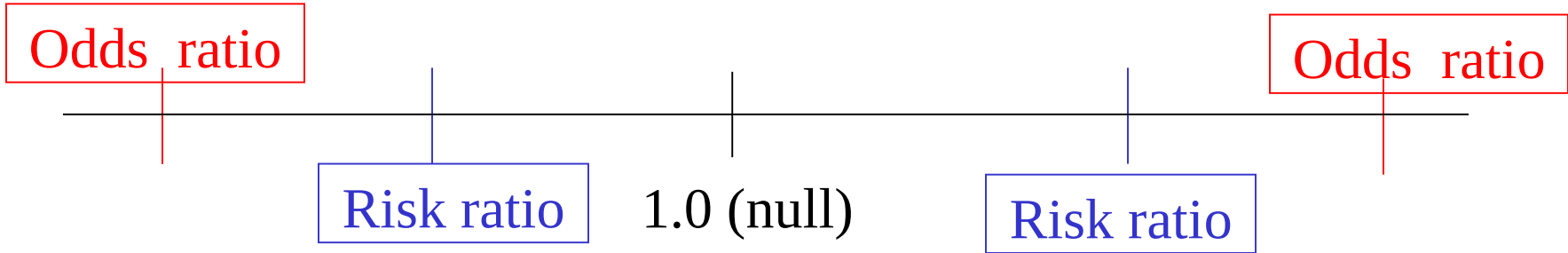
- Corresponding Odds ratio: $\frac{\frac{60\%}{40\%}}{\frac{20\%}{80\%}} = 6.0$

The odds ratio vs. the risk ratio

Rare Outcome



Common Outcome



Interpretation of the odds ratio:

- Odds ratios can be interpreted as risk ratios for rare outcomes
  - Rule of thumb for defining "rare": outcome occurs in <10% of the reference/control group
- But, when the outcome is common, odds ratio distort the effect size and need to be interpreted cautiously.

Example: Study of caloric labeling

- Researchers studied the beverage purchases of teenagers at 4 stores; each store was measured at baseline and under 3 "caloric conditions" (signs posted outside the store):
  - Absolute calories: "Did you know that a bottle of soda or fruit juice has about 250 calories?"
  - Relative calories: "Did you know that a bottle of soda or fruit juice has about 10% of your daily calories?"
  - Exercise equivalents: "Did you know that working off a bottle of soda or fruit juice takes about 50 minutes of running?"

Bleich SN, Herring BJ, Flagg DD, Gary-Webb TL. Reduction in purchases of sugar-sweetened beverages among low-income black adolescents after exposure to caloric information. *Am J Public Health*. February 2012, Vol. 102, No. 2, pp. 329-335.

The Results…

Condition	What percent of drinks purchased were sugary beverages?
Pre-intervention (no information)	93.3%
Absolute calories	87.5%
Relative calories	86.5%
Exercise equivalent	86.0%
Any caloric information (overall)	86.7%

What conclusions would you draw from the data?

The Results…

Condition	Percent sugary beverages
Pre-intervention (no information)	93.3%
Absolute calories	87.5%
Relative calories	86.5%
Exercise equivalent	86.0%
Any caloric information	86.7%

How big is the *absolute* drop in risk?

93.3% - 87.5%
= ~ 6% drop

93.3% - 86%
= ~7% drop

The Results…

Condition	Percent sugary beverages
Pre-intervention (no information)	93.3%
Absolute calories	87.5%
Relative calories	86.5%
Exercise equivalent	86.0%
Any caloric information	86.7%

How big is the *relative* drop in risk, or risk ratio?

$$\frac{87\%}{93\%} = 0.94$$

$$\frac{86\%}{93\%} = 0.92$$

Interpretation: 6%-8% drop in relative risk

Headlines…

- ’Exercise labels’ beat out calorie counts in steering consumers away from junk food
- Exercise labels are better at keeping teens away from junk food, researchers say

Media coverage…

- The researcher said: "*The results are really encouraging. We found that providing any information (via the three signs) relative to none,* ***reduced the likelihood that they would buy a sugary beverage by 40 per cent.***
- *"Of those three signs,* ***the one that was most effective was the physical activity equivalent****.*
- *"We found that when that sign was posted,* ***the likelihood that they would buy a sugary beverage reduced by around 50 per cent****."*

How does a 6 or 7 percent drop become a 40 or 50 percent drop?

Odds ratios from logistic regression!

Condition	Unadjusted Percentage of sugary drinks	Adjusted **Odds ratio**
Pre-intervention (no information)	93.3	1.00 (ref)
Absolute calories	87.5	0.62
Relative calories	86.5	0.59
Exercise equivalent	86.0	0.51
Any caloric information	86.7	0.56

These interpretations are mistaken! Odds ratios tell you about the change in odds not in risk/likelihood.

"40 percent drop in likelihood"

"50 percent drop in likelihood"

Odds ratio vs. risk ratio…

- Risk ratio: $\frac{86\%}{93\%} = 0.92$

- Corresponding Odds ratio: $\frac{\frac{86\%}{14\%}}{\frac{93\%}{7\%}} = 0.46$

We cannot interpret the odds ratio as indicating a "54% drop in likelihood"! There is a 54% drop in odds, but only an 8% drop in likelihood (risk)!

