Lesson 4
Part 2

Describing Relationships Between Two Nominal Characteristics

Measuring relationship between two variables

- The Relative Risk and the Odds Ratio are measures used to describe the relationship (or association) between two binary variables
- For Numerical data, the Pearson correlation coefficient describes the relationship
- The Spearman Rank correlation coefficient is used to describe the relationship between ordinal or skewed variables

Outline for Lesson 4 Part 2

- Relative Risk
- Absolute Risk Reduction and Absolute Risk Increase
- Number Needed to Treat and Number Needed to Harm
- Relative Risk Reduction
- Odds Ratio

This Lesson will refer to the Lesson 4 Part 2 Practice Exercises

Ratio

- A ratio is calculated as an expression of the form a / b where a and b are similar quantities measured from different groups.

- Examples of ratios
  - Male:Female ratio of students
  - Odds of winning a bet
  - Risk of disease for exposed group compared to risk of disease for unexposed group

- A ratio compares the magnitude of one quantity relative to another

Proportion, Rate, Ratio

Proportions, Rates and Ratios have different properties

- Proportion
  - the numerator is a subset of the denominator
  - Always between 0 and 1 (or 0% and 100% when expressed as %)
- Rate
  - Number of events per unit of time – these rates are not proportions
  - Number of events per population where events are counted over a specified time interval – these rates are similar to proportions
  - Change rate – not a proportion
- Ratio
  - Not a proportion
  - Similar quantities from two different groups: the numerator is not a subset of the denominator

Ratio compared to Proportion

- In a class of 100 with 60 women and 40 men
  - The proportion of women = =
  - The proportion of men = =
  - The ratio of women:men = =
  - The ratio of men:women = =
- Ratios range from 0 to large positive. If the denominator group has a count of 0, the ratio cannot be calculated

Relative Risk: general definition

- **The Relative risk** is the ratio of risks for two different populations

$$\text{Relative Risk} = \frac{\text{disease risk in group 1}}{\text{disease risk in group 2}}$$

- If the risk of having disease is 2/10 in one population and 1/10 in the reference population, then the *relative* risk is:

(2/10) / (1/10) = 2.0

Calculate RR for Exposed / Unexposed

	Disease	No Disease	Total
Group 1	a	b	a+b
Group 2	c	d	c+d

Risk of Disease for Group 1 = a / (a+b)

Risk of Disease for Group 2 = c / (c+d)

$$RR = a/(a+b) \div c/(c+d)$$

Relative Risk

Relative risk addresses the question: "How many times more likely are the *exposed* persons to become diseased than *nonexposed* persons**?"** (Fletcher et al, 1988, p102).

Relative Risk from cohort study or a cross-sectional study

$$RR = \frac{\text{risk of lung cancer for smokers}}{\text{risk of lung cancer for non-smokers}}$$

- Relative Risk is a measure of the strength of association between the exposure and the disease.

Relative Risk from Clinical Trial

- In a clinical trial, if there is a ‘control’ group and an ‘experiment’ or ‘treatment’ group
- $RR = \frac{\text{risk for experimental group}}{\text{risk for control group}} = \frac{EER}{CER}$

- EER = experimental event rate
- CER = control event rate

Interpretation of RR:

For RR: risk of group1/ risk of group2

- RR > 1.0: the risk for group 1 is greater than the risk for group 2
  - Being in group 1 risk factor

- RR < 1.0: the risk for group 1 is less than the risk for group 2
  - Being in group 1 protective factor

- RR = 1.0 or close to 1.0: the risk in the two groups is the same.

Strength of Association

- The further RR is from 1.0, *in either direction,* the stronger the association between exposure and outcome.

- Which indicates a stronger association?
  - RR = 8 or RR = 1.2
  - RR = 0.9 or RR = 0.1

RR for Nonfatal MI

	Fatal MI	No Fatal MI	Total
Aspirin group	10	11,027	11,037
Placebo group	26	11,008	11,034

Risk of Fatal MI for aspirin group =

Risk of Fatal MI for placebo group =

RR aspirin vs. placebo =
0.000906 / 0.002356 = 0.384

Interpretation of RR

- The Relative Risk of Fatal MI = 0.384
- Since the RR < 1.0 the exposure (aspirin) is a protective factor.

- The reciprocal of the RR provides the increased risk of Fatal MI in the placebo group: 1 / 0.384 = 2.6

- Physicians in the placebo group were 2.6 times more likely to have a Fatal MI than physicians in the aspirin group.

