NEW YORK INSTITUTE OF TECHNOLOGY

College of Osteopathic Medicine

Epidemiology II

Bhuma Krishnamachari, PhD
Assistant Dean of Research
bkrishna@nyit.edu

Do.
Make.
Heal.
Innovate.
Reinvent the Future.

Session Objectives

1. Students will be able to apply basic epidemiological concepts to specific disease areas as described in lecture when presented with a topic following that lecture
2. Students will be able to calculate basic epidemiological measures for a given circumstance as described in lecture following that lecture
3. Students will be able to interpret basic epidemiological results as described in lecture following that lecture
4. Students will be able to evaluate an epidemiological study for statistical significance as described in lecture following that lecture
5. Students will be able to describe an epidemiological study from beginning to end as described in lecture following that lecture

Source: Course Syllabus

NEW YORK INSTITUTE OF TECHNOLOGY

College of Osteopathic Medicine

Summary Slide

NEW YORK INSTITUTE OF TECHNOLOGY
College of Osteopathic Medicine

- There are many study designs, each with different benefits and limitations
- Each of these have different measures that can be used to quantify the relationship between exposures and disease.

- Core References:
  - (Gordis, Epidemiology) 7th Edition by Leon Gordis MD MPH DrPH

Case

NEW YORK INSTITUTE OF TECHNOLOGY
College of Osteopathic Medicine

When you were a child, your mother constantly told you that you “should not go out in the winter without a hat as you will catch a cold.” Now, as a medical professional, you are ready to prove her wrong. You decide to dedicate your life to investigating this issue.

Cross-Sectional Study

NEW YORK INSTITUTE OF TECHNOLOGY
College of Osteopathic Medicine

- A one time sweep through a time point to assess the prevalence of variables, diseases and potential risk factors
- You can collect data and then divide people into groups for comparisons
- You cannot conclude anything about “risk” or “incidence” because this was a one-time measurement with no element of time.

(Gordis, Epidemiology) 7th Edition by Leon Gordis MD MPH DrPH, Chapter 7

Cross-Sectional Study

NEW YORK INSTITUTE OF TECHNOLOGY
College of Osteopathic Medicine

How would you design a cross-sectional study?

- Without any regard for people's "cold status" or "use of hats" you can send out a survey to a general population assessing both, and then see if you find associations between the two.
- Problem- if everyone gets cold, or if everyone wears hats, you cannot do an analysis, because you don't have comparison groups.

Case-Control Studies

NEW YORK INSTITUTE OF TECHNOLOGY
College of Osteopathic Medicine

- In a case-control study with two groups, one group has the disease of interest (cases) and a comparable group is free from the disease (controls).
- The case-control study identifies possible causes of disease by finding out how the two groups differ with respect to exposure to some factor.

(Gordis, Epidemiology) 7th Edition by Leon Gordis MD MPH DrPH, Chapter 7

Designing a case-control study

NEW YORK INSTITUTE OF TECHNOLOGY
College of Osteopathic Medicine

- How would you design a Case-Control study?
- First you would recruit people who meet your "inclusion criteria." That is, how will you define "people who get colds?" ICD codes, self-report, etc. Will you recruit from a clinic?
- You then need healthy controls- where will you find them? Sources to recruit controls: General population controls, general medical clinics. Or, if conducting a matched study, will you use the spouses of cases as controls? Friends of the controls?
- You can then survey the groups and ask in detail about their use of hats.
- The goal is to compare hat wearing in the cases to hat wearing in the controls.

(Gordis, Epidemiology) 7th Edition by Leon Gordis MD MPH DrPH, Chapter 7

Selecting Controls

NEW YORK INSTITUTE OF TECHNOLOGY
College of Osteopathic Medicine

- General population controls
- Most often used when cases are selected from a defined geographic population
- Sources: random digit dialing, residence lists, drivers' license records

(Gordis, Epidemiology) 7th Edition by Leon Gordis MD MPH DrPH, Chapter 7

Selecting Controls

NEW YORK INSTITUTE OF TECHNOLOGY
College of Osteopathic Medicine

Advantages of general population controls

- Because of selection process, investigator is usually assured that they come from the same base population as the cases.

