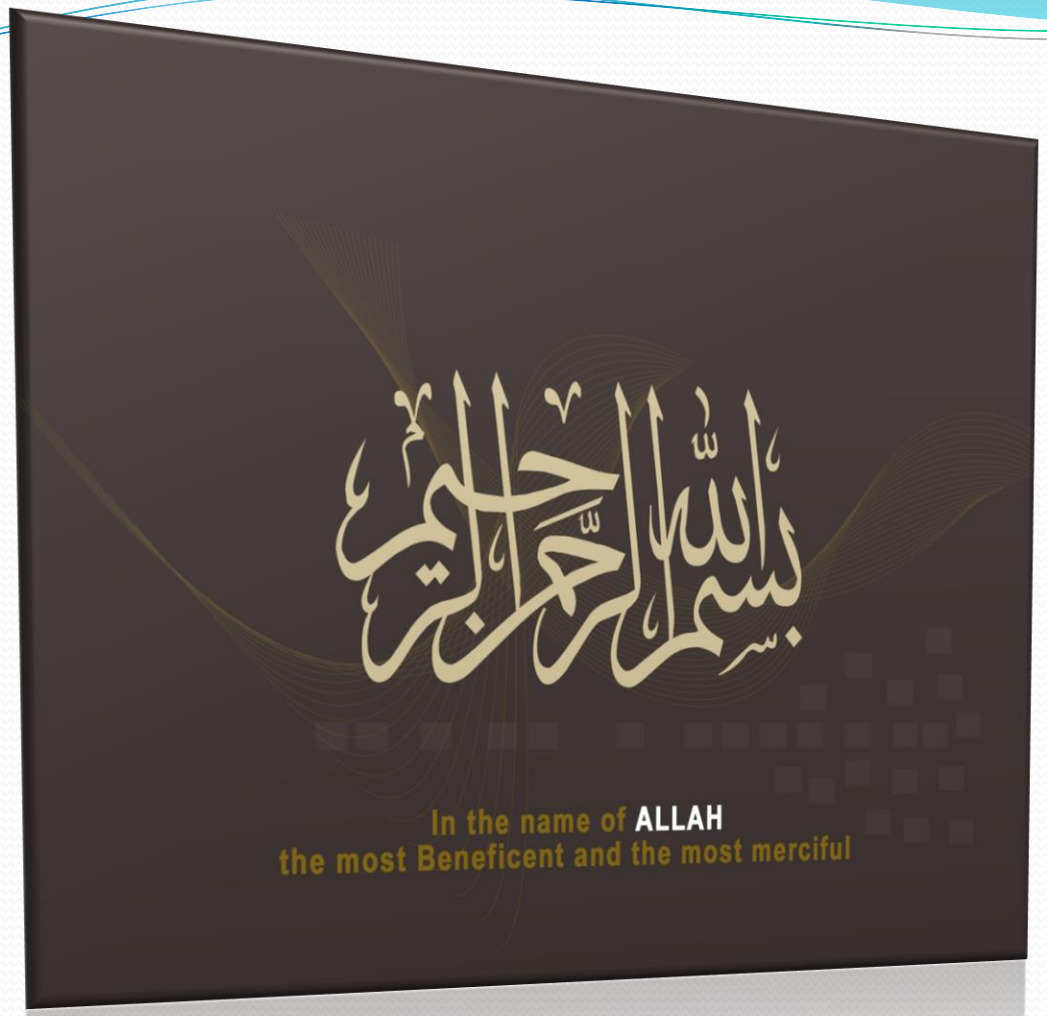
بسم الله الرحمن الرحيم
In the name of ALLAH
the most Beneficent and the most merciful

COHORT STUDY

COHORT STUDY

- Cohort study is another type of analytical (observational) study which is usually undertaken to obtain additional evidence to refute or support the existence of an association between suspected cause and disease.

COHORT STUDY

- Cohort study is known by a variety of names :
- prospective study, longitudinal study, incidence study, and forward-looking study.
- The most widely used term, however, is "cohort study"

The distinguishing features of cohort studies are :

- a. the cohorts are identified prior to the appearance of the disease under investigation
- b. the study groups, so defined, are observed over a period of time to determine the frequency of disease among them
- c. the study proceeds forward from cause to effect.

