Analytical study designs

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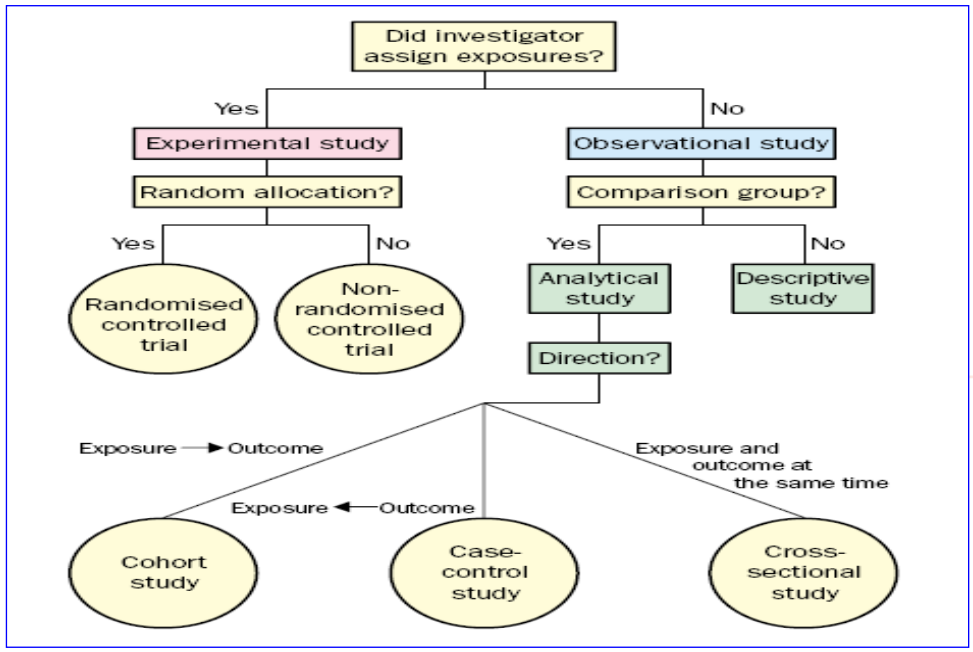

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Analytical studies

- Investigator does not assign the exposure
  - Makes careful measurement of patterns of exposure and disease in populations
- Comparison group
  - Make inferences about exposure and disease

Cohort study

- Cohort
  - 300 to 600 man unit in Roman Army
- Cohort
  - Group of people sharing some common characteristics (ex. Birth cohort)

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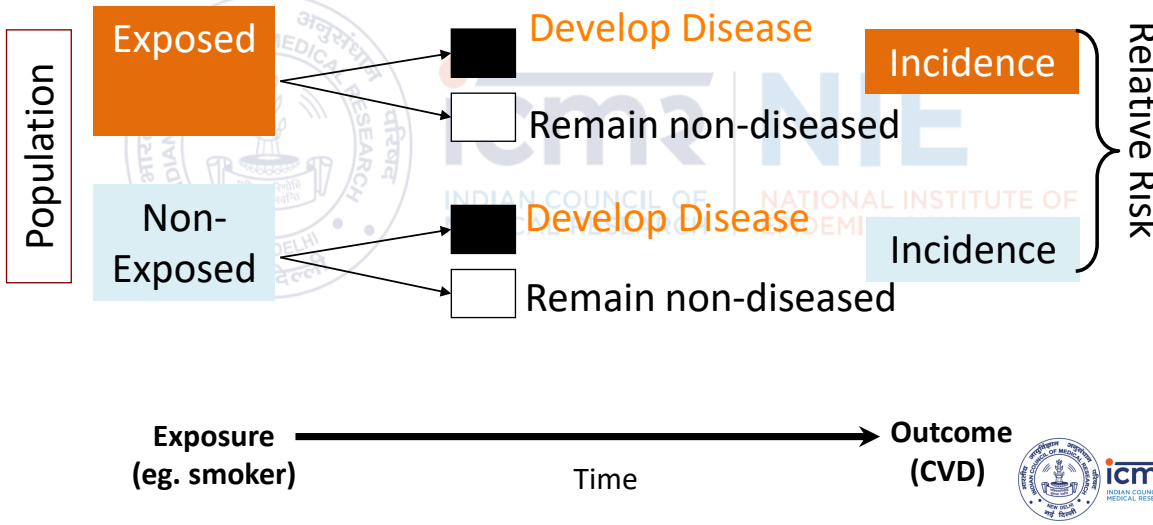
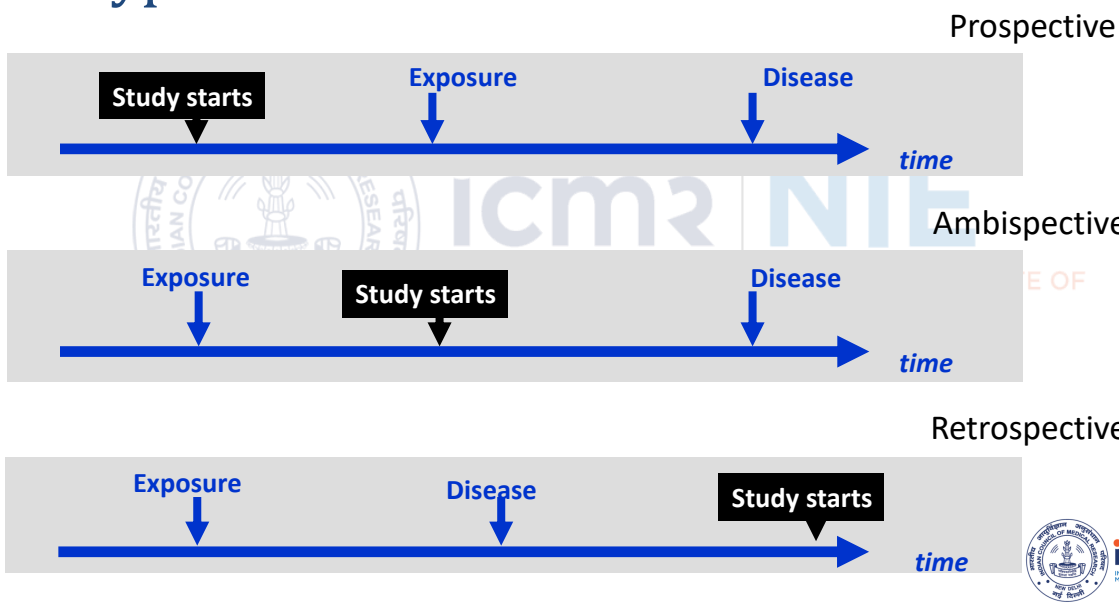
Design of cohort study