You can convert "adjusted" odds ratios from logistic regression to "adjusted" risk ratios!

Condition	Adjusted Odds ratio	Adjusted Risk ratio*
Pre-intervention (no information)	1.00 (ref)	1.00 (ref)
Absolute calories	0.62	0.96
Relative calories	0.59	0.96
Exercise equivalent	0.51	0.94
Any caloric information	0.56	0.95

6 percent drop in risk

5 percent drop risk

*Calculated by converting adjusted odds ratios from logistic regression into adjusted risk ratios, using the formula:
RR=OR/(1-pref+OR*pref)

Converting odds ratios to risk ratios...

Odds ratio from logistic regression

Conversion formula:

$$RR = \frac{OR}{(1 - p_{ref}) + (p_{ref} \times OR)}$$

risk/prevalence of the outcome in the reference group

Example:

$$RR = \frac{0.51}{(1 - 0.933) + (0.933 \times 0.51)} = 0.94$$

Zhang J. What's the Relative Risk? A Method of Correcting the Odds Ratio in Cohort Studies of Common Outcomes *JAMA.* 1998;280:1690-1691.

Mathematical proof:

Example 2, wrinkle study…

- A cross-sectional study on risk factors for wrinkles found that heavy smoking significantly increases the risk of prominent wrinkles.
  - Adjusted OR=3.92 (heavy smokers vs. nonsmokers) calculated from logistic regression.
  - Interpretation: heavy smoking increases risk of prominent wrinkles nearly 4-fold??
  - The prevalence of prominent wrinkles in non-smokers is roughly 45%. So, it's not possible to have a 4-fold increase in risk (=180%)!

Raduan et al. *J Eur Acad Dermatol Venereol*. 2008 Jul 3.

Risk ratios have ceilings!

- If the outcome has a 10% prevalence in the reference group, the *maximum* possible RR=10.0.
- For 20% prevalence, the maximum possible RR=5.0
- For 30% prevalence, the maximum possible RR=3.3.
- For 40% prevalence, maximum possible RR=2.5.
- For 50% prevalence, maximum possible RR=2.0.

Convert OR to RR…

$$RR_{\text{smokers vs. non-smokers}} = \frac{3.92}{(1-.45)+(.45\times 3.92)} = 1.69$$

So, the risk (prevalence) of wrinkles is increased by 69%, not 292%.

Zhang J. What's the Relative Risk? A Method of Correcting the Odds Ratio in Cohort Studies of Common Outcomes *JAMA.* 1998;280:1690-1691.

Statistics for Health Care

Module 6:

Communicating risks clearly: absolute vs. relative risks

Relative vs. absolute risks

- Authors love relative risks!
- A dramatic increase in relative risk may correspond to only a small increase in absolute risk:

.003%/.001% = 3.0

Versus:

.003%-.001% = .002%

Example

- Women's Health Initiative: large randomized, double-blind study of postmenopausal hormones versus placebo
- Halted in 2002 because hormones were found to significantly increase the risks of breast cancer and heart disease
- 14 million women were on hormones at the time the study was halted

Media coverage (well done!)

- "The data indicate that if 10,000 women take the drugs for a year, 8 more will develop invasive breast cancer, compared with 10,000 who were not taking hormone replacement therapy. An additional 7 will have a heart attack, 8 will have a stroke, and 18 will have blood clots. But there will be 6 fewer colorectal cancers and 5 fewer hip fractures."

Rates/risks for breast cancer

Rate in the hormone group	Rate in the Placebo group	Rate difference per 10,000 women-years	**Relative risk***	**Relative risk interpretation**
38 per 10,000 women-years	30 per 10,000 women-years	8 additional events per 10,000 women-years	**1.26**	**"26% increase in risk"**

*This is an adjusted relative rate (hazard ratio), so it is close to 38/30, but not quite equal to this.

26% increased risk of breast cancer sounds impressive and scary, but the absolute increase in risk is .08% per year!

Rates/risks for heart attack

Rate in the hormone group	Rate in the Placebo group	Rate difference, per 10,000 women-years	**Relative risk***	**Relative risk interpretation**
37 per 10,000 women-years	30 per 10,000 women- years	7 additional events per 10,000 women-years	**1.29**	**"29% increase in risk"**

*This is an adjusted relative rate (hazard ratio), so it is close to 38/30, but not quite equal to this.

29% increased risk of heart attack sounds impressive and scary, but the absolute increase in risk is .07% per year!

Number needed to harm…

	Absolute rate difference, per 10,000 women-years	Number needed to harm one woman
Heart attack	7 additional events per 10,000 women-years	1429
Invasive breast cancer	8 additional events per 10,000 women-years	1250

Tips for presenting risk:

- Most people have an easier time understanding whole numbers than percentages and decimals
- Absolute risks give a more accurate picture of the true risk than relative risks
- Public health risk can be large even when the risk to a given individual is small