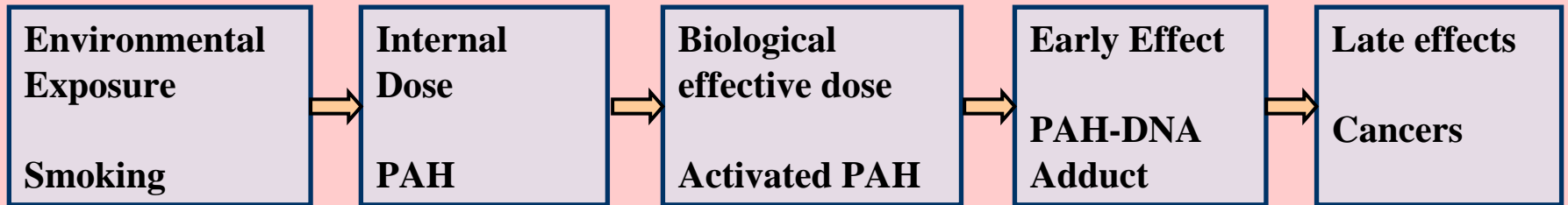# Study Designs

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Epidemiology

- Epidemiology is study of distribution and determinants of health events in population.

- What does this mean?
  – Distribution
  – Determinants

Environmental Exposure and Health Effects

| Environmental Exposure

Smoking | → | Internal Dose

PAH | → | Biological effective dose

Activated PAH | → | Early Effect

PAH-DNA Adduct | → | Late effects

Cancers |

How these Relations were Explored?

- Through posing questions
- Developing hypothesis
- Defining objectives
- Design and conduct of studies
- Measuring exposure and effect
- Statistical Analysis
- Inference

Questions

- How many textile mill workers have COPD?

- What is lead level of children in Karachi City?

- Does regular use of wood and cow dung increases risk of COPD among rural women?

- Does chromium causes skin cancer?

Measuring Disease Occurrence

$$\text{Incidence} = \frac{\text{Number of new cases of disease in a specific time period}}{\text{Population at risk at that time}}$$

Example:

3 cases of lung cancer per 1000 men over age 18 each year in 2001

Measuring Disease Occurrence

$$\text{Prevalence} = \frac{\text{Number of cases at a specific time}}{\text{Population at risk}}$$

- Example:

- 6% of a textile mill workers had asthma in June 2003

- 2 men per 1000 had lung cancer in 1999 in Karachi
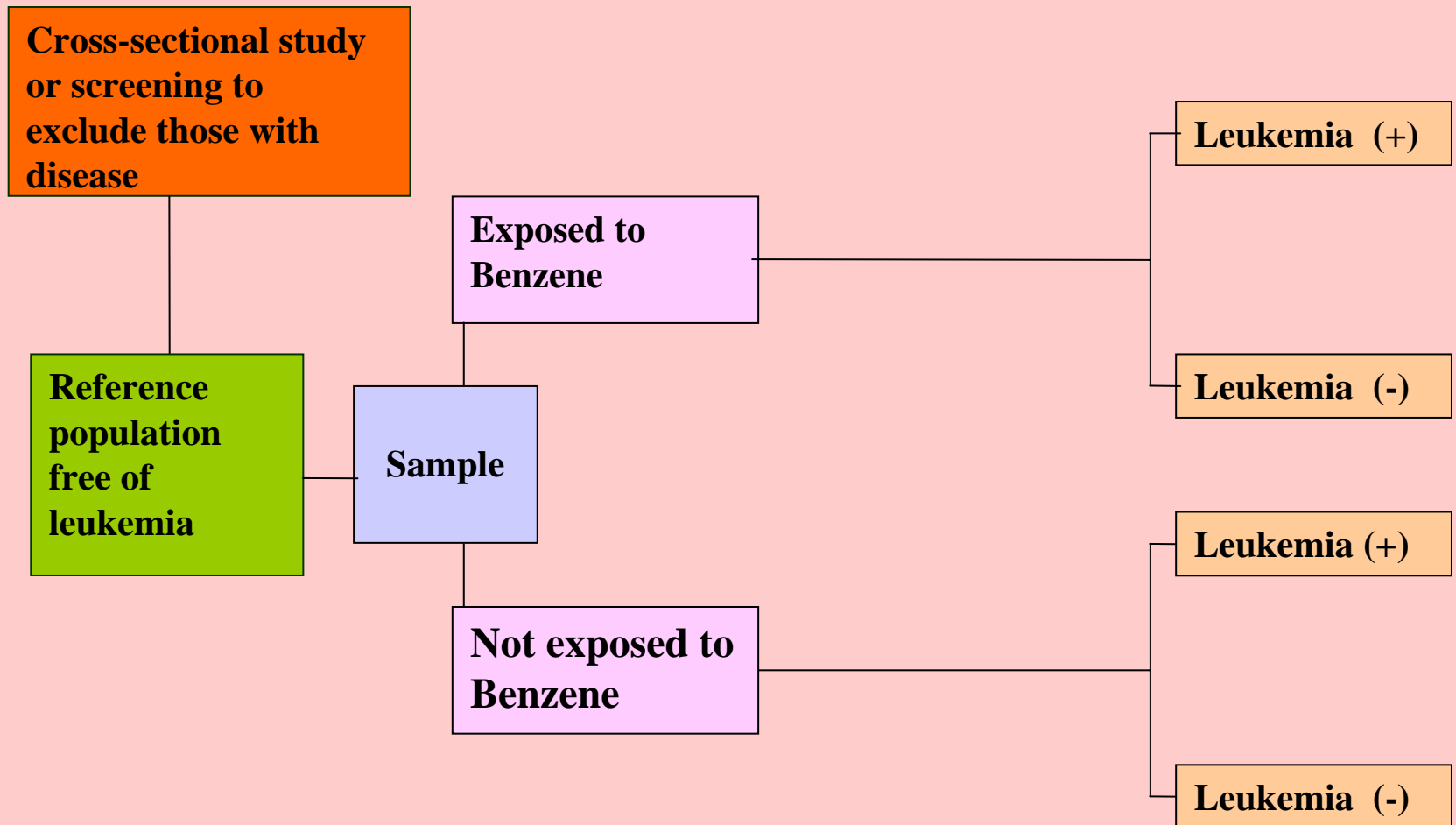
Measuring Disease Occurrence

