CMED 305

Case Control Studies

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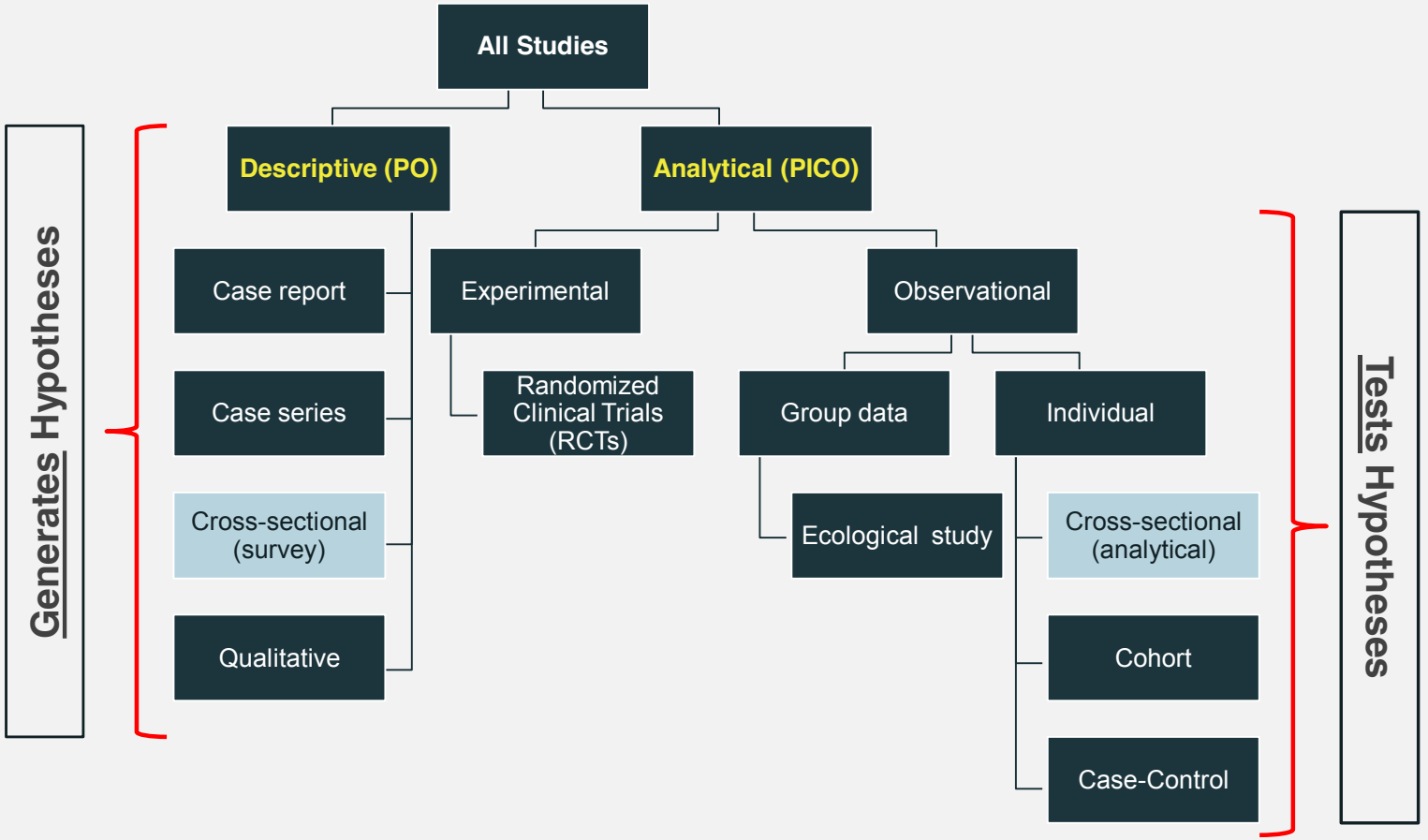
Learning Objectives: By end of this session students will be able to:

1. Describe the design of case-control studies
2. Identify steps for conducting case-control studies
3. Identify issues in the design of case-control studies
4. Describe the strengths and weaknesses of case-control studies

1 Design of Case-Control Studies


All Studies
Descriptive (PO)
Analytical (PICO)
Case report
Case series
Cross-sectional (survey)
Qualitative
Experimental
Randomized Clinical Trials (RCTs)
Observational
Group data
Individual
Ecological study
Cross-sectional (analytical)
Cohort
Case-Control
Generates Hypotheses
Tests Hypotheses

A case-control study is a study that **compares** *patients* who have a disease or outcome of interest **(cases)** with *patients* who do not have the disease or outcome **(controls**), and **looks back retrospectively** to compare how frequently the exposure to a risk factor is present in each group to determine the relationship between the risk factor and the disease.

