Epidemiologic Measures of Association and Impact Part II

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Welcome to the second part of this series focused on epidemiologic measures of association and impact.

Overview

1. **Estimating risk:**
    - Is there an association between exposure and disease?
    - How strong is the association?

2. **Estimating potential for prevention:**
    - What is the amount of disease incidence that can be attributed to an exposure?

3. **Interpretation of study results**

This three-part series will focus on the estimation of risk. We will learn about epidemiologic measures that can be used to determine if there an association between exposure and disease. Furthermore, we will learn about measures that can be used to summarize the strength of the association between exposure and disease outcome. Next, we will lean about epidemiologic measures that can be used to quantify the potential for prevention. Specifically, we will learn about measures that can be used to quantify the amount of disease incidence that can be attributed to a particular exposure. Throughout this series, we will focus on the interpretation of study results, and in particular, measures of the association between exposure and disease outcome.

Measures of Association

- Cohort study:
  - Relative risk (RR)
  - Incidence rate ratio (IRR)
  - Odds ratio (Disease OR)

- Case-control study: OR (for exposure)

- Cross-sectional study: PPR (ratio of prevalence proportions)

In this module, we will focus on the interpretation of measures of association that can be calculated from case-control and cross-sectional studies.

Odds Ratio (OR)

- Case-control

- Can also be calculated for Cohort and Cross-sectional studies

We will first focus on the odds ratio as a measure of association and will focus on the calculation of an odds ratio for exposure calculated from a case-control study.

Note that you can also calculate an odds ratio for a cohort study and for cross-sectional studies.

Case-Control Study
Sample on Disease

Exposure	Disease		Total
	Present	Absent	
Present			
Absent			
Total	*Fixed total*	*Fixed total*	

Recall that when conducting a case-control study, we sample groups of individuals based on their disease status, either the patient has the disease of interest or the patient does not have the disease, and then we review the exposure histories of the cases and controls and compare the exposure status between the cases and controls to determine if disease status is associated with exposure. The number of cases and controls is fixed. As an example, we might enroll 100 patients with lung cancer and 100 patients without lung cancer. We would then review the smoking histories of the study participants and would compare the odds of smoking between the cases and controls.

Odds Ratio

Breaking apart

- Odds ratio = Ratio of two odds

$$\frac{\text{Odds of exposure in cases}}{\text{Odds of exposure in controls}}$$

- Odds = Ratio of two probabilities

Odds 1: $\dfrac{\text{Probability of exposure among cases}}{1 - \text{Probability of exposure among cases}}$

Odds 2: $\dfrac{\text{Probability of exposure among controls}}{1 - \text{Probability of exposure among controls}}$

In a case-control study, the odds ratio is calculated as the ratio of the odds of exposure among the cases compared to the odds of exposure among the controls.

Recall that the odds are calculated as the probability of the event, exposure in this case, divided by 1 minus the probability of the event.

Odds Ratio

- OR for a case control study = Exposure odds ratio

- Exposure OR = ratio of odds of exposure among cases to the odds of exposure among controls

$$\text{Odd ratio} \ = \ \frac{\dfrac{p(E\mid D)}{p(\overline{E}\mid D)}}{\dfrac{p(E\mid \overline{D})}{p(\overline{E}\mid \overline{D})}} = \frac{\dfrac{a}{c}}{\dfrac{b}{d}} = \frac{a}{c}x\frac{d}{b} = \frac{ad}{bc}$$

In terms of our standard 2x2 table notation, the odds ratio in a case control study is calculated as shown on this slide, the ratio of the odds of exposure among the cases divided by the odds of exposure among the controls.

Odds Ratio

OR = Cross Product Ratio

Exposure	Disease	
	Present	Absent
Present	a	b
Absent	c	d
Total	*Fixed total*	*Fixed total*

$$OR = \frac{a \times d}{b \times c}$$

In terms of standard 2x2 table notation where the columns represent disease, or case status, and the rows correspond to exposure, the odds ratio is calculated as (a times d) divided by (b times c).

Odds Ratio – Example

	Cancer	No Cancer	Total
OC use	15	30	45
No OC use	35	70	105
Total	50	100	150

$$OR = \frac{15 \times 70}{30 \times 35} = \frac{1050}{1050}$$

$$= 1.0$$

Let's consider an example investigating the association between breast cancer and oral contraception use.

In this example, investigators enrolled 50 patients with a diagnosis of breast cancer and 100 patients without a history of breast cancer.

Among the 50 patients with breast cancer, 15 had a history of oral contraception use compared to 30 of 100 patients with no breast cancer.

We can calculate the odds ratio as (15 times 70) divided by (30 times 35), resulting in a value of 1.0.

Odds Ratio – Example

- Interpretation of exposure odds ratio
    OR = 1.0

    No association between disease and exposure

In this case, because the odds ratio is 1, this indicates that the odds of oral contraception use among the women with a history of breast cancer is equal to the odds of oral contraception use among the women with no history of breast cancer. The odds of exposure are equal between the cases and controls and therefore, cancer is not associated with a history or oral contraception use.

Odds Ratio – Interpretation

- OR = 1.5
    - The <u>odds of **exposure**</u> in those with the disease are 1.5 times the odds among those without the disease.

- OR = 0.60
    - The <u>odds of **exposure**</u> in those with the disease are 0.60 times the odds of exposure in those without the disease.
    - i.e., the odds of exposure are 40% lower in those with the disease than in those without the disease

If the resulting odds ratio value is greater than 1, say 1.5, we could conclude that the odds of **exposure** in those with the disease are 1.5 times the odds among those without the disease. The odds of exposure are higher among the cases compared to controls.