$$\text{Relative Risk (RR)} = \frac{\text{Incidence}_{\text{exp}}}{\text{Incidence}_{\text{unexp}}}$$
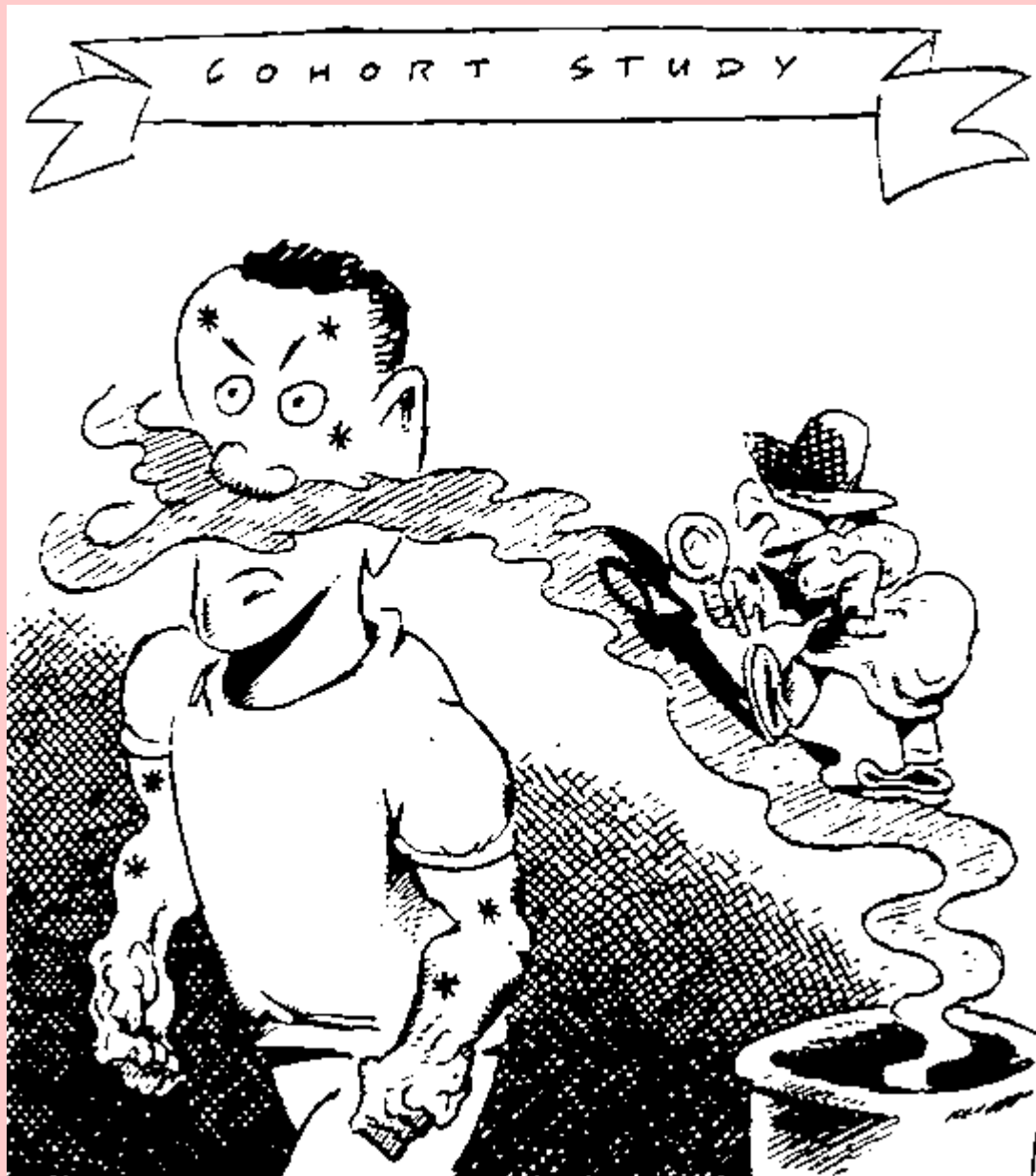
$$\text{Odds Ratio (OR)} = \frac{\text{Odds}_{\text{exp}}}{\text{Odds}_{\text{unexp}}}$$

