Research
442

Revised by
Deema · Fatima · Talal · Ahmed · Mohammed

Case Control Studies

Lecture No. 9

Objectives:

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

~ This lecture was presented by **Dr. Kholood Altassan**
~ It is included in the **Midterm Exam**
~ We highly recommended reading the **Ayah** in the first page

Slides

Color code

Original text
Dr. Notes
Important
Golden note
Extra

Editing file

Introduction

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.

سُورَةُ الحُجُرَاتِ

يَٰٓأَيُّهَا ٱلَّذِينَ ءَامَنُواْ ٱجْتَنِبُواْ كَثِيرًا مِّنَ ٱلظَّنِّ إِنَّ بَعْضَ ٱلظَّنِّ إِثْمٌ ۖ وَلَا تَجَسَّسُواْ وَلَا يَغْتَب بَّعْضُكُم بَعْضًا ۚ أَيُحِبُّ أَحَدُكُمْ أَن يَأْكُلَ لَحْمَ أَخِيهِ مَيْتًا فَكَرِهْتُمُوهُ ۚ وَٱتَّقُواْ ٱللَّهَ ۚ إِنَّ ٱللَّهَ تَوَّابٌ رَّحِيمٌ ﴿١٢﴾

المختصر في التفسير

يا أيها الذين آمنوا بالله وعملوا بما شرع، ابتعدوا عن كثير من التهم التي لا تستند لما يوجبها من أسباب وقرائن، إن بعض الظن إثم، كسوء الظن بمن ظاهره الصلاح، ولا تتبعوا عورات المؤمنين من ورائهم، ولا يذكر أحدكم أخاه بما يكره، فإنّ ذِكْره بما يكره مثل أكل لحمه ميتًا، أيحب أحدكم أن يأكل لحم أخيه ميتًا؟! فاكرهوا اغتيابه فهو مثله، واتقوا الله بامتثال أوامره، واجتناب نواهيه، إن الله تواب على من تاب من عباده، رحيم بهم.

When to Conduct a Case-Control Study

1. The **outcome** of interest is **rare**.
2. **Multiple exposures** may be associated with a **single outcome**.
3. **Funding** or **time** is **limited.**

HERE is a link of an 'Epidemiology' article from ***AMBOSS.***

It's a huge topic, so you can find Case-control study under Observational studies section.

1. To investigate cause-effect

when **experimental trials** (e.g. RCT) are **not ethical or feasible**, (lung cancer & smoking).

2. To investigate cause-effect

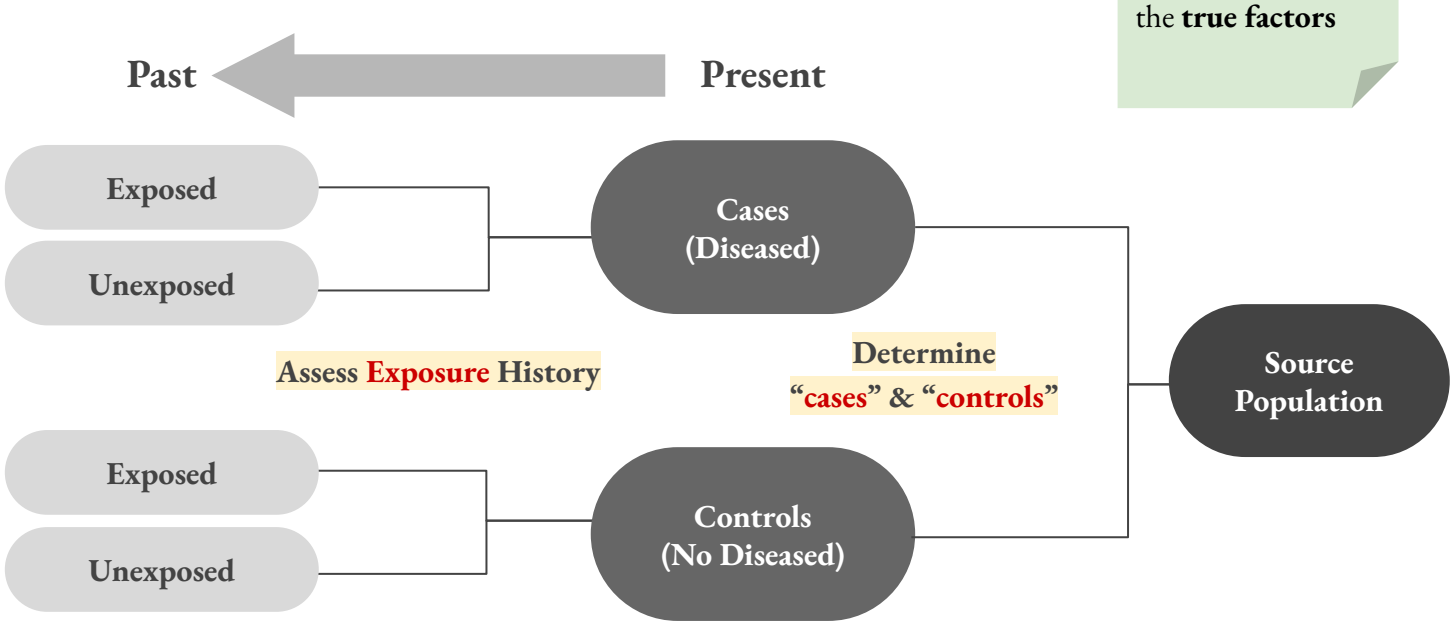
When **cohort studies** are **expensive or non-feasible** e.g. (to investigate etiology of rare disease e.g. cancer).