Indications for cohort studies

- Cohort studies are indicated :
- (a) when there is good evidence of an association between exposure and disease,
- (b) when exposure is rare, but the incidence of disease high among exposed, e,g., special exposure groups like those in industries, exposure to X-rays, etc

Indications for cohort studies

- (c) when attrition of study population can be minimized, e.g., follow-up is easy, cohort is stable, cooperative and easily accessible, and
- (d) when ample funds are available.

ELEMENTS OF A COHORT STUDY

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

1. Selection of study subjects

- The subjects of a cohort study are usually assembled in one of two ways - either from general population or select groups of the population that can be readily studied (e.g., persons with different degrees of exposure to the suspected causal factor).

1. Selection of study subjects

- (a) General population : When the exposure or cause of death is fairly frequent in the population, cohorts may be assembled from the general population, residing in well defined geographical, political and administrative areas (e.g., Framingham Heart Study).

1. Selection of study subjects

- If the population is very large, an appropriate sample is taken, so that the results can be generalized to the population sampled. The exposed and unexposed segments of the population to be studied should be representative of the corresponding segments of the general population.

1. Selection of study subjects

- (b) Special groups : These may be special groups or exposure groups that can readily be studied :
- (i) Select groups : These may be professional groups (e.g., doctors, nurses, lawyers, teachers, civil servants), insured persons, obstetric population, college alumni, government employees, volunteers, etc. These groups are usually a homogeneous population. Doll's prospective study on smoking and lung cancer was carried out on British doctors listed in the Medical Register of the UK in 1951

1. Selection of study subjects

- (ii) Exposure groups : If the exposure is rare, a more economical procedure is to select a cohort of persons known to have experienced the exposure. In other words, cohorts may be selected because of special exposure to physical, chemical and other disease agents. A readily accessible source of these groups is workers in industries and those employed in high-risk situations (e.g., radiologists exposed to X-rays).

2. Obtaining data on exposure

- Information about exposure may be obtained directly from the
- (a) Cohort members : through personal interviews or mailed questionnaires. Since cohort studies involve large numbers of population, mailed questionnaires offer a simple and economic way of obtaining information.
- For example, Doll and Hill used mailed questionnaires to collect smoking histories from British doctors.

2. Obtaining data on exposure

- (b) Review of records: Certain kinds of information (e.g., dose of radiation, kinds of surgery, or details of medical treatment) can be obtained only from medical records.
- © Medical examination or special tests : Some types of information can be obtained only by medical examination or special tests, e.g., blood pressure, serum cholesterol, ECG.

2. Obtaining data on exposure

- (d) Environmental surveys : This is the best source for obtaining information on exposure levels of the suspected factor in the environment where the cohort lived or worked. In fact, information may be needed from more than one or all of the above sources.

3. Selection of comparison groups

(a) Internal comparisons

- In some cohort studies, no outside comparison group is required. The comparison groups are in-built. That is, single cohort enters the study, and its members may, on the basis of information obtained, be classified into several comparison groups according to the degrees or levels of exposure to risk (e.g., smoking, blood pressure, serum cholesterol) before the development of the disease in question.

3. Selection of comparison groups

(b) External comparisons

- When information on degree of exposure is not available, it is necessary to put up an external control, to evaluate the experience of the exposed group, e.g., smokers and nonsmokers, a cohort of radiologists compared with a cohort of ophthalmologists, etc. The study and control cohorts should be similar in demographic and possibly important variables other than those under study.

3. Selection of comparison groups

(c) Comparison with general population rates

- If none is available, the mortality experience of the exposed group is compared with the mortality experience of the general population in the same geographic area as the exposed people, e.g., comparison of frequency of lung cancer among uranium mine workers with lung cancer mortality in the general population where the miners resided; comparison of frequency of cancer among asbestos workers with the rate in general population in the same geographic area

4. Follow-up

- One of the problems in cohort studies is the regular follow up of all the participants.
- The procedures required comprise :
- (a) periodic medical examination of each member of the cohort
- (b) reviewing physician and hospital records
- (c) routine surveillance of death records, and
- (d) mailed questionnaires, telephone calls, periodic home visits - preferably all three on an annual basis.