Disadvantages of general population controls

- Time consuming, expensive, hard to contact and get cooperation; may remember exposures differently than cases

(Gordis, Epidemiology) 7th Edition by Leon Gordis MD MPH DrPH, Chapter 7

Selecting Controls

NEW YORK INSTITUTE OF TECHNOLOGY
College of Osteopathic Medicine

Advantages of hospital controls

- Same selection factors that led cases to hospital led controls to hospital
- Easily identifiable and accessible (so less expensive than population-based controls)
- Accuracy of exposure recall comparable to that of cases since controls are also sick
- More willing to participate than population-based controls

(Gordis, Epidemiology) 7th Edition by Leon Gordis MD MPH DrPH, Chapter 7

Selecting Controls

NEW YORK INSTITUTE OF TECHNOLOGY
College of Osteopathic Medicine

Disadvantages of hospital controls

- Since hospital based controls are ill, they may not accurately represent the exposure history in the population that produced the cases

- Hospital catchment areas may be different for different diseases

(Gordis, Epidemiology) 7th Edition by Leon Gordis MD MPH DrPH, Chapter 7

Selecting Controls

NEW YORK INSTITUTE OF TECHNOLOGY
College of Osteopathic Medicine

What illnesses make good hospital controls?

- Those illnesses that have no relation to the risk factor(s) under study

  Example: Should respiratory diseases be used as controls for a study of smoking and myocardial infarction? Do they represent the distribution of smoking in the entire population that gave rise to the cases of MI?
- Special control groups like friends, spouses, siblings, and deceased individuals.

(Gordis, Epidemiology) 7th Edition by Leon Gordis MD MPH DrPH, Chapter 7

Matching in Epidemiology

NEW YORK INSTITUTE OF TECHNOLOGY
College of Osteopathic Medicine

Types

- Individual matching
- Frequency matching

Data are analyzed in terms of case-control pairs rather than for individual subjects

(Gordis, Epidemiology) 7th Edition by Leon Gordis MD MPH DrPH, Chapter 7

Matching in Epidemiology

- Can be time efficient, cost effective, and improve statistical power
- The more variables that are chosen as matching characteristics, the more difficult it is to find a suitable control to match to the case
- Once a variable is used for matching, no relationship can be discerned between this variable and the disease
- Don’t match on anything you think might be a risk factor!

(Gordis, Epidemiology) 7th Edition by Leon Gordis MD MPH DrPH, Chapter 7

Odds Ratio: Calculated in Case-Control Studies

Odds Ratio=

$$\frac{\text{Odds of exposure in diseased}}{\text{Odds of exposure in healthy}}$$

or

$$\frac{\text{Odds of disease in exposed}}{\text{Odds of disease in unexposed}}$$

(Gordis, Epidemiology) 7th Edition by Leon Gordis MD MPH DrPH, Chapter 7

Analysis of case-control studies

	Disease Status		
Exposure Status	Yes	No	ODDS
Yes	A	B	A/B
No	C	D	C/D

Odds Ratio=[A/B]/[C/D]= [A x D]/[B x C]

Or [A/C]/[B/D]= [A x D]/[B x C]

(Gordis, Epidemiology) 7th Edition by Leon Gordis MD MPH DrPH, Chapter 7

Analysis of case-control studies

EXAMPLE: Case control study of Parkinson's Disease (PD)and coffee consumption

		Case (Has PD)	Control (healthy)
Coffee Drinker	Yes	42	247
No Coffee	No	107	825

Odds ratio = [(a/b) / (c/d)] = [(42/247) / (107/825)] = 1.3

"A PD patient is 1.3 times as likely as a healthy individual to have been a coffee drinker"

