Epidemiology

→ The study of the distribution and deter
of health related states or events in a
specified population and the application o
the study to control of health problems

Epidemiologic methods :-

① Observational studies :-

a) Descriptive studies

b) Analytical studies

1) Ecological or Correlation with popula
as unit of ob

2) Cross sectional or Prevalence with individu

3) Case Control or Case reference " "

4) Cohort or Follow up. " "

② Experimental or Interventional studies

1) Randomized Controlled or clinical → Patients.
trial trial

2) Field trial → Healthy
People

3) Community trials or Community → Commun
intervention

Descriptive epidemiology

⇒ The best study of mankind is man. Shows that the importance of observations on individuals or populations exposed to suspected factors.

⇒ It is the first phase of an epidemiological investigation.

⇒ It is concerned with observing the distribution of the diseases.

- Who (Person)
- When (Place)
- Where with the population. (Time)

Procedures in descriptive studies

① Defining the Population

⇒ It means not only total number, but also age, sex, occupation, cultural characters, etc.

⇒ The population should be large enough.

⇒ The population should be stable without migration in or out of area.

⇒ Health Facility should be close enough to obtain the information.

⇒ "Defined population" is important because it provider denominator for calculating rates which are essential to measure frequency of disease, its distribution and determinants.

⇒ Epidemiologist are therefore given the name men in search of denominators.

② Defining the disease under study

⇒ Here the clinician and epidemiologist diverge-

- Clinician may not need precise diagnosis for patient case - But epidemiologist need accurate information about the diagnosis in a population.
→ Eg: Tonsillitis caused by S. Pyrogens.
→ The disease should be large enough and it provides the denominator.

3) Defining the disease.

⇒ By Time; Place; Person:

(i) Time distribution.

(a) Short term fluctuation:

⇒ Best example is: epidemic which is defined as "the occurrence in a community or region of cases of illness or other health-related events clearly in excess than normal expected"

A) Types of epidemics.

a) Common source epidemics:

a) Single source. (Point source)

→ Eg:- Food poisoning.

→ The epidemic curve will rise and fall rapidly with no secondary wave.

→ Time interval will be virually less.

→ Most frequently infectious cause.

b) Repeated exposure (Continuous exposure)

→ Eg:- Prostitute continuously injecting gonorrhea to the people connected to her.

Epidemic Curve?

B) Propagated epidemics.

⇒ a) Person to person ⇒ Hepatitis A or Polio.
   b) Arthropod borne.
   c) Animal borne

⇒ Curve will rise gradually and fall slowly Usually depends upon herd immunity and secondary attack rate & susceptible individual.

(b) Periodic fluctuation

A) Seasonal trend

⇒ URT, during winter, Measles during spring, GIT infection during summer.

⇒ It depends upon the temperature, humidity, rainfall, crowding, life cycle of vector.

⇒ Dengue start in July peak in September, oct and coinciding lated summer & rain.

B) Cyclic trend

⇒ Over short period of time every.

⇒ Measles (2-3 years), Rubella 6-9 years, Influenza (10 years).

(C) Long term or Secular trends

⇒ Progressive increase or decrease over a long period of time; generally years or decades.

⇒ ↑ in CHD, Lung Ca, Diabeter.
   ↓ in TB, Typhoid, Diptheria.

(II) Geographic or Place distribution

a) International Variation.

- Ca stomach in Japanese & Ca Oral & Cervix in India

b) National variation.

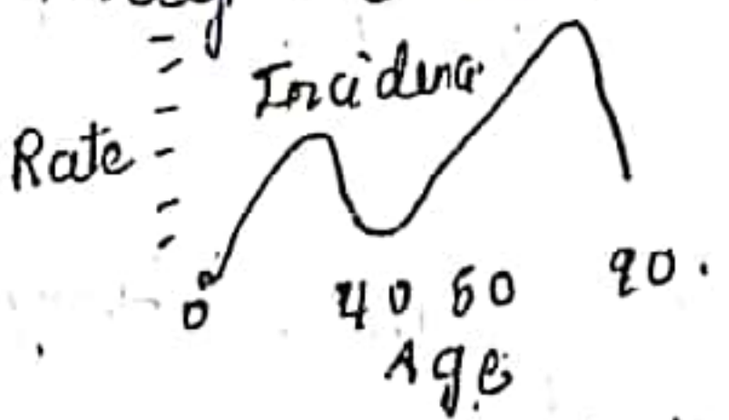
- Goitre in Himalayan Belt, Lathyrism, Fluorosis

