Cohort Study Design

Objectives:

- Definition of cohort design
- Design advantages and disadvantages
- Framework of cohort design
- Indications for cohort studies
- Types of cohort study designs
- Elements of cohort study
- Review of measures of disease occurrence (risk, relative risk and attributable risk)
- Potential biases and confounding effect
- Example of a cohort study

Team Members:

Ghaida Alsaeed - Doaa Walid - Hatem Alnddah - Abdulmohsen Alghannam

Team Leaders: Rawan Alwadee & Mohammed ALYousef

Revised By: Basel almeflh

Resources:

- 436 Lecture Slides + Notes

Important – Notes

436researchteam@gmail.com

Editing file

Feedback link

Cohort study

Steps:

- A group of people without the outcome is identified
- Followed
- Outcome ascertainment

Elements of Cohort Study

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

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

Strengths:

- Is of a particular value when the exposure is rare
- Can examine multiple effects of a single exposure
- Can elucidate temporal relationship between exposure and disease
- If prospective, minimizes bias in the ascertainment of exposure
- Allows direct measurement of incidence of disease in the exposed and nonexposed groups

436 TEAMS
436 Research Team

Cohort Study

- Term "**cohort**" is defined as a group of people 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). You take a group and you follow them over time
- 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.
- Cohort study is another type of analytical (observational) study.
- It is usually undertaken to obtain additional evidence to refute or support the existence of an association between suspected cause and disease. In Cohort study there are two groups: 1- Main group 2- Comparison group.
- The objective of a cohort study is to investigate whether the incidence of an event is related to a suspected exposure In Cohort study we measure the incidence to calculate the relative risk " احفظه مثلا ، اسمك "

Steps

1- A group of people without the outcome is identified

2- Followed

3- Outcome ascertainment

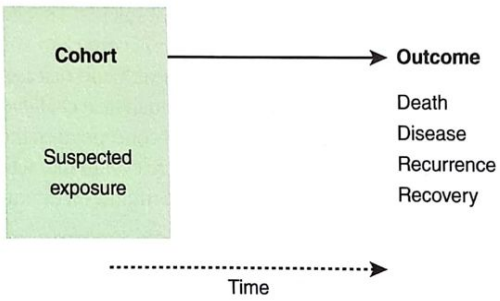
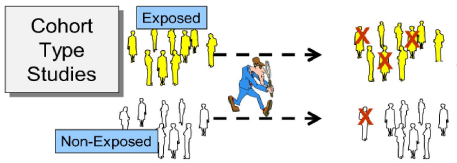


FIGURE 1-12 Basic components of a cohort study: exposure, time, and outcome.

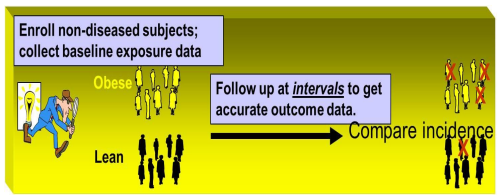
Elements of Cohort Study

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



The data are analyzed in terms of:

1. Incidence rates of outcome among exposed and non-exposed
2. Estimation of risk



Analysis of data

- Statistics from cohort study;
  - Crude rates of outcome
  - Standardized rates and ratios of outcome
  - Risk ratio of outcome
- **Crude Rates**
  - Number of individuals with the outcome out of the total cohort study size

$$(a + b) / n$$

Table 1.			
	Exposed to risk factor:		
Outcome	Yes	No	Total
Yes	a	b	a+b
No	c	d	c+d
Total	a+c	b+d	N

*e.g. The effect of Methotrexate (drug for rheumatoid arthritis) on developing cardiovascular disease in Rheumatoid patients;
The exposure: is the drug / The population: is rheumatoid patients / The outcomes: cardiovascular disease.
يعني نجيب مجموعيتين من مرضى الروماتويد وحدة منهم تاخذ ميثاتروكسيت والثانية ما تخذ ميثاتروكسيت؛ ونشوف مين منهم يجيه أمراض القلب, وهل فعلا في علاقة بين الميثاتروكسيت والإصابة بأمراض القلب؟

Comparison group can be one of two ether **General population or **Internal** comparison group.
يعني لو طبقنها على المثال إلي قبل يعتبر انتيرنال؛ لأن كل القروبين مرضى روماتويد، بينما لو قروب مرضى روماتويد والقروب الآخر من عامة الناس هنا يعتبر جينيرال.
!The internal is better

