Basic Concepts and Principles of Epidemiology

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- Epidemiology is the **basic science** of Preventive and Social Medicine.
- Epidemiology is **scientific discipline** of public health to study diseases in the community to acquire knowledge for health care of the society. **(prevention, control and treatment).**

- Epidemiological principles and methods are applied in –
- Clinical research,
- Disease prevention,
- Health promotion,
- Health protection and
- Health services research.
- The results of epidemiological studies are also used by other scientists, including health economists, health policy analysts, and health services managers.

MODERN EPIDEMIOLOGY

- Infectious disease Epidemiology.
- Chronic disease Epidemiology.
- Clinical Epidemiology.
- Genetic Epidemiology.
- Occupational Epidemiology.
- Cancer Epidemiology.
- Neuro-Epidemilogy.

Definition

"The study of the distribution and determinants of health-related states or events in specified populations, and the application of this study to the prevention and control of health problems" .

As defined by **John M. Last** (1988)

Box 1.2. Definition of epidemiology[a]

The word "epidemiology" is derived from the Greek words: *epi* "upon", *demos* "people" and *logos* "study". This broad definition of epidemiology can be further elaborated as follows:

Term	Explanation
Study	includes: surveillance, observation, hypothesis testing, analytic research and experiments.
Distribution	refers to analysis of: times, persons, places and classes of people affected.
Determinants	include factors that influence health: biological, chemical, physical, social, cultural, economic, genetic and behavioural.
Health-related states and events	refer to: diseases, causes of death, behaviours such as use of tobacco, positive health states, reactions to preventive regimes and provision and use of health services.
Specified populations	include those with identifiable characteristics, such as occupational groups.
Application to prevention and control	the aims of public health—to promote, protect, and restore health.

Ultimate Aim of Epidemiology

- 1. To eliminate or reduce the health problems of community.
- 2. To promote the health and well-being of society as a whole.

Aims & Objectives of Epidemiology

1. To describe the **distribution and magnitude** of health and disease problems in human population.
2. To identify **etiological factors (risk factors)** in the pathogenesis of disease.
3. To provide data essential to **the planning, implementation and evaluation of services** for the **prevention, control and treatment of disease** and setting priorities among those services.

(Acc. to International Epidemiological Association)

Distribution

- Distribution of disease occurs in a PATTERN.
- PATTERN- Time, Place, Person .
- PATTERN – Hypothesis for Causative/Risk factor – **Etiological Hypothesis**.
- **Descriptive Epidemiology.**

Determinants

- Identifying the causes and risk factors for diseases.
- **Testing the Hypothesis –** *(Biostatistics)*
- **Analytical Epidemiology**

Scope of Epidemiology

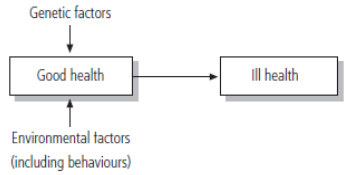
- 1. Causation of the disease.
- 2. Natural history of the disease.
- 3. Health status of the population.
- 4. Evaluation of Interventions.

1. Causation of the disease.

- Most of diseases are caused by interaction between *genetic and environmental factors*. (Diabetes)
- *Personal behaviors* affect this interplay.
- Epidemiology is used to study their **influence and the effects** of *preventive interventions* through health promotion.

1. Causation of the disease.

Figure 1.3. Causation

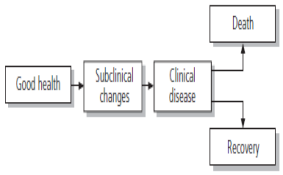


2. Natural history of the disease

Epidemiology is also concerned with the course and outcome (natural history) of diseases in individuals and groups.

2. Natural history of the disease

Figure 1.4. Natural history

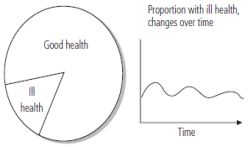


3. Health status of the population

- Epidemiology is often used to describe the *health status of population*.
- Knowledge of the **disease burden in populations** is essential for *health authorities*.
- To use *limited resources* to the best possible effect by **identifying priority health programmes** for prevention and care.

3. Health status of the population

Figure 1.5. Describing the health status of populations

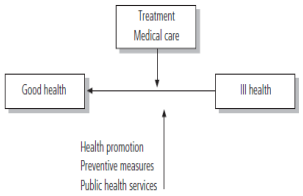


4. Evaluation of Interventions

- To evaluate the **effectiveness and efficiency** of health services.
- This means determining things such as –
- Impact of Contraceptive use on Population Control.
- the efficiency of sanitation measures to control diarrheal diseases and
- the impact of reducing lead additives in petrol.

4. Evaluation of Interventions

Figure 1.6. Evaluating interventions



- Applying *epidemiological principles and methods* to problems encountered in the *practice of medicine* has led to the development of-

"Clinical Epidemiology"

Applications of epidemiology in public health

1. Preventing disease and promoting health.
2. Community health assessment *(Community Diagnosis)* and priority setting.
3. Improving diagnosis, treatment and prognosis of clinical diseases.
4. Evaluating health interventions and programmes.

Epidemiology and public health

- Public health, refers to *collective actions* to improve population health.
- Epidemiology, *one of the tools* for improving public health, is used in several ways.

