

Formulation of a hypothesis

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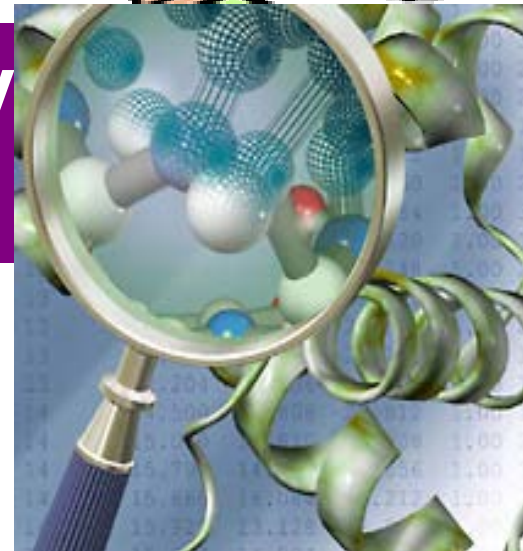
Formulation of a hypothesis

▶ **Observation**

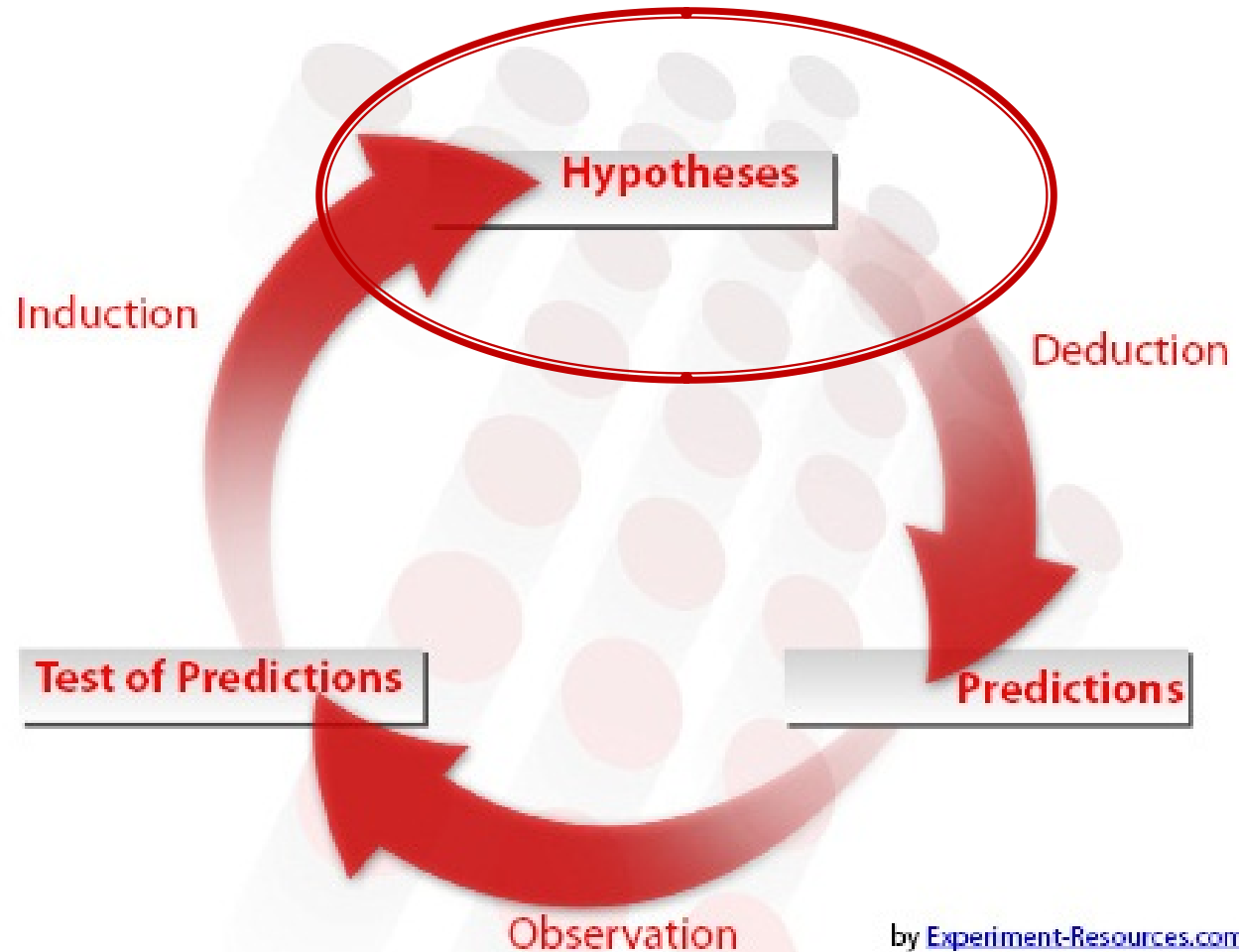
• **Hypothesis**

• **Confirmation and verification by criticism and experimentation**

Law



FORMULATING A RESEARCH PROBLEM



Research Hypothesis

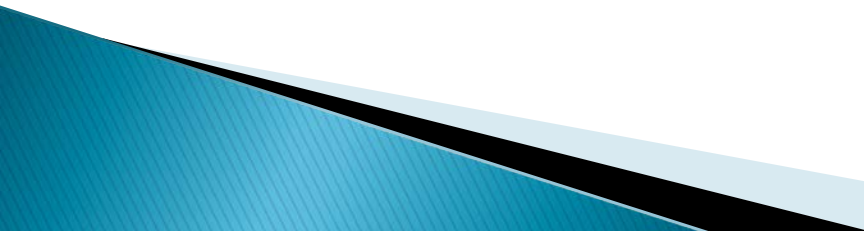
“ Research hypothesis is a statement of the research question in a measurable form”

The practice of science involves formulating and testing *hypotheses*, assertions that are falsifiable using a test of observed data.

Research Hypothesis (conti)

- ▶ A hypothesis can be defined as a prediction or explanation of the relationship between one or more independent variables(PREDISPOSING/RISK FACTORS) and one dependent variable (OUTCOME/CONDITION/DISEASE)).
- ▶ A hypothesis, in other words, **translates the problem statement into a precise, clear prediction of expected outcomes.**
- ▶ It must be emphasized that hypotheses are not meant to be haphazard guesses, but should reflect the depth of knowledge, imagination and experience of the investigator.

Research Hypothesis (conti.)

- ▶ **Null hypothesis:** Corresponds to a general or default position. For example, the null hypothesis might be that there is no relationship between two measured phenomena, or that a potential treatment has no effect.
 - ▶ **Alternative hypothesis:** Null hypothesis is typically paired with a second hypothesis, the alternative hypothesis, which asserts a particular relationship between the phenomena. The alternative need not be the logical negation of the null hypothesis and predicts the results from the experiment if the alternative hypothesis is true.
- 