Statistical Significance

NEW YORK INSTITUTE OF TECHNOLOGY
College of Osteopathic Medicine

- P is short for probability: the probability of getting something more extreme than your result, when there is no effect in the population.
- P-values below 0.05 are often considered significant
- *Usually report a 95% CI*
- You can be 95% confident you will get a number between your reported range if experiment is repeated
- IF your CI includes 1, then you automatically will NOT have statistically significant results (this will be supported by a p-value)

NEW YORK INSTITUTE OF TECHNOLOGY

College of Osteopathic Medicine

Strengths of case-control studies

- Efficient for rare diseases and diseases with long induction and latent period.
- Can evaluate many risk factors for the same disease so good for diseases about which little is known

(Gordis, Epidemiology) 7th Edition by Leon Gordis MD MPH DrPH, Chapter 7

Weaknesses of case-control studies

- Inefficient for rare exposures
- Vulnerable to bias because of retrospective nature of study
- May have poor information on exposure because retrospective
- Difficult to infer temporal relationship between exposure and disease

(Gordis, Epidemiology) 7th Edition by Leon Gordis MD MPH DrPH, Chapter 7

NEW YORK INSTITUTE OF TECHNOLOGY

College of Osteopathic Medicine

You decide that the case-control study is not the optimal way of conducting your study, and instead opt to conduct a cohort study.

COHORT STUDIES

NEW YORK INSTITUTE OF TECHNOLOGY

College of Osteopathic Medicine

- Definition: A study in which two or more groups of people that are free of disease and that differ according to the extent of exposure (e.g. exposed and unexposed) are compared with respect to disease incidence. Can be prospective or retrospective.

- Cohort studies are the observational equivalent of experimental studies but the researcher cannot allocate exposure -he must locate a natural experiment to observe the relationship between the exposure and disease

(Gordis, Epidemiology) 7th Edition by Leon Gordis MD MPH DrPH, Chapters 8,12,13

How would you design a Cohort study?

NEW YORK INSTITUTE OF TECHNOLOGY
College of Osteopathic Medicine

- First you would recruit people who meet wear hats. Here again, you must decide on your “inclusion criteria.”
- Then you would find a control group with people who do not wear hats.
- You would then follow them through time to calculate an incidence rate of colds in the hat wearers vs the non-hat wearers.

(Gordis, Epidemiology) 7th Edition by Leon Gordis MD MPH DrPH, Chapters 8,12,13

Strengths of Cohort Studies

NEW YORK INSTITUTE OF TECHNOLOGY
College of Osteopathic Medicine

- Efficient for rare exposures
- In a retrospective cohort study, efficient for diseases with long induction and latent periods
- Can evaluate multiple effects of an exposure
- If prospective, good information on exposures, less vulnerable to bias, and clear temporal relationship between exposure ad disease

(Gordis, Epidemiology) 7th Edition by Leon Gordis MD MPH DrPH, Chapters 8,12,13

Weaknesses of Cohort Studies

NEW YORK INSTITUTE OF TECHNOLOGY
College of Osteopathic Medicine

- Inefficient for rare outcomes
- If retrospective, poor information on exposure and other key variables, more vulnerable to bias
- If prospective, expensive and time consuming, inefficient for diseases with long induction and latent period
- Keep these strengths and weaknesses in mind for comparison with case-control studies

(Gordis, Epidemiology) 7th Edition by Leon Gordis MD MPH DrPH, Chapters 8,12,13

Analysis of cohort studies

NEW YORK INSTITUTE OF TECHNOLOGY
College of Osteopathic Medicine

- Basic analysis involves calculation of incidence of disease among exposed and unexposed groups.
- Recall set up of 2 x 2 tables.