1. Incidence rates:
who developed the disease over the total.

Among exposed= a/a+b
Among non-exposed= c/c+d

Cohort	Disease		Total
	Yes	No	
Exposed to a putative etiologic factor	a	b	a+b
Non exposed to a putative etiologic factor	c	d	c+d

2. Relative risk (RR) = a/(a+b) /c/(c+d)
The Incidence of exposed over the incidence of non-exposed.

Cohort	Disease		Total
	Yes	No	
Exposed to a putative etiologic factor	a	b	a+b
Non exposed to a putative etiologic factor	c	d	c+d

3. **Attributable risk (AR)=** is the difference in the disease rates in exposed and unexposed individuals

Cohort	Disease		Total
	Yes	No	
Exposed to a putative etiologic factor	a	b	a+b
Non exposed to a putative etiologic factor	c	d	c+d

- **Q: When the event of interest is a newly developed disease, what we should do with the prevalent cases?**

- Incidence can be estimated as the number of events occurring during the follow-up period divided by the number of subjects in the cohort at baseline minus one-half of the losses

- 4/[1000-(1/2 X 7)] = 4.01/1000

- In this example,
- 1000 people started the study and followed up
- 4 eventually have the outcome " events "
- 7 lost to follow up " see the arrows "
- **Incidence** = number of outcome / (number of subjects started the study - 0.5 * number of subjects who lost to follow up)

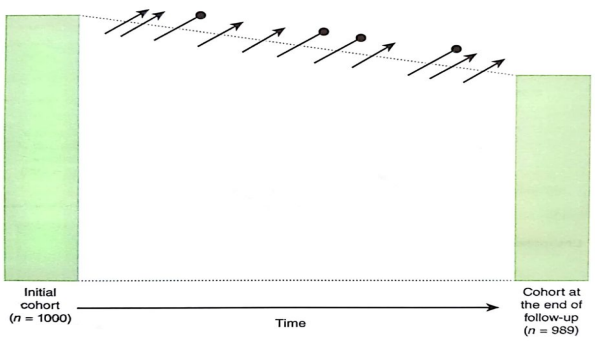


FIGURE 1-13 Diagram of a hypothetical cohort of 1000 subjects. During the follow-up, four disease events (line segments ending in dots) and seven losses to follow-up (arrows) occur so that the number of subjects under observation at the end of the follow-up is 989.

H36 Research Team

- The subjects are classified according to their exposure status
- Then, the incidence of the outcome of interest (usually a disease) is ascertained and compared across exposure categories

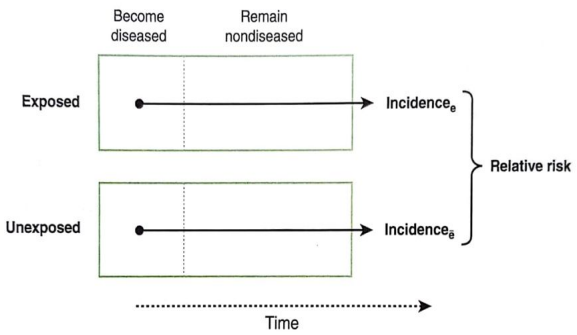


FIGURE 1-14 Basic analytical approach in a cohort study.

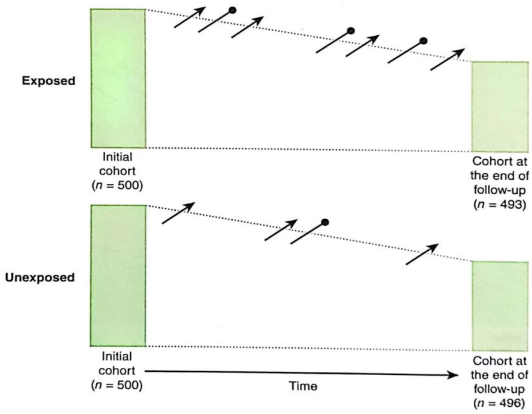


FIGURE 1-15 Same cohort study as in Figure 1-13, but the ascertainment of events and losses to follow-up is done separately among those exposed and unexposed.

Example

- Calculate the incidence of disease in exposed

3 / 500 - (0.5 * 4) = 0.006

- Calculate the incidence of disease in unexposed

1 / 500 – (0.5 * 3) = 0.002

- Calculate the relative risk (risk ratio)

0.006 / 0.002 = 3 There is association because it is > 1

- > 1 There is association
- < 1 Protective role
- = 1 No risk nor Protection

➢ An important assumption for the calculation of incidence in a cohort study is that individuals who are lost to follow-up are similar to those who remain under observation

436 TEAMS
436 Research Team

Types of cohort studies

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:

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

** Don't get confused with Retrospective and case control, even we go back in time we still looking for the exposure first !!