Observation,
Questioning

• Hypothesis

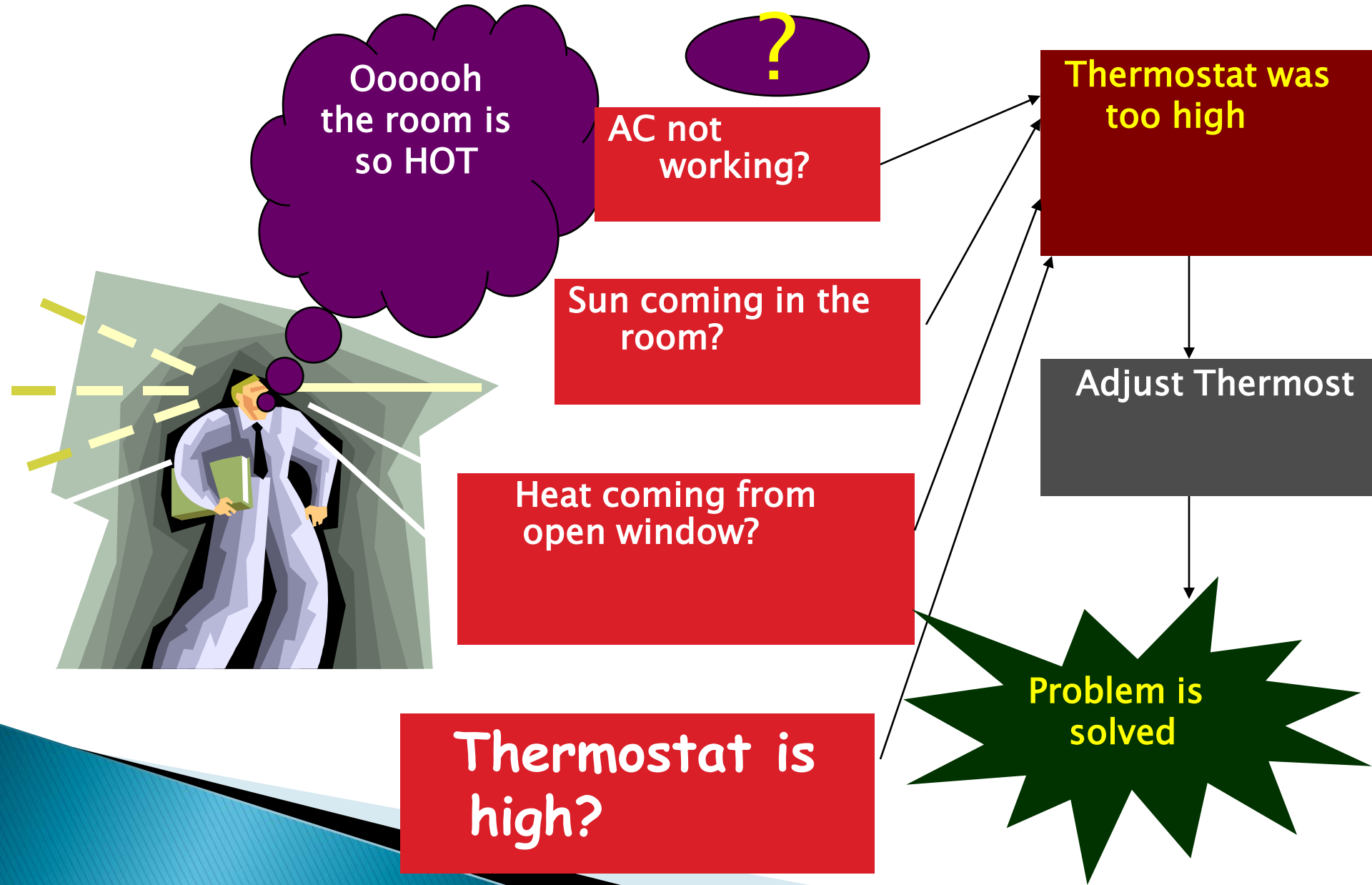


• Confirmation and verification by

- exploring
- problem solving
- experimenting
- inventing
- critical analysis

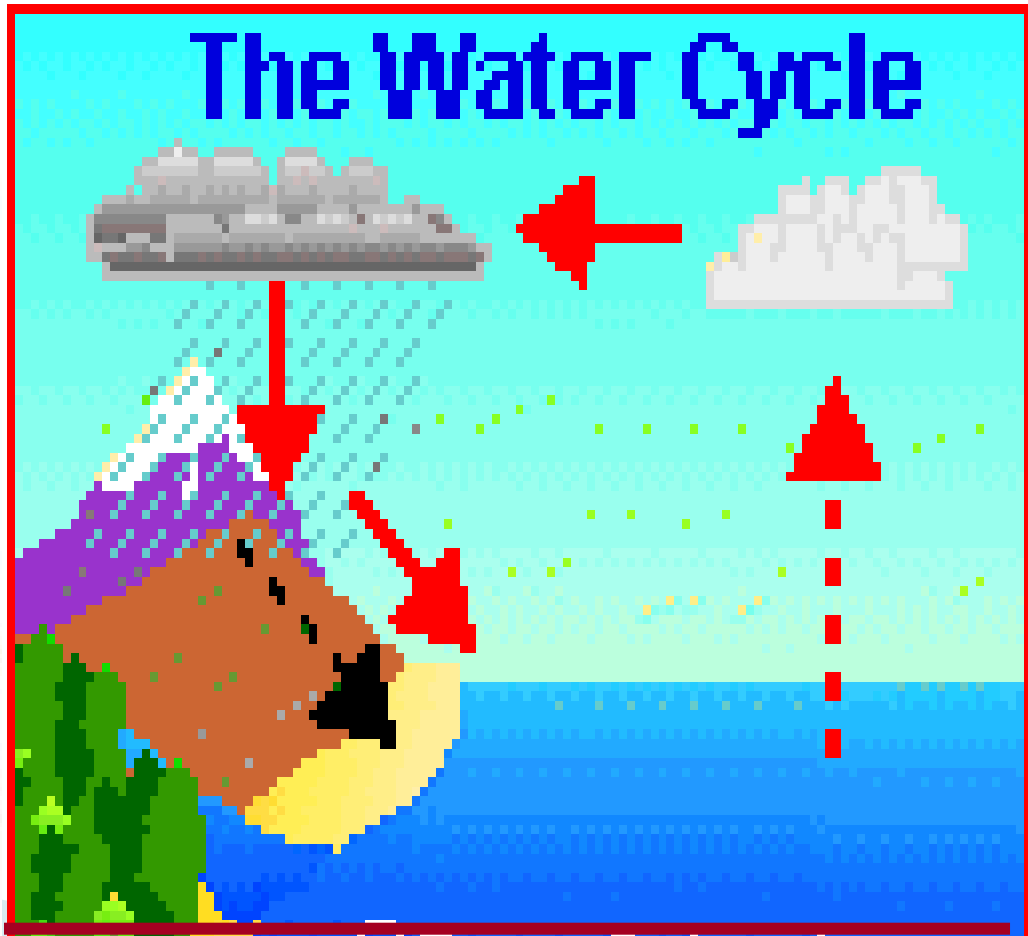
Learning a new thing

Problem solving---example

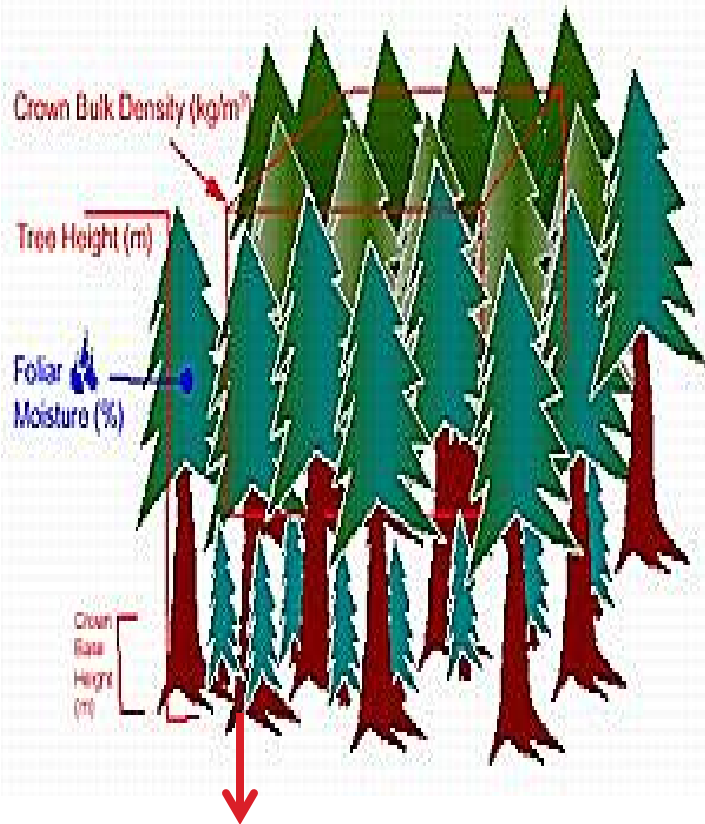


Exploring--examples

- ▶ How does rain fall?



Experimenting--example



What does a stem do?

Color the water;
Wait a day




What happened?
How did it happen?



Experiment

Example: (Interventional Study)

- ▶ **Research area: cardiology**
 - ▶ **Research topic: ischemic heart disease (IHD)**
 - ▶ **Goal: to contribute to prevention of IHD**
 - ▶ **Primary objective: to determine the effect of reducing LDL on the occurrence of MI**
 - ▶ **Secondary objective: to describe the side effects of lowering LDL**
 - ▶ **Research question: does hypocholesterolemic agent “A” decrease the risk of MI?**
 - ▶ **Research hypothesis: the risk of MI among patients treated with hypocholesterolemic agent “A” is lower than the risk among controls not treated with hypocholesterolemic agents**
- 

Research Methodology and Design

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Research

- ▶ Earliest recorded use of the term “Research” was in 1577
- ▶ Derived from the French "*recerche*", which means "to go about seeking or searching"
- ▶ Searching for
 - knowledge or as any systematic investigation
- ▶ In order to:
 - find an answer
 - establish novel facts,
 - solve new or existing problems,
 - prove new ideas,
 - develop new theories
- ▶ **Scientific Research:** using scientific methods.

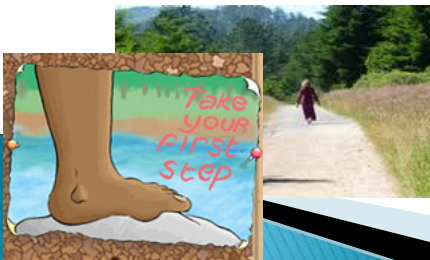
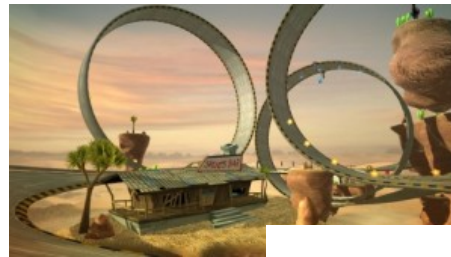


Research is an organised and creative journey



Research has a route map

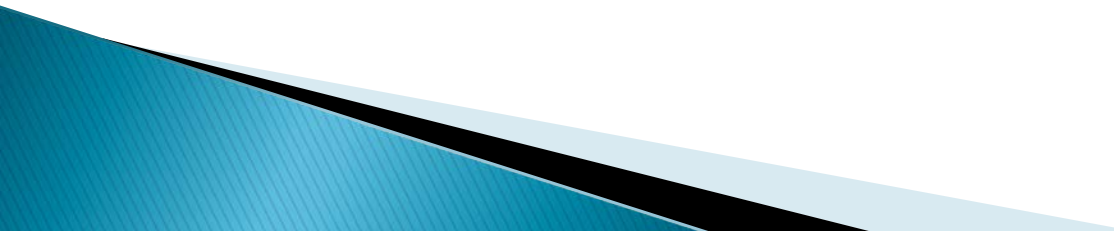
- What makes us want to start a journey?- Research question
- How do we know which direction to move in?-Hypothesis
- What exactly is the first step?- Research design
- What do we do when the road gets too tough?- Modify design
- What happen if we do nothing and ignore?- Failure



Proper designing, common sense and clear thinking necessary for the management of the entire research endeavor.



Research design

- ▶ **The strategy, the plan, and the structure of conducting (performing) a research** in order to fulfill the planned objective.
 - ▶ Gives **direction** and **systematizes** research.
 - ▶ Depends on the type of research.
 - ▶ Correct and suitable designing will ensure **reliable and dependable** results.
- 

Factors affecting Research Design

▶ Research design depends on different factors:

- Research question-research topic
- The objectives of the study
- Scientific theory and literature available on the topic
- Type of research-qualitative or quantitative
- Research methodology
- Ethical consideration
- Budget and financial constrain
- Time allowed for the research



Research Methods

- ▶ **Description**
 - ▶ **Experimentation**
 - ▶ **Comparison**
 - ▶ **Modeling**
- 

Research methodology

- ▶ Descriptive
- ▶ Experimental

Relationships Among Research Type, Question, and Design

Type of Research

Descriptive

Research Question

What is happening?

How is something happening?

Why is something happening?

Research Design

Simple Descriptive

Comparative Descriptive

Correlational

Type of Research

Experimental

Research Question

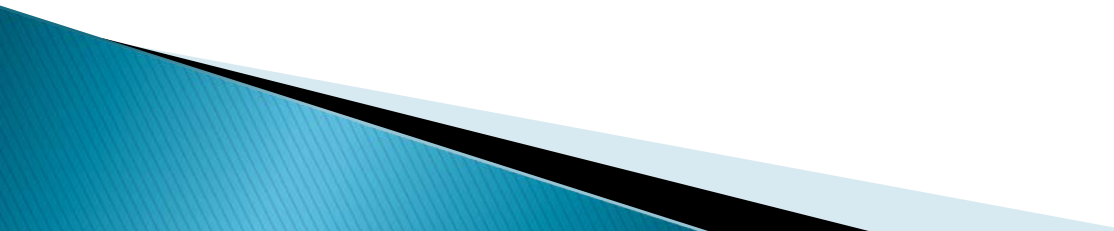
Does something cause an effect?

Research Design

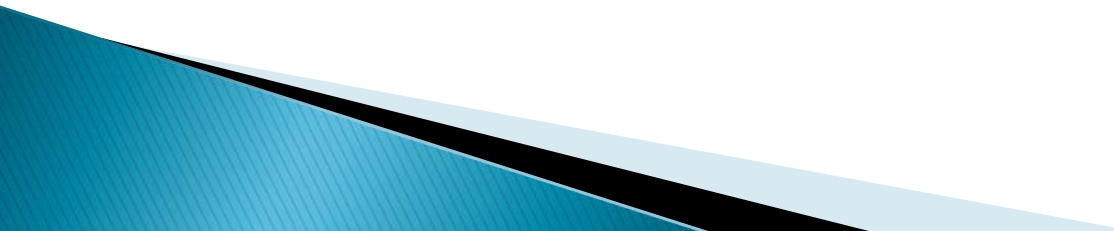
Experimental

Quasi-Experimental

Description

- ▶ Description is used to gather data regarding natural phenomena and natural relationships and includes observations and measurements of behaviors.
 - ▶ A classic example of a descriptive study is Copernicus's observations and sketches of the movement of planets in the sky in an effort to determine if the Earth or the Sun is the orbital center of those objects.
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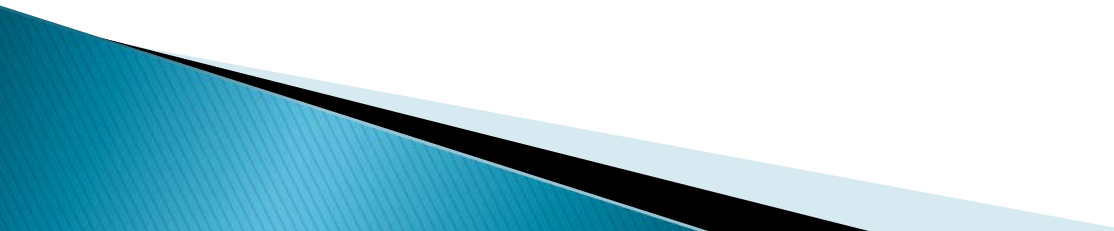
Experimentation

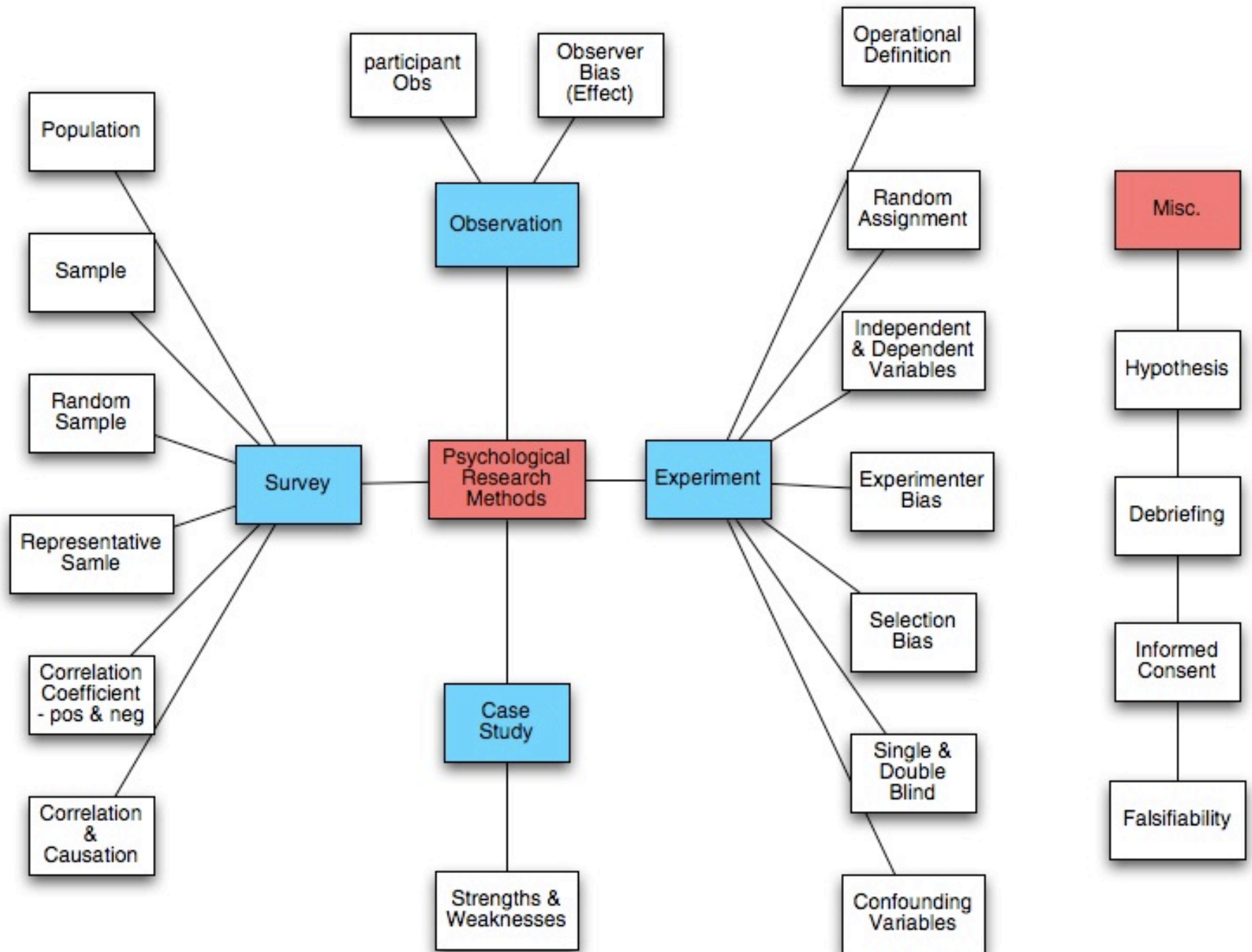
- ▶ Experimental methods are used to investigate the relationship(s) between two or more variables when at least one of those variables can be intentionally controlled or manipulated.
 - ▶ The resulting effect of that manipulation (often called a treatment) can then be measured on another variable or variables.
- 

Comparison

- ▶ Comparison is used to determine and quantify relationships between two or more variables by observing different groups that either by choice or circumstance are exposed to different treatments.
- ▶ Examples: in the 1950s investigations initiated to study the relationship between **cigarette smoking and lung cancer** in which scientists compared individuals who were smoking with non-smokers and correlated smoking with various health problems including lung cancer.