Epidemiology & Clinical Medicine

- 1. In **Clinical Medicine** the *unit of study* is a 'case', but in the **Epidemiology** the unit of study is *'defined population'* or *'population at risk'*.
- **Physician** is concerned with the *disease* in the *individual patient*, whereas **Epidemiologist** is concern with the *disease pattern in entire population.*
- So, the Epidemiology is concern with the both ***Sick & Healthy.***

- 2. In **Clinical Medicine**, the physician seeks to *diagnosis* for which he derives *prognosis* and prescribes *specific treatment*.
- The **Epidemiologist** is confronted with the relevant data derived from the particular *epidemiological study. (Community Diagnosis)*
- He seek to identify the **source of infection, mode of transmission, and an etiological factor** to determine the **future trends, prevention and control measure**.

- 3. In **Clinical Medicine** patient comes to the Doctor.
- **Epidemiologist**, goes to the community to find out the *disease pattern* and suspected *causal factors* in the question.

Epidemiological approach

- 1. Asking questions.
- 2. Making Comparisons.

1. Asking questions

Related to Health Events	Related to Health Action
1. What is the event? (Problem)	1. What can be done to reduce the problem?
2. What is magnitude?	2. How can be prevented in future?
3. Where did happen?	3. What action should be taken by community?
4. When did happen?	4. What resources required?
5. Who are affected?	5. How activities to be organized?
6. Why did it happen?	6. What difficulties may arise?

Epidemiology is *"a means of learning by asking questions and getting answers that lead to further questions."*

- These questions can be referred to as:

1. **Case definition** - (what)
2. **Person** - (who)
3. **Place** - (where)
4. **Time** - (when)
5. **Causes** - (why)

2.Making Comparisons

- To find out the *differences* in the AGENT, HOST and ENVIRONMENT conditions between two groups.
- *Weighs, balances and contrasts* give clues to ETIOLOGICAL HYPOTHESIS.

Basic Measurements in Epidemiology

Defining health and disease

Definition **–**

"health is a state of complete physical, mental, and social well-being and not merely the absence of disease or infirmity"

(WHO in 1948)

- This definition – criticized because of the *difficulty in defining and measuring* **well-being** – remains an ideal.
- The **World Health Assembly** resolved in **1977** that all people should attain a *level of health permitting them to lead socially and economically productive lives by the year **2000*** **(Health for All by 2000)**

- **Practical definitions** of health and disease are needed in **epidemiology**, which concentrates on aspects of health that are *easily measurable and amenable to improvement*.
- Definitions of health states used by epidemiologists tend to be simple, for example,

"disease present" *or* ***"disease absent"***

- **There is often no clear distinction between normal and abnormal.**
- Specially, for *normally distributed* **continuous variables** that may be associated with several diseases.
- Examples-
  - ✓ Cut of point for Blood Pressure- HTN.
  - ✓ Cut of point of Hemoglobin- Anaemia.
  - ✓ Normal Range of Blood Cholesterol.

BLOOD CHOLESTEROL (mg%)	FREQUENCY
125 - 135	5
135-145	22
145-155	25
155-165	130
165-175	140
175-185	260
185-195	274
195-205	282
205-215	268
215-225	270
225-235	135
235-245	135
245-255	24
255-265	24
265-275	8
TOTAL	2000

MEASURING DISEASE FREQUENCY

Incidence and Prevalence

- These are fundamentally different ways of **measuring disease frequency.**
- The **incidence** of disease represents the rate of occurrence of **new cases** arising in a given period in a specified population, while
- **prevalence** is the number of **existing cases (old+ new)** in a defined population at a given point in time.

Incidence

- "Number of **new cases** occurring in *defined population* during *specified period of time*"
- **Incidence** = Number of new cases during given period **/** Population at risk x 1000

Prevalence

- *Prevalence is* ***total no of existing cases (old + new)*** *in a defined population* at a particular point in time or specified period.
- **Prevalence** = Total no of cases at given point of time **/** Estimated population at time x 100

Relation between Incidence & Prevalence

Prevalence = Incidence x Mean duration of d/se.

P = I x D

Example – if,
I= 10 cases per 1000 per year.
D = 5 years.

P = 10 x 5
50 cases per 1000 population.

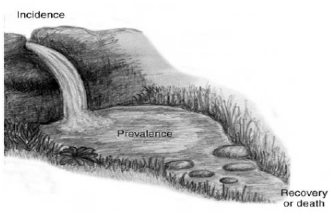
- 1. **Point Prevalence**

  Prevalence for given point of time.

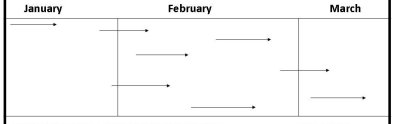
- 2. **Period Prevalence**

  Prevalence for specified period.

Relation between Incidence & Prevalence



Cases of cold infections in class 4J : Class size = 20



What is the period prevalence during February?	6/20=30.0%
What is the point prevalence on the 28th February?	1/20=5.0%
What is the incidence in February?	4/18=22.2%

Factors influencing the prevalence

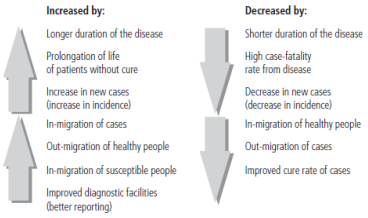


Table 2.2. Differences between incidence and prevalence

	Incidence	Prevalence
Numerator	Number of new cases of disease during a specified period of time	Number of existing cases of disease at a given point of time
Denominator	Population at risk	Population at risk
Focus	Whether the event is a new case Time of onset of the disease	Presence or absence of a disease Time period is arbitrary; rather a "snapshot" in time
Uses	Expresses the risk of becoming ill The main measure of acute diseases or conditions, but also used for chronic diseases More useful for studies of causation	Estimates the probability of the population being ill at the period of time being studied. Useful in the study of the burden of chronic diseases and implication for health services

Note: If incident cases are not resolved, but continue over time, then they become existing (prevalent) cases. In this sense, prevalence = incidence × duration.

