# 08

# COHORT STUDY DESIGN

KSU COLLEGE OF MEDICINE
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## ACKNOWLEDGMENTS

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# LECTURE **OBJECTIVES**


**By the end of this lecture, I am able to:**

- Describe the types and design of cohort studies
- Identify steps and issues in the design and conducting of cohort studies
- Describe strength and weakness of cohort studies

# COHORT STUDIES

## Cohort Study

- A cohort study is an analytical observational study in which a **group of people** with a common characteristic is **followed over time** (at intervals) to find how many reach a certain health outcome of interest (disease, condition, event, death, or a change in health status or behavior).
- Term **"cohort"** is defined as a group of people, usually 100 or more in size, who share a common characteristic or experience within a defined time period (e.g., age, occupation, exposure to a drug or vaccine, pregnancy, and insured persons).
- The **comparison group** may be the general population from which the cohort is drawn, or it may be another cohort of persons thought to have had little or no exposure to the substance in question, but otherwise similar. from same source population

- A cohort study is as good as it can get when it comes to observational studies, this is where you can get the best evidence from an observational study incase you are looking into an association that gives the incidence of a disease.
- cohort studies are incidence studies while cross-sectional studies are prevalence studies.
- the Hallmark of cohort studies is **follow up.**

## Types of Cohort Study

**Three types of cohort studies have been distinguished on the basis of the time of occurrence of disease in relation to the time at which the investigation is initiated and continued**

Cohort studies always **start from the exposure**.the Timing of an exposure and an outcome are the factors that determine the type of cohort study;

1. if the exposure occurs once the investigation is initiated and followed up from there then this is a **prospective study**,
2. if the exposure took place in the past and the outcome also occurred in the past the study is **retrospective**
3. sometimes the exposure takes place in the past however the outcome have not yet occured , meaning we are still following up with the participants, akin to taking an exposure from a retrospective study and an outcome from a prospective study. resulting in a **mixed cohort study design.**

sometimes studies report the design as a cohort study but students often get confused on why no specific type was mentioned and that is because it's a mixed cohort study.

# COHORT STUDIES

## Types of cohort studies:

1. **Prospective cohort studies (concurrent): forward**

When the cohort is assembled at the present time and is followed up toward the future

2. **Retrospective cohort studies (nonconcurrent, historical):backward**

A cohort is identified and assembled in the past on the basis of existing records and is "followed" to the present time

3. **A combination of retrospective and prospective cohort studies**

A cohort is identified and assembled in the past on the basis of existing records and is followed up toward the future

## When to Conduct a Cohort Study:

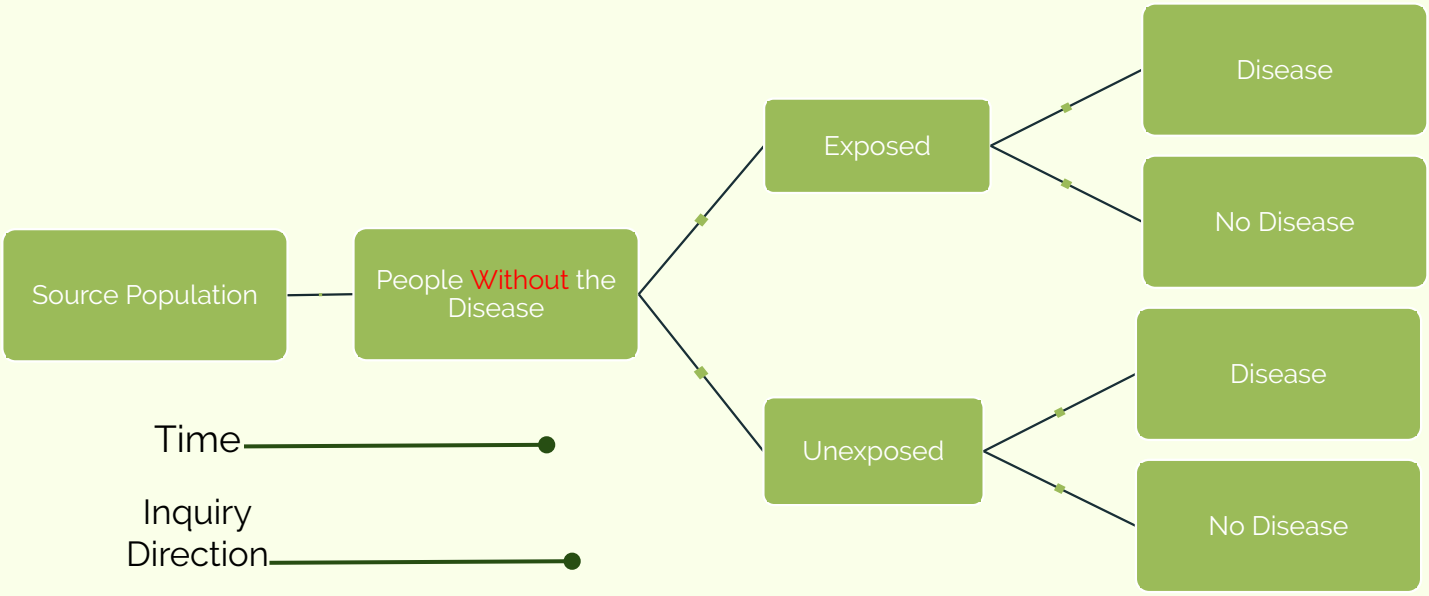
- When there is **good evidence of an association** between exposure and disease **(If we observe an association between an exposure and a disease or another outcome, the question is: Is the association causal?)**
- When **exposure is rare**, but the **incidence of disease high** among exposed, e.g. special exposure groups like those in industries, or exposure to X-rays
- When **attrition** (loss during follow up) of study population **can be minimized**, e.g. follow-up is easy, cohort is stable, cooperative and easily accessible
- When **funds and time are available**