Absolute Risk Reduction (ARR)

- If the risk is lower in the treatment group than in the control group, the risk reduction can be calculated as EER – CER
- The absolute value of this difference is the ARR= | EER – CER |

- EER – CER is negative when the treatment reduces risk

Absolute Risk Increase (ARI)

- If the risk is greater in the treatment group than in the control group, the risk increase is calculated as EER – CER
- The absolute value of this difference is the ARI= | EER – CER |

- EER – CER is positive when the treatment increases risk

ARR and ARI

- Both ARR and ARI are calculated as the absolute value of the EER – CER difference
- ARR: difference is negative – usually the treatment is expected to *reduce* risk
- ARI: difference is positive – useful for measuring increase in side-effects of the treatment

NNT and NNH

- NNT = Number Needed to Treat = the number of people who need to receive the treatment to prevent one event = 1/ARR
- NNH = Number Needed to Harm = the number of people who need to receive the treatment to result in one event = 1/ARI
- NNT and NNH provide a basis for weighing the costs/benefits of a treatment

Relative Risk Reduction: RRR

- The Relative Risk Reduction = the risk reduction (EER – CER) relative to the baseline risk.
  - The denominator for RRR is the risk for the control group = CER
  - The numerator for RRR is ARR = | EER- CER |
- RRR = ARR / CER

ARR, RRR and NNT

	Fatal MI	No Fatal MI	Total
Aspirin group	10	11,027	11,037
Placebo group	26	11,008	11,034

Calculate the Absolute Risk Reduction_____

Calculate the Relative Risk Reduction_____

Calculate the Number Needed to Treat _____

ARR, RRR and NNT

	Fatal MI	No Fatal MI	Total
Aspirin group	10	11,027	11,037
Placebo group	26	11,008	11,034

ARR = | 0.000906 – 0.00236|= |-0.00145| = 0.00145

RRR = ARR / CER = 0.00145 / 0.00236 = 0.615

NNT = 1/ ARR = 1/ 0.00145 = 689

Interpretations of ARR, RRR, NNT

- The ARR = 0.00145. Multiply this by 100,000
  - the absolute risk reduction in fatal MI = 145 per 100,000 people.
- The RRR = 0.615.
  - Relative to the baseline fatal MI risk in the placebo group, taking aspirin reduces the risk of fatal MI by 61.5%.
- NNT = 689.
  - One fatal MI is prevented for every 689 people* taking aspirin.

* Assuming that results of this study that enrolled physicians can be generalized to the general population

Odds ratio

- The Relative Risk is not an appropriate measure in a Case-Control study.
  - The investigator decides how many subjects with and without the disease to study. The proportion of diseased vs. not is not reflective of the population.
- When data are collected in a case control study use the Odds Ratio (OR)

Disease Odds Ratio

- The disease odds ratio compares the odds of disease for those in one group compared to the odds of disease in another group

$$\text{disease OR} = \frac{\text{odds of disease for group 1}}{\text{odds of disease for group 2}}$$

Odds Ratio: Definitions

- Odds of disease for one group=

  $\frac{\text{\# diseased}}{\text{\# not diseased}}$

Disease OR Formula

	D+	D-
Group 1	**a**	**b**
Group 2	**c**	**d**
Total	**a + c**	**b + d**

Odds of Disease for Group 1 = a/b

Odds of Disease for Group 2 = c/d

$$\mathbf{OR = a/b \div c/d = a*d \,/\, b*c}$$

Note: this formula is only valid for a table arranged as above

TRH Hormone Study

- Case control study
- Using thyroid hormone (TRH) to stimulate fetal lung development.
- Q: Is there a difference in the odds of death for those exposed to TRH compared to those not exposed to TRH?

Disease OR for TRH example

	Death (cases)	Alive (controls)	Total
TRH (n = 392)	**43**	**349**	**392**
Placebo (n = 377)	**42**	**335**	**377**
Total	**85**	**684**	**769**

Odds of death for TRH Exp = _____

Odds of death for Placebo = _____

Disease OR = _____

Calculate the Odds and the Odds Ratio before moving to the next slide

Interpretation of disease OR

- If OR > 1.0: the odds of disease for group 1 is greater than the odds of disease for group 2

- If OR < 1.0: the odds of disease for group 1 is less than the odds of disease for group 2

- If OR = 1.0 or close to 1.0: the odds of event in the two groups is the same or similar which indicates no association between disease and outcome.

TRH Example

- The OR for the TRH example = 0.98 indicating that there is probably not association between TRH disease and infant death.