(Gordis, Epidemiology) 7th Edition by Leon Gordis MD MPH DrPH, Chapters 8,12,13

Analysis of cohort studies

NEW YORK INSTITUTE OF TECHNOLOGY
College of Osteopathic Medicine

Exposure Status	Disease Status: Yes	No	Totals	Incidence Rate
Yes	A	B	A+B	A/(A+B)
No	C	D	C+D	C/(C+D)

Relative Risk =
[A/A+B]/[C/C+D]=
Incidence rate in exposed/incidence rate in unexposed

Attributable Risk =[A/A+B]-[C/C+D]= incidence rate in exposed-incidence rate in unexposed
or {[A/A+B]-[C/C+D]}/ [A/A+B]= (incidence rate in exposed-incidence rate in unexposed)/ incidence rate in exposed

(Gordis, Epidemiology) 7th Edition by Leon Gordis MD MPH DrPH, Chapters 8,12,13

NEW YORK INSTITUTE OF TECHNOLOGY

College of Osteopathic Medicine

Relative Risk: Calculated in a Cohort Study

$$\text{Relative risk} = \frac{\text{Incidence rate (risk) in the exposed}}{\text{Incidence rate (risk) in the non-exposed}}$$

(Gordis, Epidemiology) 7th Edition by Leon Gordis MD MPH DrPH, Chapters 8,12,13

Interpreting Relative Risk

NEW YORK INSTITUTE OF TECHNOLOGY
College of Osteopathic Medicine

- Relative Risk = 1.0 No Risk

(meaning the rate of poor outcome among those with risk factor is the same as those without)

- Relative Risk > 1 Elevated Risk

(meaning the rate of poor outcome is more common among those with the risk factor present)

- Relative Risk < 1 Reduced Risk

(meaning the rate of poor outcome is less common among those with the risk factor present)

(Gordis, Epidemiology) 7th Edition by Leon Gordis MD MPH DrPH, Chapters 8,12,13

NEW YORK INSTITUTE OF TECHNOLOGY

College of Osteopathic Medicine

You decide that you would really like to conduct a randomized controlled trial, since this is the gold standard in epidemiology studies. You spend all of your time, money and effort on creating a controlled "winter chamber" and recruit 400 people to live under a controlled setting where you will randomize people to the "hat" or "no hat" groups.

Analysis is the same as a cohort study!

(Gordis, Epidemiology) 7th Edition by Leon Gordis MD MPH DrPH, Chapters 10,12

Use of Placebo and Blinding

NEW YORK INSTITUTE OF TECHNOLOGY
College of Osteopathic Medicine

Placebos are used to make the groups as comparable as possible (recall laboratory experiment)

Blinding: subjects do not know if they are receiving treatment or placebo (single blind); neither subjects nor investigators know who is receiving treatment or placebo (double blind).

Purpose of blinding: To avoid bias in ascertainment of outcome

Placebo allows study to be blind

(Gordis, Epidemiology) 7th Edition by Leon Gordis MD MPH DrPH, Chapters 10,12

Number Needed to Treat (NNT)

NEW YORK INSTITUTE OF TECHNOLOGY
College of Osteopathic Medicine

Number of persons who would have to receive an intervention for 1 to benefit.

NNT = 1/ (rate in untreated group-rate in treated group)=1/Absolute risk reduction)

- To determine absolute risk reduction subtract incidence with treatment from incidence without treatment : 0.0043 − 0.0028 = 0.0015 = Absolute Risk Reduction
- The number needed to treat is the inverse of the Absolute risk reduction: 1/0.0015=667
- This means that if 667 individuals are exposed to the risk factor, 1 case will be prevented (NNT).
- Number Needed to Harm (NNH) is similar but is 1/attributable risk when you are looking at the harmful side effects of a drug.