Study Designs: case scenario

- You are Medical Advisor of a Petrochemical Industry. There had been concern that workers handling various products may get exposed to the benzene. Benzene is potentially carcinogenic and cause leukemia (blood cancer). Level of benzene vary across work stations.

- You have been asked by your seniors who were pressurized by trade union and govt. to investigate if there is any effect of benzene exposure on occurrence of leukemia or any other disease?

Cohort Studies

Cross-sectional study or screening to exclude those with disease

Reference population free of leukemia

Sample

Exposed to Benzene

Not exposed to Benzene

Leukemia (+)

Leukemia (-)

Leukemia (+)

Leukemia (-)

Cohort studies start with an exposure and go forward to diseases.

Drawing by:

Nick Thorkelson

Cohort Studies

	Leukemia Positive	Leukemia Negative	
Benzene Exposure	**a**	**b**	**a+b**
Non Exposed to Benzene	**c**	**d**	**c+d**
	a+c	**a+d**	**a+b+c+d**

Cohort Studies

- Used to test hypothesis about causation of disease

- Groups of people are defined on particular characteristics before the appearance of disease under study-defining exposed and non exposed

- Observation of groups over period of time to determine and compare frequency study disease among them

Cohort Studies

Analysis:

- Relative Risk= (a/a+b)/(c/c+d)

- Advantages & disadvantages:
    – Good for rare exposures
    – Can ascertain multiple outcome of single exposure
    – Demonstrate temporal relationship
    – Time consuming and costly
    – Loss to follow up (participants can leave in between)

Examples of Cohort Studies

- **Associations between lifetime lead exposure with intelligence among children**

- **Lead exposure and motor functioning in 4(1/2)-year-old children: the Yugoslavia prospective study; to investigate associations between lead exposure and early motor development**

Study Designs: scenario

- The study (cohort) you are planning is
  - Time consuming
  - Costly
  - and some of your workers may leave till completion of study

- What you can do?

Retrospective Cohort Study

- If exposure measurements/records and job histories are available can get evidence about exposures

- If medical records are available you can get information about "how many developed Leukemia"?

Study Designs

- You went back to your friends and discussed?

- Group work to come with solution?

- Work finished!

Study Designs

- Information required for retrospective cohort was not available!

- You went back to your seniors and told them that work is not doable

- Seniors were insistent on doing some thing and asked you :

  - Would you be able to tell us causes of leukemia only among workers in a way that cost less?