Modeling

- ▶ Both physical and computer-based models are built to mimic natural systems and then used to conduct experiments or make observations.
 - ▶ E.g. Weather forecasts are an example of scientific modeling, where data collected on temperature, wind speed, and direction are used in combination with known physics of atmospheric circulation to predict the path of storms and other weather patterns.
- 



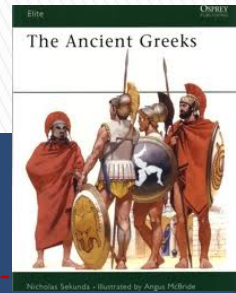
Main approaches to a research problem

Quantitative Research

- ▶ Involves quantitative experiments-measures quantity
- ▶ Use mathematical and statistical means for data analysis
- ▶ Generate a hypothesis to be proved or disproved
- ▶ Frequently uses control group
- ▶ Results obtained are real and unbiased
- ▶ Is reproducible.

Qualitative Research

- ▶ The oldest of all scientific techniques
- ▶ Regarded as a precursor of quantitative research to formulate a realistic and testable hypothesis
- ▶ Measures quality, not quantity.
- ▶ Based on interviews, survey design techniques and individual case studies



Conti:

Quantitative Research

- ▶ Sample size is essential
- ▶ Generates numerical data or information that can be converted into numbers
- ▶ Ideal for later phases of research projects
- ▶ Provides the researcher a clearer picture of what to expect in his research compared.
- ▶ Instruments used: tools such as questionnaires, surveys and other equipment, scientific instruments to collect numerical or measurable data.

Qualitative Research

- ▶ Does not depend on a sample size
- ▶ Generates non-numerical data. It focuses on gathering of mainly verbal data rather than measurements.
- ▶ Ideal for earlier phases of research projects
- ▶ Gives an idea, that has to be confirmed by quantitative research
- ▶ Instruments used: individual in-depth interviews, structures and non-structured interviews, focus groups, narratives, content or documentary analysis, participant observation and archival research

Types of design depending on different types of research methods

- ▶ **Descriptive Designs**
 - ▶ **Correlational Studies**
 - ▶ **Semi-Experimental Designs**
 - ▶ **Experimental Designs**
 - ▶ **Reviewing Other Research**
 - ▶ **Test Study Before Conducting a Full-Scale Study**
- 

A- Descriptive Designs

Aim of descriptive research: Observe and Describe

1. Descriptive Research
2. Case Study
3. Naturalistic Observation
4. Survey (the questionnaire is also a technique used in many types of research designs)



1- Descriptive Research

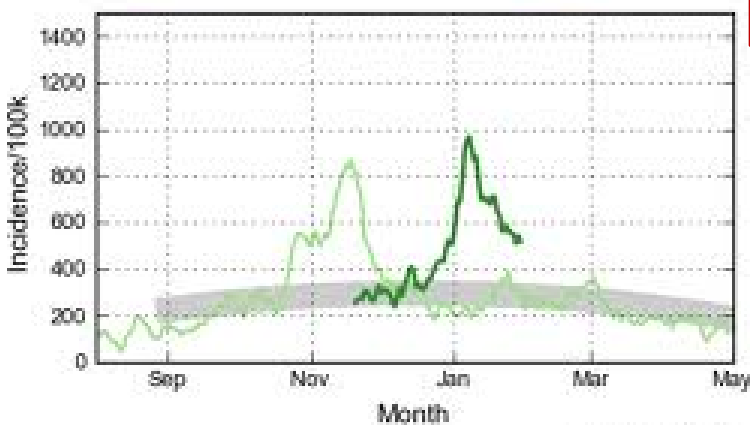
- ▶ Also known as **statistical research**, describes data and characteristics about the population or phenomenon being studied.
- ▶ Descriptive research answers the questions *who, what, where, when*, "why" and *how*



e.g. H1N1 in a population?

Influenzanet The Netherlands
ILI Incidence

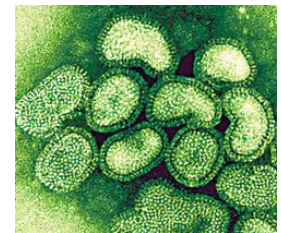
— 2009 - 2010 — Baseline — 2010 - 2011



Prevalence in different cities?

What causes H1N1?

How many people vaccinated?



2- Case study



- ▶ Analysis of an individual unit (e.g., a person, group, or event) stressing developmental factors in relation to context.
- ▶ Common in social sciences and life sciences.
- ▶ May be **descriptive** or **explanatory**. The latter type is used to **explore causation** in order to find underlying principles.
- ▶ May be **prospective** in which criteria are established and cases fitting the criteria are included as they become available, or **retrospective**, in which criteria are established for selecting cases from historical records for inclusion in the study.



Case: Tomatoes not good in the market

1. Identify the problem in the case.



2. Identify the cause of the problem.



Tomato plants suffering from infection



3. Work on solution.



4. Implementation plan.



5. Backup plan.



3- Naturalistic observatio

- ▶ A research method in which a subject is observed in its natural habitat without any manipulation by the observer.
- ▶ Widely used in such fields as psychology, biology, anthropology, ecology, and others
- ▶ Researchers take great care to avoid interfering with the behavior they are observing by using unobtrusive methods.
- ▶ In the context of a naturalistic observation the environment is in no way being manipulated or created by the observer

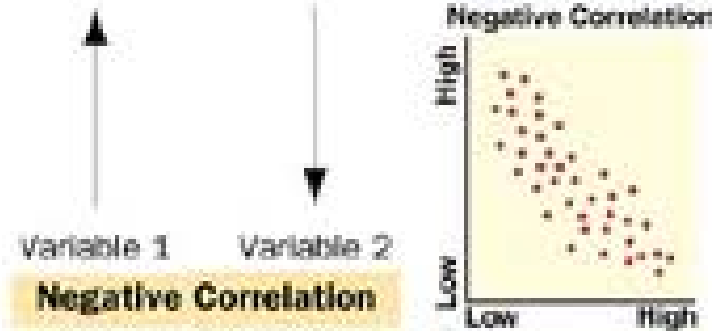


4- Survey

- ▶ **A method of Quantitative research**
- ▶ Using questionnaires, Delphi method, interviews, normative
- ▶ e.g. Statistical survey, a method for collecting quantitative information about items in a population
- ▶ In Astronomy, medicine, physics, metallography

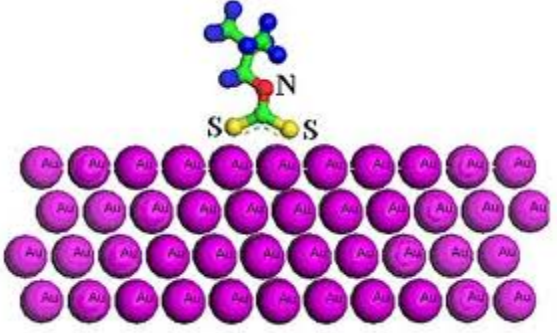
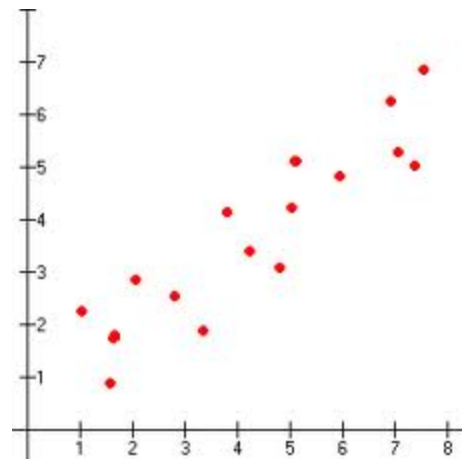


B-Correlational Studies



Aim: Predict

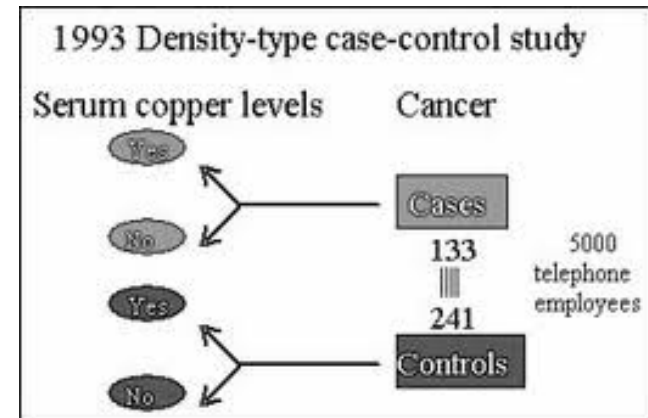
1. Case Control Study
2. Observational Study
3. Cohort Study
4. Longitudinal Study
5. Cross Sectional Study
6. Correlational Studies in general



Structure-Property **Correlation Studies** Using Electronic Structure

1- Case-control study

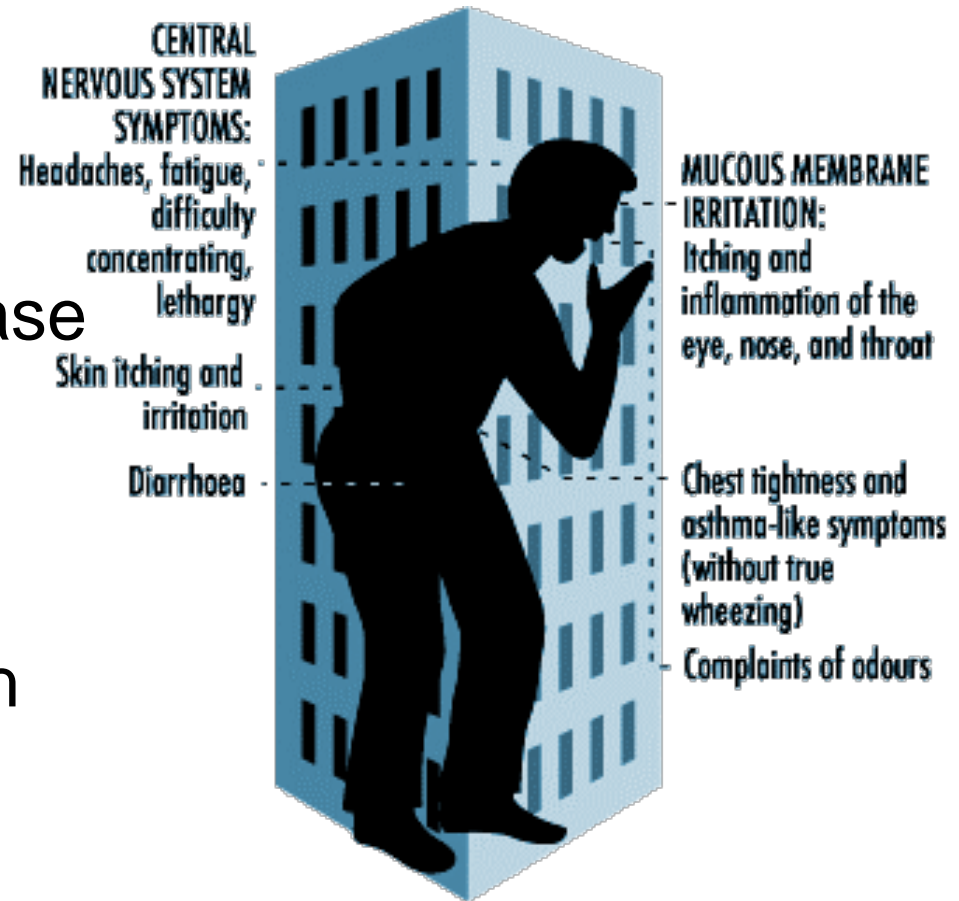
- ▶ Frequently used type of epidemiological study
- ▶ Requires cases and controls
- ▶ Used to identify factors that may contribute to a medical condition by comparing subjects who have that condition (the 'cases') with patients who do not have the condition but are otherwise similar (the 'controls').
- ▶ Relatively inexpensive
- ▶ Can be carried out by small teams or individual researchers in single facilities.