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

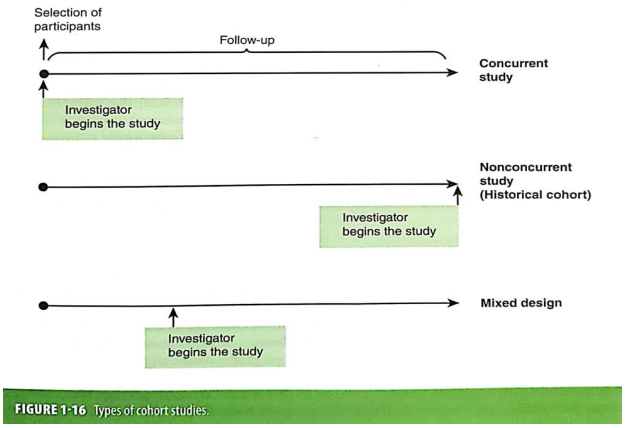
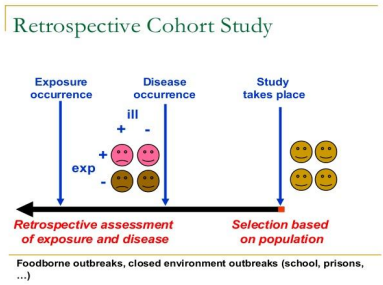
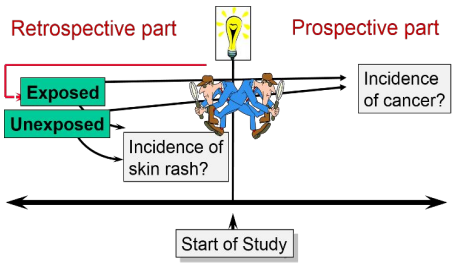


FIGURE 1-16 Types of cohort studies.





Strengths

- Is of a particular value when the exposure is rare
- Can examine multiple effects of a single exposure
- Can elucidate temporal relationship between exposure and disease
- If prospective, minimizes bias in the ascertainment of exposure
- Allows direct measurement of incidence of disease in the exposed and nonexposed groups

Limitations

- Is inefficient of the evaluation of rare diseases " the best design for rare diseases **CASE CONTROL** "
- If prospective, can be extremely expensive and time consuming
- If retrospective, requires the availability of adequate records
- Validity of the results can be seriously affected by losses to follow-up " especially if the losses are in one group more than other or all of the losses are sharing the same demographic characteristics "

436 Research Team
436 TEAMS

Advantages and disadvantages of cohort studies

Advantages	Disadvantages
Incidence, Relative Risk and Attributable Risk can be calculated.	It involves a large number of people
Several possible outcomes related to exposure can be studied simultaneously. You can calculate many outcomes	It takes a long time to complete the study and obtain results. And very expensive.
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.	Selection of comparison groups which are representative of the exposed and unexposed segments of the population is a limiting factor.
Since comparison groups are formed before disease develops, certain forms of bias can be minimized like mis-classification.	There may be changes in the standard methods or diagnostic criteria of the disease.

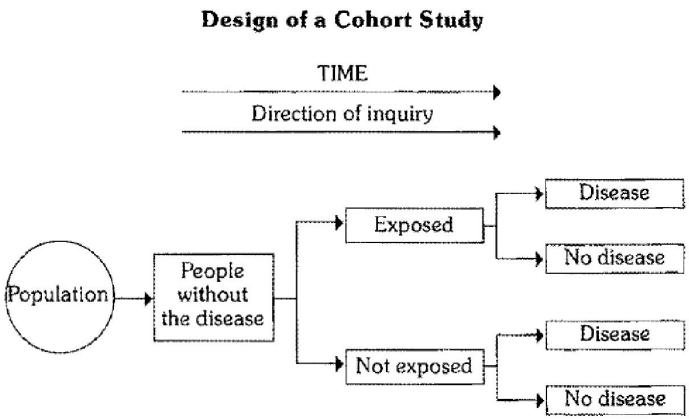
Framework of a cohort study

In contrast to case control studies which proceed from "**effect to cause**", the basic approach in cohort studies is to work from "**cause to effect**"

Case control is the opposite to Cohort
Case control > we start from the **disease**
Cohort > we start from **Exposure or risk factor**
E.g. you recruited 100 patients and you want to study the risk of smoking, dose the researcher start from the outcomes (disease) or start from the Exposure?
If they start with the exposure it is **Cohort**
If they start with the disease it is **Case-Control**

So in **Cohort**, there is a group of ppl who **don't** have the disease but they are Exposed to Risk factor.
The main purpose of Cohort is to measure the association between the risk factor or exposure and the disease, and we want to see will this risk factor lead to a certain disease or not.