TOOLS OF MEASUREMENTS

Numerator and Denominator

- Numerator – Number of events in a *population during specified time.*
- Denominator -

1. Total population

- Mid-year population
- Population at risk

2. Total events

Tools of Measurements

Basic tools are -

- 1. Rate
- 2. Ratio
- 3. Proportion
  - **Used for expression of disease magnitude.**

Rate

- A "Rate" measures the *occurrence of some specific event* in a population during given *time period*.
- Example –

Death Rate = total no of death in 1 yr / Mid-year population x 1000.

ELEMENTS –
Numerator (a) is a part of Denominator (b) and multiplier is 1000 or 10,000 or 100,000 or so on…. .

Ratio

- Ratio measures the *relationship of size of two random quantities*.
- Numerator is **not** component of denominator and BOTH numerator & denominator are unrelated.
- Ratio = x / y
- Example-
- Sex – Ratio

Proportion

- Proportion is **ratio** which indicates the *relation in a magnitude of a part of whole.*
- The Numerator is always part of Denominator and multiplier is 100.
- always expressed in **percentage (%)**.

Examples of Tools of Measurement in Epidemiology

Parameter	Formula	Numerator (N) & Denominator (D)	Conclusion
Infant mortality rate (IMR)	No. of infant deaths / No. of Live births x 1000	N is a part of D; multiplier NOT 100	Rate
Maternal mortality rate (MMR)[2]	No. of maternal deaths / No. of Live births x 100000	N is NOT a part of D; both unrelated	Ratio
Sex ratio (SR)	No. of females / No. of males x 1000	N is NOT a part of D; both unrelated	Ratio
Incidence[2]	No. of new cases / Total population x 1000	N is a part of D; multiplier NOT 100	Rate
Prevalence[2]	No. of new + old cases / Total population x 100	N is a part of D; multiplier 100	Proportion
Case fatality rate[2] (CFR)	No. of deaths / No. of cases X 100	N is a part of D; multiplier 100	Proportion
Relative risk (RRP)	Incidence among exposed / Incidence among non-exposed	N is NOT a part of D; both unrelated	Ratio

Indicators of Health

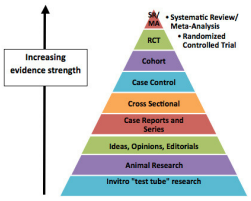
SCOPE OF MEASUREMENTS IN EPIDEMIOLOGY

Measurements in Epidemiology

1. Measurement of mortality.
2. Measurement of morbidity.
3. Measurement of disability.
4. Measurement of natality.
5. Measurement of presence or absence of attributes.
6. Measurement of health care need.
7. Measurement of environmental & other risk factors.
8. Measurement of demographic variables.

EPIDEMIOLOGIC RESEARCH METHODS

Position in the evidence hierarchy



Evidence pyramid in research

- Meta-analysis (Highest clinical relavence: Gold standard)
- Systemic review
- Cohort study
- Case control study
- Case series
- Case report
- Ideas, editorial, opinions
- Animal research
- In vitro (Test-tube) lowest clinical relevance)

Epidemiological Studies

1. Observational Studies

- Observational studies allow nature to take its course.
- The investigator measures but does not intervene.

2. Experimental Studies

- Active involvement to change disease determinants.
- such as an exposure or a behaviour – or the progress of a disease through treatment.
- are similar in design to experiments in other sciences.

Observational Studies

1. **Descriptive Study**

- is often the **first step** in an epidemiological investigation.
- is limited to a description of the occurrence of a disease in a population.
- Formulation of Hypothesis.

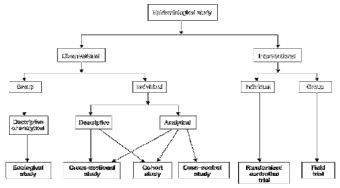
2. **Analytical Study**

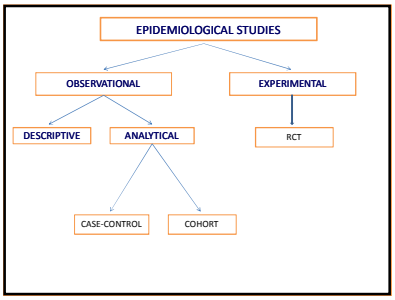
- analyze relationships between health status and other variables.
- Testing of Hypothesis.

Types of Epidemiologic Study Designs

Type of study	Alternative name	Unit of study
Observational studies		
Descriptive studies		
Analytical studies		
Ecological	Correlational	Populations
Cross-sectional	Prevalence	Individuals
Case-control	Case-reference	Individuals
Cohort	Follow-up	Individuals
Experimental studies	***Intervention studies***	
Randomized controlled trials	Clinical trials	Individuals
Cluster randomized controlled trials		Groups
Field trials		
Community trials	Community intervention studies	Healthy people Communities

Types of Epidemiologic Study Designs





OBSERVATIONAL - EPIDEMIOLOGY

Descriptive Epidemiologic Studies

- A simple description of the health status of a community.
- Based on routinely available data or data obtained in special surveys.
- is often the first step in an epidemiological investigation.