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**
5. ★ Decide on **Matching Cases & Controls**
6. **Estimate sample size**
7. **Select Cases & Controls**
8. **Measure Exposure** (Risk Factors)
9. **Analyze the date**

1st Step: Population

We need "to create a pool to choose the sample from it" and that sample will be used to determine the **true factors**



Steps in conducting a case-control study, cont.

2nd Step: 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** [1] (newly diagnosed cases). - **Prevalent cases** [2] (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.	

3rd Step: Study Subjects: "Controls"

Hospital-Based controls
Advantages:

- Subjects are easily accessible.
- Patients usually have time to participate.
- Patients are often motivated to cooperate with investigators.
- Controls and cases may be drawn from similar social & geographical environment.
- Differential recalls of prior exposure is likely to be minimized.

Disadvantages

- Differential hospitalization patterns may introduce selection bias.
- Difficult to blind disease status from cases and controls.
- An underestimate of the study effect may result if control's disease is etiologically similar to cases' disease.

Community-Based controls
Advantages

- Reduction of selection bias.
- Generalization of study results is more valid.
- May provide convenient control of extraneous (confounding) variables.

Disadvantages

- Time and money consuming.
- May suffer low participation rate.
- Cases and control may exhibit differential recall of period exposure.

1. Incident cases comprise cases newly diagnosed during a defined time period. The use of incident cases is considered as preferential, as the **recall of** past **exposure** may be more accurate among newly diagnosed cases. In addition, the **temporal sequence of exposure and disease** is easier to assess among incident cases.

2. Prevalent cases comprise individuals who have had the outcome under investigation for some time. The use of prevalent cases may give rise to **recall bias** as prevalent cases may be less likely to accurately report past exposures. As a result, the interpretation of results based on prevalent cases may prove more problematic, as it may be more difficult to ensure that reported events **relate** to a time **before** the **development** of **disease rather than** to the **consequence** of the **disease** process **itself**. For example, individuals may modify their exposure following the onset of disease. In addition, unless the effect of exposure on duration of illness is known, it will not be possible to determine the extent to which a particular characteristic is related to the prognosis of the disease once it develops rather than to its cause.

Steps in conducting a case-control study Cont.

3rd Step: Study Subjects "Controls", cont. [4]

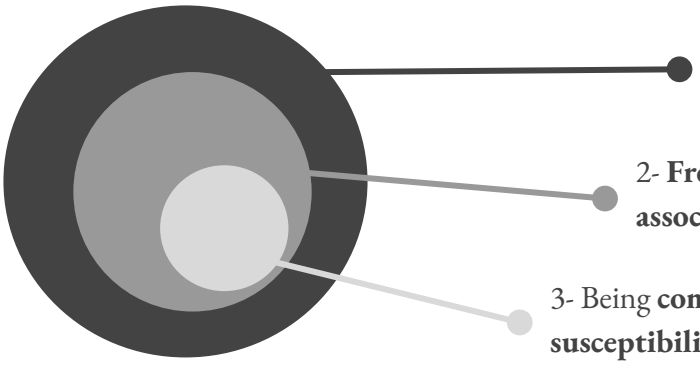
Selection of Controls:

- 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.