where fluke, lathyrism, fluorine, Malaria in hilly
c) Rural - Urban variation → CH - Bronchitis & Accidents
↓ ↓ in urban.
Helminthasis & Soil transmitted

d) Local distribution:
→ Spot map or shaded maps are plotted.
for identifying clustering of cases & prevention

③ Person distribution.

a) Age → Eg:- Measles in childhood, CA in middle, & or
atheromatous in old people.
→ Chronic disease with advancing age.
Bimodality → There are two separate peaks
instead of one in the age incidence. Eg →
Hodgkin lymphoma 15-35 years and after 50 years
→ It is a special interest of epidemiologist and
there may be two causal features operative.



b) Sex → Women → Diabetes, obesity. Hyperthyroid
Men → CA lung. CHD. etc.
c) Ethnicity → Difference between racial & ethnic group
d) Marital status →
→ Mortality rate is ↓ in married men & women.
→ But ↑ in CA cervix.
e) Occupation. Depending upon their occupation
altering habits eg: Sleep, alcohol, smoking, night
coal mining etc.
f) Social class: Life expectancy ↑ed in UC than
LIG - UIG has CAD, Hypertension, diabetes ↑ risk.
g) Behaviour → Smoking, Alcohol, Sedentary
h) Others. i) Migration - of rural to urban vice versa

(4) Measurement of disease

* Disease load in the population should be available in terms of mortality, morbidity, disability.

Morbidity is measured by Incidence & Prevelance

Cross sectional (Prevelance study) → Not the natural history of disease.

Longitudinal (Incidence & Prevelance) → Follow up examination.

(5) Comparison with known indices

⇒ Comparing with different population and subgroups of same population.

(6) Formulation of Hypothesis:

⇒ Hypothesis is supposition, gained from observation, it can be rejected or accepted.

It should specify.

a) Population. b) Specific cause c) The expected outcome.

d) Dose response relationship e) Time response relationship.

Eg: Cigratte smoking causes cancer lung is incomplete.

Improved formulation →

Smoking 30-40 cigarrete per day causes lung cancer in 10% of smoker after 20 years of exposure.

Uses: ① Provides data for disease load (Mortality, Morbidity)

② Provides clue to aetiology.

③ Provide data for planning, organizing, evaluating.

④ Contribute to research by describing variation in disease occurence by time, Place, Person.

Analytical Epidemiology

⇒ Second major type of Epidemiology.
⇒ In this the study of interest is individual in the population not the population itself but the inference is to the population they selected.

1) Case Control
2) Cohort study.

CASE CONTROL STUDY

⇒ Also called "Retrospective studies" and common first approach to form causal hypothesis.
3 main features.
1) Exposure and outcome before the study.
2) study from backwards effect to cause.
3) Control or comparison group to support the result
⇒ By definition ⇒ It involves two populations.
Cases ⇒ Have a certain outcome.
Control ⇒ Not having outcome.
and the focus is on the disease that has already occured.
⇒ They are Comparison studies - Comparable with confounding factors like, age, sex, occupation etc
⇒ Questions are asked about exposures before

Framework of ce study.

Risk factors suspected	Case	Control.
Present	a	b
Absent	c	d
	a+c	b+d.

If $\frac{a}{a+c} > \frac{b}{b+d}$ then the risk factor is present.

Four Basic steps

① Selection ② Matching ③ Measurement of exposure.
④ Analysis and interpretation.

① Selection of Cases and Control.

① Cases Selection

a) Definition of Cases:.

i) ⇒ Diagnosing Criteria ⇒ Diagnosis and stage of the disease before the study, should not be changed.

ii) ⇒ Eligibity Criteria ⇒ Newly diagnosed more than old advanced cases (Incidence than Prevelance).

b) Sources of Cases:.

i) ⇒ Hospitals ⇒ Single or multiple hospital.

ii) General population ⇒ In same geographic location. duration of D with a survey, hospital registry.