Strength of Association

- An OR > 1.0 or < 1.0 indicates a possible relationship (or association) between disease and outcome.
- The further the OR is from 1.0, *in either direction,* the stronger the association between disease and event.
- Which indicates a stronger association?
  - OR = 7 or OR = 2
  - OR = 0.8 or OR = 0.15

Disease OR and Exposure OR

- Exposure OR = Disease OR

Exposure OR Formula

	D+	D-
Exposed	**a**	**b**
Not Exposed	**c**	**d**
Total	**a + c**	**b + d**

Odds of exposure for D + = a/c

Odds of exposure for D- = b/d

$$\mathbf{OR = a/c \div b/d = a*d \,/\, b*c}$$

Note: this formula is only valid for a table arranged as above

Relative Risk for rare events

- Risks can be calculated from prospective cohort studies: follow an exposed group and an unexposed group over time and observe the number of events and follow-up time in each group.
- When the event is rare, it can be difficult to estimate the risk without a long (and usually expensive) prospective cohort study
- For *rare events*, the Disease Odds Ratio can provide an estimate of the Relative Risk

Odds Ratio and Relative Risk

- Calculate the RR and Disease OR from this table

		Disease		
		Yes	**No**	
	Yes	A	B	A+B
disease	**No**	C	D	C+D

- Relative Risk= $\frac{A/(A+B)}{C/(C+D)}$
- Odds Ratio= $\frac{A/B}{C/D}$

Relationship between RR and OR for rare events

$$RR = \frac{A/A+B}{C/C+D} \qquad OR = \frac{A/B}{C/D}$$

These ratios are NOT equivalent.

However, if the disease (or event) is rare, A+B is approximately equal to B and C+D is approximately equal to D because, for rare events, the A and C cells will be small.

In these cases, the RR can be approximated by the OR:

$$RR \approx \frac{A/B}{C/D} = OR$$

Odds Ratio and Relative Risk

- Both RR and OR measure the strength of association between two nominal variables

- **Odds ratios** are used in case-control studies
  - Cases and controls are selected in the present
  - Level of disease is determined retrospectively

- **Relative risks** are used in cohort studies & cross-sectional studies

  - For very rare outcomes, the OR can be used as an estimate of the RR. This approximation is valid when the prevalence of the disease or outcome is < 0.05

EXAMPLE 1:
A multicenter study was conducted to assess the occurrence of death following angioplasty to reopen occluded coronary arteries. The study involved 4030 patients undergoing angioplasty. Among 3000men in the study, 7 died in the hospital following the procedure. Among the 1030 women in the study, 27 died in the hospital following the procedure.

Define the events:
D+ =Death following angioplasty
D- =Survival following angioplasty
M =Patient is Male
F =Patient is Female

Postprocedure Outcome

Gender	D+	D-	Total
M	7	2993	3000
F	27	1003	1030
Total	34	3996	4030

D+ =Death following angioplasty
D- =Survival following angioplasty
M =Patient is Male
F =Patient is Female

What is the risk of death following angioplasty for men?

1. 0.0023
2. 0.0023
3. 0.2059
4. 0.0084
5. Cannot be determined

What is the risk of death following angioplasty for women?

1. 0.0023
2. 0.0084
3. 0.2556
4. 0.0262
5. Cannot be determined

What is the relative risk of death following angioplasty for women compared to men?

1. 41.89
2. 0.02387
3. 0.09
4. 11.24
5. Cannot be determined

EXAMPLE 2:

Alcohol and esophageal cancer. Data from a case-control study of 200 esophageal cancer cases and 775 community-based controls are shown below. Detailed dietary data were obtained by interview. This example addresses the relation between alcohol consumption (dichotomized at 80 grams per day) and esophageal cancer.

[source:http://www.sjsu.edu/faculty/gerstman/StatPrimer/case-control.pdf]

	D+	D-	Total
>80 g/day	96	109	205
≤80 g/day	104	666	770
Total	200	775	975

What is the risk of esophageal cancer for those who consume more than 80 g/day of alcohol?

1. 0.468
2. 0.098
3. 0.135
4. 3.467
5. Cannot be determined.

What is the odds of esophageal cancer for those who consume more than 80 g/day of alcohol compared to those who consume 80 g/day or less?

1. 5.64
2. 0.18
3. 6.62
4. 0.15
5. Cannot be determined.

RR and OR in EXCEL

- To calculate RR or OR in EXCEL you only need division (/) and multiplication (*)
- Use ( ) around the terms in the numerator and denominator of the ratio so that the division is done correctly.
- Data in tables are not always set up in the same format so check the labels carefully to identify the correct numerator and denominator before calculating RR and OR.

Readings and Assignments

- Reading Chapter 3 pgs. 50 – 58
- Work through Practice Exercises
- Excel Module 4: the last 6 worksheet
- Complete Homework 2: Problems 3 – 5 and submit by the due date
- Review for Exam 1 - Tuesday