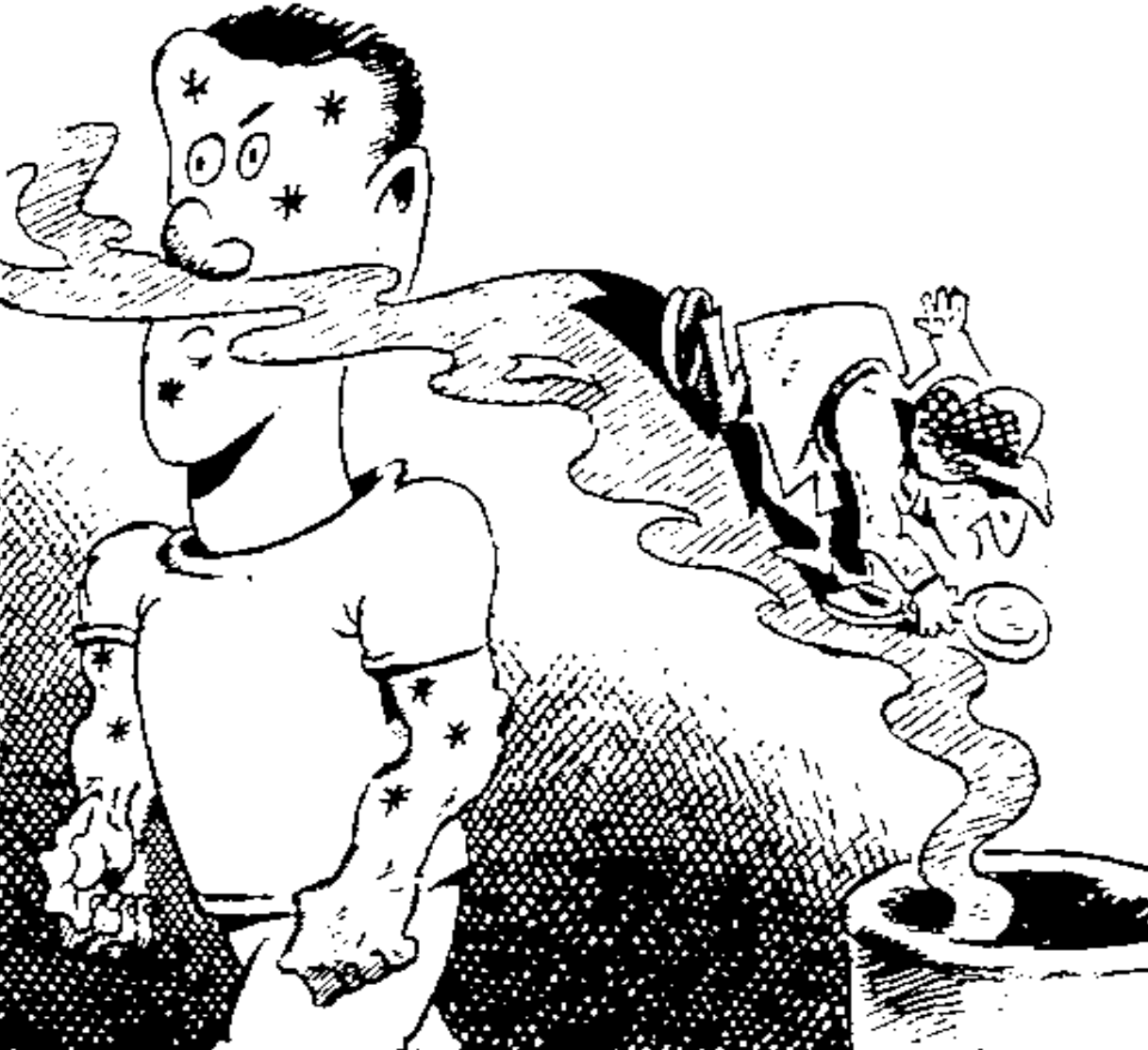# Study Designs

- You went back to your friends and discussed

- What options do you have?

- what you can do?

Solution: Case Control Study

Leukemia pts

Benzene (+)

Benzene (-)

Ask about exposures

Healthy Controls
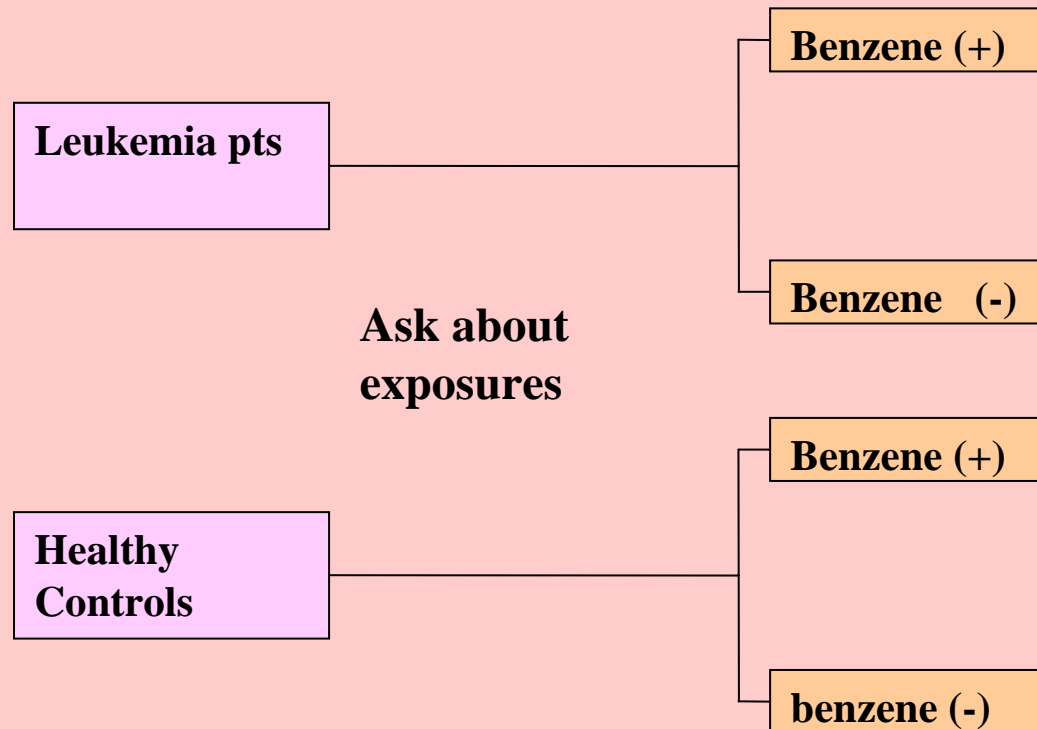
Benzene (+)

benzene (-)

CASE-CONTROL STUDY

Case-control studies start with a disease and go back to exposures.