- **cohort vs experimental studies**: in cohort the researcher does not assign an exposure he only asks whether the participant have been subjected to the exposure or not.
- **cross-sectional vs cohort**: in contrast to the association measured by a cross-sectional study. the associations in a cohort study are causal.;cause and effect. due to the researcher introducing the time dimension (follow up).
- example on **rare exposures**: one of the possible causes of multinodular goiter, a common condition in saudi Arabia ( high incidence), is radiation which is considered a rare exposure among common population.
- When **funds and time are available:** cohort studies are similar to RCT's in the sense that they require patience, lots of money and a long duration

# Design and Conduct of a Cohort Study

## Design and Steps in conducting a cohort study:

1. Define a **source population**
2. Select **Study Populations (subjects & controls): two methods:** based on **exposure status OR** based **on factor other than exposure** e.g. geographic location
3. Measure the **exposure**
4. **Follow up** at intervals to get accurate **outcome data**
5. **Analyze** data




- Cohort studies looking into **"health disparity" :** a fairly new field in preventive medicine that looks beyond populations of clinical setting ; interested in the factors differentiating people ,eg: age, gener, geographic location.
- **example:** we take those who are located in riyadh and those located in jeddah and follow up with a sample of their population. we inquire about what diseases they have obtained ,or a disease of interest, from the moment participants started living in the city until 20 yrs. and compare results.

# Design and Conduct of a Cohort Study

## Measurement:

| Measuring Exposure | Measuring Outcome |
|---|---|
| • Levels of exposure (e.g. packs of cigarettes smoked per year) are measured for **each individual** at:<br>1. baseline at the beginning of the study<br>2. assessed at intervals during the period of follow-up.<br>• A particular problem occurring in cohort studies is whether **individuals in the control group are truly unexposed.** For example, study participants may start smoking or they may fail to correctly recall past exposure. Similarly, those in **the exposed group may change their behaviour in relation to the exposure** such as diet, smoking suddenly decided to stop! we cannot stop them since it's not ethical. or alcohol consumption.you may never be sure! researchers try to ensure the validity of the exposure status in several way.<br>• **Sources for Exposure data:** medical or employment records, standardized questionnaires, interviews and by physical examination. | • **Sources for outcome data:** routine surveillance of cancer registry data, death certificates, medical records or directly from the participant.<br>• Method used to ascertain outcome must be **identical for both exposed and unexposed groups.** |

## Analysis:

**The data are analyzed in terms of:**

1-**Incidence rates** of outcome among exposed and non-exposed

2-**Estimation of risk:**

- Relative risk (Also known as risk ratio) (RR)
- **Attributable Risk (AR)** how to confirm that the outcome is actually a result of that rik

# Design and Conduct of a Cohort Study

## Equations:

| Cohort | Diseased | non-Diseased | Total |
|---|---|---|---|
| **Exposed** | A | B | A+B |
| **non-Exposed** | C | D | C+D |
| **Total** | A+C | B+D | A+B+C+D |

- in the example of multinodular goiter : exposure statues may be confirmed by asking the participants as well as performing periodic biological tests to assess their exposure to radiation

1. **Incidence rates:**

who developed the disease over the total.