Hypothesis

- ▶ Smoking causes Peripheral vascular disease.
- ▶ Smoking causes lung cancer.
- ▶ Eating eggs causes increase in blood cholesterol
- ▶ Too much water spoils indoor plants
- ▶ Water containing too much fluoride spoils the teeth

Sick building syndrome



Smoking and Peripheral Vascular Disease (PVD)

Ever smoked?  PVD

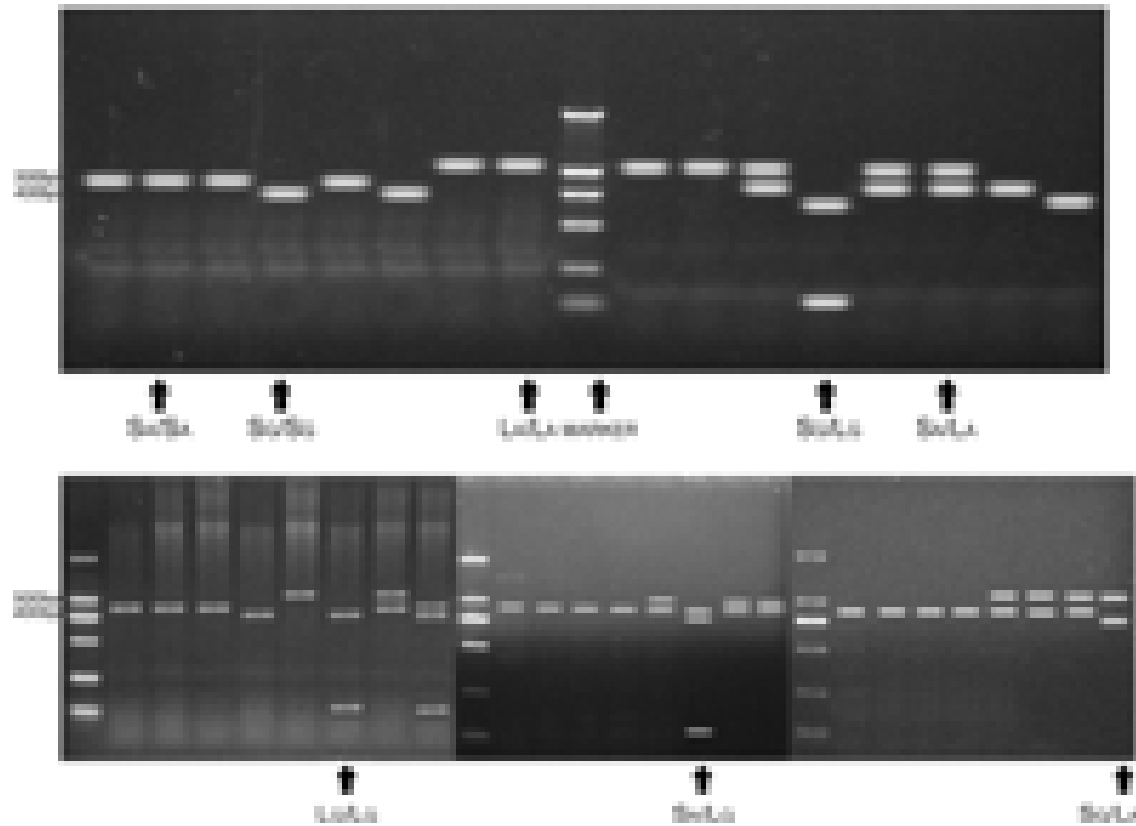
	Smoked		Total
	Ever	Never	
PVD	23	8	31
No PVD	1704	1291	2995
Total	1727	1299	3026

$$\frac{.013}{.006} = 2.2$$

Ever smokers:

2.2 x more likely to have PVD than never-smokers.

Serotonin Transporter Gene Polymorphism in Chinese Patients With Poststroke Depression A Case-Control Study



Advantages and disadvantages of Case-control studies

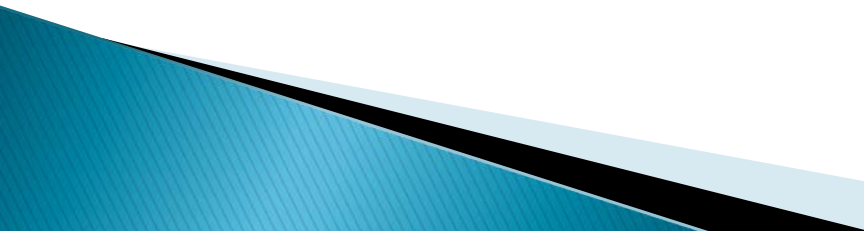
Advantages:

- ▶ Relative to cohort, quicker
- ▶ Usually smaller sample size
- ▶ Better with rare diseases than cohort
- ▶ Better with diseases of long latency periods
- ▶ Can evaluate multiple exposures

Disadvantages

- ▶ Only one outcome can be studied (in contrast to cohort)
- ▶ Does not allow direct assessment of risk
- ▶ More susceptible to certain biases
- ▶ Not efficient for studying rare exposures

2- Observational study

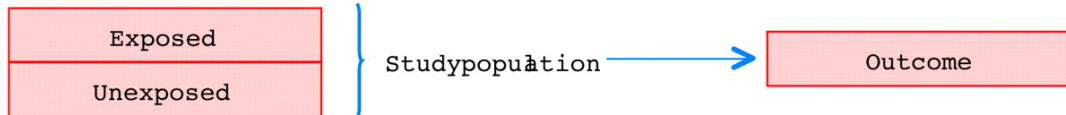
- ▶ By observing a specific group versus a control group to draw an inferences. e.g. about the possible effect of a treatment on subjects
 - ▶ Used frequently in epidemiology and statistics
 - ▶ The assignment of subjects into a treated group versus a control group is outside the control of the investigator.
 - ▶ [This is in contrast with controlled experiments, such as randomized controlled trials, where each subject is randomly assigned to a treated group or a control group before the start of the treatment].
- 

Hum...the alpine butterflies are darker than species at lower elevations, which could be caused by natural selection for heat absorption. If this theory applies, I'd expect coloration to affect the butterflies' body temperature.

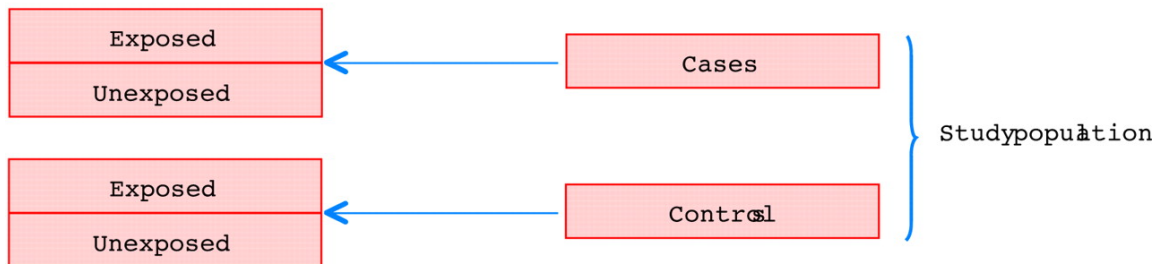


The three main study designs used in observational studies: cohort (follow up), case-control, and cross sectional.

Cohort design



Case-control design



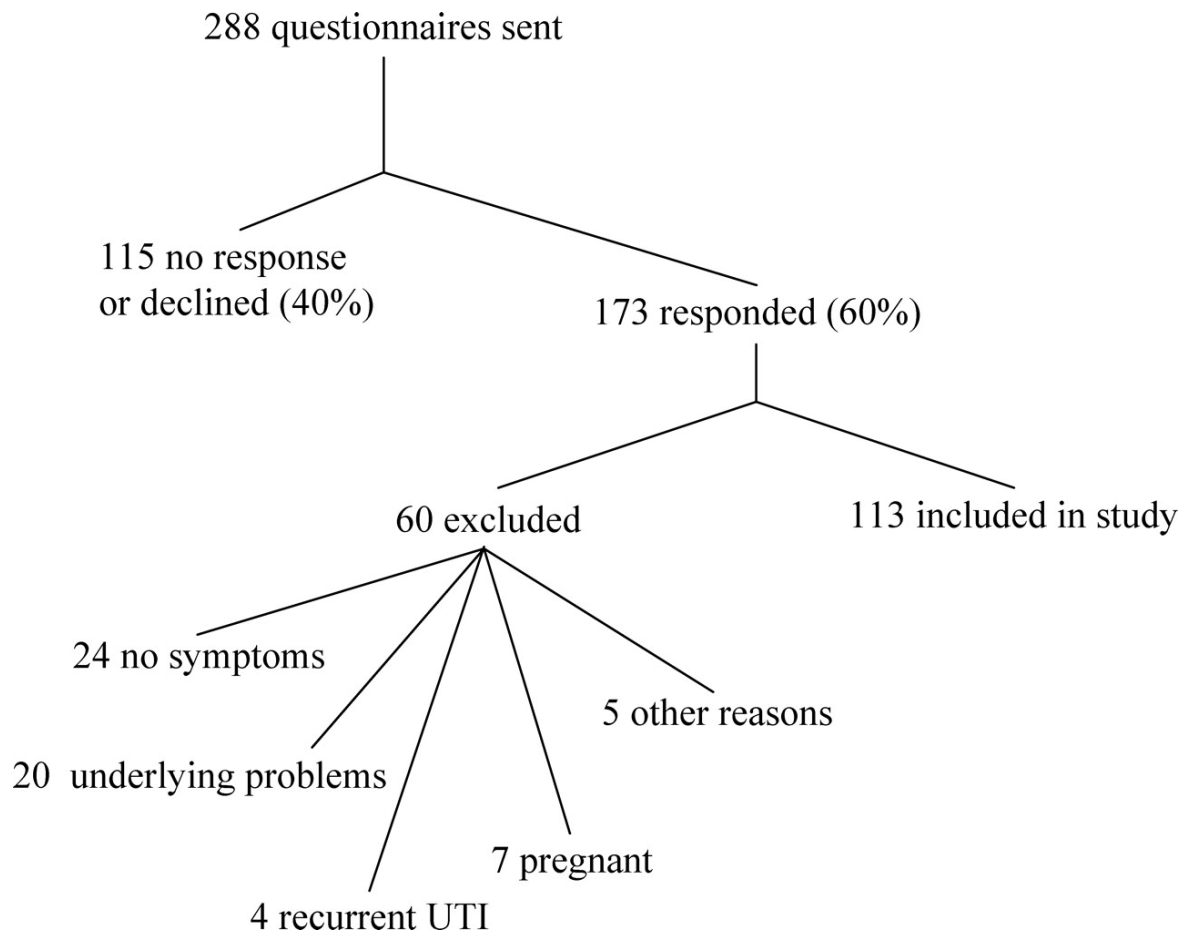
Cross sectional studies



Jepsen P et al. Heart 2004;90:956-960

An observational study of empirical antibiotics for adult women with uncomplicated UTI in general practice

Response rates and exclusions.



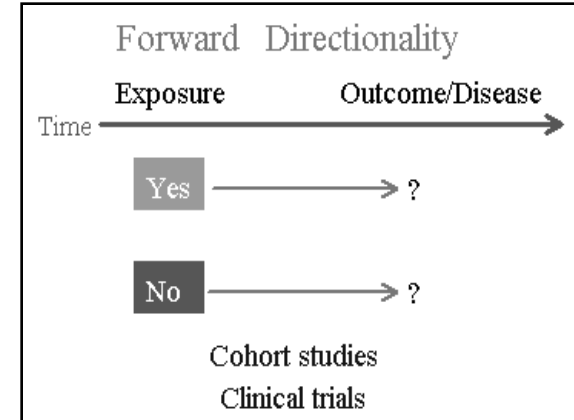
O'Brien K et al. *J. Antimicrob. Chemother.* 2007;59:1200-1203