Drawing by:

Nick Thorkelson

Case Control Studies

	Leukemia Patients	Healthy Controls	
Benzene Exposed	a	b	a+b
Benzene Non exposed	c	d	c+d
	a+c	a+d	a+b+c+d

Case Control Studies

- Selection of study subjects is on the basis of disease status

<u>Case</u>:

Those suffer from disease under study

<u>Control</u>:

Those are free from the disease under study

Selection of cases and control

- Select cases
- Controls are selected from the same study base as cases were
- Control if acquire disease, you should able to select it.

Sources of controls

- Community

- Neighborhood

- Hospitals

- Friends

Important issues

- Recall
  - Recall bias
  - Imperfect recall
- Temporality
- Selection

Case Control Studies

Analysis
- Calculation of Odds Ratio- as measure of association
- OR = ad/bc

Advantages & disadvantages:
- Good for rare disease as cancers
- Short duration and inexpensive
- Rely on recall
- Finding appropriate comparison group difficult
- Sequence of event is difficult to establish

# Examples of Case Control Studies

- To asses the risk factors for acute hepatitis B

- To evaluate the association between lead exposure, as reflected in bone lead levels, and adjudicated delinquency

- The effect of Pb exposure from automobile exhaust on renal integrity among traffic policemen

- To test the hypothesis that Essential tremors (ET) is associated with lead exposure.

Study Designs: another scenario

- Social Security Institute was asked by govt. that there are reports of poor safety measures in leather industry and handling of chromium is very poor?

- Occupational health expert was called and asked go and plan an investigation and tell us what is the magnitude of problem say prevalence of chrome ulcer among workers.

Solution: Cross-sectional Study
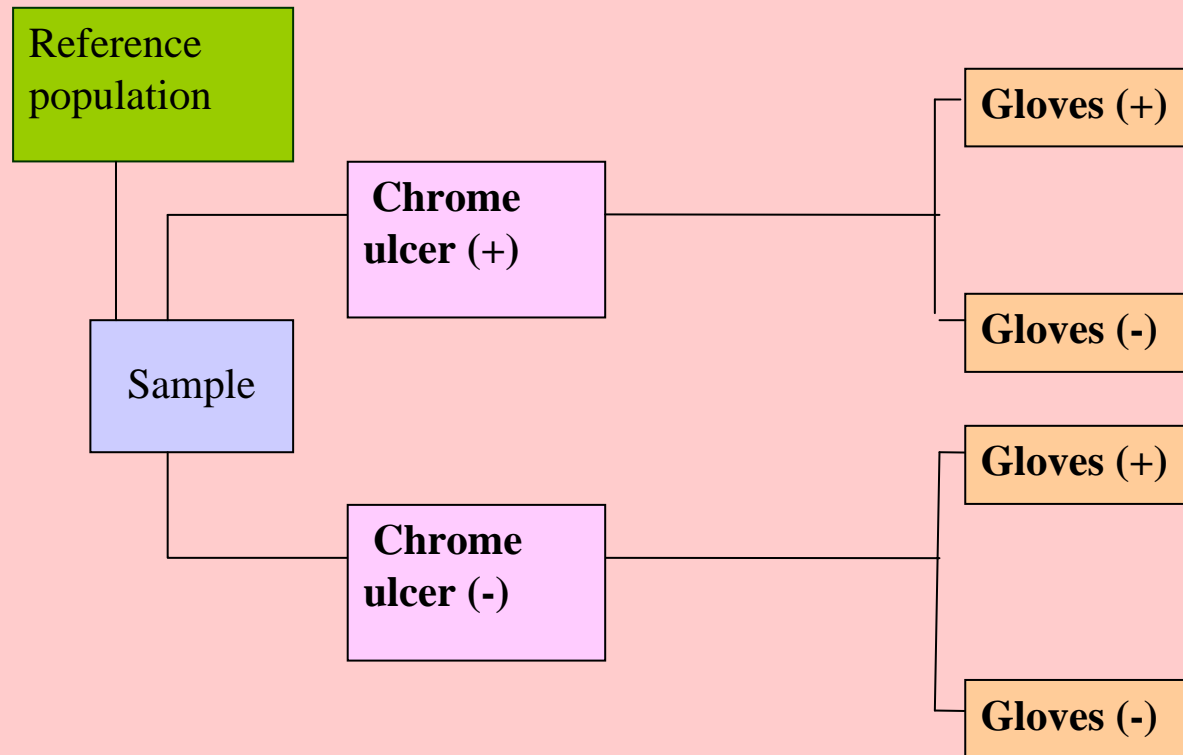
Cross-sectional Studies