Procedure in Descriptive Studies

1. Defining population to be studied.
2. Defining disease under study.
3. Describing disease by
   - Time
   - Place
   - Person
4. Measurement of disease.
5. Comparing with known indices.
6. Formulation of etiological hypothesis.

1. Defining population to be studied.

- It is a 'Population study' not of an individual.
- Defining population by total number and composition (age, sex, occupation etc.)
- Defined population- can 'whole population' or 'a representative sample'.
- It provides 'denominator' for calculating rates and frequency.

2. Defining disease under study.

- Operation Definition - of disease is essential for measuring the disease in defined population.
- 'Case definition' should be adhered throughout the study.

3. Describing disease

- Describing the disease frequency and distribution in terms of Time, Place and Person.

TIME	Year, month, week, season, duration.
PLACE	Country, region, climatic zone, urban/rural, community, Cities, towns.
PERSON	Age, Sex, marital status, occupation, education, socioeconomic status.

4. Measurement of disease.

- To obtain the clear picture of 'disease load' in the population.
- In terms of Mortality, Morbidity and Disability.
- Morbidity has two aspects –
  - Incidence – Longitudinal Studies
  - Prevalence - Cross-sectional studies.

5. Comparing with known indices.

- Basic epidemiological approach –

1. making comparisons.
2. Asking questions.

- Making comparison with known indices in population.
- By making comparisons - clues about
  - disease etiology and
  - high risk population.

6. Formulation of etiological hypothesis.

- A **hypothesis** is supposition arrived at observation or reflection.

- Hypothesis should specify –

1. Population.
2. Specific cause – risk factors/exposures.
3. Outcome – disease/disability.
4. Dose-response relationship.
5. Time response relationship.

***Hypothesis** should be formulated in a manner that it can be **tested** with above parameters.*

- Hypothesis-

"Cigarette smoking causes lung cancer"

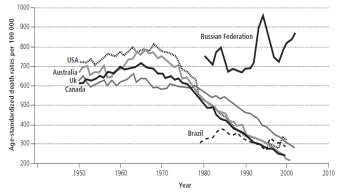
- Improved-

"Smoking 30-40 Cigarette /day for 20 years of causes lung cancer in 10% of smokers."

TESTING OF HYPOTHESIS

'Hypothesis' can be accepted or rejected by using the techniques of **Analytical Epidemiology**

Example- Descriptive study



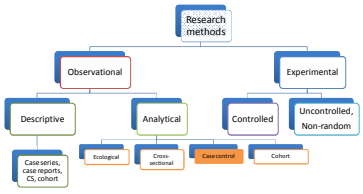
Death rates from heart disease among men aged over 30 years. 1950–2002

Uses of Descriptive Epidemiology

1. Provide data of magnitude of problem- **disease load**.
2. Provide clues for etiology.
3. Provide background data for planning, organizing and evaluating the preventive and curative services.
4. Contributes to research.

ANALYTICAL EPIDEMIOLOGY

Classification of research methods



Analytical Studies

- analyzing relationships between health status and other variables.
- The objective is testing the hypothesis.
- Subject of interest is individual, but inference applied to population.

TYPES

1. **Case-control studies**. (Case reference studies)
2. **Cohort studies.** (Follow-up studies)

1. **Case-control studies**.
2. **Cohort studies.**

By analytical studies we can determine-

1. **Statistical association.** (between disease and suspected factor)
2. **Strength of association**.

Case-control studies

- It is first approach to **testing causal hypothesis,**
- especially for rare disease.

- Three features-

1. Both exposure and outcome (disease) has occurred.
2. Study proceeds backwards from effect to cause.
3. It uses a control group to support or refuse a inference.

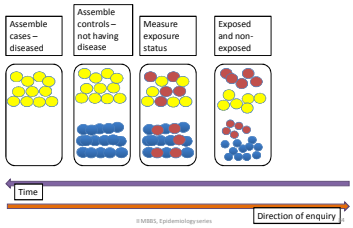
Introduction

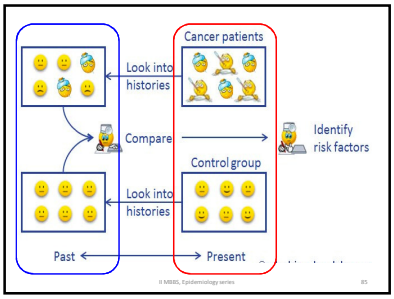
- Synonyms – retrospective study
- A study that compares two groups of people: those with the disease or condition under study (cases) and a very similar group of people who do not have the disease or condition (controls).
- Essential elements
  - Both exposure and disease have occurred
  - Proceeds from effect to cause
  - Uses a comparison 'control' group

2 by 2 table

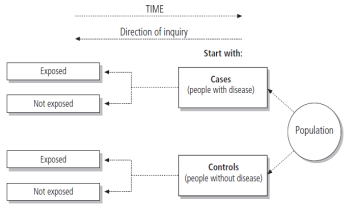
	Diseased - Cases	Non-diseased – Controls	Total
Exposed	A	B	A+B
Non-exposed	C	D	C+D
Total	A+C	B+D	A+B+C+D

Dogma of case control study





Design of a case-control study



Basic steps in Case-control study

1. Research Question
2. Selection of cases and controls.
3. Matching.
4. Measurement of exposure.
5. Analysis and interpretation.

