RESEARCH DESIGN 1 (OBSERVATIONAL)

RAZMAN MOHD RUS
DEPARTMENT OF COMMUNITY MEDICINE
KULLIYYAH OF MEDICINE

LEARNING OBJECTIVES

At the end of this lecture, participants should be able to:

- Discuss the various types of observational study design
- Explain the advantages & disadvantages of study designs

RESEARCH DESIGN

1) Observational
   a) Descriptive: *case reports, case series, cross sectional*
   b) Analytical: *case – control, cohort*
2) Experimental: *Randomized Controlled Trial (RCT), community trial*

OBSERVATIONAL STUDY DESIGN

Important criteria:

- ❑ non-experimental
- ❑ no individual intervention – no manipulation of study factor by the investigator
  - no "control" over doses, treatments, exposures
- individuals can be observed prospectively, retrospectively, or currently

STUDY DESIGNS (OBSERVATIONAL)

Descriptive	Analytical
1. Cross-sectional	1. Case control
2. Case series	2. Cohort
3. Case report	

OBSERVATIONAL STUDY DESIGN: TYPES

Descriptive epidemiology:

- ❑ measure/describe the frequency in which diseases occur *e.g. prevalence of hypertension, diabetes*
- ❑ collect descriptive data on possible causal factors - *e.g. proportion (%) of smokers, obese subjects, lack of exercise*
- ❑ e.g. - case reports, case series, cross sectional
- ❑ hypothesis generating

OBSERVATIONAL STUDY DESIGN: TYPES

Analytic epidemiology:

- attempts to specify in more detail the relationship between the dependent (outcome) variable & the independent variable
  - *looking for association – e.g. association between smoking & lung cancer, association between shift work & breast cancer*
- case- control, cohort
- hypothesis testing

GRADES OF EVIDENCE

TABLE 1. GRADES OF EVIDENCE FOR THE PURPORTED QUALITY OF STUDY DESIGN.*

I	Evidence obtained from at least one properly randomized, controlled trial.
II-1	Evidence obtained from well-designed controlled trials without randomization.
II-2	Evidence obtained from well-designed cohort or case–control analytic studies, preferably from more than one center or research group.
II-3	Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of the introduction of penicillin treatment in the 1940s) could also be regarded as this type of evidence.
III	Opinions of respected authorities, based on clinical experience; descriptive studies and case reports; or reports of expert committees.

*The grades are those of the U.S. Preventive Services Task Force7

Most difficult study.

Concato J, Shah N, Horwitz RI. Randomized, controlled trials, observational studies, and the hierarchy of research designs. N Engl J Med. 2000 Jun 22;342(25):1887-92.

SLIDE 8

OBSERVATIONAL STUDY: DESCRIPTIVE

CASE REPORTS

- Detailed presentation of a single case or handful of cases
- Generally report a new or unique finding *e.g.*
  - previous undescribed disease, unexpected link between diseases, unexpected new therapeutic effect or unexpected adverse events

CASE SERIES

- Experience of a group of patients with a similar diagnosis
- Cases may be identified from a single or multiple sources
- Generally report on new/unique condition
- May be only realistic design for rare disorders

- STRENGTH
  - Useful for hypothesis generation
  - Informative for very rare disease with few established risk factors
  - Characterizes averages for disorder
- LIMITATIONS
  - Cannot study cause & effect relationships
  - Cannot assess disease frequency

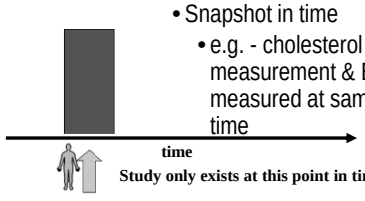
Case Report → **One case of unusual findings**

Case Series → **Multiple cases of findings**

Descriptive Epidemiology Study → **Population-based cases with denominator**

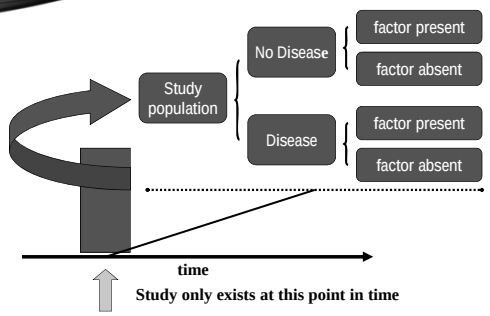
CROSS-SECTIONAL STUDY

- classifies a population or group with respect to both outcome & exposure
- measures both exposures & disease status at a single point in time
- measures prevalence, not incidence of disease
- suitable for conditions that are relatively frequent with long duration of expression (nonfatal, chronic conditions)
- also known as – survey, prevalence study



