جامعة الملك سعود
King Saud University

CMED 305

Case Control Studies

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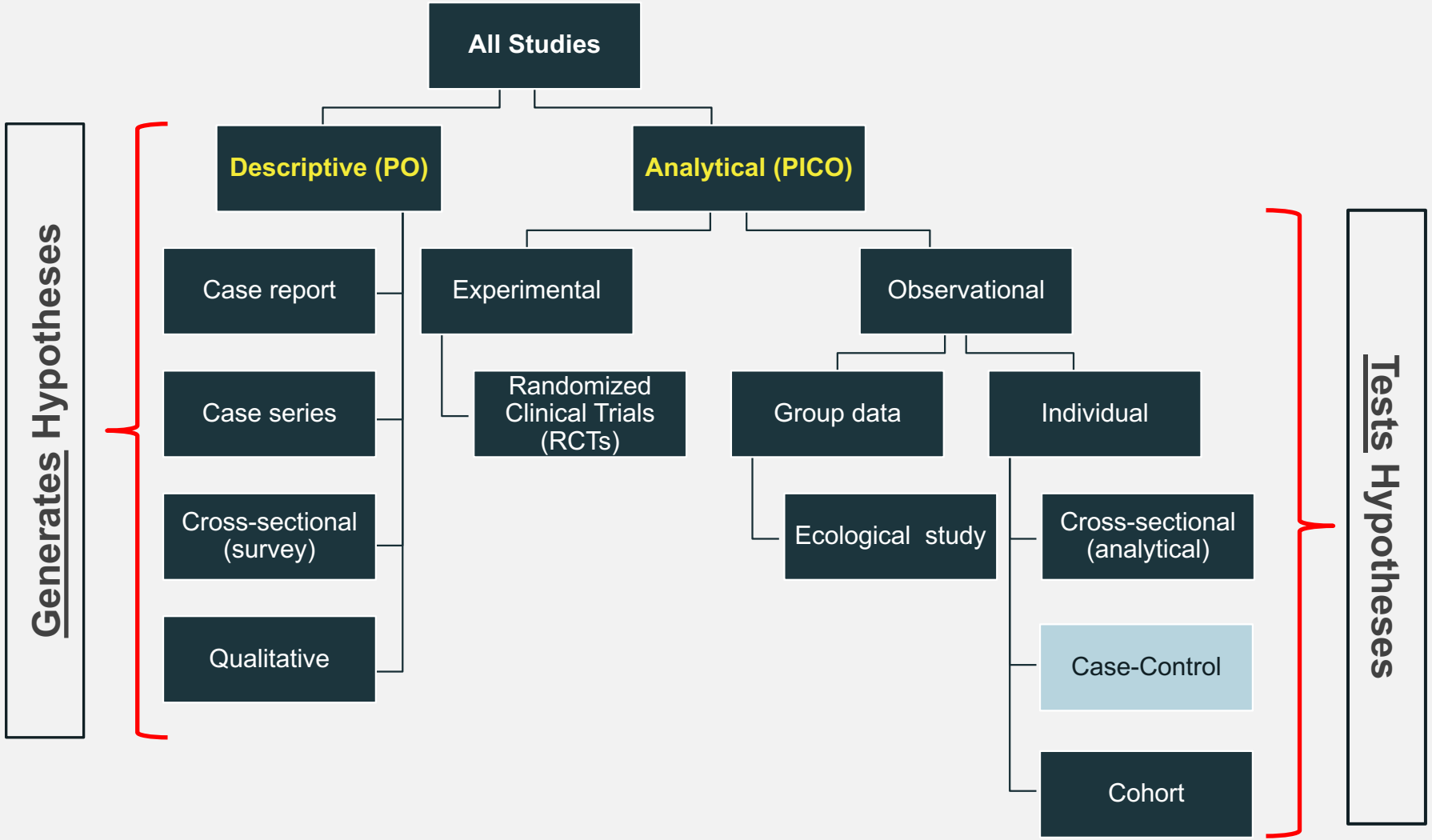
Learning Objectives: By end of this session students will be able to:

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)
Case-Control
Cohort
Generates Hypotheses
Tests Hypotheses

A case-control study is a study that **compares** subjects who have a disease or outcome of interest ***(cases)*** with subjects who do not have the disease or outcome ***(controls)*** by looking back **retrospectively** at the frequency of exposure to a risk factor in each group.