Type of cohort studies



Framingham heart study

Framingham town (population: 28,000)

Objectives

Identify Risk factors for cardio-vascular diseases

Have risk factor

Don't have risk factor

Hypertensive

Normotensive

Compare incidence of CVD

Start of study

Aniline dyes and urinary bladder cancer

Employees working in dye industry (n=4622)

Exposure to aniline dyes

Death due to bladder tumors

Expected cases of bladder cancer using national statistics

Start of study

1920 1930 1940 1950

Case R et al, Brit J Industr Med, 1954

Closed (fixed) and open cohort

- Closed cohort
- Once cohort is enrolled and follow-up begins, no one can be added
- Cohort size always get smaller over time
- Ex: Victims of Bhopal gas tragedy

- Open cohort
- Members can leave, or added in the cohort over time
- Ex: Framingham study

Elements of cohort study

1. Selection of study populations
2. Gathering baseline information
3. Follow-up
4. Analysis

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Selection of study population

- General population cohorts or a sub-set
  - Framingham heart study
  - Nurses health study
- Special exposure cohorts
  - Occupational groups

Gathering baseline information

- Objective
  - Valid assessment of exposure status of members of cohort
    - Identification data
    - Exclude individuals having disease at baseline
    - Define individuals at risk
    - Obtain data on co-variables (other exposure variables)

Sources of baseline information

- Existing records
  - Hospital records, employment records
- Interviews
  - Personal interviews/mailed questionnaires etc.
- Examinations
  - Medical and other special examination
- Measurement of environment
  - E.g. air pollution, exposure to radiation

Choice of comparison group

- Internal comparison group
  - Unexposed persons in the population
- External comparison group
  - When internal comparison group not available
  - Ex: Observed number of bladder cancer deaths in aniline dye industry compared with expected cases

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Follow-up

- Objectives
  - Uniform and complete follow-up of all cohort members
    - Uniform surveillance in exposed and unexposed groups
  - Complete ascertainment of exposures and outcome/s
  - Standardized diagnosis of outcome events

Presentation of the data in a cohort study in a 2 x 2 table

	Diseased	Non-diseased	Total
Exposed	a	b	a+b
Unexposed	c	d	c+d
	a+c	b+d	a+b+c+d

Known at the start of the study

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Relative risk

	Diseased	Non-diseased	Total
Exposed	a	b	a+b
Unexposed	c	d	c+d
	a+c	b+d	a+b+c+d

Incidence of disease in exposed = a/a+b

Incidence of disease in unexposed = c/c+d

Interpreting Relative risk

- RR=1
  - Incidence in exposed and unexposed is same
  - Exposure is not associated with disease
- RR > 1
  - Incidence in exposed is higher than unexposed
  - Exposure is positively associated with disease
- RR < 1
  - Incidence in exposed is lower than unexposed
  - Exposure is negatively associated with disease