② Control Selection

⇒ They should be free from the disease, and should be be similar to cases except free from disease and identified before the study.

⇒ Selection is difficult if the disease is in subclinical.

- Source of Control.

i) Hospital ⇒ People with other disease but might cause a selection bias.

ii) Relatives ⇒ Sibiling (Not in genetics) & Spouse.

iii) Neighourhood ⇒ Locality, School, Occupation.

iv) General Population ⇒ Random samples.

⇒ It is important to conduct more than one CCS to rely upon them.

③ Matching

⇒ Process by which we select control in such a way that are similar to cases with regard to certain variables (eg: age).

→ If the variable is correctly matched, it confounder can confound the results.
→ Confounding factors is the one associated with exposure and disease but distributed unequally more especially although associated with exposure it itself a risk factor independently.
Eg → Alcohol, Age.
→ Aetiology should never be matched.
→ Two types of matching → Pairing.
Case person of same in case and other control
↳ But difficult.
Group matching
(Age, occupation sub class)

(3) Measurement of exposure
→ It is collected by questionnaires, studying past records, of hospital, employment, interviews etc
→ Information about exposures should be obtained in same manner from both case and control.

(4) Analysis and interpretation
a) Exposure rates.

	Cases (Ca)	Control (without Ca)	Total
Smokers (less than 5 cigarettes per day)	33 (a)	55 (b)	a+b
Non smokers	2 (c)	27 (d)	c+d
	35 (a+c)	82 (b+d)	n = a+b+c+d

Cases = a/a+c = 33/35 = 94.2%.
Control = b/(b+d) = 55/82 = 67.01, P < 0.0001

b) Estimation of risk :-

→ Calculated with the help of Relative risk.

RR = Incidence among exposed / Incidence among non exposed.

Odd ratio → Association between outcome & risk factor.

$\left(\frac{a}{b}\right) / \left(\frac{c}{d}\right) = \frac{ad}{ca} = \frac{33 \times 27}{2 \times 55} = 8.1$

- So 8.1 times risk than non smokers.

Bias in case control studies

⇒ Bias is any systematic error between the exposure and disease.

a) Confounding factor.
b) Memory or recall bias ⇒ Past history and habits.
c) Selection Bias :-
d) Berksonian Bias :⇒ Hospital case & controls.
e) Interviewer Bias → ⓘ

Advantages

1) Easy to carry out
2) Rapid and inexpensive.
3) Require few subjects.
4) Suitable for rare disease.
5) Several aetiology.
6) Risk Factors.
7) No ethical problems
8) No attrition problems.
9) No risk to subjects.

Disadvantages

1) Bias
2) Selection of control.
3) Cannot find incidence.
4) Cannot find difference between cases & associated factors.

Examples :-

① Adenocarcinoma of Vagina and use of Diethylstilbestrol (DES)
② OCP ~ Thromboembolic disease. ③ Thalidomide therapy

Uses of Epidemiology:

→ A means of learning by asking questions which getting answers leads to other questions.

① To study historically rise and fall of disease in a population → Fluctuation of disease, Epidemic is identified.

② Community diagnosis → Mortality and Morbidity rates and nations priority in the control.

③ Planning and evaluation → Hospital with disease training, screening, Immunization. Sanitary services.