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

5- Decide on **Matching Cases and Controls**

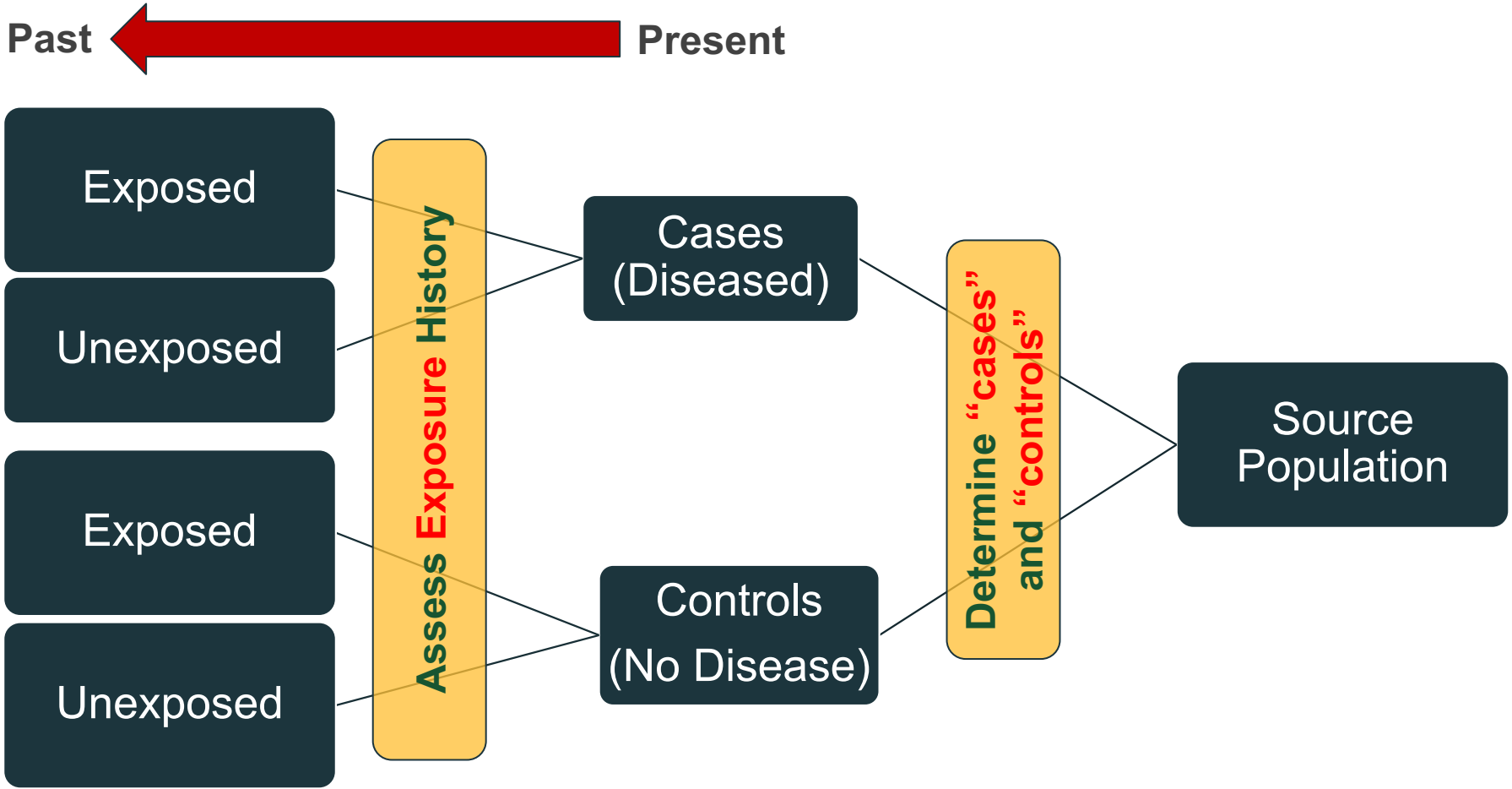
6- Estimate **sample size**

7- Select **Cases and Controls**

8- Measure **Exposure (Risk Factor(s))**

9- Analyze the **data**

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"

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 ongoing cohort study	
	Cases reported or diagnosed during a survey or surveillance system	
	Employment records	

Determine Study Subjects: "Controls"