(Gordis, Epidemiology) 7th Edition by Leon Gordis MD MPH DrPH, Chapters 10,12

Confounding

NEW YORK INSTITUTE OF TECHNOLOGY
College of Osteopathic Medicine

- An alternate explanation for observed association between an exposure and disease.
- What if you see that those who wear hats get fewer colds. BUT, then you find out the same people who wear hats wear gloves and scarves. What if it is really the scarf that protects against colds?
- This is why you collect data on variables other than the ones you are studying- namely, confounders.
- Common confounders are age, gender and race.
- Can address by stratification OR with more complicated regression analysis

(Gordis, Epidemiology) 7th Edition by Leon Gordis MD MPH DrPH, Chapter 15

Stratified Analysis-Confounding

Composite OR=2.15

Female

		Case	Control
Smoking	**Yes**	5	8
	No	45	72

Stratum-specific OR = 1

Male

		Case	Control
Smoking	**Yes**	25	10
	No	25	10

Stratum-specific OR = 1

- In this case control study of smoking and risk of heart attack. Gender is a confounder.

NEW YORK INSTITUTE OF TECHNOLOGY
College of Osteopathic Medicine

Interaction (Effect Modification)

- When an exposure behaves differently in different groups.
- For example, if you find smoking increases the risk for heart attacks much more in males than females (these are fictional numbers and not based on fact!)

(Gordis, Epidemiology) 7th Edition by Leon Gordis MD MPH DrPH, Chapter 15

Stratified Analysis-Interaction (Effect Modification)

NEW YORK INSTITUTE OF TECHNOLOGY

College of Osteopathic Medicine

NEW YORK INSTITUTE OF TECHNOLOGY

College of Osteopathic Medicine

How would you address interaction and/or confounding in an analysis?

Stratification!

Both issues, though very different from one another, have the same solution

Bias

NEW YORK INSTITUTE OF TECHNOLOGY
College of Osteopathic Medicine

Bias is a systematic error that results in an incorrect (invalid) estimate of the measure of association

- Can create spurious association when there really is none (bias away from the null)
- Can mask an association when there really is one (bias towards the null)
- Bias is primarily introduced by the investigator or study participants

(Gordis, Epidemiology) 7th Edition by Leon Gordis MD MPH DrPH, Chapter 15

Bias

NEW YORK INSTITUTE OF TECHNOLOGY
College of Osteopathic Medicine

- Bias does not mean that the investigator is "prejudiced."
- Bias can arise in all study types: experimental, cohort, case-control
- Bias occurs in the design and conduct of a study. It can be evaluated but not fixed in the analysis phase.

Selection Bias

NEW YORK INSTITUTE OF TECHNOLOGY
College of Osteopathic Medicine

- Results from procedures used to select subjects into a study that lead to a result different from what would have been obtained from the entire population targeted for study.

(Gordis, Epidemiology) 7th Edition by Leon Gordis MD MPH DrPH, Chapter 15

Recall bias

NEW YORK INSTITUTE OF TECHNOLOGY
College of Osteopathic Medicine

People with disease remember or report exposures differently (more or less accurately) than those without disease.

Can result in over- or under-estimate of measure of association. (see following slide)

Solutions: Use controls who are themselves sick; use standardized questionnaires that obtain complete information, mask subjects to study hypothesis

(Gordis, Epidemiology) 7th Edition by Leon Gordis MD MPH DrPH, Chapter 15

Many other types of Bias…too many to cover in one lecture. BUT, the concept is always the same- the study is designed in a way that it is getting you flawed results.

Take-home

- There are many study designs, each with different benefits and limitations
- Bias, confounding and Effect modification can occur with any study design
- Each of these should be addressed in any given research study.

NEW YORK INSTITUTE OF TECHNOLOGY
College of Osteopathic Medicine

NEW YORK INSTITUTE OF TECHNOLOGY

College of Osteopathic Medicine

This concludes this epidemiology session. Please make certain you understand all of the listed objectives.

Lecture and Lab Feedback Form:

NEW YORK INSTITUTE OF TECHNOLOGY

College of Osteopathic Medicine

https://comresearchdata.nyit.edu/redcap/surveys/?s=HRCY448FWYXREL4R