Among exposed= **A/(A+B)**

Among non-exposed= **C/(C+D)**

2. **Relative risk (RR) =**

"What is the ratio of the risk of disease in exposed individuals to the risk of disease in unexposed individuals?"

**[A/(A+B)] /[C/(C+D)] or A(C+D) / C(A+B)**

The Incidence of exposed over the incidence of non-exposed.

3. **Attributable risk (AR)=**

"How much the disease can be prevented if we have an effective measure of eliminating the exposure?"

**[A/(A+B) -C/(C+D)]/[A/(A+B)]*100**

is the difference in the disease rates in exposed and unexposed individuals over the incidence of exposed

In cohort studies these specific **questions** are often asked: (vaping example)

- what were the **incidence rates** among the exposed group in comparison to the non exposed?
- what is the **relative risk** of actually vaping fi you have seen an add? **RR**
  answer: people are 3.5 times more likely to vape if they have seen an add in comparison to those who did not see an add.
- how to prove that this risk of vaping actually happened because of seeing an add and not due to another factor, eg: smoking?
- how can you attribute the risk of vaping to adds?
  for the answer we will look into the 3.5 relative risk and dissect it further with **attributable risk.**

Attributable risk is a very important concept in cohort study.

eg: 90% Attributable risk indicates that 90% of cases vaped because of the add, so if you see an add there is a 90% chance you will vape in comparison to other factors
the significance: public health will conclude that if we do something about the add (prohibition, prevention,...) we will prevent 90% of the outcome (vaping)

# Vaping and Pulmonary Illness (Example)

Cohort study of vaping and pulmonary illness followed for 1 year.

**Exposure:** vaping **Outcome:** pulmonary illness

| Cohort | Pulmonary Illness | No Pulmonary Illness | Total |
|---|---|---|---|
| **vaping** | 42 | 27,000 | 27,042 |
| **No vaping** | 7 | 63,000 | 63,007 |
| **Total** | 49 | 90,000 | 90,049 |

1. **Incidence rates:**

Incidence Rate among exposed= 1.5/1000/year

Incidence Rate among unexposed= 0.1/1000/year

2. **Relative risk (RR) = 15**

**What does 15 mean?**

The risk of pulmonary illness is 15 times higher among vapors than non-vapers

3. **Attributable risk (AR)= 93%**

**What does 93% mean?**

93% of the morbidity from pulmonary illness among vapers may be attributable to vaping and could be prevented by elimination of vaping

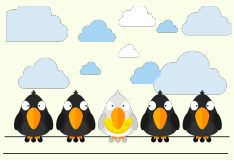
# In Comparison

Difference between Cohort and Case-Control Study :

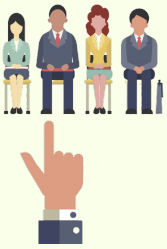
| Case-Control | Cohort |
|---|---|
| Proceeds from "effect to cause" | Proceeds from "cause to effect" |
| Starts with the disease | Starts with people exposed risk factor or suspected cause |
| Tests whether the suspected cause occurs more frequently in those with the disease than among those without the disease | Tests whether disease .occurs more frequently in those exposed, than in those not similarly exposed |
| Involves fewer number of subjects | Involves larger number of subjects |
| Yields relatively quick results | Long follow-up period often needed, involving delayed results |
| Suitable for the study of rare diseases | Inappropriate when the disease or exposure under investigation is rare |
| Generally yields only estimate RR or OR | Yields incidence rates, RR and AR |
| **CANNOT** yield information about diseases other than that selected for study | **CAN** yield information about more than one disease outcome |

# Identify issues in a Cohort Study

**Loss to Follow Up**



**Differential Misclassification of Subjects**



**Selection Bias**


**Confounding**

"We hope this doesn't happen to your coffee (: "

# Identify issues in a Cohort Study

## Loss to Follow Up

- Cohort members may die, migrate, change jobs or refuse to continue to participate in the study.
- In addition, losses to follow-up may be related to the exposure, outcome or both. change in statues of exposure or outcome
- For example, individuals who develop the outcome may be less likely to continue to participate in the study.