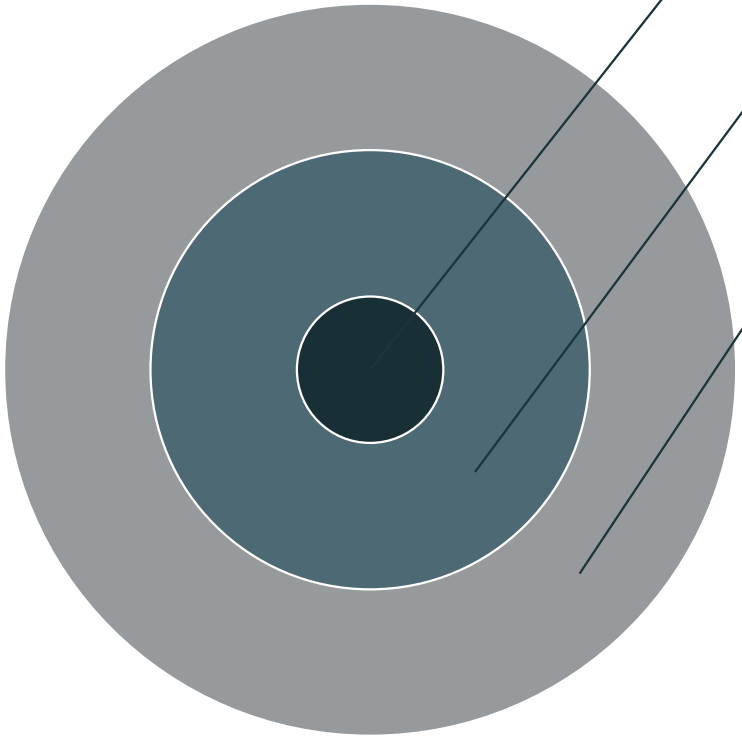
Aim of selecting controls:

- To compare the exposure rate among those with outcome and those without (e.g., % smoking among cases and controls)
- To confirm/refute if that the risk factor has occurred more frequently among the cases vs the controls using a measurement of association.

Selection of Controls:

- Ideal controls are healthy ones (very challenging!)
- It is crucial to select control group from population we are certain do not have the specified disease / condition.

Determining **controls**



3) Comparable to cases in terms of susceptibility

2) Free from health problems associated with the exposure under investigation

1) Free from the outcome under investigation

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. Minimize recall bias because they are sick, but with a different diagnosis.	1. Differing hospitalization patterns may introduce selection bias. 2. Difficult to blind disease status from cases and controls. 3. May have disease that share risk factors with outcome of interest (Berkson's bias).	1. Reduction of selection bias. 2. Generalization of study results is more valid. 3. More likely to be healthy.	1. Time and money consuming. 2. May suffer low participation rate. 3. Cases and control may exhibit differential recall of prior exposures.

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.

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

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


Calculating measures of associations

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 an OR of 4.5 mean?

Subjects who vaped were 4.5 times more likely to develop pulmonary illness than those who did not.

{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 "retrospectively".
- 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

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

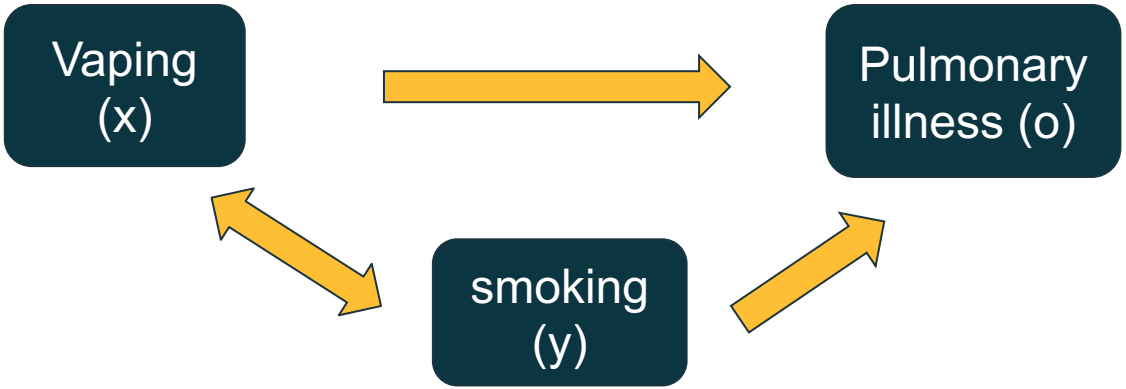
3. Confounding

Confounding in Case-control studies

- A confounding variable is one that is associated with both the exposure and the outcome.

E.g. Looking at the association between vaping and pulmonary illness, cigarette smoking is a likely confounder

- Males who vape are more likely to smoke, and smoking is strongly associated with pulmonary illness.



{4 Strengths & Weaknesses }

Strengths

- Cost effective relative to other analytical studies such as cohort studies.
- 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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