# Online Only Lectures - Statistics

*Speaker: Khalil Ghanem, MD*

IDBR INFECTIOUS DISEASE BOARD REVIEW AUGUST 20-24 2022

## Statistics

Khalil G. Ghanem, MD, PhD
Professor of Medicine
Division of Infectious Diseases
Johns Hopkins University School of Medicine

6/15/2022

IDBR INFECTIOUS DISEASE BOARD REVIEW AUGUST 20-24 2022

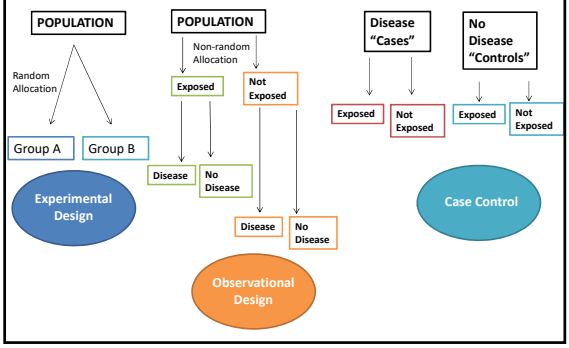
**Disclosures of Financial Relationships with Relevant Commercial Interests**

- None

## Overview

- Study designs
- Incidence & Prevalence
- Relative risk, relative odd, & attributable risk
- Confidence intervals
- Number needed to treat
- Sensitivity, specificity, positive predictive value, negative predictive value
- Bias and confounding

## Study Designs




## Example: Study Designs

- Choose the most appropriate study design for the following scenarios:
  - You are trying to determine what caused 35 people to experience fever and severe hemorrhagic complications upon returning from a Caribbean cruise
  - You are trying to get a novel influenza vaccine approved by the FDA
  - You are trying to determine whether hormonal contraception increases your risk of HIV

## Incidence vs. Prevalence

- **Incidence**= *new* infection occurring during a specified period of time in a population at risk for developing the infection
  - A measure of events (a disease that develops in someone who did not have it), thus, a measure of *risk*
- **Prevalence:** number of affected persons present in the population at a given time(i.e. *existing* infections) divided by the total number of people in the population
- **Prevalence=Incidence X duration of disease**

# Online Only Lectures - Statistics

*Speaker: Khalil Ghanem, MD*

### Example: Incidence vs. Prevalence

- **In a population that includes HIV-infected persons who exhibit high medication adherence, what would the impact of HAART be on HIV incidence and prevalence over a 10 year period?**

  -Incidence= new HIV infections. HAART should decrease the risk of transmission of HIV and thereby **decrease** the incidence

  -Prevalence= all existing HIV infections. HAART allows people with HIV to live longer so it may **increase** the prevalence of HIV

### Estimating Risk

- **Relative Risk (RR)**= Incidence in exposed/ Incidence in nonexposed
  - If the RR=1, there is no association
  - If the RR >1, the risk in exposed > nonexposed
  - If the RR<1, the risk in exposed < nonexposed
- **Hazards Ratio(HR)**: A form of RR; HR is instantaneous while RR is cumulative.
- **Odds**= Probability that disease developed/Probability that it did not develop
- **Odds Ratio:**
  - **Cohort study:** ratio of odds of disease occurring in exposed to the odds of disease occurring in non-exposed
  - **Case Control**: ratio of the odds that the cases were exposed to the odds that the controls were exposed
  - If the OR=1, there is no association between exposure and disease
  - If the OR>1, the exposure is positively related to the disease
  - If the OR<1, the exposure is negatively related to the disease

### Example: Estimating Risk

- **In a population of 1000 people, 400 were having unprotected sex. Infection-Y occurred in 100 of the 400 who were having unprotected sex and in 5 of the 600 who were not.**
- **What is the RR of Y in those having unprotected sex?**
- **What are the relative odds (odds ratio) of Y in those having unprotected sex?**

- RR: 100/400/5/600= 31.3
- OR: 100/300/5/595=41.3

- The odds ratio is a good estimate of the relative risk when the disease being studied is RARE

### Estimating Risk 2

- The **attributable risk** is the proportion of disease incidence that can be attributed to a specific exposure

  **AR= Incidence in exposed- Incidence in non-exposed**
- This is one of the most important measures when deciding *how* to spend money and resources in public health

### Example: Estimating Risk 2

**A new deadly fungal infection is described with a mortality rate of 30%. You are given 1 million dollars to spend on prevention in your state.**