Association of empirical antibiotic prescription with urine culture result

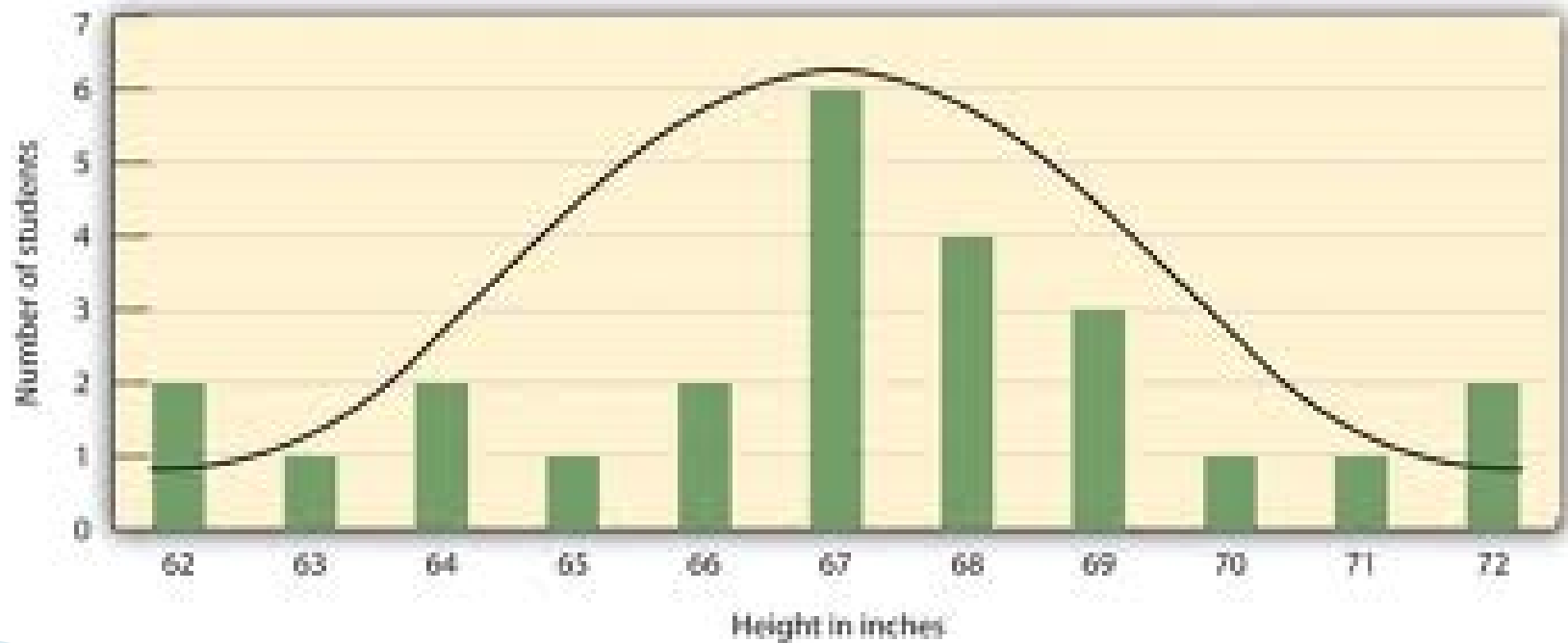
Empirical decision by GP	Positive culture	Negative culture	Total
Antibiotics prescribed	27	41	68
No antibiotics	9	34	43
Total	36	75	111

3- Cohort study or panel study

- ▶ A form of **longitudinal study** (a type of **observational study**) used in medicine, social science, actuarial science and ecology.
- ▶ A **cohort** is a group of people who share a common characteristic or experience within a defined period (e.g., are born, are exposed to a drug or vaccine or pollutant, or undergo a certain medical procedure).
- ▶ An analysis of **risk factors and follows** a group of people who do not have the disease, and uses correlations to determine the absolute risk of subject contraction.
- ▶ A type of clinical study design and should be compared with a cross-sectional study.
- ▶ Cohort studies are largely about the life histories of segments of populations, and the individual people who constitute these segments.



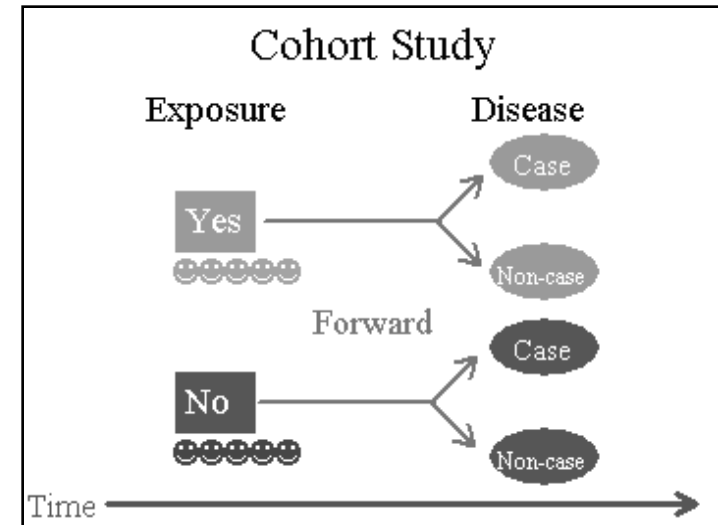
Height distribution in a group of students



Cohort studies

- ▶ Prospective
- ▶ Retrospective
- ▶ Ambidirectional

Prospective

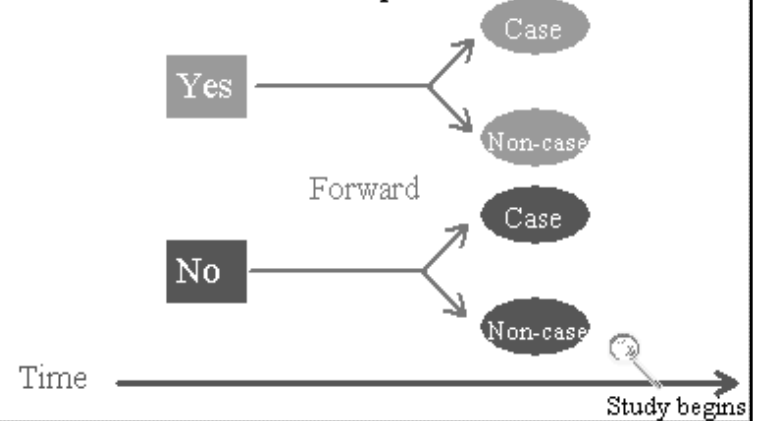


Retrospective
Cohort Study



VDT's

Spontaneous abortions



Advantages and disadvantages of cohort studies

Advantages of cohort studies:

- ▶ Of observational studies, tends to be least prone to bias
- ▶ Can address several diseases in same study
- ▶ With retrospective, can be relatively low cost, quick
- ▶ Can be used with rare exposures

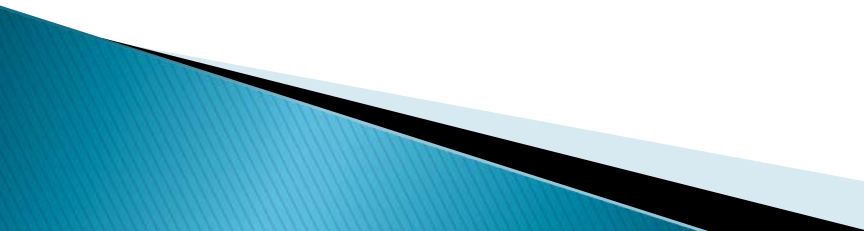
Disadvantages of cohort studies

- ▶ Loss to follow-up a potential problem
- ▶ Usually larger sample size than case-control
- ▶ Prospective – can be expensive & time-consuming
- ▶ Prospective – inefficient with rare diseases, diseases of long latency

4- Clinical Trials

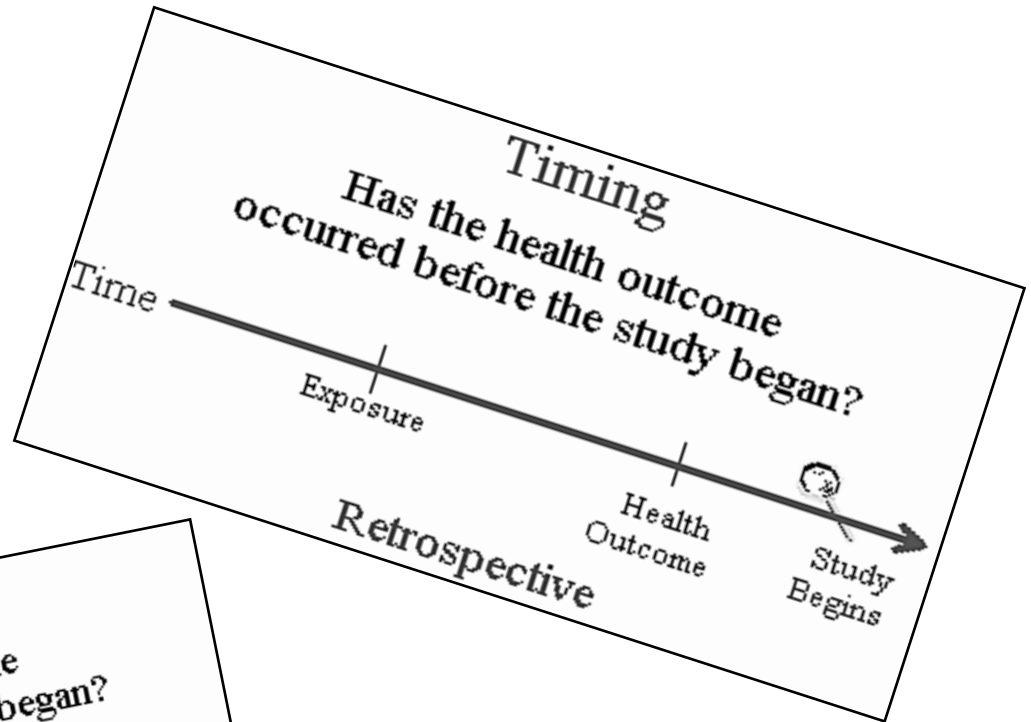
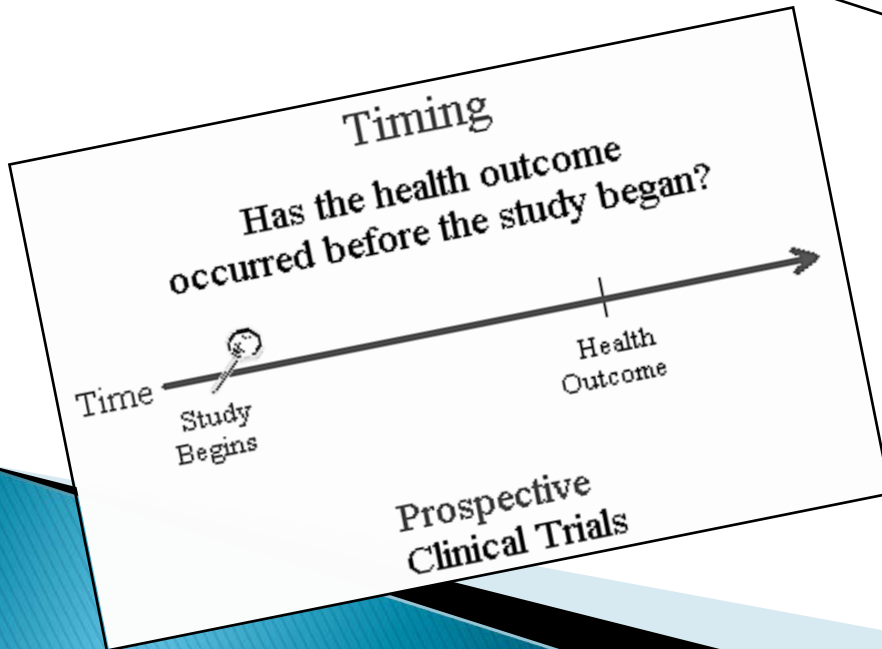
- ▶ **Experimental design**
- ▶ **Assess therapeutic effects/health benefits**

Key features:

- ▶ **Randomization**
 - ▶ **Blinding**
 - ▶ **Ethical concerns**
 - ▶ **Intention to treat analysis (analyze-as-randomized, effectiveness) vs. Treatment-received analysis (efficacy)**
- 