## Differential Misclassification of Subjects

- A major source of potential bias in cohort studies arises from the degree of accuracy with which subjects have been classified with respect to their exposure or disease status.
- Differential misclassification can lead to an over or underestimate of the effect between exposure and outcome. classifying someone as exposed when he is not or vise versa. especially in studies measuring determinants rather than risk factors.

## Selection Bias

- Selection bias is more common in case-control studies.
- However, **it can happen in cohort studies if:**

1. The completeness of follow-up is different among exposed and unexposed. ie: excellent follow up in the exposed group in comparison to non exposed. loss of follow up in control group results in more data for the exposed vs those who are not ultimately leading to overestimation.
2. Outcome ascertainment differs between exposed and unexposed.

## Confounding

- Confounding is a distortion (inaccuracy) in the estimated measure of association that occurs when the primary exposure of interest is mixed up with some other factor that is associated with the outcome.
- For example about the association between heart disease and physical inactivity, the primary goal is to ascertain the strength of association between physical inactivity and heart disease. Age is a confounding factor because it is associated with the exposure (meaning that older people are more likely to be inactive), and it is also associated with the outcome (because older people are at greater risk of developing heart disease).

# Strength & Weakness of Cohort Study

## Advantages and disadvantages of cohort studies:

| Advantages | Disadvantages |
|---|---|
| Incidence, can be calculated. | It involves a large number of people |
| Several possible outcomes related to exposure can be studied simultaneously. | It takes a long time to complete the study and obtain results. |
| It provides a direct estimate of relative risk. | It is unusual to lose a substantial proportion of the original cohort. |
| Dose response ratios can also be calculated. | There may be changes in the standard methods or diagnostic criteria of the disease. |
| Since comparison groups are formed before disease develops, certain forms of bias can be minimized like mis-classification. | Selection of comparison groups which are representative of the exposed and unexposed segments of the population is a limiting factor. |

## Weaknesses & Strengths

| Weaknesses | Strengths |
|---|---|
| • Costly and time consuming.<br>• Prone to bias due to loss to follow-up.<br>• Prone to confounding.<br>• Participants may move between one exposure category.<br>• Knowledge of exposure status may bias classification of the outcome.<br>• Being in the study may alter participant's behavior.<br>• Poor choice for the study of a rare disease (rare outcome).<br>• Classification of individuals (exposure or outcome status) can be affected by changes in diagnostic procedures. | • Multiple outcomes can be measured for any one exposure.<br>• Can look at multiple exposures.<br>• Exposure is measured before the onset of disease (in prospective cohort studies).<br>• Good for measuring rare exposures.<br>• Demonstrate direction of causality.<br>• Can measure incidence and prevalence. |

# COHORT STUDY

## Summary

**Issues in the design of cohort studies:**

- Loss to Follow Up
- Differential Misclassification of Subjects
- Selection Bias
- Confounding

**How to conduct a Cohort study?**

1. selection of study subjects
2. Obtaining data on exposure
3. Selection of comparison groups
4. Follow-up
5. Analysis of data

Cohort Study

**Types of cohort study** :

- **Prospective cohort (concurrent):**

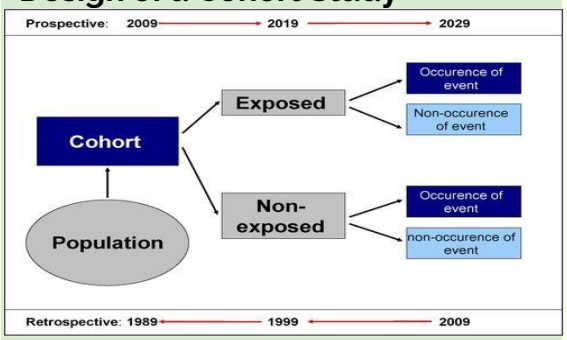
When the cohort is assembled at the present time and is followed up toward the future

- **Retrospective cohort (nonconcurrent, historical):**

A cohort is identified and assembled in the past on the basis of existing records and is "followed" to the present time

- **Mixed**

**Design of a Cohort Study**




**Strengths:**

- Multiple outcomes can be measured for any one exposure.
- Can look at multiple exposures.
- Exposure is measured before the onset of disease (in prospective cohort studies).
- Good for measuring rare exposures.
- Demonstrate direction of causality.
- Can measure incidence and prevalence.

**Weaknesses:**

- Costly and time consuming.
- Prone to bias due to loss to follow-up.
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- Participants may move between one exposure category.
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- Being in the study may alter participant's behavior.
- Poor choice for the study of a rare disease (rare outcome).
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