Research question

- Begin with broad and ambitious question
- Later, narrow and more precise
- Considerations of time, cost
- Eg.
  1. Does tobacco cause cancer?
  2. Does smoking tobacco cause bronchogenic CA?
  3. Do persons having broncho. CA have h/o greater exposure to tobacco smoking as compared to persons w/o the disease?

1. Selection of cases and controls

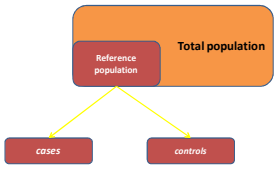
- **CASES**
  - Case definition – (Diagnostic criteria and Eligibility criteria.)
  - Source of Cases – (Hospital or General population)
- **CONTROLS**
  - Free from the disease under study.
  - Similar to the cases in all other aspects.
  - Source-

Hospital, Relative, Neighbourhood, General population

Source of Control

Source	Advantage	Disadvantage
Hospital based	Easily identified. Available for interview. More willing to cooperate. Tend to give complete and accurate information (↓recall bias).	Not typical of general population. Possess more risk factors for disease. Some diseases may share risk factors with disease under study. Berkesonian bias
Population based	Most representative of the general population. Generally healthy.	Time, money, energy. Opportunity of exposure may not be same as that of cases. (location, occup.)
Neighbourhood controls/ Telephone exchange random dialing	Controls and cases similar in residence. Easier than sampling the population.	Non cooperation. Not representative of general population.
Best friend control/ Sibling control	Accessible, Cooperative. Similar to cases in most aspects.	Overmatching.

Selection process - 1



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Selection process - 2

- Cases
  - In practice; we use all eligible cases within a defined time period
    - From disease registry or hospital
    - We are implicitly sampling from a subset of total population of cases
- Controls
  - Sampling is most pertinent here because in rare diseases, the no. of controls greatly exceed no. of cases

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Selection of cases - 1

- ***Representativeness***
  - Ideally, cases sh. be a random sample of all cases of interest in the source population (e.g. from vital data, registry data)
  - But commonly they are a selection of available cases from a medical care facility. (e.g. from hospitals, clinics)
- **Method of Selection**
  - Selection may be from incident or prevalent cases
  - Incident cases are those derived from ongoing ascertainment of cases over time
  - Prevalent cases are derived from a cross-sectional survey

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Selection of cases - 2

- Incident cases are more optimal
- These should be all newly diagnosed cases over a given period of time in a defined population. (However we are excluding patients who died before diagnosis)
- Prevalent cases do not include patients with a short course of disease (patients who recovered early and those who died will not be included)
- Can be partly overcome by including deceased cases as well as those alive

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Selection of controls - 1

- The four principals of *Wacholder*

1. The study base
2. De-confounding
3. Comparable accuracy
4. Efficiency

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Selection of controls - 2

- Should the controls be similar to the cases in all respects other than having the disease? i.e. ***comparable***
- Should the controls be representative of all non-diseased people in the population from which the cases are selected? i.e. ***representative***

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Selection of controls - 3

- Representativeness
  - Sh. be representative of the general population in terms of probability of exposure to the risk factor
- Comparability
  - Sh. also have had the same opportunity to be exposed as the cases have
- *Not* that both cases and controls are equally exposed; but only that they have had the same opportunity for exposure.

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Selection of controls - 5

- The ***study base*** is composed of a population at risk of exposure over a period
- Cases emerge within a study base. Controls should also emerge from the same study base, except that they are not cases.
- Eg. If cases are selected exclusively from hospitalized patients, controls must also be selected from hospitalized patients.

98

Selection of controls - 6

- ***Comparability*** is more important than ***representativeness*** in the selection of controls
- The control should resemble the case in all respects except for the presence of disease

99

Selection of controls - 7

- Number of controls
  - Large study; equal numbers
  - Small study; multiple controls
- Use of multiple controls
  - Controls of same type
  - Multiple controls of different types
    - Hospital and neighborhood controls
    - e.g. case - children with brain tumor, control- children with other cancer, normal children

2. Matching.

- **Matching** is process by we selecting controls in a manner that they are similar to cases in all variables.
- Matching is essential for comparability and for elimination of confounding bias.

2. Matching

- A Confounding factor is a factor which associated with both exposure and disease and unequally distributed in study and control groups.
- Exm- 1. Alcohol in esophageal cancer, smoking is confounding factor.
  2. Age for steroid contraceptive are causative in Breast cancer.
- **Matching procedure** –
- Group matching (Strata matching).
- Pair matching.

Biases

- Bias due to confounding
- Memory or recall bias
- Selection bias
- Berkesonian bias
- Interviewer bias

3. Measurement of exposure.

- Information of exposure of risk factor should be obtain in same manner for both cases and controls.
- Information obtain by-
- Questionnaire.
- Interviews.
- Hospital records.
- Employment records.

4. Analysis and interpretation

1. **Exposure rates**
Estimation of rates of exposure of suspected factor among cases & controls.

2. **Odds Ratio**
Estimation of disease risk associated with exposure among cases & controls.