So here you follow them over time to see, how many who are exposed develop the disease, and how many who are not exposed develop the disease



Schematic diagram of the design of cohort studies

4. Indications for cohort studies:

1. When there is good evidence of an **association** or causal relationship between exposure and disease.*
2. 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.
3. When attrition of study population can be minimized, e.g. **follow-up is easy**, cohort is stable, cooperative and easily accessible.
4. When ample **funds and time** are available.

* e.g. Does eating too much sugar increase the risk of diabetes?
Does drinking too coffee cause heart disease?

436 Research Team
436 TEAMS

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

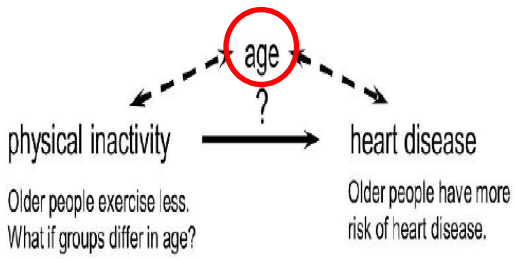
The key of any question if you have a scenario in the exam .

Potential Biases: main biases with Cohort study

1. Non response > no response from people, so the results will be underestimated > false results > error.
2. Loss to follow up with time > Long time > people may die or refuse to continue. The main problem in cohort.
3. Measurement errors in exposure > errors in the tools of measurement.

Confounding Effect

- 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.
- In the figure, 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).



For a confounding factor, It is important to associate or link with both the exposure and the outcomes.

Summary

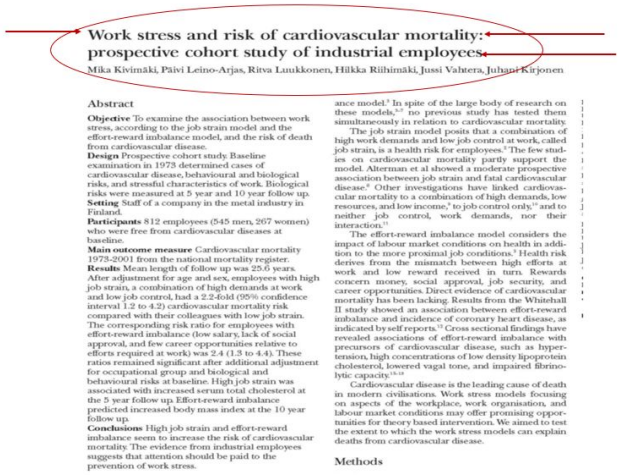
•Cohort studies are observational in nature and are useful in comparing risks in subgroups of populations within a specific time frame

•Availability of data from previous years can lead to less expensive estimates for Risk, RR, and AR, using a retrospective cohort study

•Prospective Cohort studies are expensive in time and resources, in addition to estimates of Risk, RR and AR , provide a causal link between risk factors and disease/other outcomes e.g. cancer.

Female slides

Example of Cohort Study:



Work stress and risk of cardiovascular mortality: prospective cohort study of industrial employees

Mika Kivimäki, Päivi Leino-Arjas, Ritva Luukkonen, Hilkka Riihimäki, Jussi Vahtera, Juhani Kirjonen

Abstract

Objective To examine the association between work stress, according to the job strain model and the effort-reward imbalance model, and the risk of death from cardiovascular disease.

Design Prospective cohort study. Baseline examination in 1973 determined cases of cardiovascular disease, behavioural and biological risks, and stressful characteristics of work. Biological risks were measured at 5 year and 10 year follow up.

Setting Staff of a company in the metal industry in Finland.

Participants 812 employees (545 men, 267 women) who were free from cardiovascular diseases at baseline.

Main outcome measure Cardiovascular mortality 1973-2001 from the national mortality register.

Results Mean length of follow up was 25.6 years. After adjustment for age and sex, employees with high job strain, a combination of high demands at work and low job control, had a 2.2-fold (95% confidence interval 1.2 to 4.2) cardiovascular mortality risk compared with their colleagues with low job strain. The corresponding risk ratio for employees with effort-reward imbalance (low salary, lack of social approval, and few career opportunities relative to efforts required at work) was 2.4 (1.3 to 4.4). These ratios remained significant after additional adjustment for occupational group and biological and behavioural risks at baseline. High job strain was associated with increased serum total cholesterol at the 5 year follow up. Effort-reward imbalance predicted increased body mass index at the 10 year follow up.