**-Persons with ExposureA have a RR of 16 for getting infected.**

**-Persons with ExposureB have a RR of 2 for getting infected.**

➢ **How are you going to spend your money?**

### Example: Estimating Risk 2

- ExposureA is spelunking and ExposureB is gardening
- NOW how are you going to spend your money?
- Even though the relative risk of spelunking is far more than gardening, most of the cases in your state are likely the result of gardening (a lot more people garden).
- The attributable risk of gardening, therefore, is much greater than that of spelunking

| Exposure | Incidence | Relative Risk | Attributable Risk |
|---|---|---|---|
| Spelunking | 32 per million | 16 | 30 per million |
| No Spelunking | 2 per million | | |
| Gardening | 640 per million | 2 | 320 per million |
| No Gardening | 320 per million | | |

# Online Only Lectures - Statistics

*Speaker: Khalil Ghanem, MD*

## Confidence Intervals

- Confidence intervals (CI) are used to indicate the reliability of an estimate
  - CI is *directly* related to the standard deviation and *indirectly* related to the sample size (i.e. the larger the sample size, the smaller the CI)
- In simple terms, a 95% CI means: If you were to repeat this experiment many times, in 95% of the time, your results will fall within this range.
  - The wider the CI surrounding the point estimate, the more uncertainty there is about the reliability of that point estimate

## Example: Confidence Intervals

- Match each scenario to the more likely prevalence point estimate and CI:
  - **Scenario 1**: We test 100 people in the population for HIV.
  - **Scenario 2**: We test 3500 people in the population for HIV

A. The prevalence of HIV is 1.3% (95%CI: 1.1 %-1.5%)

B. The prevalence of HIV is 3.3% (95%CI: 0.3%-7.2%)

## Number Needed to Treat (NNT)

- NNT= 1/(Rate in untreated)- (Rate in treated)

## Example: NNT

**RCT for a new Ebola vaccine: the mortality rate in the experimental group is 20% while the mortality rate in the control group is 85%. How many people do we need to vaccinate to prevent one death from Ebola?**

**NNT= 1/(0.85-0.20)=1.5**

Approximately 2 people need to be vaccinated to prevent a single death from Ebola. This would be a GREAT public health intervention in endemic areas.

## Sensitivity, Specificity, Positive Predictive Value (PPV), Negative Predictive Value (NPV)

| | Disease | No Disease |
|---|---|---|
| Positive | True Positive | False positive |
| Negative | False negative | True negative |

**Sensitivity**= TP/ TP + FN
**Specificity**= TN/ TN +FP
**PPV**= TP/ TP + FP
**NPV**= TN/TN +FN

**Sensitivity and specificity are INDEPENDENT of prevalence whereas PPV and NPV are DEPENDENT on prevalence**

- **Sensitivity**= the ability of a test to correctly identify those who have a disease
- **Specificity**=the ability of a test to correctly identify those who do not have a disease
- **PPV**= the proportion who test positive and actually have the disease
- **NPV**=the proportion who test negative and actually don't have the disease

## Example: Sensitivity Specificity, PPV, NPV

**The glycoprotein-G- based antibody tests for the detection of HSV-2 antibodies have a sensitivity of 99% and specificity of 98.5%. We plan to test two populations: (A) 1000 commercial sex workers (B) 1000 nuns confined to a convent.**

**In which population will the tests have a higher: Sensitivity? Specificity? PPV? NPV?**

- Sensitivity and specificity are INDEPENDENT of prevalence of disease. As such, the sensitivity and specificity of these tests will be the same in both populations
- Population A likely has a higher prevalence of HSV-2 compared to population B. As such, the PPV of the test will be higher in population A and the NPV will be higher in population B

# Online Only Lectures - Statistics

*Speaker: Khalil Ghanem, MD*

### Definitions

- **Precision**: How close do the results cluster to ***each other***?
- **Accuracy**: How close do the results cluster to ***the truth***?
- **Bias**: systematic error leading to a decrease in accuracy
  - Bias is reduced by careful study design
- **Confounding**: a distortion in the degree of association between an exposure and an outcome due to a mixing of effects between the exposure and an incidental factor, which is known as the confounder
  - You must adjust for confounding; otherwise, it will lead to misinterpretation of results
- **Effect Modification** (i.e. interaction): a variable that differentially (positively and negatively) modifies the observed effect of a risk factor on disease status. Different groups have different risk estimates when effect modification is present
  - Effect modification is a true phenomenon that should be reported. You do NOT need to adjust for it.

### Example: Definitions

- We find no cases of InfectionY in infants but many cases in children and adults. The RR of infection in those >1 year old is 45 as compared to those who are < 1 year old. We later find out that InfectionY is only transmitted when walking barefoot on the beach.
- Age is an example of _____