1. Exposure rates

	CASES (Lung Cancer)	CONTROLS (Without Lung Cancer)	TOTAL
SMOKERS	33 (a)	55 (b)	88 (a+b)
NON-SMOKERS	2 (c)	27 (d)	29 (c+d)
TOTAL	35 (a+c)	82 (b+d)	N= a+b+c+d

Exposure rates-
a. Cases = a / (a+c) = 33/35 = 94.2%.
b. Controls = b/ (b+d) = 55/82 = 67%.
(p value is p<0.001)

Whether the exposure is significant associated to cause lung cancer.
TESTS OF SIGNIFICANCE
(p value)

2. Odds Ratio
(Cross-product Ratio)

- It is estimation of risk of disease associated with exposure.
- It measures **strength of association** of risk factor and outcome(disease).

Odds Ratio = ad / bc

- Odds Ratio = 33 x 27 / 55 x 2 = 8.1
- *Smokers have risk of developing lung cancer 8.1 times higher than non-smoker.*

Other Example

- E.g. 1. Depression and Vegetable eating

	Individuals With Depression (Cases)	Individuals Without Depression (Controls)	Total
Eat Vegetables	90	90	180
Do Not Eat Vegetables	130	130	260
Total	220	220	440

- Odds of exposure among cases: a/c = 90/130 = 0.6923
- Odds of exposure among controls: b/d = 90/130 = 0.6923
- Odds ratio = 0.6923/0.6923 = 1.0

- For the odds ratio to be a good approximation, the cases and controls must be representative of the general population with respect to exposure.
- However, because the incidence of disease is unknown, the **relative risk** can not be calculated.

Thalidomide Tragedy

A classic example of Case-control study

- A classic example of a case-control study was the discovery of the relationship between **thalidomide and limb defects** in babies born in the Federal Republic of Germany in 1959 and 1960.
- The study, **done in 1961**, compared affected children with normal children.
- Of **46 mothers** whose babies had **malformations**, **41 had been given thalidomide** between the fourth and ninth weeks of pregnancy, whereas **none of the 300 control mothers**, whose children were normal, had taken the drug during pregnancy.
- Accurate timing of the drug intake was crucial for determining relevant exposure.

Other Examples

- Adenocarcinoma of vagina and DES
- OCP and thrombosis

Pros & Cons

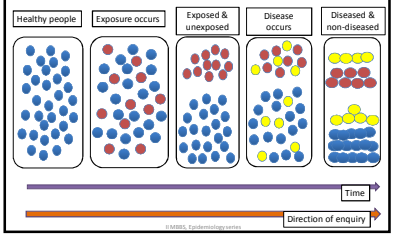
Advantages	Disadvantages
Easy to carry out	Subject to several biases
Rapid results	Selection of controls difficult
Inexpensive	Incidence can' t be measured
Suitable for rare diseases	Association doesn't mean causation
No risk to subjects	Not practical for rare exposure
Minimal attrition	
Multiple exposures can be studied	

Case Control Studies	Cohort Studies
Proceeds from effect to cause	Proceeds from cause to effect
Starts with the disease	Starts with people exposed to the risk factor or suspected cause
Tests whether the suspected cause occurs more frequently in those with disease than those without disease	Tests whether disease occurs more frequently in those exposed than in those not exposed
Usually the 1st approach to the testing of hypothesis, but also useful for exploratory studies	Reserved for the testing of precisely formulated hypothesis
Involves fewer study subjects	Involves larger number of subjects
Yields results relatively quickly	Long follow-up, delayed results
Suitable for study of rare diseases	Inappropriate when disease or exposure under investigation is rare
Generally, yields only estimate of relative risk (Odds ratio)	Yields incidence rates, relative risk, attributable risk
Cannot yield information about disease other than that under study	Can give information about more than one disease outcome
Relatively inexpensive	Expensive

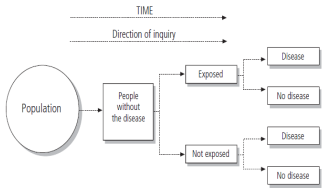
Cohort Studies

- **Cohort is group of people with common characteristics or experience within a define time period.**
  - **Birth cohort**
  - **Exposure cohort**
  - **Marriage cohort**
- also called **follow-up** or **incidence studies.**
- Begin with a group of people who are free of disease.
  - Study cohort
  - Control cohort
- Whole cohort is followed up to see the effect of exposure.

Dogma of cohort study



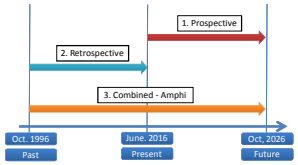
Study design of a cohort study



Types of Cohort Studies

1. Prospective cohort studies. (Current cohort study)
   1. Dolls & Hills-Smoking with lung carcinoma
   2. Framingham heart study
   3. OCP & health by Royal College of General Practitioner
2. Retrospective cohort studies. (Historical cohort study)
   1. Birth cohort 1969 to 1975 with Electronic foetal monitoring
   2. Lung carcinoma in Uranium miners
   3. Angiosarcoma of liver with PVC
3. Combination of retrospective and prospective cohort studies.
   1. Radiation therapy for Anchylosing Spondylitis with Aplastic anaemia or Leukemias

Types of cohort study



Elements of Cohort studies

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

1. Selection of study subjects.

- General population
  - Framingham heart study
- Special group (Doctors, Teachers, Lawyers, former military).
  - Dolls & Hills
- Exposure group-Cohort should be selected from the group with special exposure under study.
  - Radiologist for X-ray exposure
  - Uranium miners

2. Obtaining data on exposure.

a. Cohort members- questionnaire, interview.
b. Review of records.
c. Medical Examination or tests.
d. Environmental surveys.