When to Conduct a Case-Control Study

- The outcome of interest is rare
- Multiple exposures may be associated with a single outcome
- Funding or time is limited

(1) To investigate cause-effect when experimental trials (e.g. RCT) are not ethical or feasible, (lung cancer and smoking)

(2) To investigate cause-effect when cohort studies are expensive or non-feasible e.g. (to investigate etiology of rare disease e.g. cancer)

2 How to conduct a case-control study?

Steps in conducting a case-control study

1- Define a **source population**

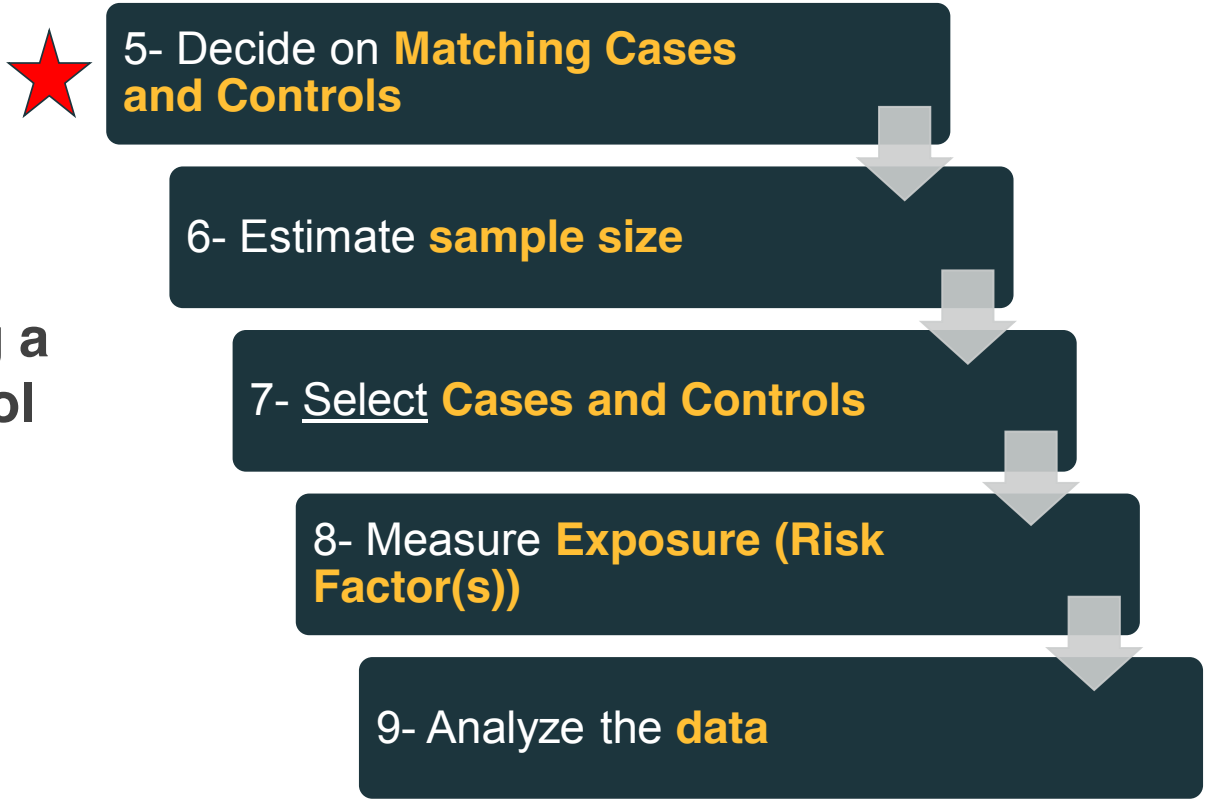
2- Determine **Study Subjects: "Cases"**
(**Case-subjects:** They have the disease or outcome of interest)