5. Analysis

- The data are analyzed in terms of :
- (a) Incidence rates of outcome among exposed and non exposed,
- (b) Estimation of risk.

5. Analysis

- (a) Incidence rates
- In a cohort study, we can determine incidence rates directly in those exposed and those not exposed.

A hypothetical example is given showing how incidence rates may be calculated

	Disease + Lung cancer +	Disease – No Lung cancer	
Study Cohort Smoking +	70 (a)	6930 (b)	7000 a+b
Control Cohort Smoking -	3 (c)	2997 (d)	3000 c+d
	a+c	b+d	1000

5. Analysis

- Incidence rates
- (a) among smokers = 70/7000, =10 per 1000
- (b) among non-smokers = 3/3000 = 1 per 1000
- Statistical significance : $P < 0.001$

5. Analysis

(b) Estimation of risk

- Having calculated the incidence rates, the next step is to estimate the risk of outcome (e.g., disease or death) in the exposed and non-exposed cohorts.
- This is done in terms of two well-known indices:
- (a) relative risk, (b) attributable risk.

5. Analysis

RELATIVE RISK

- Relative risk (RR) is the ratio of the incidence of the disease (or death) among exposed and the incidence among non-exposed.
- Some authors use the term "risk ratio" to refer to relative risk.

5. Analysis

$$RR = \frac{\text{incidence of disease among exposed}}{\text{Incidence of disease among non-exposed}}$$

$$= \frac{a/a+b}{c/c+d}$$

5. Analysis

- Incidence of lung cancer among smokers

  70/7000 = 10 per 1000

- Incidence of lung cancer among non-smokers

  3/3000 = 1 per thousand

RR = 10 / 1 = 10

(lung cancer is 10 times more common among smokers than non smokers)

5. Analysis

- A relative risk of one indicates no association; relative risk greater than one suggests "positive'.' association between exposure and the disease under study. A relative risk of 2 indicates that the incidence rate of disease is 2 times higher in the exposed group as compared with the unexposed. Equivalently, this represents a 100 per cent increase in risk

5. Analysis

- A relative risk of 0.25 indicates a 75% reduction in the incidence rate in exposed individuals as compared with the unexposed

5. Analysis

- In our hypothetical example, the relative risk is 10. It implies that smokers are 10 times at greater risk of developing lung cancer than non-smokers.

ATTRIBUTABLE RISK

- Attributable risk (AR) is the difference in incidence rates of disease (or death) between an exposed group and non exposed group. Some authors use the term "risk difference" to attributable risk.

ATTRIBUTABLE RISK

- Attributable risk is often expressed as a per cent. This is given by the formula
- Attributable Risk

$$AR = \frac{\text{Incidence of disease among exposed} - \text{incidence of disease among non exposed}}{\text{Incidence of disease among exposed}}$$

$$AR = \frac{a/a+b - c/c+d}{a/a+b}$$

ATTRIBUTABLE RISK

AR = 10 – 1 / 10 x 100

= 90 %

(90% of the cases of lung cancer among smokers are attributed to their habit of smoking)

- Attributable risk indicates to what extent the disease under study can be attributed to the exposure. The figure in our example indicates that the association between smoking and lung cancer is causal, 90 per cent of the lung cancer among smokers was due to their smoking. This suggests the amount of disease that might be eliminated if the factor under study could be controlled or eliminated.

POPULATION-ATTRIBUTABLE RISK

- It is the incidence of the disease (or death) in the total population minus the incidence of disease (or death) among those who were not exposed to the suspected causal factor

Lung cancer death rates among smokers and non-smokers : UK physicians

Deaths per 100,000 person-years		
Heavy smokers	224	Exposed to suspected factor (a)
Non-smokers	10	Non-exposed to suspected causal factor (b)
Deaths in total population	74 (c)	
Individual RR	a/b 224/10 = 22.40	

Population AR (c-b)/c = 86 per cent

POPULATION-ATTRIBUTABLE RISK

- The concept of population attributable risk is useful in that it provides an estimate of the amount by which the disease could be reduced in that population if the suspected factor was eliminated or modified. In our example one might expect that 86 per cent of deaths from lung cancer could be avoided if the risk factor of cigarettes were eliminated.