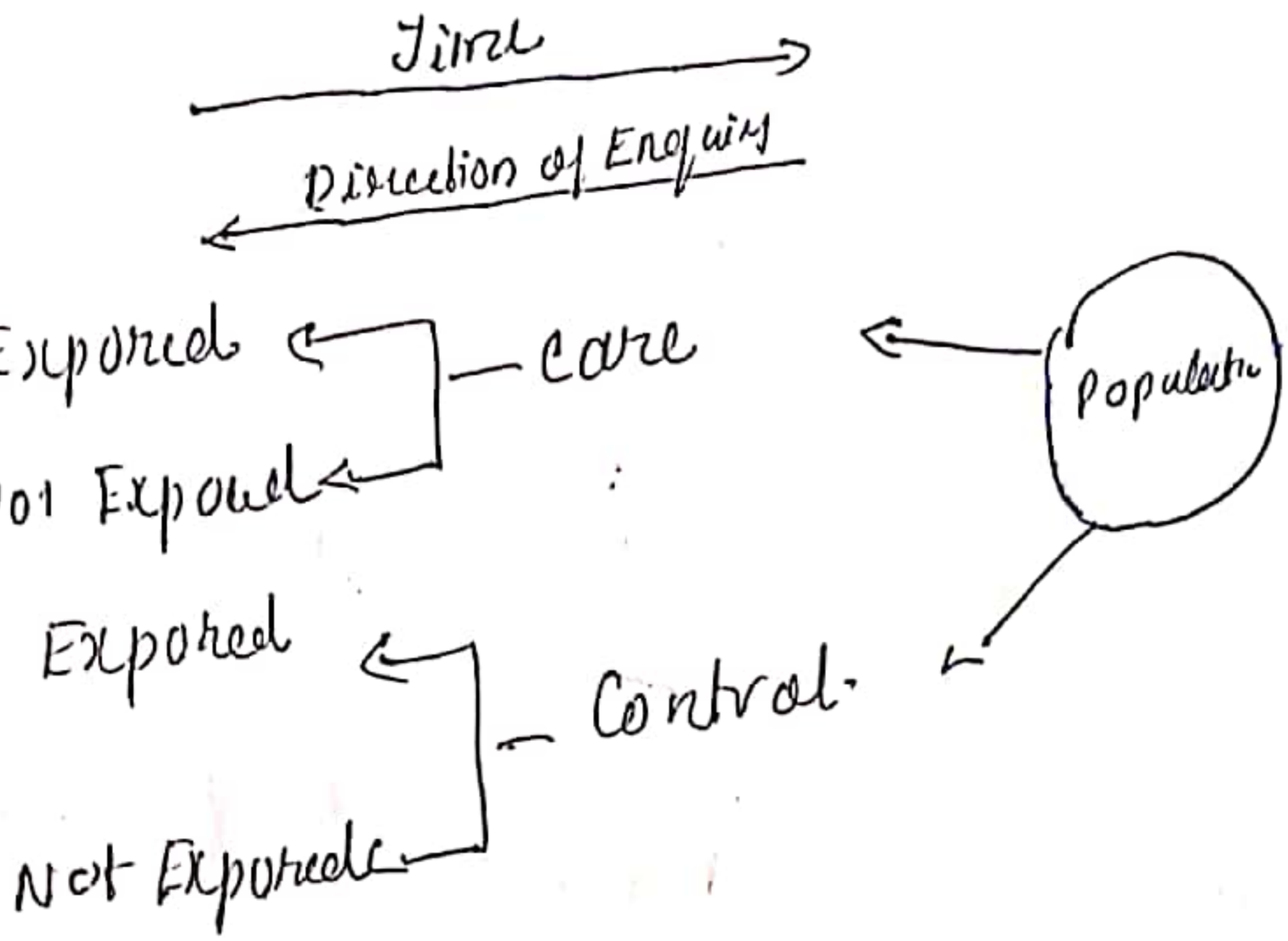
④ Evaluation of Individual risk & chances:
→ Clinically Hereditary problems, Smoking etc.

⑤ Syndrome identification:
→ Frequently associated findings.
→ Define and redefine syndrom.