Categorized according to exposure –
1. Whether exposed or not exposed to special causal factor.
2. Degree of exposure.

3. Selection of comparison group.

1. Internal comparison.
   - Subjects are categorized in group according to degree of exposure & mortality and morbidity compared.
   - Framingham Heart Study

2. External comparison.
   - When degree of exposure not known.
   - Control group with similar in other variable.
   - Radiologists with Ophthalmologists

3. Comparison with general population.
   - Comparison with the general population as exposed group.
   - Asbestos worker with General population of same geographic area
   - Expected values & Observed values

4. Follow-up.

- Regular follow-up of all participants.
- Measurement of variable depends upon outcome.

- Procedure-

1. Periodical medical examination.
2. Review of hospital records.
3. Routine surveillance and death records.
4. Mailed questionnaire and phone calls, periodic home visits on annual basis.

5. Analysis.

- Data are analyzed in terms of –

a. Incidence rates.
   - Among exposed and non-exposed

b. Estimation of risk.
   - Relative Risk.
   - Attributable Risk.

- Incidence of disease in exposed
- Incidence of disease in non-exposed =
- Relative risk (RR) =

Measures of association

- Relative risk (RR) = $I_{(e)} / I_{(ue)}$
- Risk difference = $I_{(e)} - I_{(ue)}$
- Attributable risk = $[I_{(e)} - I_{(ue)}] / I_{(e)}$
- Population attributable risk = $[I_{(tp)} - I_{(ue)}] / I_{(tp)}$ X100

Incidence rates.

SMOKING	DEVELOPED LUNG CANCER	DID NOT DEVELOPED LUNG CANCER	TOTAL
YES	70 (a)	6930(b)	7000 (a+b)
NO	3(c)	2997 (d)	3000 (c+d)

- Incidence among smoker = 70/7000 = 10 per 1000.
- Incidence among non-smoker = 3/3000= 1per 1000.

Test of significance = p< 0.001

Relative Risk (Risk ratio)

- Relative risk is the ratio of the incidence of disease among exposed and incidence among non-exposed.

RR of Lung cancer = 10/1 = 10

- It is direct measure of strength of the association between suspected cause and effect.
- It does not necessary implies the causal relationship.

Attributable Risk
(Risk difference)

- AR is the difference in incidence rates of disease among exposed and non-exposed group.
- AR= I.R. among exposed - I.R. among non-exposed /Incidence among exposed x 100

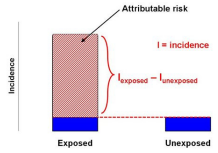
Example - A.R.= 10-1/ 10 x 100 = 90 %

- AR is the proportion of disease due to particular risk factor exposure.
- Exm – 90% of lung cancers are due to smoking.
- ***That means- amount of disease eliminated if the suspected risk factor is removed.***

Population Attributable Risk

- **Population A. R.** = I.R. in total population – I.R. among non-exposed /I.R. in total population X 100
- Population Attributable Risk is useful concept as it give the magnitude of disease that can be **reduced** from the population if the suspected risk factor is eliminated or modified.

Attributable risk



Fraction, proportion & percentage

Fraction	Proportion	Percentage
1/3	0.33	33%
2/3	0.66	66%
3/4	0.75	75%
1/4	0.25	25%
2/4	0.50	50%
2/5	0.40	40%

Example of calculations

	Lung cancer	Normal	Total
Smoker	70	6930	
Non-smoker	3	2997	
Total			

- Incidence of disease in exposed = 0.01 or 1%
- Incidence of disease in non-exposed = 0.001 or 0.1%
- Relative risk = 10
- Risk difference = 0.009 or 0.9%
- Attributable risk = 0.9 or 90%

Example of calculations

- **Population Attributable Risk** = I.R. in total population – I.R. among non-exposed /I.R. in total population X 100

Deaths per 100,000 person years		
Heavy Smokers	224	Exposed to suspected factor(a)
Non-smokers	10	Non exposed to suspected causal factor (b)
Death in total population	74	(c)
Individual RR	a/b=224/10	22.40
Population AR	(c-b)/c=74-10/74	86%

- The relative and attributable risks of Cardiovascular complications in women taking oral contraceptives:
-

Cardiovascular risk 100,000 patients years	Age	
	30-39	40-44
Relative risk	2.8	2.8
Attributable risk	3.5	20.0

- Risk assessment, smokers v/s non-smokers

Cause of Death	Death rate/1000			
	Smokers	Non-smokers	RR	AR(%)
Lung Cancer	0.90	0.07	12.86	92.2
CHD	4.87	4.22	1.15	13.3

Advantages

- Incidence and RR can be calculated
- One exposure and multiple outcomes
- Dose response ratios
- Recall bias reduced

Disadvantages

- Unsuitable for rare outcomes
- Long duration
- Administrative problems
- Loss to follow up
- Selection of representative groups
- Diagnostic criteria may change over time
- Expensive
- People may alter their behaviour
- Ethical problems

Examples of famous cohort studies

- British doctors study on smoking and lung cancer
- The Framingham heart study
- Oral contraceptives study

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EXPERIMENTAL EPIDEMIOLOGY

- **Interventional or experimental study** involves attempting to change a variable in subjects under study..
- This could mean the elimination of a dietary factor thought to cause allergy, or testing a new treatment on a selected group of patients.
- The effects of an intervention are measured by comparing the outcome in the experimental group with that in a control group.