	Disease	Non disease	
Exposed	a	b	a+b
Non Exposed	c	d	c+d
	a+c	a+d	a+b+c+d

Cross-sectional Studies

- **Objectives:**
  - To examine the health problem and disease frequency
  - To examine relationship between exposure and disease frequency or health problem

- **Unit of Analysis:** individual

- Exposure and disease status is assessed at the same time

Advantages

- Short duration study
- Start with reference population so generalization possible
- Provide prevalence estimates

Examples of Cross-sectional Studies

- Blood lead levels and risk factors for lead toxicity in children from schools and an urban slum in Delhi
- Prevalence of dermatitis among leather tannery workers

Design in Epidemiology

- Design choice depends on the objectives of study.

- When you want to know *"How much is disease": distribution of disease* ⟶ descriptive study

- and when you want to answer *"why"* ⟶ Analytical studies

Analytical Designs

- Observational
  - Case-control
  - Cohort

- Interventional
  - Randomized Controlled Trials
    - Clinical and Community Trials
  - Pre post comparison

Randomized Controlled Trial

- These studies are used test the interventions

- Interventions could be
    - Drugs or clinical procedures
    - Health education programme
    - A new measure for hazard prevention or decreasing exposure at workplace

Randomized Controlled Trial

Patient with Breast Cancer

Random allocation

Radical mastectomy
- Recurrence of cancer
- No Recurrence of cancer

Radical mastectomy with more limited resection
- Recurrence of cancer
- No Recurrence of cancer
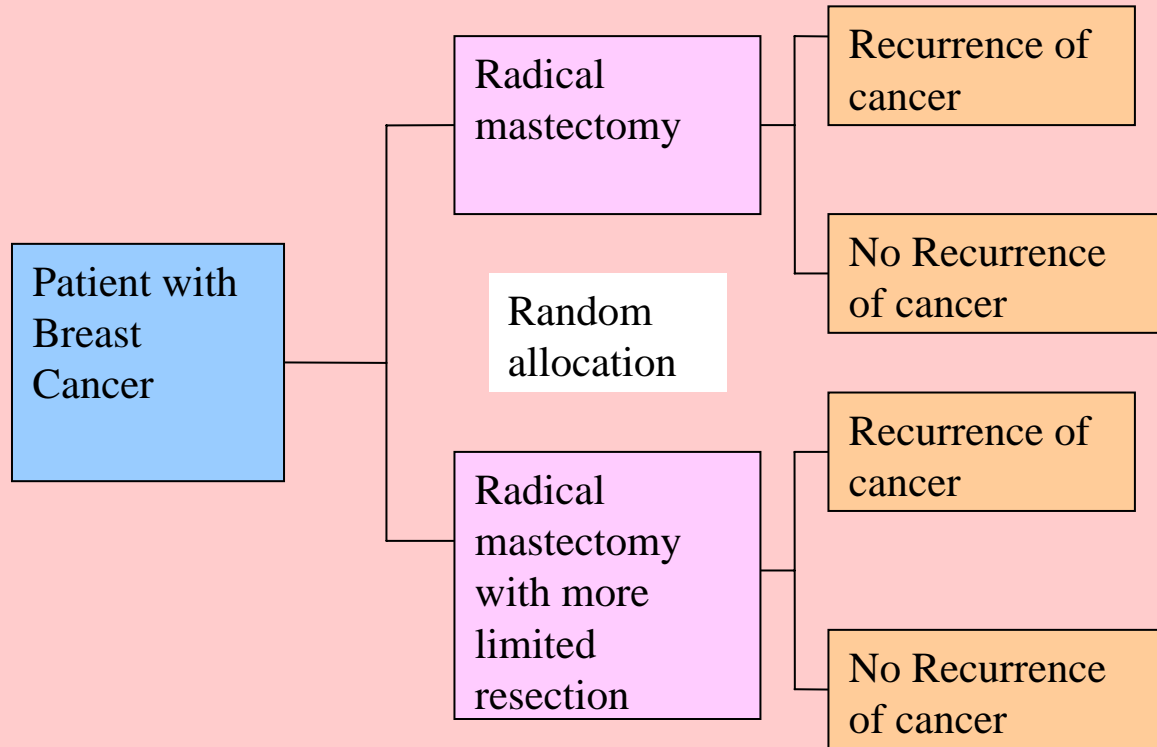
Randomized Controlled Trial