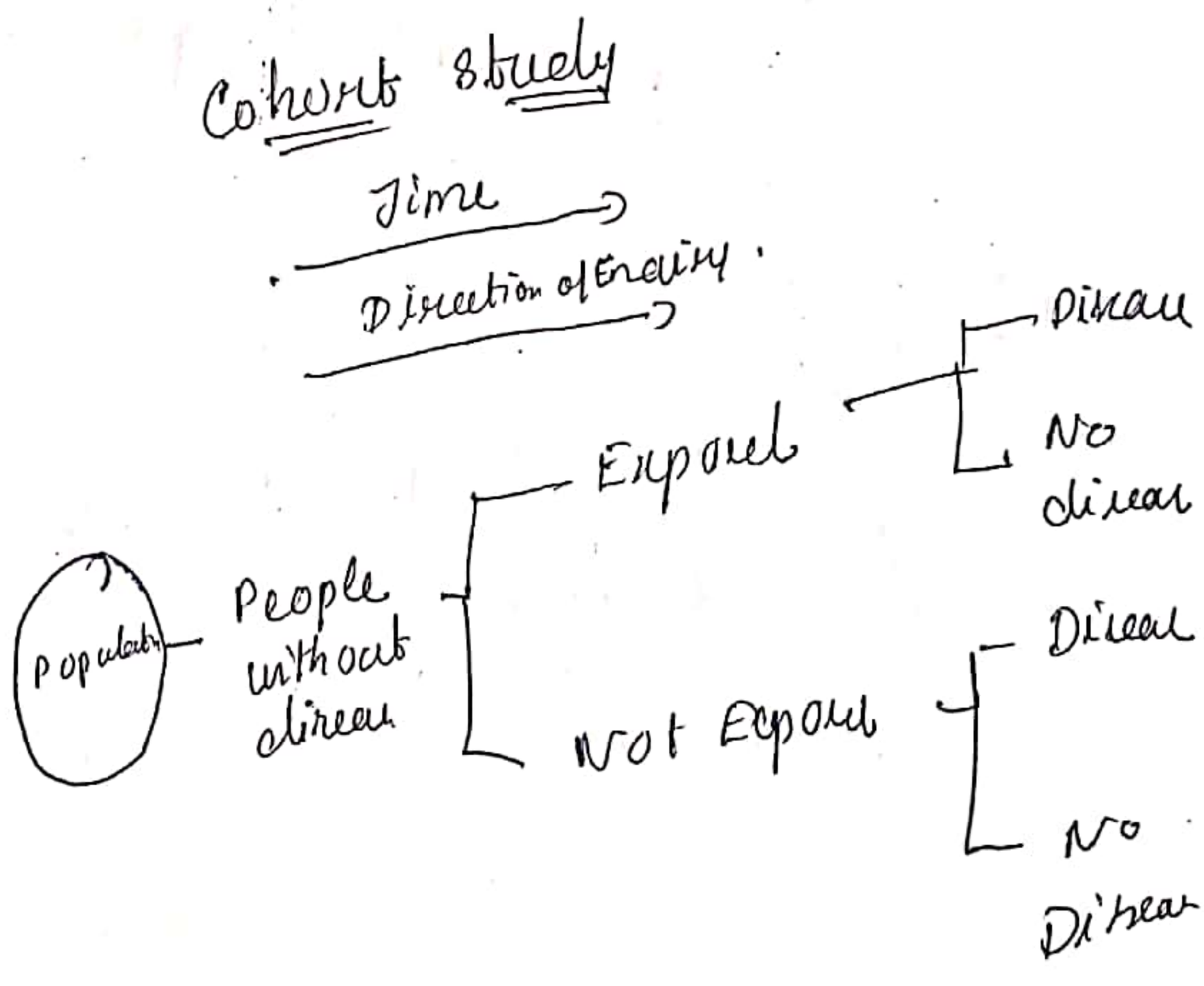
⑥ Completing the natural history of disease.
→ Agent, host, Environment.

⑦ Searching for Causes and risk factors.
→ Smoking & CA lung, Rubella and Congenital defect in Babies etc.

Case Control study



Cohort study



Cohort Study

- It is a type of analytical study which is usually done to obtain evidence to support the existence of an association between cause and disease.
- Also called as Prospective study, Longitudinal study, Incidence study, forward looking study.
- The distinguishing features are:
  i) The cohorts are identified prior to the appearance of the disease
  ii) The study group is observed for a period of time to determine frequency of disease
  iii) It is from cause to effect.

Concept of Cohort:

- "Cohort" is defined as a group of people who share a common characteristics or experience within a definite time period.
  Eg: People born on same day, same year.
  Birth cohort, Married on the same day, same time period, - Marriage cohort. Exposed to common drug, vaccine → Exposure cohort

Indications:

i) When good evidences between exposure and disease supported by Descriptive & Case control.
ii) When exposure is rare but high among exposed eg- X-rays
iii) When a study population is small.
iv) When ample funds are available.