Relative risk versus attributable risk

- Relative risk is important in aetiological enquiries. Its size is a better index than is attributable risk for assessing the aetiological role of a factor in disease. The larger the relative risk, the stronger the association between cause and effect

Relative risk versus attributable risk

- But relative risk does not reflect the potential public health importance as does the attributable risk. That is, attributable risk gives a better idea than does relative risk of the impact of successful preventive or public health programme might have in reducing the problem.

Advantages and disadvantages of cohort studies

- Advantages

(a) Incidence can be calculated.

(b) Several possible outcomes related to exposure can be studied simultaneously - that is, we can study the association of the suspected factor with many other diseases in addition to the one under study. For example, cohort studies designed to study the association between smoking and lung cancer also showed association of smoking with coronary heart disease, peptic ulcer, cancer oesophagus and several others.

Advantages

- (c) Cohort studies provide a direct estimate of relative risk.
- (d) Dose response ratios can also be calculated, and
- (e) Since comparison groups are formed before disease develops, certain forms of bias can be minimized like mis-classification of individuals into exposed and unexposed groups.

Disadvantages

- Cohort studies also present a number of problems :
- (a) Cohort studies involve a large number of people. They are generally unsuitable for investigating uncommon diseases or diseases with low incidence in the population.

Disadvantages

- (b) It takes a long time to complete the study and obtain results (20-30 years or more in cancer studies) by which time the investigators may have died or the participants may have changed their classification.
- Even in very common chronic diseases like coronary heart disease, cohort studies are difficult to carry out. It is difficult to keep a large number of individuals under medical surveillance indefinitely.

Disadvantages

- (c) Certain administrative problems such as loss of experienced staff, loss of funding and extensive record keeping are inevitable.

Disadvantages

- (d) It is not unusual to lose a substantial proportion of the original cohort they may migrate, lose interest in the study or simply refuse to provide any required information.

Disadvantages

- (e) Selection of comparison groups which are representative of the exposed and unexposed segments of the population is a limiting factor. Those who volunteer for the study may not be representative of all individuals with the characteristic of interest.

Disadvantages

- (f) There may be changes in the standard methods or diagnostic criteria of the disease over prolonged follow-up. Once we have established the study protocol, it is difficult to introduce new knowledge or new tests later.
- (g) Cohort studies are expensive.

Disadvantages

- (h) The study itself may alter people's behaviour. If we are examining the role of smoking in lung cancer, an increased concern in the study cohort may be created. This may induce the study subjects to stop or decrease smoking.
- (i) With any cohort study we are faced with ethical problems of varying importance.

Disadvantages

- (j) Finally, in a cohort study, practical considerations dictate that we must concentrate on a limited number or factors possibly related to disease outcome.

Main differences between case control and cohort studies

Case control study

- 1. Proceeds from "effect to cause".
- 2. Starts with the disease.
- 3. Tests whether the suspected cause occurs more frequently in those with the disease than among those without the disease.

Cohort study

- Proceeds from "cause to effect".
- Starts with people exposed risk factor or suspected cause.
- Tests whether disease occurs more frequently in those exposed, than in those not similarly exposed.

Main differences between case control and cohort studies

Case control study	Cohort study
4. Usually the first approach to the testing of a hypothesis, but also useful for exploratory studies.	Reserved for testing of precisely formulated hypothesis.
5. Involves fewer number of subjects.	Involves larger number of subjects.
6. Yields relatively quick results.	Long follow-up period often needed, involving delayed results.
7. Suitable for the study of rare diseases.	Inappropriate when the disease or exposure under investigation is rare.

Main differences between case control and cohort studies

Case control study	Cohort study
8. Generally yields only estimate of RR (odds ratio).	Yields incidence rates, RR as well as AR.
9. Cannot yield information about diseases other than that selected for study.	Can yield information about more than one disease outcome.
10. Relatively inexpensive	Expensive.


Thanks