- Snapshot in time
  - e.g. - cholesterol measurement & ECG measured at same time

Study only exists at this point in time



STRENGTH

- Short term, inexpensive
- Design less complex
- Fewer resources required
- Offer important clues for further studies, generate hypothesis
  - *e.g. Does drinking coffee associated with pancreatic cancer related? Does type A personality & heart attack associated?*

LIMITATIONS

- Not suitable to measure rare disease
- Not suitable to measure highly fatal disease
- Not possible to establish temporal relationship between exposure & disease
  - *e.g. does high cholesterol precede CHD?*

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EXAMPLE 1:

- A researcher would like to test the hypotheses concerning the association between feelings of stress & the use of medical services.
- A random sample was drawn involving 18,000 people
- The researcher might ask whether people had visited a doctor in the last 2 weeks, & if they were under stress in the last year.

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		Doctor visit in the last 2 weeks?		
		Yes	No	Total
Stress in the last year?	Yes	1,442	3,209	4,651
	No	2,633	11,223	13,856
	Total	4,075	14,432	18,507

1. Of those who suffered stress in the last year, 31% (1442/4651) visited their doctor in the last 2 weeks compared with only 19% (2633/13856) of those who did not suffer stress.
2. Of those who visited their doctor in the last 2 weeks, 35% (1442/4075) suffered stress in the previous year, compared with 22% (3209/14432) of those who did not visit their doctor.

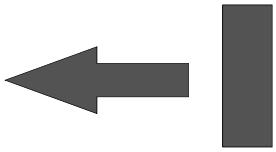
OBSERVATIONAL STUDY: ANALYTICAL

CASE –CONTROL STUDY

- an "observational" design
- compare exposures in disease cases vs. healthy controls from same population
- exposure data collected retrospectively
  - *population followed BACKWARD in time – look for exposure in the past*
- most feasible design where disease outcomes are rare

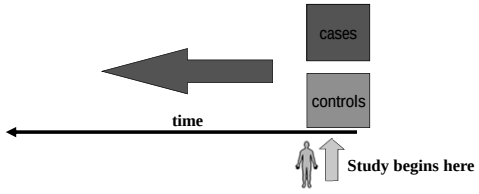
CASE-CONTROL STUDIES

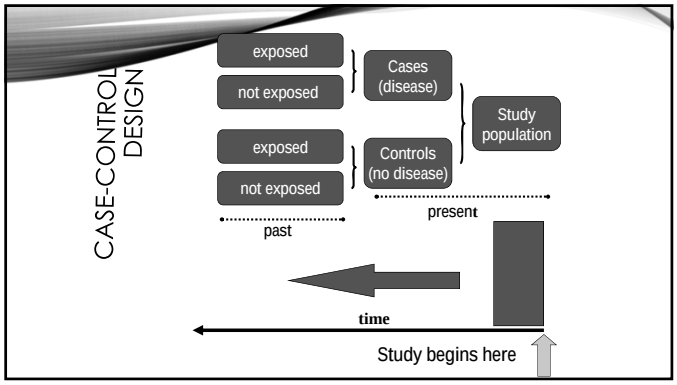
Cases: Disease
Controls: No disease



TIMEFRAME OF STUDIES

- Retrospective Study - "to look back", looks back in time to study events that have already occurred





CASE-CONTROL STUDY

- STRENGTH
  - Less expensive & time consuming
  - Efficient for studying rare diseases
- LIMITATIONS
  - Inappropriate when disease outcome for a specific exposure is not known at start of study
  - Exposure measurements taken after disease occurrence – tend to rely on recall for exposure measure
  - Disease status can influence selection of subjects

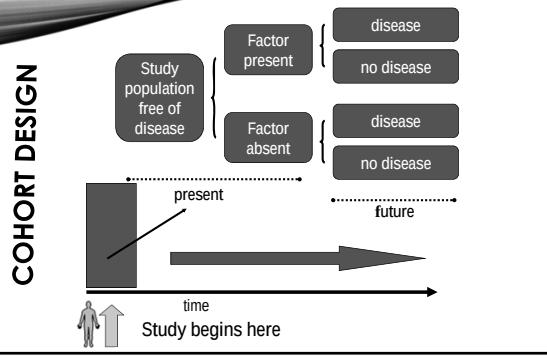
COHORT STUDY

- refer to ancient Roman military unit
- in research context - group of persons who share certain characteristics
  - E.g. age, birth date
- followed up for a specified period of time