Framework of Cohort study:

Cohort	Disease Yes	Disease No	Total
Exposed to aetiologic factor	a	b	a + b
Not exposed to aetiologic factor	c	d	c + d

Crucial considerations

1) Cohorts must be free from disease they have to be identified before
2) Both group should be equally susceptible to the disease (Males over 35 year - Lung Cancer).
3) Both group should be comparable in all variable which may influence the frequency of disease.
4) The diagnosis and eligibility criteria should be defined beforehand.

a + b = Exposed to factor under study.

a = Developed disease during follow up period

c + d = Persons not exposed.

c = Become case

Aim → Follow up if it is found that the incidence of the disease in exposed a/(a+b) significantly higher than the non-exposed then it is risk factor. the disease and cause are associated.

Types of Cohort Study:

i) Prospective cohort study.
- It is the one in which the outcome (ie disease) has not yet occured at the time of investigation begins.
- Eg: Uranium exposure persons are compared with non-Exposed for lung cancer.

ii) Retrospective Cohort study.
- Historical cohort study.
- It is the one in which the outcomes have all occured before the investigator gets licensed 10 to 30 years and studies them with the part employment records. Eg. Occupational.

iii) Combination of Both:
- The cohort is identified from part record and is assured of data for the outcome.

Elements of a Cohort Study

1) Selection of study subjects:
a) General Population: where the exposure of cause of death is fairly frequent in population.
b) Special group: (Doctors, Nurses, Lawyers).
i) Select groups → Professional group.
ii) Exposure group → The persons who are exposuring to manufacture
↓
Doll prospective study.. on smoking and lung CA on British doctors.
↓
Radiologists, X ray

2) Obtaining data on exposure.

a) Cohort members - By personal interview and questionnaires, Eg: Doll & Hill by questionnaires to doctors.

b) Review of the medical records (doctors, surgery, treatment).

c) Medical examination. (BP, cholesterol, ECG)

d) Environment surveys (Living + working)

Information about exposure should be like,

i) According to whether they are exposed to suspected factors.

ii) According to the level or degree of exposure.

3) Selection of Comparision Groups

a) Internal Comparision.

→ The cohorts are put into group according to the degree of exposure and compared with morbidity and mortility.

b) External Comparision.

→ When degree of ~~com~~ exposure is not available, they are compared externally.

Eg: ~~Sm~~ Non-Smokers and Smokers.

Cohort of Radiologist are compared with cohorts of opthamalogists.

c) Comparision with general population rate

- If nothing is available the exposed group is compare with the mortality experience of the same population [Lung cancer in same area population to the Uranium exposure]

4) Follow up :-
- It is the main problem.
- Periodic medical examination, routine surveillance, Mailed questionnaires, telephone calls.
- They have follow up due to death, change of residence, migration, withdrawal from occupation.

5) Analysis :-
a) Incidence rate :-
It is direct. For example.

Smoking	Developed Lung cancer	Not developed lung cancer	Total
Yes	a (70)	6930 (b)	7000 (a+b)
No	b (8)	2992 (d)	3000 (c+d)

i) Among Smokers = $\frac{a}{a+b} = \frac{70}{7000}$ = 10 per 1000
= 1 per 100.

ii) Among Non-Smokers = 8/3000

b) Estimation of risk :-
a) Relative risk :-

RR = $\frac{\text{Incidence of disease among exposed}}{\text{Incidence among non exposed}} = \frac{10}{1} = 10$

- It is the direct measure between the cause and effect.
- A relative risk of one indicated no association.
- A relative risk of 2 indicates that the incidence rate of disease is 2 times higher in the exposed group compared to not exposed.

In our hypothetical example the relative risk is 10. It says, that smokers are 10 times at greater risk in lung cancer. - The larger the RR, the greater the strength between the suspected factor and disease.

ii) Attributable Risk:

- Incidence rate among exposed - Not exposed / Incidence among exposed x 100,

$= \frac{10 - 1}{10} \times 100 = 90\ \%$

Advantages:

- Incidence can be calculated.
- Several other factor with association is calculated.
- Relative risk;
- No misclassification, Bias minimised;

Disadvantages

- Large number of people
- Large time,
- Costs of life, Follow up
- Expensive,
- withdrawal
- Change of occupation
- Ethical problem
- Attrition problem

Examples: ① Smoking & lung Cancer.