Objectives of Experimental Studies

1. To provide 'scientific proof' for etiology of disease and risk factor which may allow modification of occurrence of disease.
2. To provide a **method of measurement** for effectiveness and efficiency of therapeutic / preventive measure for disease.
3. To provide **method to measurement** for the efficiency health services for prevention, control and treatment of disease.

Types of Experimental Studies

1. Randomized Control Trials.
2. Field Trials & Community Trials.

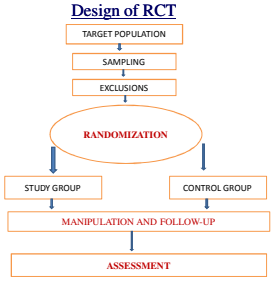
Randomized Control Trials
(RCT)

- RCT is a **planned experiment** designed to asses the **efficacy of an intervention** in human beings by comparing the **effect of intervention** in a study group to a control group.
- The allocation of subjects to study or control is determined purely by chance **(randomization)**.
- For new programme or new therapy RCT is best method of evaluation.

Basic Steps in RCT

1. Drawing-up a protocol.
2. Selecting reference and experimental population.
3. Randomization.
4. Manipulation or Intervention.
5. Follow-up.
6. Assessment of outcome.

Design of RCT



The Protocol

- Study conducted under strict protocol.
- Protocol specifies –
  - aim, objectives, criteria for selection of study and control group, sample size, intervention applied, standardization and schedule and responsibilities.
- Pilot study –
  - some time small preliminary study is conducted to find out feasibility or operational efficiency.

Reference and Experimental population

- **Reference population** **(Target Population)**
  - Is the population in which the results of the study is applicable.
  - A reference population may be – Human being, country, specific age, sex, occupation etc.
- **Experimental Population** **(Study Population)**
  - It is derived from the target population.
  - Three criteria-
  - 1. they must be representative of RP.
  - 2. qualified for the study.
  - 3. ready to give informed consents.

Randomization

- It is statistical procedure to allocate participants in groups – **Study group** and **Control group**.
- Randomization gives equal chance to participants to be allocated in Study or Control group.
- Randomization is an attempt to eliminate 'bias' and allow 'comparability'.

- Randomization eliminates 'Selection Bias'.
- Matching is for only those variable which are known.
- Randomization is best done by the table of random numbers.
- In Analytical study there is no randomization, we already study the difference of risk factor. So only option is Matching.

Manipulation or Intervention

- Manipulation by **application of therapy** or **reduction or withdrawal** of suspected causal factor in Study and control group.
- This manipulation creates *independent variable* whose effect is measured in *final outcome*.

Follow-up

- **Follow-up** of both study and control group in **standard manner** in **definite time period**.
- Duration of trial depends on the changes expected in duration since study started.
- Some loss of subjects due to migration, death is k/as **Attrition.**

Assessment

- Final step is assessment of outcome in terms of **positive and negative results.**
- The incidence of positive and negative results are compared in both group- **Study group and Control group**.
- Results are tested for **statistical significance**. (p value)

Potential errors in epidemiological studies (Bias)

- **Bias** may arise from the **errors of assessment** of outcome due to human element.
- **Three sources** –

1. Bias on part of subject.
2. Observer bias.
3. Bias in evaluation.

Blinding

- *Blinding is procedure to eliminate bias*.
- **Thee types** -

1. Single blind trial.
Participant not aware of study.
2. Double blind trial.
Examiner and participant both not aware.
3. Triple blind trial.
Participant, examiner and person analyzing the data not aware of the study.

Field trials

- Field trials, in contrast to clinical trials, involve people who are healthy but presumed to be at risk.
- **Data collection takes place "in the field**," usually among non-institutionalized people in the general population.
- Since the subjects are disease-free and the purpose is to prevent diseases.

Community Trials

- In this form of experiment, the treatment groups are communities rather than individuals.
- This is particularly appropriate for diseases that are influenced by social conditions, and for which prevention efforts target group behaviour.
- Example –
  - IDD and Iron def Anaemia.
  - Fortification of food.

Ethical issues in Epidemiological Studies

1. Informed consent.
2. Confidentiality.
3. Respect for human rights.
4. Scientific integrity.

ASSOCIATION AND CAUSATION

- **Descriptive studies-**
  - Identification of disease problem in community.
  - Relating agent, host and environmental factor.
  - Etiological hypothesis.
- **Analytical and Experimental studies**
  - Tests the hypothesis derived from the descriptive studies.
  - Accept or reject the association between the suspected cause and disease.
- *Epidemiologists are now proceed from demonstration of statistical association to* ***causal association***.

- **Association** is defined as - *the concurrence of two variables more often than would be expected by chance.*
- So association does necessarily imply a ***causal relationship***.

- **Correlation –** is strength of association between two variable.
- Correlation coefficients ranges from - 1 to + 1.
- +1 = perfect linear positive relationship.
- -1 = perfect linear negative relationship.

- ***Causation implies association and correlation but correlation and association do not necessarily imply causation.***

TYPE OF ASSOCIATION

1. Spurious association.

Exp- IMR in home and institutional deliveries.

2. Indirect association.

Exp- Endemic goitre and altitude

3. Direct or Causal association.

a. **One to one causal association.**

Exm- streptococcus- tonsilitis.

b. **Multi-factorial causation.**

Exm- CHD- multiple factors.

THANK YOU