Conclusions High job strain and effort-reward imbalance seem to increase the risk of cardiovascular mortality. The evidence from industrial employees suggests that attention should be paid to the prevention of work stress.

ance model.[3] In spite of the large body of research on these models,[3,4] no previous study has tested them simultaneously in relation to cardiovascular mortality.

The job strain model posits that a combination of high work demands and low job control at work, called job strain, is a health risk for employees.[3] The few studies on cardiovascular mortality partly support the model. Alterman et al showed a moderate prospective association between job strain and fatal cardiovascular disease.[5] Other investigations have linked cardiovascular mortality to a combination of high demands, low resources, and low income,[6] to job control only,[7] and to neither job control, work demands, nor their interaction.[8]

The effort-reward imbalance model considers the impact of labour market conditions on health in addition to the more proximal job conditions.[3] Health risk derives from the mismatch between high efforts at work and low reward received in turn. Rewards concern money, social approval, job security, and career opportunities. Direct evidence of cardiovascular mortality has been lacking. Results from the Whitehall II study showed an association between effort-reward imbalance and incidence of coronary heart disease, as indicated by self reports.[9] Cross sectional findings have revealed associations of effort-reward imbalance with precursors of cardiovascular disease, such as hypertension, high concentrations of low density lipoprotein cholesterol, lowered vagal tone, and impaired fibrinolytic capacity.[10-13]

Cardiovascular disease is the leading cause of death in modern civilisations. Work stress models focusing on aspects of the workplace, work organisation, and labour market conditions may offer promising opportunities for theory based intervention. We aimed to test the extent to which the work stress models can explain deaths from cardiovascular disease.

Methods

Study population

The study sample was drawn from the employees (n=4570 in 1973) of the Valmet factories in Jyväskylä, central Finland, which manufacture paper machines, tractors, firearms, gauges, and so on. The work tasks varied from foundry work and heavy engineering to precision engineering and clerical and administrative work. The study population comprised people who had been employed by Valmet for at least 15 months in

Work stress questionnaire

We used self assessment scales used to measure the components of the job strain model and the effort-reward imbalance model.[16] The four questions on work demands deal with the degree of responsibility at work, task difficulty, and mental load (Cronbach's α reliability=0.67), and the 12 questions on job control concern decision authority and skill discretion (α=0.78). (Sample questions: "How mentally straining do you consider your work?" "Do you learn new things in your work?") The nine questions on effort at work indicate pace of work and physical and mental load (α=0.72), and the 16 questions on rewards measure satisfaction with income, fairness of supervision, job security, and promotion prospects (α=0.80). (Sample questions: "How great is the strain due to haste in your work?" "If changes or reorganisation take place at your workplace, how great is your risk of getting laid off?") All the questions required responses on Likert-type response formats (for example, 1="no strain" to 5="very great strain"). Each scale was constructed by summing the response scores on the individual questions. We divided the resulting scores into thirds to indicate low, intermediate, and high levels on each

Cardiovascular mortality

We collected mortality data from the Statistics Finland national mortality register, using the participants' personal identification codes. We obtained the date and cause of death for all participants who died between the date of their clinical examination (which took place between 5 February and 30 June 1973) and 1 November 2000. The causes of death were coded according to the ICD-8 (international classification of diseases, eighth revision) in 1973-86, the ICD-9 in 1987-95, and the ICD-10 in 1996-2000. Statistics Finland provided a classification that converted the different codes (up to 1997; subsequent deaths were classified on the basis of the death certificates) to the following categories: ischaemic heart diseases (I20-I25 in ICD-10), other heart diseases (I30-I52), cerebrovascular diseases (I60-I69), and other diseases of the cardiovascular system (I00-I19, I26-I29, I70-I99). We pooled these categories to indicate death due to cardiovascular diseases. We used information on the basic cause of death.

Assessment of work stress with self reports is apparently not a source of major bias in our study. Previous studies using subjective and objective methods have tended to give reasonably consistent results,[19] and the correlations between subjective assessments and expert ratings of job conditions are high.[5]

However, excess health risk in employees with high stress might not exclusively reflect a causal relation. For example, a selection into a stressful work environment may partly reflect early risk factors and adverse environments during childhood and adolescence.[24] Research on organisational interventions is needed to evaluate the additional gains achievable from efforts to change work life.

436 Research Team

436 TEAMS

THE END