② Framingham Heart study ⇒ Risk factors & Heart d

③ OCP & health

Immunity:

1) Active Immunity:- Body produces antibody or c
   1) Humoral Immunity -
      - Antibody mediated immunity (Eg CIAMED).
      - Produced by B cells.
   2) Cellular Immunity
      - T cell mediated immunity.
   3) Combination of the above.
2) Passive Immunity :→ From another body transp
   - By administering Ig or antiserum
   - By Maternal placenta (Ig G), Mothers Milk (Ig

Herd Immunity:
When the vaccination of a portion of people protects the unprotected individuals.

Vaccines:
a) Live Modified, b) Inactivated or killed c) Toxoids
d) Extracellular fractions. e) Combination,
a) Live Vaccines: (MMR, Rotavirus, BCG, Varicella),
- Prepared from live or attenuated organisms. they have been repeatedly in tissue culture or chick embryo and lost their capacity and lost their capacity to produce full disease but retain their immunogenicity.
- It should not be administered to persons with immunodeficiency diseases or during pregnancy.
- A single dose is usually enough but another dose is given to ensure maximum protection.
- It produces durable immunity but not always like not the natural infection.
- They should be stored properly for its effectiveness.

b) Inactivated or killed vaccines:
- Inactivated vaccines are produced by growing viruses or bacteria in culture media and then inactivating them with heat or formalin.
- They are usually safe but less efficacious than live vaccines.
- It requires series of 2 or 3 doses to produce antibodies and requires a booster dose.
- It is administered by subcutaneous or intramuscular.
- Because it is inactivated it can be given to immunodeficient persons also.
- Only contraindication is severe reaction to the previous dose.
- Hepatitis, Cholera, Typhoid, Diphtheria, Influenza.

c) Subunit Vaccine:
- Vaccine produced by single or multiple antigenic components that are capable of producing immune response is used.

d) Toxoids:
- Certain organisms produce exotoxin (Diphtheria & Tetanus)
- These toxins are detoxified and used.

2) Protein vaccine.
- When single or multiple protein is sufficient to protect immune then it is used
- Pertussis, Influenza.

3) Recombinant protein Vaccine:
- Prepared from DNA of viruses

4) Polysaccharide - based vaccine.
- Prepared from polysaccharide coating of the bacteria.

5) Conjugated vaccines, (Ex- Pneumococci, Meningococci).
- Polysaccharide + Protein vaccine
  ↓ ↓
  Antibodies T cells.

d) Combinations:

- It is more than one kind of immunizing agents.
- It is used to reduce the cost, storage cost, Timeline of vaccination.
- No evidence exist that combination increases the burden of the immune systems.

DPT, DT, DP, DPT, Diphtheria, MMR, Pentavalent vaccine

Vaccine	When to give	Dose	Route	Site
BCG	Birth	0.1ml 0.06 in infants	~~Oral~~ Intradermal	left upper arm
OPV	Birth, 6, 10, 14 weeks 16-24 month, 5 years	2 drops	Oral	
Hepatitis B	Birth, 6, 10, 14	0.5 ml	Intra-muscular	Anterolateral side of Mid thigh
DPT	6, 10, 14 weeks, 16-24 months, 5 years	0.5ml	Intramuscular	Upper left arm " "
Hemophilus Influenza B	6, 10, 14 weeks	0.5ml	Intramuscular	
Rota Virus	6, 10, 14 weeks	5 drops	Oral	
IPV	At 14 weeks	0.5ml	Intramuscular	Right thigh
Measles	9 m-12 months 16-24 months	0.5 ml	Subcutaneous	Right upper arm
Japanese Encephalitis	9-12 months 16-24 months.	0.5ml	Subcutaneous	Rt hip- upper arm
MMR	15 months	0.5 ml	Oral	
Vitamin A (2nd dose)	9 month along with measles 16 month, after that one dose every 6 month	1 ml 2 ml		
JJ	10 & 16 years.	0.5ml	Intramuscular	Upper arm
Pregnancy	2 doses, 1 month apart If already immunized then booster dose	0.5ml	Intramuscular	Upper arm