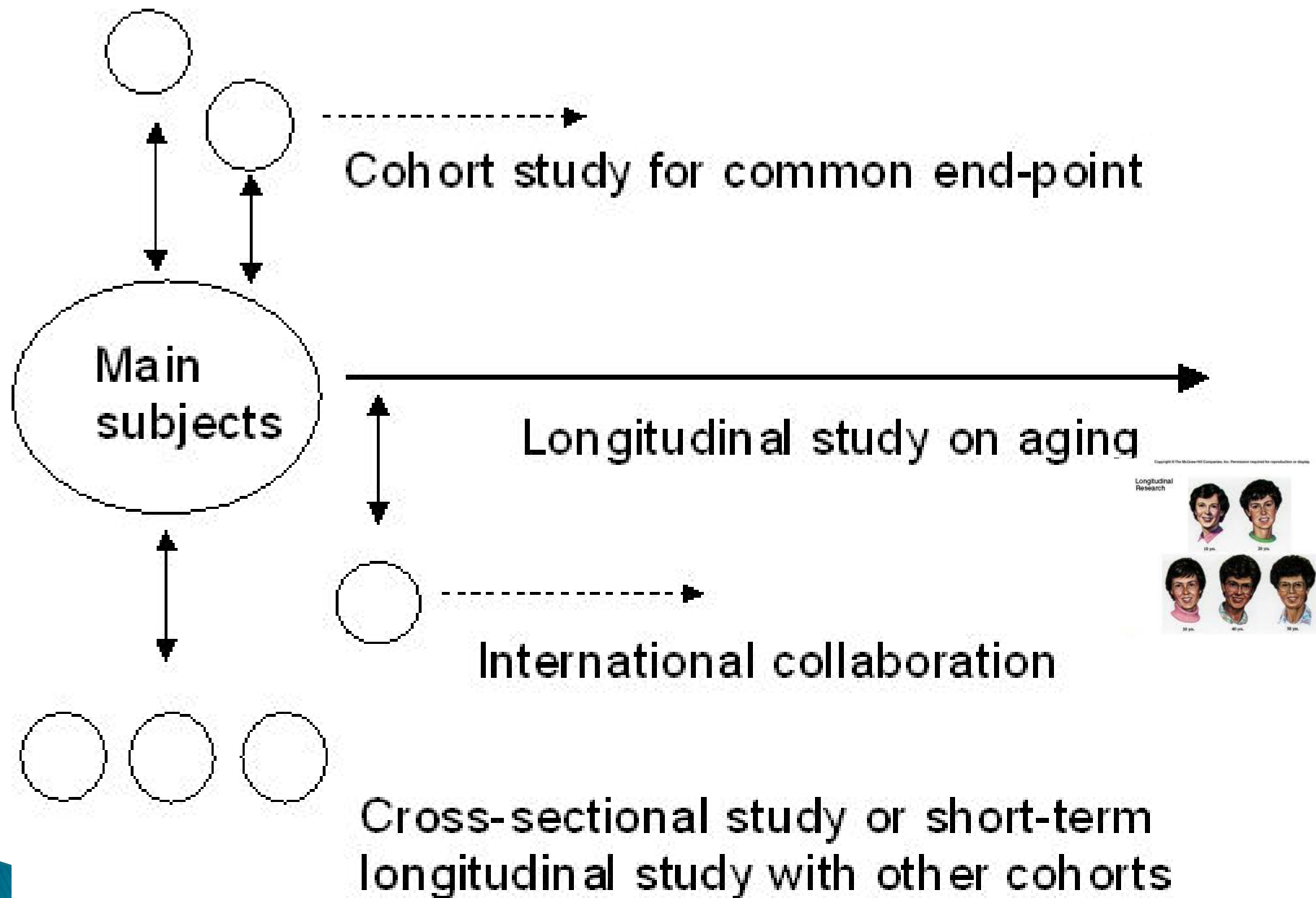
Clinical trials

- ▶ Prospective
- ▶ Retrospective

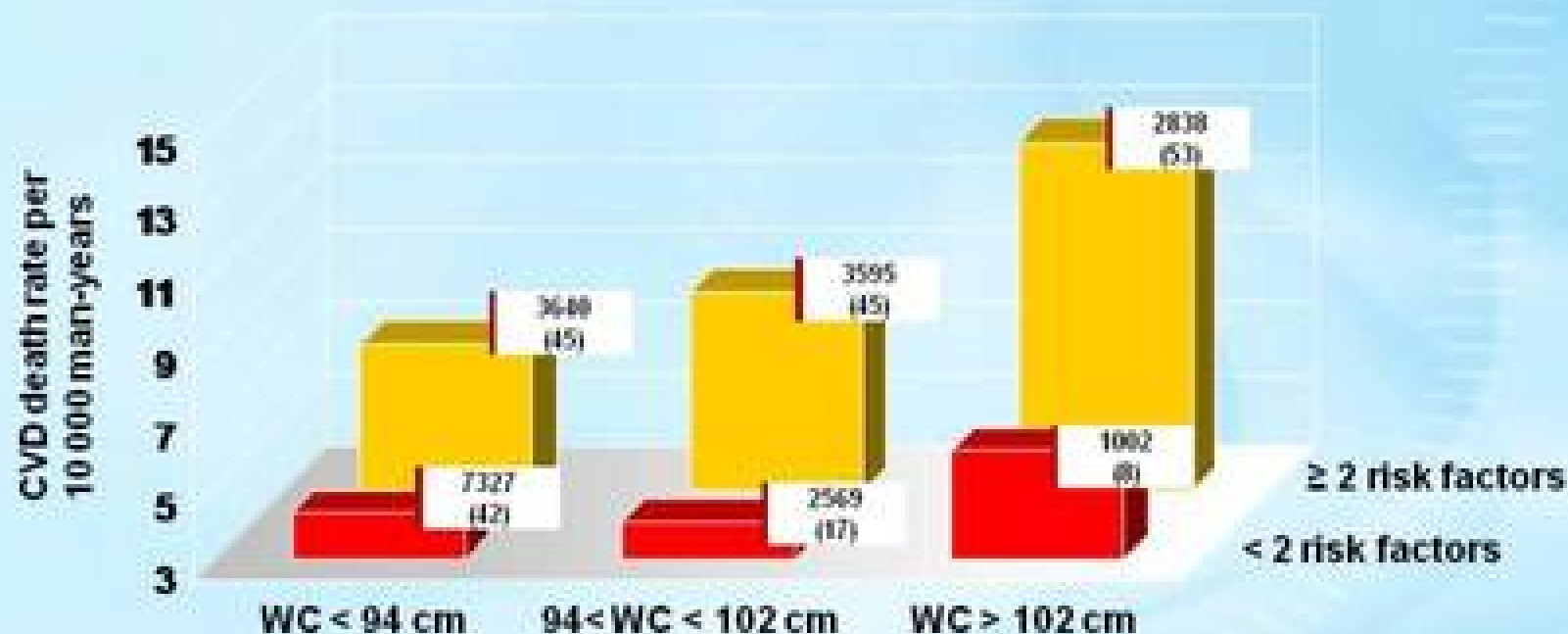


5– Longitudinal study

- ▶ A correlational research study
- ▶ Involves repeated observations of the same variables over long periods of time — often many decades.
- ▶ A type of observational study.
- ▶ Often used in psychology to study developmental trends across the life span, and in sociology to study life events throughout lifetimes or generations.
- ▶ Track the same people, and therefore the differences observed in those people are less likely to be the result of cultural differences across generations.
- ▶ Make observing changes more accurate
- ▶ Applied in various other fields e.g. in medicine, the design is used to uncover predictors of certain diseases.



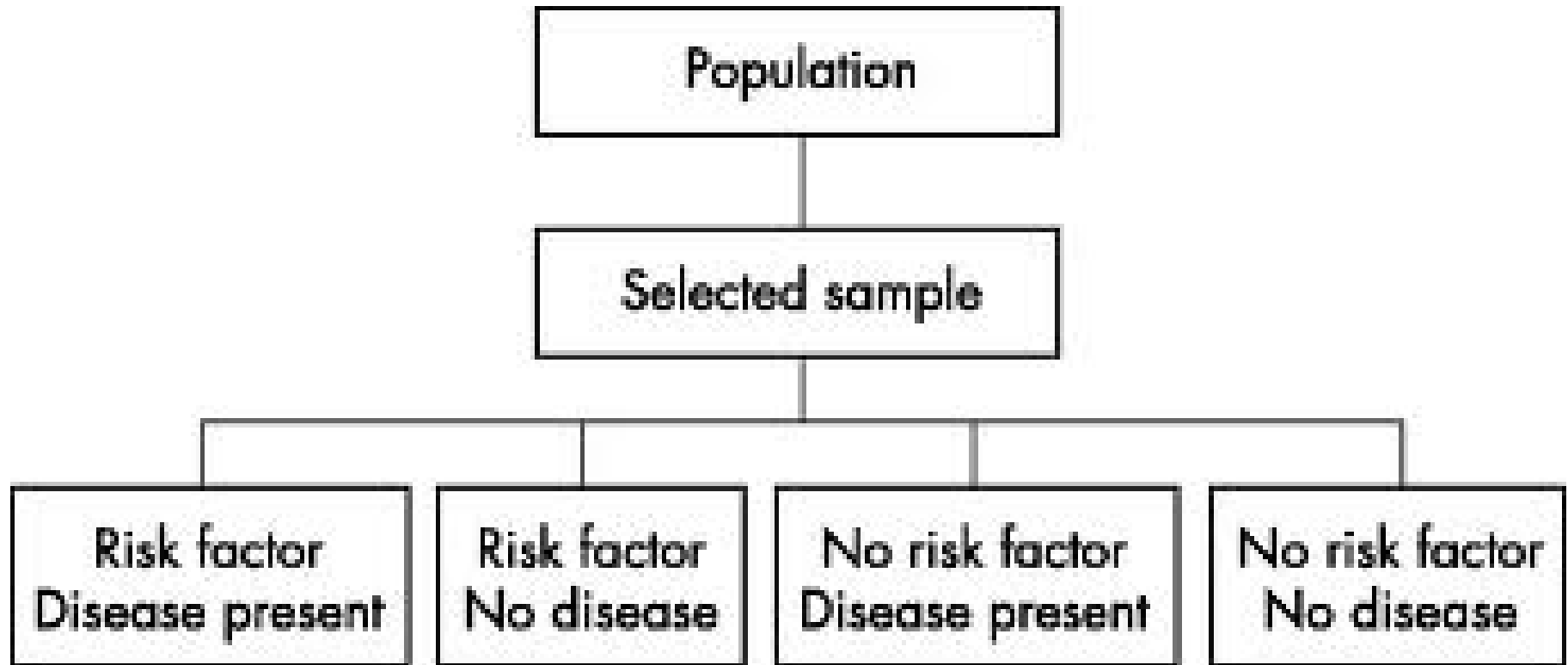
CVD death rates in the Aerobics Center Longitudinal Study according to categories of waist circumference (WC) and the presence or absence of two or more other metabolic syndrome risk factors



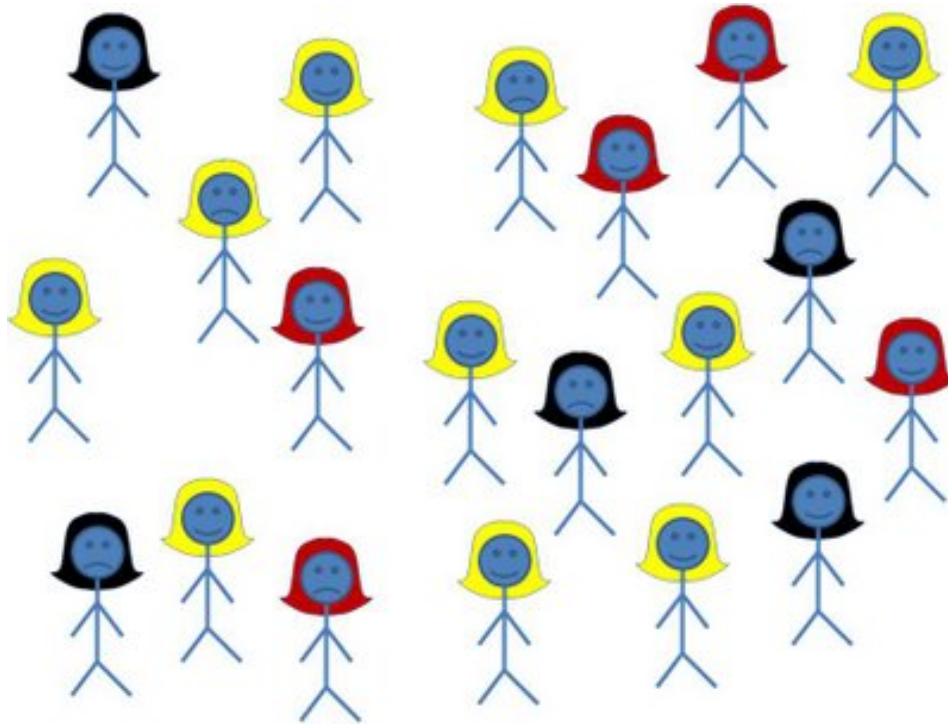
6- Cross-sectional studies

- ▶ A class of research methods that involve observation of all of a population, or a representative subset, at one specific point in time.
- ▶ Aim to provide data on the entire population under study.
- ▶ Are descriptive studies (neither observational nor experimental).
- ▶ Can be used to describe absolute risks and relative risks.
- ▶ May be used to describe some feature of the population, such as prevalence of an illness, or they may support inferences of cause and effect.