3- Determine **Study Subjects: "Controls"**
(**Control-subjects:** They DO NOT have the disease or outcome of interest)

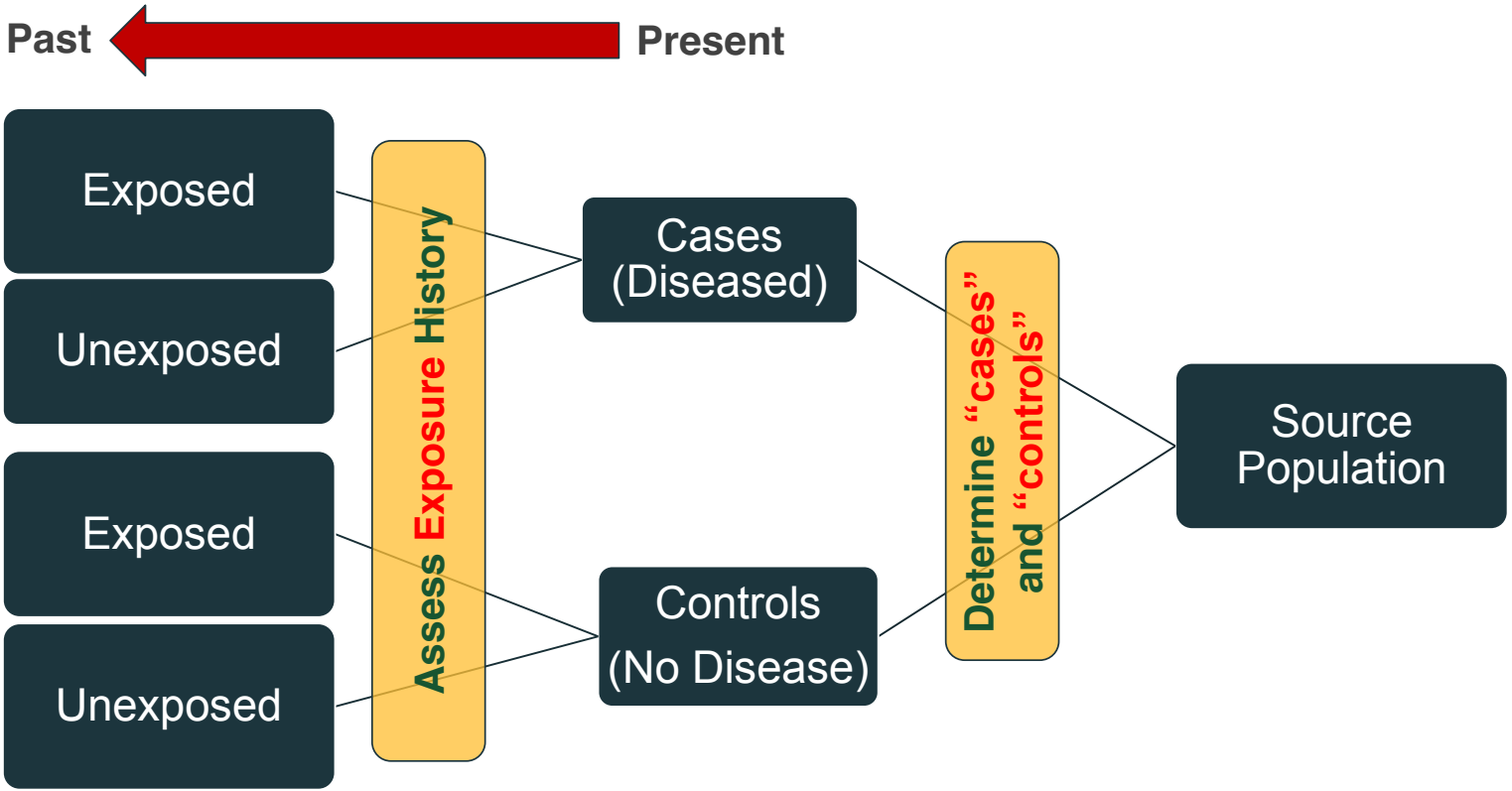
4- Decide on the **Ratio of Cases to Controls**

Important principles in case-control study design – will discuss more later

Steps in conducting a case-control study



Important principles in case-control study design – will discuss more later


Past
Present
Exposed
Unexposed
Exposed
Unexposed
Assess Exposure History
Cases
(Diseased)
Controls
(No Disease)
Determine "cases" and "controls"
Source Population

