Measuring Association in Contingency Tables

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Outline

1. Contingency tables and probability
2. Study design, odds, and odds ratios

Introduction

- Lately we've been using the Chi-squared test of association to identify *statistically significant* relationships between two categorical variables
- This presentation will focus on how to report the *clinical significance* of the observed effect following a significant Chi-squared test

Contingency tables and probability

- Statisticians define the **probability** of an outcome as it's long-run relative frequency
  - For example, the probability of a coin flip resulting in "heads" is 0.5 because over a very large number of coin flips you'll see "heads" half of the time

Contingency tables and probability

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  - For example, the probability of a coin flip resulting in "heads" is 0.5 because over a very large number of coin flips you'll see "heads" half of the time
- Under this definition, it's reasonable to *estimate* an outcome's probability using the corresponding *sample proportion* (ie: $\hat{p}$)

Diagnostic tests

Probability is often applied to contingency tables in applications involving *diagnostic testing*:

	Positive	Negative
Present	True Positive	False Negative
Absent	False Positive	True Negative

- Here, subjects are grouped according to the presence or absence of a disease or exposure (rows)
  - Their outcome on a diagnostic test is recorded as either positive (suggesting they have the disease) or negative (suggesting they do not have the disease)

Diagnostic tests

Diagnostic tests:

	Positive	Negative
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- If the diagnostic test is effective, you'd expect the proportion of "true positives" in the "present" group to be high
  - The probability corresponding to this proportion is the test's **sensitivity**

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  - The probability corresponding to this proportion is the test's **sensitivity**
- You'd also expect the proportion of "true negatives" in the "absent" group to be high
  - The probability corresponding to this proportion is the test's **specificity**

Practice

Radionuclide ventriculography (RNV) is a non-invasive approach to diagnosing coronary artery disease (CAD). Summarized below are data collected from a population at high risk of coronary artery disease:

	positive	negative
CAD Present	302	179
CAD Absent	80	372

1) Use StatKey to perform a Chi-squared test to determine if there's a *statistically significant* relationship between an individual's RNV result and the presence CAD.
2) Estimate the sensitivity and specificity of RNV, then comment upon it's *clinical significance* as a diagnostic test.

Practice (solution)

1) Using StatKey, $X^2 = 195.907$ and the p-value is nearly zero, so there is overwhelming statistical evidence of an association.
2) The sensitivity is $302/481 = 0.628$ and the specificity is $372/452 = 0.823$; so, while the relationship is highly statistically significant, the clinical significance might only be considered moderate

Epidemiology is a branch of the biomedical sciences that focuses on relationships between health-related exposures and outcomes:

	Disease	Absent
Exposed		
Unexposed		

- It is common to compare *risks* of the disease among the exposed and unexposed
  - "Risk" is defined as the estimated probability of having the disease given your exposure status (ie: row proportion)
  - The exposed and unexposed are sometimes compared using *risk differences* or *risk ratios* (relative risk)

Epidemiology

Two important study designs used in epidemiology are:

1) *Cohort studies* - a single group is followed forward in time and both variables (exposure status and disease status) are directly observed
2) *Case-control studies* - separate groups of disease-positive (cases) and disease-negative (controls) are asked about their past exposures

Study design directly influences whether or not risks can be accurately estimated.

Case-control studies

A well-known case-control study published in 1969 examined the relationship between oral contraceptive (OC) use and the risk of blood clots. Data from the study is summarized in the table below:

	Cases (blood clots)	Controls (no clots)
Didn't use OC	42	145
Used OC	42	23

- Notice that 42 of 65 individuals (64.6%) in this study that had used OC also had developed blood clots
  - Based upon your prior knowledge, does this seem like an accurate estimate of the risk of developing blood clots for an OC user?

Case-control studies

- 64.6% is nowhere close to the actual probability of an OC user developing blood clots (the real probability is less than 1%)
- In a case-control study, we cannot use conditional proportions to estimate the risk of an outcome given an exposure
  - So, the *risk difference* and *relative risk* cannot be estimated in a case-control study!

Odds

- The **odds ratio** (OR) can be estimated in a case-control study
  - Instead of a ratio of two probabilities (relative risk), the odds ratio is a ratio of two odds

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- The **odds ratio** (OR) can be estimated in a case-control study
  - Instead of a ratio of two probabilities (relative risk), the odds ratio is a ratio of two odds
- The **odds** of an event are the number of times that event occurs relative to the number of times it doesn't occur
  - Suppose the probability of an event is 50%, the odds here are 1 (.5/.5), which people tend to express as "1 to 1 odds"
  - Suppose the probability of an event is 75%, the odds here are 3 (.75/.25), or "3 to 1 odds"

Odds Ratios

Odds ratios have two major advantages:

1. Can be used in case-control studies
2. Symmetry - the OR for survival of cases relative to controls = the OR for death of controls relative to cases

Practice

Below are the results of the OC case-control study:

	Cases (blood clots)	Controls (no clots)
Didn't use OC	42	145
Used OC	42	23

1) Find the *odds* of blood clots for OC users
2) Find the *odds* of blood clots for those not using OC
3) Find the *odds ratio* describing the risk of blood clots for OC users relative to non-users

Practice (solution)

1) The odds of blood clots were 1.83 (42/23) for OC users
2) The odds of blood clots were 0.29 (45/145) for those not using OC
3) The odds ratio for blood clots given OC use is $1.83/0.29 = 6.31$; so the odds of blood clots were 6.31 times higher for OC users relative to those not using OC

Comments - confidence intervals

- As with any measure of effect size, it's a generally a good idea to report it using a *confidence interval estimate*
- Calculating these intervals for a relative risk or odds ratio is beyond the scope of this class
  - However, you should feel comfortable interpreting these intervals (for example, in the article review project)

Summary

This presentation covered several ways to describe the clinical significance of data displayed in a contingency table:

1) Sensitivity and specificity are used to describe the efficacy of a diagnostic test
2) Odds ratios are used to describe effect sizes in any type of study (with a particular advantage in case-control studies)