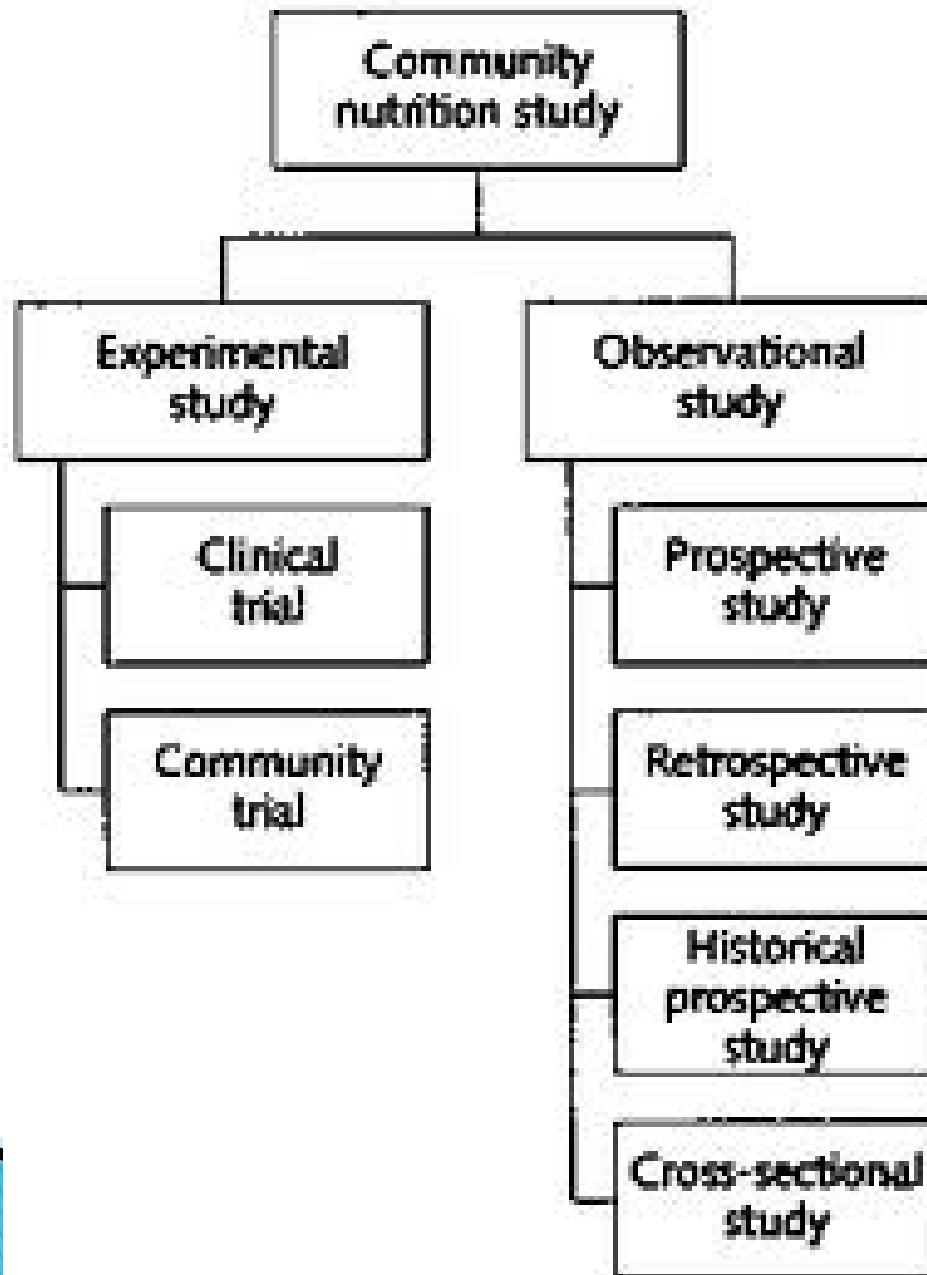
Study design for cross sectional studies



Cross sectional study on hair color and depression



- ▶ 5/10 of the women with dark hair color are depressed (frowning) and 2/10 of the women with blond hair color are depressed. Therefore the prevalence of depression among non-blonds is 50%, and the prevalence of depression among blonds is 20%.



7- Correlational research

- ▶ Examines the covariation of two or more variables.
- ▶ e.g. The early research on cigarette smoking examine the covariation of cigarette smoking and a variety of lung diseases. These two variable, smoking and lung disease were found to covary together.
- ▶ Correlational research can be accomplished by a variety of techniques which include the collection of empirical data.
- ▶ Often times, correlational research is considered a type of observational research as nothing is manipulated by the experimenter or individual conducting the research. For example, the early studies on cigarette smoking did not manipulate how many cigarettes were smoked. The researcher only collected the data on the two variables. Nothing was controlled by the researchers and therefore, no cause and effect statements could be made. Of course, further experimental research clearly demonstrated the negative effects of cigarette smoking.



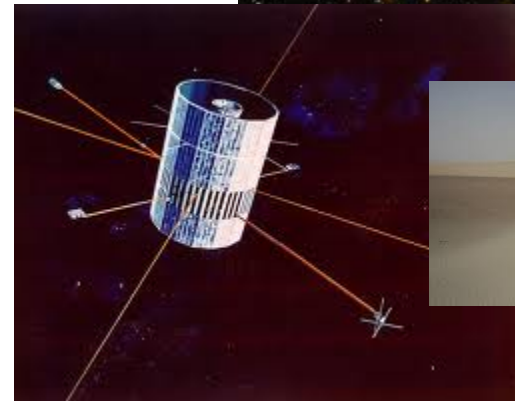
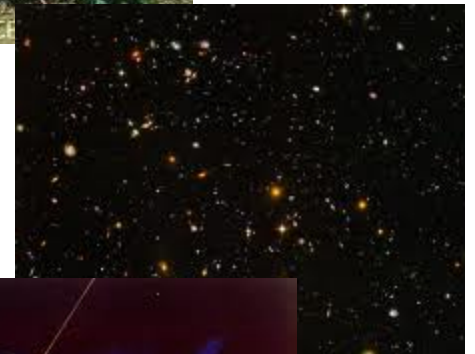
C– Semi-Experimental Designs

Aim: Determine Causes

1. Field Experiment
2. Quasi-Experimental Design
3. Twin Studies

1- Field experiment

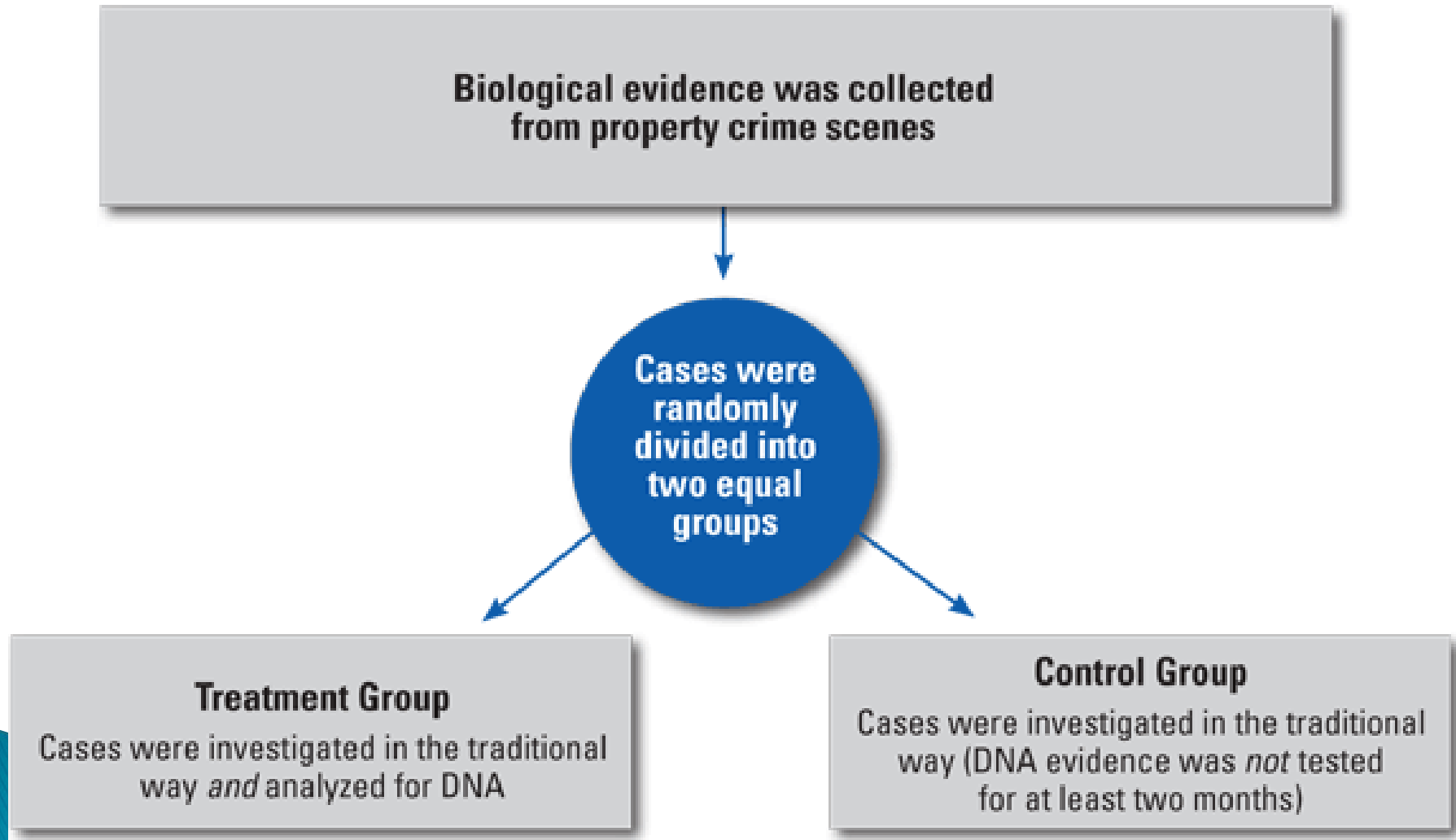
- ▶ Applies the **scientific method** to experimentally examine an intervention in the real world rather than in the laboratory.
- ▶ Field experiments, like lab experiments, generally randomize subjects (or other sampling units) into treatment and control groups and compare outcomes between these groups.
- ▶ Examples include:
 - Clinical trials of pharmaceuticals are example of field experiments.



The need for Potassium fertilization in rice and experiences from a long-term experiment in Indonesia

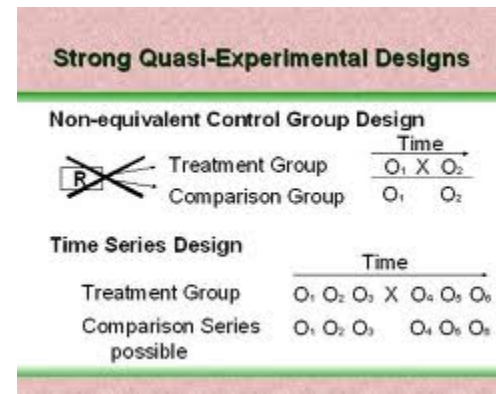
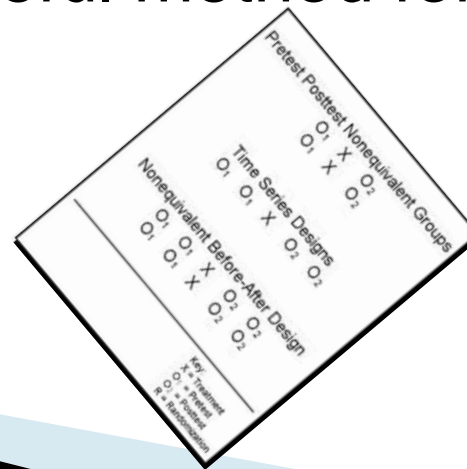


How Did the DNA Field Experiment Work?



2- Quasi-experiment design

- ▶ Involves selecting groups, upon which a variable is tested, without any random pre-selection processes.
- ▶ There is lack of random assignment.
- ▶ This method uses time series analysis, both interrupted and non-interrupted.
- ▶ Whilst regarded as unscientific and unreliable, by physical and biological scientists, the method is, nevertheless, a very useful method for measuring **social variables**.



3-Twin studies

- ▶ Help clarify the relative importance of environmental and genetic influences on individual traits and behaviors.
- ▶ Twin research is considered a key tool in behavioral genetics and related fields.
- ▶ Twins are a valuable source for observation due to their genotypes and family environments tending to be similar.
 - Monozygotic (MZ) or "identical" twins, share nearly 100% of their genetic polymorphisms, which means that most variation in pairs' traits (measured height, susceptibility to boredom, intelligence, depression, etc.) is due to their unique experiences.
 - Dizygotic (DZ) or "fraternal" twins share only about 50% of their polymorphisms. DZ twins are helpful to study because they tend to share many aspects of their environment (e.g., uterine environment, parenting style, education, wealth, culture, community) by virtue of being born in the same time and place.

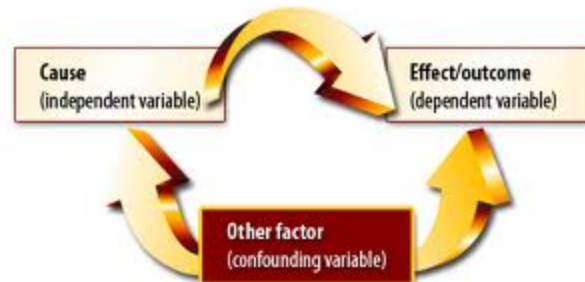
D-Experimental Designs

Aim: Determine Causes

1. True Experimental Design
2. Double-Blind Experiment

1- True Experimental Design

- ▶ **Experimental Research** - An attempt by the researcher to maintain **control over all factors** that may affect the result of an experiment. In doing this, the researcher attempts to determine or predict what may occur.
- ▶ **Experimental Design** - A blueprint of the procedure that enables the researcher to test his hypothesis by reaching valid conclusions about relationships between independent and dependent variables. It refers to the conceptual framework within which the experiment is conducted.