COHORT STUDIES

- starts with people free of disease
  - Individuals with outcome of interest at time of screening & enrollment are not eligible for study
  - Sub-clinical presentation of diseases - ***challenges*** in defining the cohort
- exposure status determined before disease detection
  - assesses *exposure* at "baseline"
  - compare individuals with a known risk factor/ exposure with others without the risk factor/ exposure
- measure *disease* status at "follow-up"
  - looking for a difference in the risk (incidence) of a disease over time between two cohorts

COHORT DESIGN



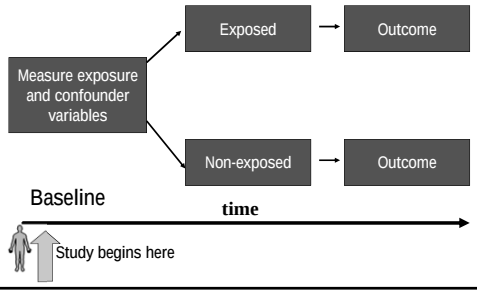
INDICATION OF A COHORT STUDY

- when there is good evidence of exposure & disease (may come from clinical observations or other types of studies)
- when exposure is rare but incidence of disease is higher among exposed (e.g rubella infection during pregnancy & development of congenital malformation in the offspring)
- when follow-up is easy (interval between exposure & development of disease is short)
- cohort is stable (both groups are accessible & available for follow up)

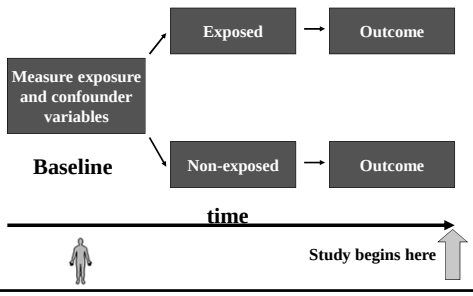
COHORT STUDY: TYPES

- Prospective cohort studies
  - Chronic Disease Cohorts (20th Century)
  - Framingham study of cardiovascular disease, 1948
  - Japanese atomic bomb survivors, 1946
  - British physician study, 1950s
  - Colorado Plateau uranium miners, 1950s
- Retrospective cohort studies
  - Aniline-dye occupational cohort, 1954

PROSPECTIVE COHORT STUDY



RETROSPECTIVE COHORT STUDY



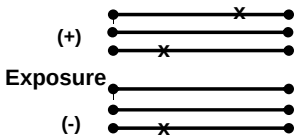
Fixed Cohort

- A group of individuals recruited and enrolled at a uniform point in the natural history of a disease or by some defining event
- Cohort does not take on new members after it is assembled
- Examples
  - Patients admitted to the ER with acute MI
  - Survivors of Hiroshima bombings
  - Children born to HIV-infected mothers

COHORT STUDIES

- Fixed Cohort

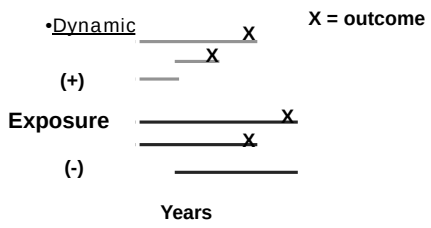
X = outcome



Open cohort

- A group of individuals recruited & enrolled through a mechanism that allows for in & out migration of people
- Defined by characteristic other than disease, e.g., geographic location, administrative unit
- Dynamic population
- Examples
  - Framingham Study

COHORT STUDIES



Important elements in a cohort study

a) Selection of study subjects (expose & non – exposed)

- ✓ presence or absence of risk factor is determined before outcome occurs.
- ✓ both the cohorts are free of the disease.
- ✓ both the groups should equally susceptible to disease
- ✓ both the groups should be comparable
- ✓ Diagnostic and eligibility criteria for the disease should be defined well in advance.