Intervention	Recurrence of breast cancer		Total
	+	-	
Radical mastectomy (RM)	a	b	a+b
Mastectomy with more limited resection (MLR)	c	d	c+d
Total	a+c	b+d	a+b+c+d

Randomized Controlled Trail

```
                              ┌──────────────┐        ┌──────────┐
                              │  Directly    │────────│ MTB(+)   │
                              │  observed    │        └──────────┘
                              │  treatment   │
                              │              │        ┌──────────┐
                              └──────────────┘────────│ MTB (-)  │
┌──────────────┐                                      └──────────┘
│ Patients of  │              ┌──────────────┐
│ MTB          │──────────────│ Random       │
│ positives    │              │ allocation   │
└──────────────┘              └──────────────┘
                              ┌──────────────┐        ┌──────────┐
                              │ Conventional │────────│ MTB(+)   │
                              │ treatment    │        └──────────┘
                              │              │
                              │              │        ┌──────────┐
                              └──────────────┘────────│ MTB (-)  │
                                                      └──────────┘
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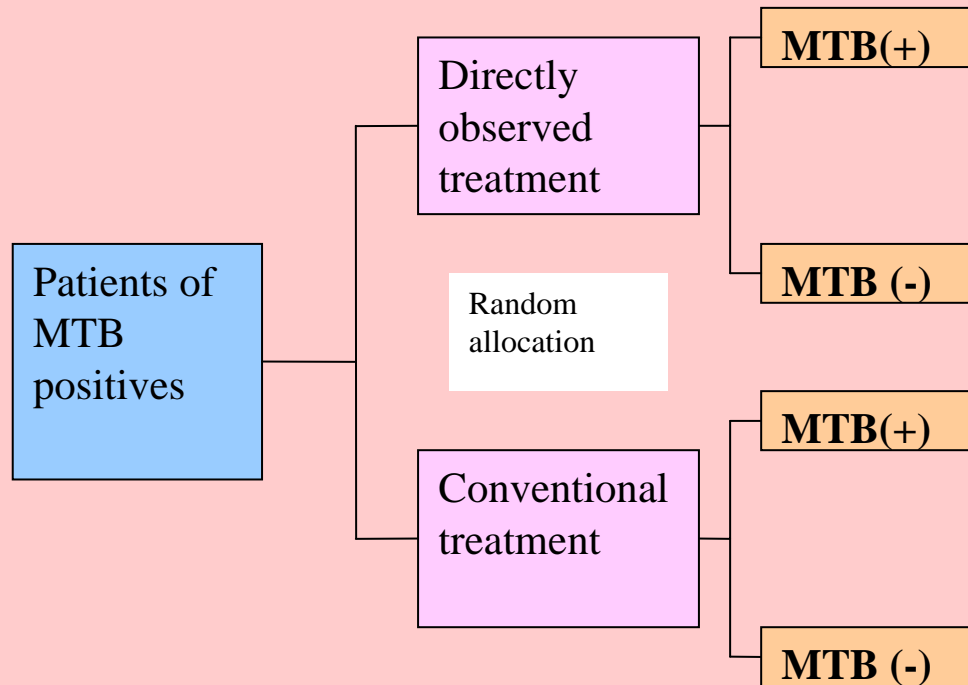
Examples

- Placebo-controlled, randomized trial of up to three courses of succimer in children with blood lead levels of 20-44 microg/dL (1.0-2.1 microM).

- Trail to assess the safety and efficacy of meso-2,3-dimercaptosuccinic acid in the treatment of children with lead toxicity

Cohort & Intervention study

	Cohort Study (Prospective)	Intervention Study
Objective	To test hypothesis regarding the causation of disease	To evaluate the efficacy of preventive or therapeutic agent or procedure
The role of investigators	To conduct observation of exposure causing the disease	To allocate the exposure to the study subjects, and observe the outcome caused by exposure

Descriptive Epidemiology