4. The challenge is this: If we conduct a case-control study and find more exposure in the cases than in the controls, we would like to be able to conclude that there is an association between the exposure and the disease in question.

The way the controls are selected is a major determinant of whether such a conclusion is valid.

Determining controls:



4th Step: 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!).

Steps in conducting a case-control study Cont.

5th Step: 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:
  1) **Creates difficulties in finding controls.**
  2) **Requires more complex statistical analysis.**
  3) **May result in overmatching.**

9th Step: 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 (in the table below)

> 1	• Means that the odds of exposure Among cases is **greater** than the odds of exposure Among controls.	The exposure may be **a risk factor** for the disease .
= 1	• Means that the odds of exposure Among cases is **same as** the odds of exposure Among controls.	The exposure is **not associated** with the disease .
< 1	• Means that the odds of exposure Among cases is **lower** than the odds of exposure Among controls.	The exposure may be **protective** against the disease .

Example of odds ratio and issues in this design

Example:

Vaping and Pulmonary "illness"

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

Exposure: vaping

Outcome: pulmonary illness

★ **OR = Odds of exposure among cases (a/c) / Odds of exposure among controls(b/d)**

= ad / bc

= (60 x 300) / (100 x 40) = 4.5

- It means:
  Those who vape are **4.5 times** more likely to develop pulmonary illness than non-vaping.

	Cases	Controls	Total
Vaping	**60** a	**100** b	**160**
No vaping	**40** c	**300** d	**340**
Total	**100**	**400**	**500**

Issues in the design of case-control studies

1. 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.

2. 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 make **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.**

Issues in the design of case-control studies, cont.

3. Bias in Case-Control Studies:

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

4. Confounding in Case-Control Studies: [5]

- 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 vape are more likely to smoke, and smoking is strongly associated with pulmonary illness. **Age could be another confounder!**
- **E.g., is vapers use associated with pulmonary illness?**

5. Control of confounding:
1- Design of the study matching cases and controls on the relevant confounding variables (E.g., matching in age)

2- Analysis phase Restrict the analysis to a limited age group-discards much of the collected information Stratification/Multivariate analysis

Note: **confounding** bias is the only type of bias that **can be controlled in the analysis** (selection bias can not be handled at the analysis stage).

- **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).

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

Weaknesses:

- 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.**

القادة:

نواف التركي — عبدالله الشهري — المتحمي

ريان الغنامي — وهى ا

الأعضاء:

عبدالله التركي — عبدالله المياح — رغد الظيف

محمد الزير — عبدالله النجرس — ريما الجريبة

عثمان الدريهم — تركي العتيبي — شهد البخاري

عبدالعزيز القحطاني — عبدالله القرني — نوف الضلعان

ناصر الغيث — عامر الغامدي — أثير الاحمري

سعد السهلي — سعد الاحمري — وعد ابو نخاع

رائد الماضي — معاذ آل صلام — ثراء الهويش

سعود الشعلان — محمد الحصيني — في الدوسري

منار الزهراني

Answer: Q1:C |Q2:B |Q3:C |Q4:B

MCQ:

Q1: The highest ratio can be taken for cases to control is?

A. 1:1
B. 1:2
C. 1:4
D. 1:5

Q2: What does it means when the odds ratio is equal to 1?

A. The exposure may be a risk factor for the disease
B. The exposure is not associated with the disease
C. The exposure may be protective against the disease

MCQ:

Q3: which type of bias occurs when the people in one group are different on some factor (other than disease)?

A. Ascertainment bias
B. Participation bias
C. Selection bias
D. Sampling bias

Q4: which of the following not considered as a strength of case-control study?

A. There is no long follow up period
B. Good for study of rare exposures
C. Efficient for study of diseases with long latency periods
D. Efficient for study rare diseases