Important elements in a cohort study

b) Obtaining data on exposure

- ✓ Measuring exposure is one of the fundamental activities of a cohort study
- ✓ Exposure measurement must be comparable for all members of the cohort
- ✓ Carefully defined in advance of study, specific attention should be given to the accuracy & precision of proposed measurements - Pilot studies often needed

- ✓ Valid means of determining exposure include:
  a. Questionnaires (e.g., age, smoking history)
  b. Laboratory tests (e.g., cholesterol, hemoglobin)
  c. Physical measurements (e.g., blood pressure, height)
  d. Special procedures (e.g., electrocardiogram, x-rays)
  a. Medical records

c) Selection of comparison group

i. Internal controls - with a one-sample (population-based) cohort, exposure is unknown until after the first period of observation *e.g.*
   - Select the cohort (such as all residents of a given neighborhood)
   - All members of the cohort are then given first round questionnaires, and/or clinical examinations, and/or testing to determine exposure
   - the cohort is then divided into exposure categories based on those results

ii. External controls
   - If everyone in a cohort is exposed (such as workers in an industry), a separate cohort as similar as possible to the exposed in terms of income, education, geography, and age should be sought
   - Example: Workers in a neighboring but unexposed industry

d) Outcome definition

- Primary outcome - the main event that will be related to the exposure
  - Failure-time outcomes
  - Death
  - Disease occurrence
  - Repeated measures
- Secondary outcomes - other events that are of interest and may corroborate the findings of the main outcome

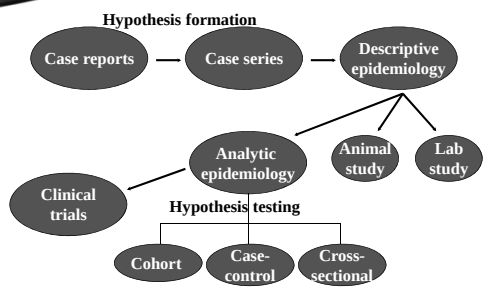
OUTCOME DEFINITION

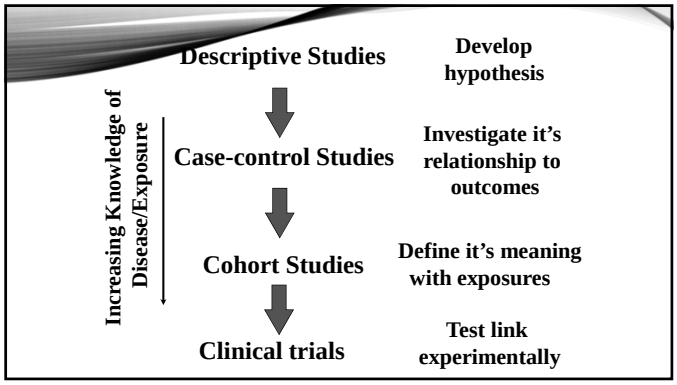
- Primary outcome - the main event that will be related to the exposure
  - Failure-time outcomes
    - Death
    - Disease occurrence
  - Repeated measures
- Secondary outcomes - other events that are of interest and may corroborate the findings of the main outcome

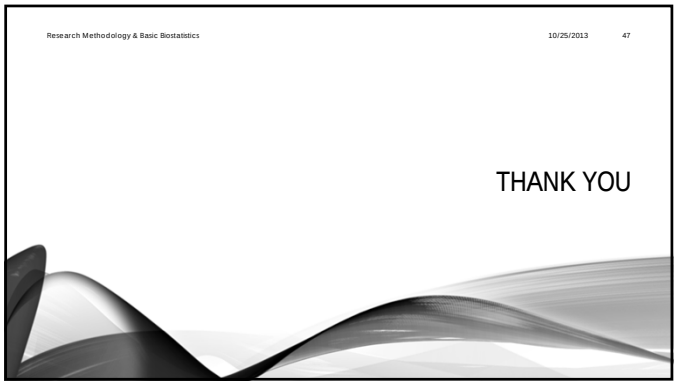
COHORT STUDY

- Strengths
  - measure incidence
  - able to establish cause-effect (clear temporal relationship)
  - efficient for rare exposure
  - several outcomes for each exposure
- Limitations
  - often requires large sample
  - expensive
  - time-consuming
  - inefficient for rare diseases or diseases with long latency
  - losses to follow-up may diminish validity

STUDY DESIGN SEQUENCE




Descriptive Studies
Develop hypothesis
Increasing Knowledge of Disease/Exposure
Case-control Studies
Investigate it's relationship to outcomes
Cohort Studies
Define it's meaning with exposures
Clinical trials
Test link experimentally


Research Methodology & Basic Biostatistics
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THANK YOU