Determine Study Subjects: "Cases"= WHO IS THE CASE

Sources for Cases		Selection of Cases
Hospital-Based	Cases admitted to or discharged from a hospital, clinic or any health care facility.	1) Establish a"standard case definition": adopt a "standard diagnostic criteria" 2) Set inclusion and exclusion criteria: Area of residence, age, gender, etc 3) Decide on the type of cases: • incident cases (newly diagnosed cases) • prevalent cases ((people who may have had the disease for some time)
Population-based	Death certificates with recorded cause of death.	
	Disease registries (e.g. Cancer registry)	
	Incident cases in a going cohort study	
	Cases reported or diagnosed during a survey or surveillance system	
	Employment records	

Determine Study Subjects: "Controls" = WHO IS THE CONTROL

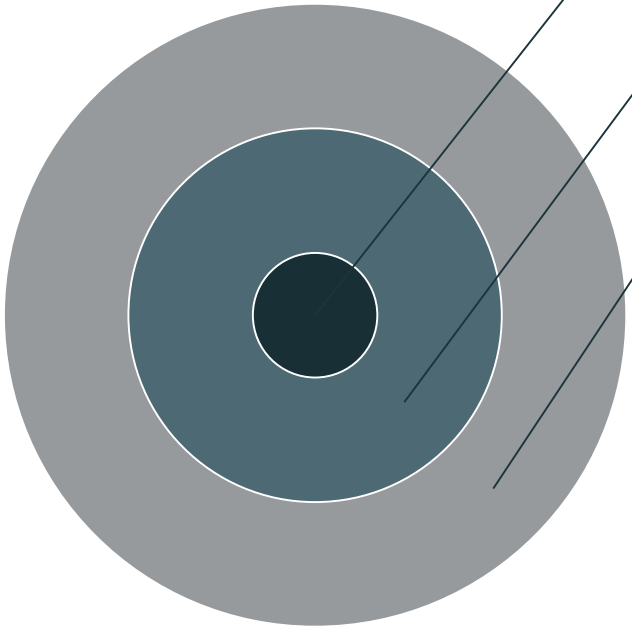
Hospital-Based Controls		Community-Based Controls	
Advantages	**Disadvantages**	**Advantages**	**Disadvantages**
1. Subjects are easily accessible. 2. Patients usually have time to participate. 3. Patients are often motivated to cooperate with investigators. 4. Controls and cases may be drawn from similar social and geographical environment. 5. Differential recalls of prior exposure is likely to be minimized.	1. Differential hospitalization patterns may introduce selection bias. 2. Difficult to blind disease status from cases and controls. 3. An underestimate of the study effect may result if control's disease is etiologically similar to cases' disease	1. Reduction of selection bias. 2. Generalization of study results is more valid. 3. May provide convenient control of extraneous (confounding) variables.	1. Time and money consuming. 2. May suffer low participation rate. 3. Cases and control may exhibit differential recall of prior exposures.

Determine Study Subjects: "Controls" = WHO IS THE CONTROL

Selection of Controls:

- The ideal "controls" are the healthy ones (very challenging!)
- It is crucial to select control group/s from people who we are certain not to have got the specified disease/condition.
- Aim of selecting controls:
  - Is to compare the exposure rate among both cases and controls (e.g. % smoking among cases and controls)
  - Then to confirm/refute if that the risk factor has occurred more frequently in the cases than in the controls using the measurement of association.

Determining **controls**



•3- Being **comparable** to cases in terms **of susceptibility**

2- **Free** from health problems **known to be associated with the exposure**

•1- **Free from the disease** / health problem under investigation

Decide on the Ratio of Cases to Controls

- The ratio of cases to control should be at least and ideally 1:1
- However, in many situations we may not be able recruit a large number of cases and it may be easier to recruit more controls for the study.
- It has been suggested that we can increase the number of controls to increase statistical power (if we have limited number of cases) of the study.
- Increase in the ratio lead to increase in “study precision”: 1:2, 1:3, 1:4
- Further increase in the ratio is associated with little increase in study precision relative to the cost involved (i.e will not add much to the study power but will add to the cost!)