- Use to describe health states or events
- Types
  - Case Report & Case series
  - Correlative studies
    - Time series analysis
    - Ecological Studies
  - Surveillance
  - Cross-sectional studies

Case Report & Case Series

- Case report: A careful and detailed report of some new finding about one case is case report. e.g., chronic CO poisoning in a child

- Case report: Case report describe characteristics of number of cases e.g., distribution of characteristics of cancer patients in a hospital

Correlation studies

- Objective: To correlate general characteristics of population with their disease frequency at same period of time; within same population at different time periods

- Unit of analysis: group

Ecological correlations

- To correlate characteristics of population with disease frequency among several group of people during same period of time

- Example:
- Average TSP in ambient of big cities and respiratory tract infections

Surveillance

- Continuous, systematic process of collection, analysis, interpretation and dissemination of information for monitoring health problems

Study Designs
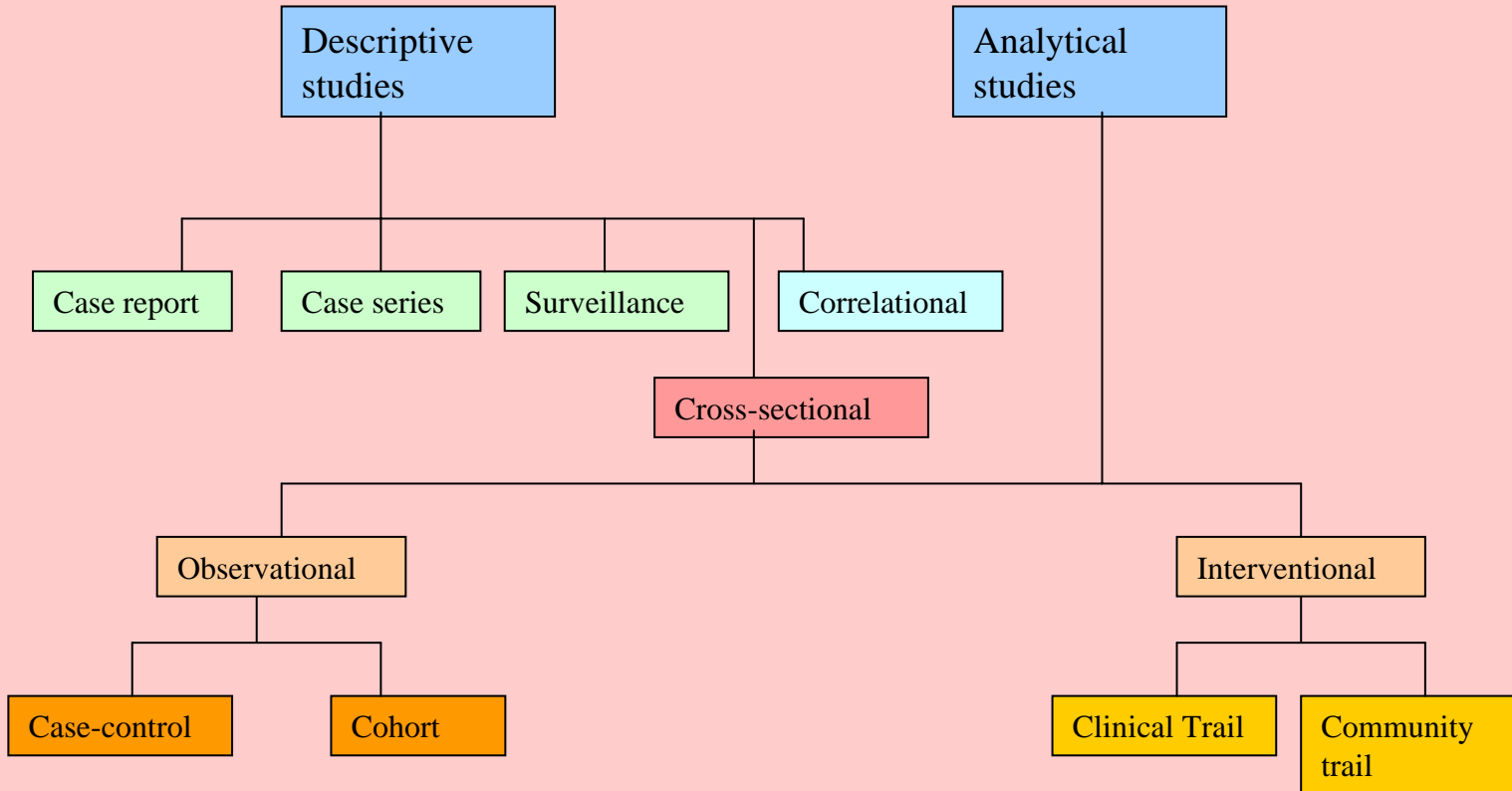
Traditional Study Designs

Design	Environmental Epidemiology	Occupational Epidemiology
Prospective follow-up	Common	Rare
Retrospective follow-up	Rare	Common
Nested case-control	Rare	Common
Registry-based case-control	Common	Common but of limited value
Cross-sectional	Common	Common
Ecologic; PMR	Becoming rare; rare	Rare; becoming rare
Descriptive & surveillance	Common for exposure & disease	Common for exposure & disease
Meta-analysis or collaborative reanalysis	Common	Common

Specific Study Designs in Relation to Research Objectives & Design Determinants

Design*	Objectives/Design Determinants					
	Etiology	Public Health	Interven-tion	Hypo-thesis	Feasibility	Credibility
PF	+		+	+		+++
RF	+				+	+
NCC	+				++	++
RBCC	+	+				++
CS	+-	+				-
Ecologic				+		-
Surv.				+		
Meta	+		+		++	+++

*PFS, prospective follow-up; RFS, retrospective follow-up; NCCS, nested case-control; RBCC, registry-based case-control; CS, cross-sectional.