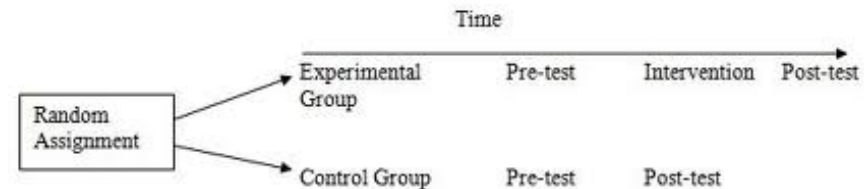
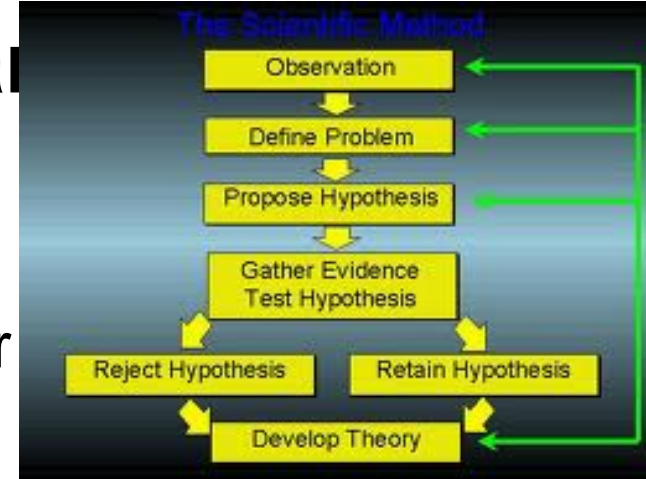
Steps involved in conducting an experimental study

Identify and define the problem.

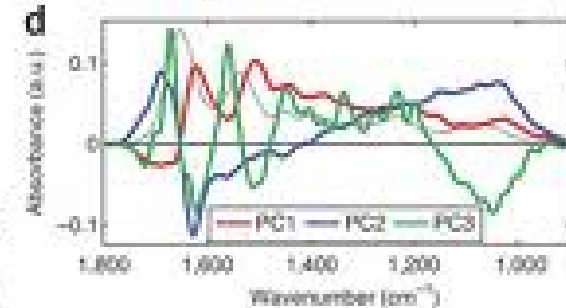
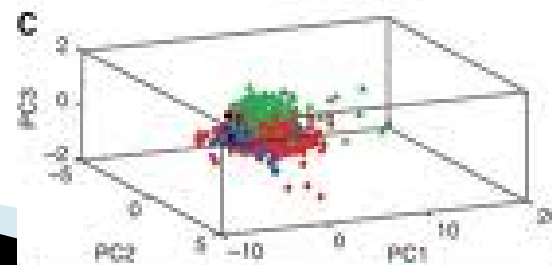
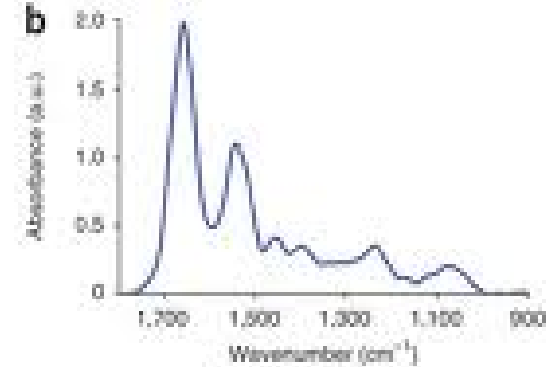
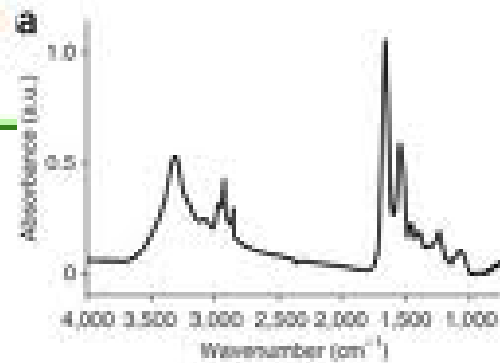
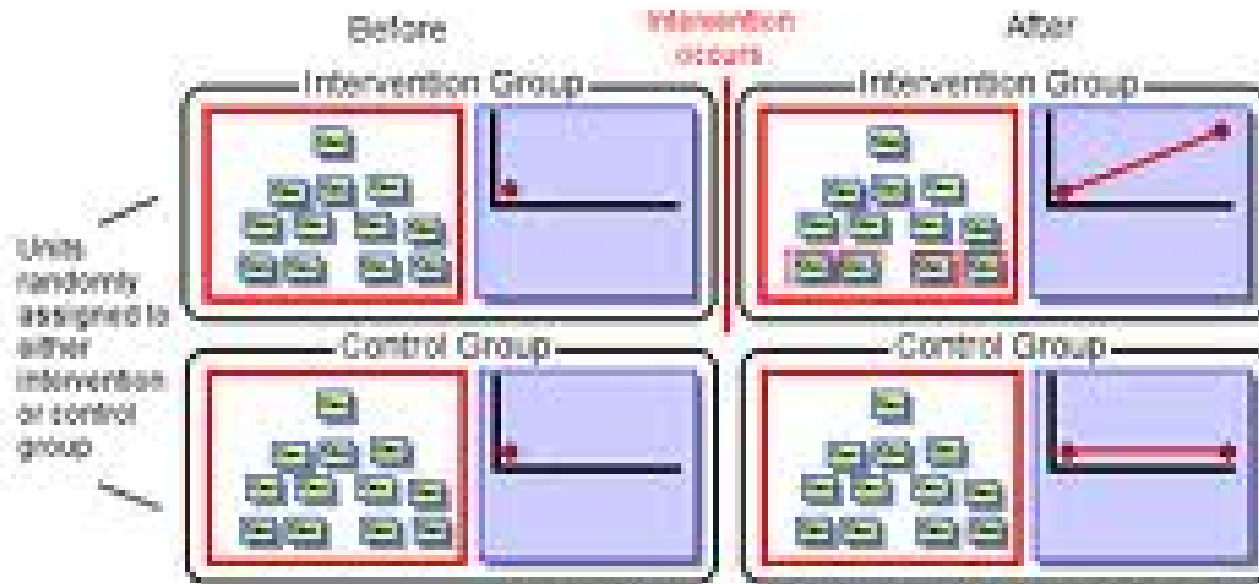
Formulate hypotheses and deduce their consequences.

Construct an experimental design that represents all the elements, conditions, and relations of the consequences.

- Select sample of subjects.
- Group or pair subjects.
- Identify and control non experimental factors.
- Select or construct, and validate instruments to measure outcomes.
- Conduct pilot study.
- Determine place, time, and duration of the experiment.
- Conduct the experiment. Compile raw data and reduce to usable form. Apply an appropriate test of significance.

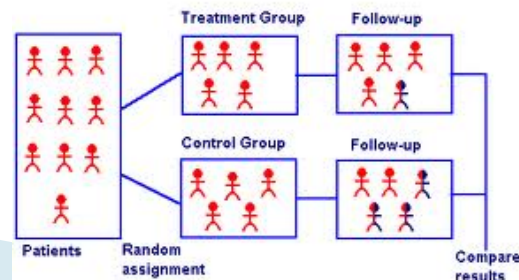


True Experimental Design



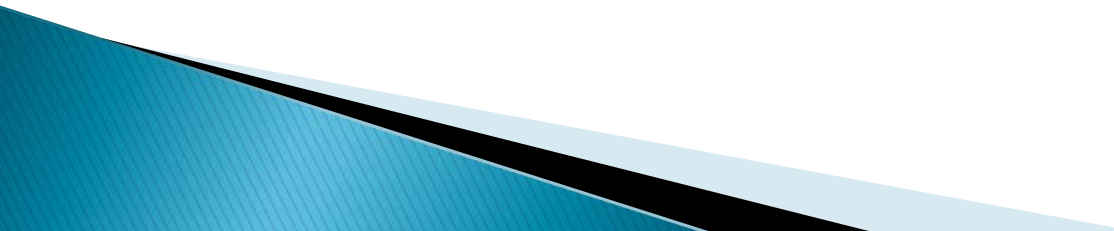
2-Double-Blind Experiment

- ▶ **Blind** or **Blinded** experiment is an experiment where some of the people involved are prevented from knowing certain pieces of information that might lead to conscious or unconscious bias on their part, invalidating the results.
- ▶ In medicine, when testing a new medicine, it is ensured that the placebo looks and tastes the same as the actual medicine.
 - A placebo is a dummy medical intervention that exploits the hope/expectancy effect from the treatment. Ideally, the subjects would not be told that a placebo was being used at all, so the patients cannot subconsciously be influenced, as they are not aware if the impact is because of the drug or the *placebo effect*.



E- Reviewing Other Research

Aim: Explain

- ▶ Literature Review
 - ▶ Meta-analysis
 - ▶ Systematic Reviews
- 

F- Test Study Before Conducting a Full-Scale Study

Aim: Does the Design Work?

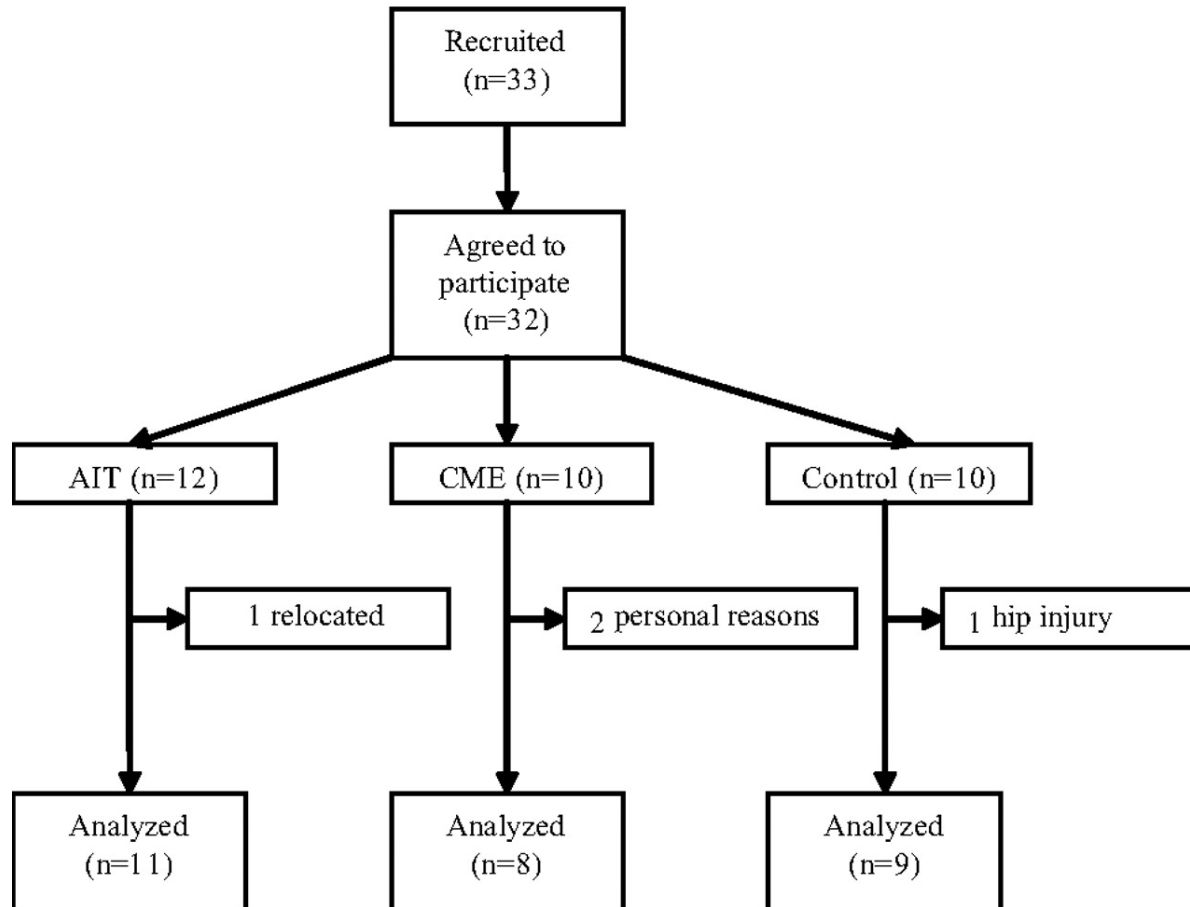
1. **Pilot Study**

A small scale preliminary study conducted in order to evaluate feasibility, time, cost, adverse events, and effect size (statistical variability) in an attempt to predict an appropriate sample size and improve upon the study design prior to performance of a full-scale research project.

Frequently carried out before large-scale quantitative research, in an attempt to avoid time and money being wasted on an inadequately designed project.

Figure 1. Flow chart of the study design.

FLOW CHART



Tjønnå A E et al. *Circulation* 2008;118:346-354

TYPICAL EXPERIMENTAL DESIGNS

SIMPLE EXPERIMENTAL TECHNIQUES

- ▶ Pretest-Posttest Design
- ▶ Control Group
- ▶ Randomization
- ▶ Randomized Controlled Trials
- ▶ Between Subjects Design
- ▶ Within Subject Design

COMPLEX EXPERIMENTAL DESIGNS

- ▶ Factorial Design
- ▶ Solomon Four-Group Design
- ▶ Repeated Measures Design
- ▶ Counterbalanced Measures Design
- ▶ Matched Subjects Design
- ▶ Bayesian Probability