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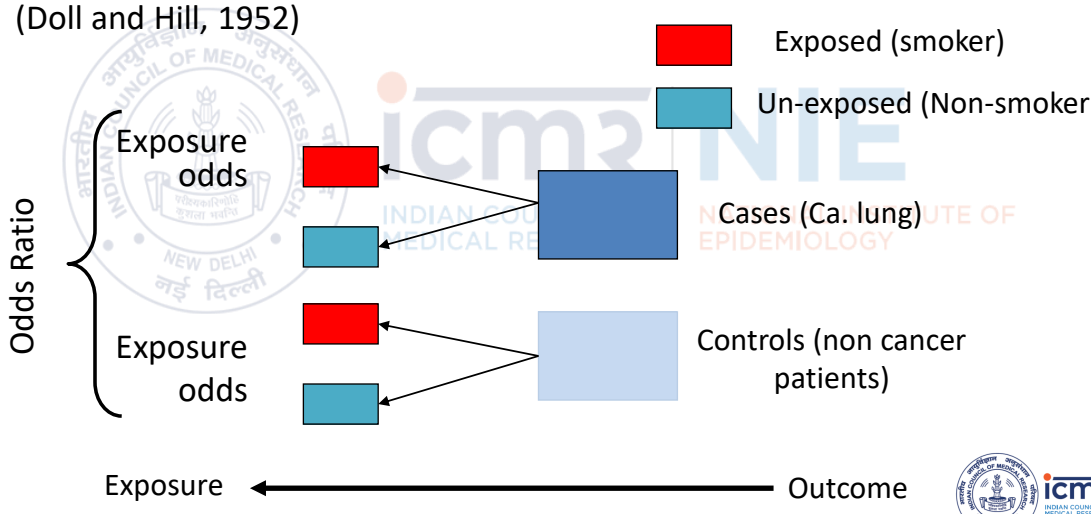
Cohort study – Strengths and weaknesses

- Strengths
  - Allows calculation of incidence
  - Examine multiple outcomes for a given exposure
  - Clarity of temporal sequence
  - Good for investigating rare exposures
- Weakness
  - May have to follow large numbers of subjects for a long time.
    - Expensive and time consuming.
  - Not good for rare diseases.
  - Not good for diseases with a long latency.
  - Differential loss to follow up can introduce bias.

Case control study

Design of case-control study

Objective: Test association between cigarette smoking and lung cancer (Doll and Hill, 1952)



Elements of case control study

1. Selection of cases
2. Selection of controls
3. Information on exposure
4. Analysis

Selection of cases

- All people in source population who develop the disease of interest
  - Sample of cases
    - Independent of the exposure under study
- Clear definition of outcome studied
- Prevalent vs. incident cases
  - Prevalent cases may be related more to survival with disease than to development of disease

Sources of cases

- Hospital/clinic based cases
  - Easier to find
  - May represent severe cases
- Population based (cancer registry)
  - not biased by factors drawing a patient to a particular hospital

Selection of controls

- Represent the distribution of exposure in the source population of cases
  - Selected from the same source population that gives rise to the cases
- Selected independently of their exposure status

Selection of controls

- Population based
  - Sampling of the general population
- Health care facility based
  - Patients with other diseases
- Case-based
  - Friends, Neighbourhood

Collecting good data on exposure

- Objectively
  - Reproducibility of exposure measurement
- Accurately
  - Information reflecting as closely as possible the effect of exposure
- Precisely
  - Quality management in exposure measurement

Presentation of the data of a case-control study in a 2 x 2 table

	Cases	Controls	Total
Exposed	a	b	a+b
Unexposed	c	d	c+d
	a+c	b+d	a+b+c+d

Known at the start of the study

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Odds ratio

	Cases	Controls	Total
Exposed	a	b	a+b
Unexposed	c	d	c+d
	a+c	b+d	a+b+c+d

Odds that case was exposed =

$$\frac{\text{Probability that case was exposed}}{\text{Probability that case was not exposed}}$$

$$\frac{=[(a/a+c)]}{=[(c/a+c)]} = a/c$$

Odds that control was exposed =

$$\frac{\text{Probability that control was exposed}}{\text{Probability that control was unexposed}}$$

$$\frac{=[(b/b+d)]}{=[(d/b+d)]} = b/d$$

Odds ratio=[a/c]/[b/d] = ad/bc

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Interpreting Odds Ratio

- OR=1
  - Odds of exposure among cases and controls are same
  - Exposure is not associated with disease
- OR > 1
  - Odds of exposure among cases are higher than controls
  - Exposure is positively associated with disease
- OR < 1
  - Odds of exposure among cases are lower than controls
  - Exposure is negatively associated with disease

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Case control study: Strengths and weaknesses

- Strengths
  - Good for examining rare outcomes or outcomes with long latency
  - Relatively quick to conduct, inexpensive
  - Requires comparatively few subjects
  - Multiple exposures or risk factors can be examined
- Weaknesses
  - Susceptible to recall bias
  - Selection of an appropriate comparison group may be difficult
  - Rates of disease in exposed and unexposed individuals cannot be determined

Thank you

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