Decide on Matching Cases and Controls

- A major concern in conducting a case-control study is that cases and controls may differ in characteristics or exposures other than the one that has been targeted for study.
- An approach to deal with this challenge: **Matching!**
- **Matching:** The process of selecting the controls so that they are similar to the cases in certain characteristics (confounders), such as age, race, gender, socioeconomic status, and occupation.
- Matching reduces the possible **confounding effect**
- Matching on several characteristics is not advisable as it:
  - Creates difficulties in finding controls
  - Requires more complex statistical analysis
  - May result in overmatching

Analysis in Case-Control Studies

- **The odds ratio (OR)** is used in case-control studies to estimate the strength of the association between exposure and outcome.

- Note that it is not possible to estimate the incidence of disease from a case control study unless the study is population based and all cases in a defined population are obtained.

- The odds ratio is a measure of the odds of disease in the exposed compared to the odds of disease in the unexposed (controls) and is calculated as: OR = ad/bc

- OR interpretations: OR>1, OR=1, OR<1

Vaping and Pulmonary “illness”

Case-control study of vaping and pulmonary illness among 100 cases and 400 controls.

Exposure: vaping **Outcome:** pulmonary illness

	cases	controls	Total
vaping	60	100	160
No vaping	40	300	340
Total	100	400	500

	cases		controls		Total
vaping	60	**a**	100	**b**	160
No vaping	40	**c**	300	**d**	340
Total	100		400		500

OR = Odds of exposure among cases (a/c)
Odds of exposure among controls(b/d)
= **ad / bc**
= (60X300) / (100X40) = 4.5

What does 4.5 mean??

Those who vape are 4.5 times more likely to develop pulmonary illness than non-vaping

{3 Issues in the design of case-control studies}

Formulation of a clearly defined hypothesis, case, and sources

- **Clearly defined hypothesis:** a case-control study should begin with the formulation of a clearly defined hypothesis.
- **Case definition:** It is essential that the case definition is clearly defined at the outset of the investigation to ensure that all cases included in the study are based on the same diagnostic criteria.
- **Source of cases:** The source of cases needs to be clearly defined.

Measuring exposure status

- In case-control studies, the measurement of exposure is established **after** the development of disease.
- As a result is prone to both **recall** and **observer bias**.
- Various methods can be used **to ascertain exposure status**, including:
  - Standardized questionnaires
  - Biological samples
  - Interviews with the subject
  - Interviews with spouse or other family members
  - Medical records
  - Employment records
  - Pharmacy records
- The procedures used for the collection of exposure data **should be the same for cases and controls**.

Bias in Case-Control Studies

1. **Selection bias: Selection bias occurs when the persons in one group are different on some factor (other than disease)**

2. **Ascertainment bias: may arise because:**
   - **Cases may recall exposure better**
   - **Investigators may search for exposure more thoroughly in cases**
   - **Different data collection instrument may be used for the controls**

3. **Confounding**

Confounding in Case-Control Studies

- The two groups differ in some characteristic which is associated with both the outcome and exposure being studied
- A confounding variable is one that **can influence both the exposure and the outcome**

E.g. in relation between vaping and pulmonary illness, cigarette smoking is a likely confounder

- Males who use vapors are more likely to smoke, and smoking is strongly associated with pulmonary illness. **Age could be another confounder!**

E.g., is vapors use associated with pulmonary illness?

- **Cases: all males admitted to hospital with pulmonary illness aged 20-49 in region X**
- **Controls: a random sample of resident males in region X; age: 20-49 who have not had pulmonary illness**
- **Exposure: vapors use during 3 months prior to interview**
- **Data collection: personal interview of cases and controls – cases in hospital, controls telephone interview**
- **Potential bias: cases are younger than controls. Age is related to both exposure (vapors use) and outcome (pulmonary illness)**

{4 Strengths & Weaknesses}

Strengths

- Cost effective relative to other analytical studies such as cohort studies.
- Case-control studies are retrospective, and cases are identified at the beginning of the study; therefore there is no long follow up period (as compared to cohort studies).
- Efficient for the study of diseases with long latency periods.
- Efficient for the study of rare diseases.
- Good for examining multiple exposures.

Weakness

- Particularly prone to bias; especially selection, recall and observer bias.
- Case-control studies are limited to examining one outcome.
- Unable to estimate incidence rates of disease (unless study is population based).
- Poor choice for the study of rare exposures.

Thank you!

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