If the resulting odds ratio value is less than 1, say 0.6, we could conclude that the odds of **exposure** in those with the disease are 0.6 times the odds among those without the disease. The odds of exposure are reduced by 40% among the cases compared to controls.

Odds Ratio

OR calculated for all three study designs:
1. Case-control
2. Cohort
3. Cross-sectional

But interpretations and inferences vary by design.

Note that the odds ratio can be calculated for data arising from a case-control design, a cohort design, and a cross-sectional design; however, the interpretation and inference will vary by design due to the process that was used to draw the sample of study participants.

Odds Ratio – Case Control Studies

- Is a ratio of the odds of exposure in cases to the odds of exposure in controls.

- Exposure OR

In a case-control study, the number of cases and the number of controls is fixed while the exposure history is variable.

For a case-control study, the odds ratio is the ratio of the odds of exposure in cases compared to the odds of exposure in controls. We are estimating the exposure odds ratio.

Odds Ratio – Cohort Studies

- Is a ratio of the odds of developing disease in exposed persons to the odds of developing disease in non-exposed persons.

- Disease OR

In a cohort study, the number of exposed and the number of unexposed is fixed while the development of disease is variable.

For a cohort study, the odds ratio is the ratio of the odds of developing disease in exposed persons to the odds of developing disease in nonexposed persons. We are estimating the disease odds ratio.

Odds Ratio – Cross-sectional Studies

- Is a ratio of the odds of having disease in persons who have the exposure to the odds of having disease in persons who don't have the exposure.

- Prevalence OR

In a cross-sectional study, the number of participants is fixed while the number of cases or controls and the number of exposed or unexposed is variable. Also, we do not follow participants for the development of disease, instead, we observe prevalent (existing) cases.

For a cross-sectional study, the odds ratio is the ratio of the odds of having disease in persons who have the exposure to the odds of having disease in persons who don't have the exposure. We are estimating the prevalence odds ratio.

Odds Ratio

Question

- When is the OR obtained in a case-control study a good approximation of the RR in the population?

In practice, it is helpful if the odds ratio estimated from a case-control study is a good approximation of the relative risk in the population. It is easier to interpret relative risk values instead of odds ratio values.

Odds Ratio

When is the OR obtained in a case-control study a good approximation of the RR in the population?

    A. When cases are representative of all cases in the population.
    B. When controls are representative of all controls in the population.
    C. When the disease is rare.

The odds ratio obtained in a case-control study is a good approximation of the RR in the population when the following conditions hold:

A. When cases are representative of all cases in the population.
B. When controls are representative of all controls in the population.
C. When the disease is rare.

Prevalence proportion ratio (PPR)
Cross-sectional studies

- In cross-sectional studies, only the presence/absence of disease is measured.

- Prevalence proportion ratio: the ratio of the prevalence of disease in the exposed to the ratio of the prevalence of disease in the unexposed.

- Mathematically identical to risk ratio but the interpretation is VERY DIFFERENT!

Now, let's turn our attention to cross-sectional studies and consider the prevalence proportion ratio that can be calculated in cross-sectional studies.

Recall that in a cross-sectional study, we only measure the presence or absence of disease for each participant and do not follow the participants prospectively for the development of disease.

The prevalence proportion ratio can be calculated from a cross-sectional study. The prevalence proportion ratio is the ratio of the prevalence of disease in the exposed to the prevalence of disease in the unexposed.

Note that the prevalence proportion ratio is mathematically identical to the risk ratio, which is calculated from a cohort study, but the interpretation is VERY DIFFERENT given the difference in sampling strategies.

Prevalence Proportion Ratio – Example

Cross-sectional study

		Has antibodies to toxoplasmosis?	
		Yes	No
Eats or ever ate undercooked lamb meat?	Yes	100	500
	No	25	375

$$PPR = \frac{100/_{100+500}}{25/_{25+375}} = \frac{100/_{600}}{25/_{400}} = \frac{0.1667}{0.0625}$$

$$= 2.67$$

Let's consider a data example.

In this example, we survey 1000 participants and ask them about their dietary habits relative to ever eating undercooked lamb meat. We also evaluate the participants' blood samples to determine if they have antibodies to toxoplasmosis.

The prevalence proportion ratio is the prevalence of disease among the exposed, 100 out of 600, compared to the prevalence of disease among the unexposed, 25 out of 400. The resulting ratio is 2.67.

Prevalence Proportion Ratio – Example

Interpretation

- The prevalence of having antibodies to toxoplasmosis among people who eat or have ever eaten undercooked lamb meat is 2.67 times the prevalence of toxoplasmosis in those who have never eaten undercooked lamb meat.

  - NOTE: it is impossible to know if eating lamb meat preceded the infection or not.

With a prevalence proportion value of 2.67, we can state that the prevalence of having antibodies to toxoplasmosis among people who eat or have ever eaten undercooked lamb meat is 2.67 times the prevalence of toxoplasmosis in those who have never eaten undercooked lamb meat. Note that given the cross-sectional assessment, it is impossible to know if eating lamb meat preceded the infection or not. We do not observe the temporal sequence between exposure and disease onset; therefore, our inference is limited to commenting on prevalence cases, not incident cases.

Summary

- **Case-control study design**

  - Sample cases and controls
  - Measures of association
    - Exposure odds ratio

- **Cross-sectional study design**

  - Measures of association
    - Prevalence odds ratio
    - Prevalence proportion ratio

In this second module, we focused on the interpretation of measures of association that can be calculated from case-control studies, namely the exposure odds ratio, and the interpretation of measures of association that can be calculated from cross-sectional studies, namely, the prevalence proportion ratio.

In the next module, we will discuss measures that can be used to quantify the potential impact of prevention programs on disease burden related to a particular exposure.