Screening and Epidemiology

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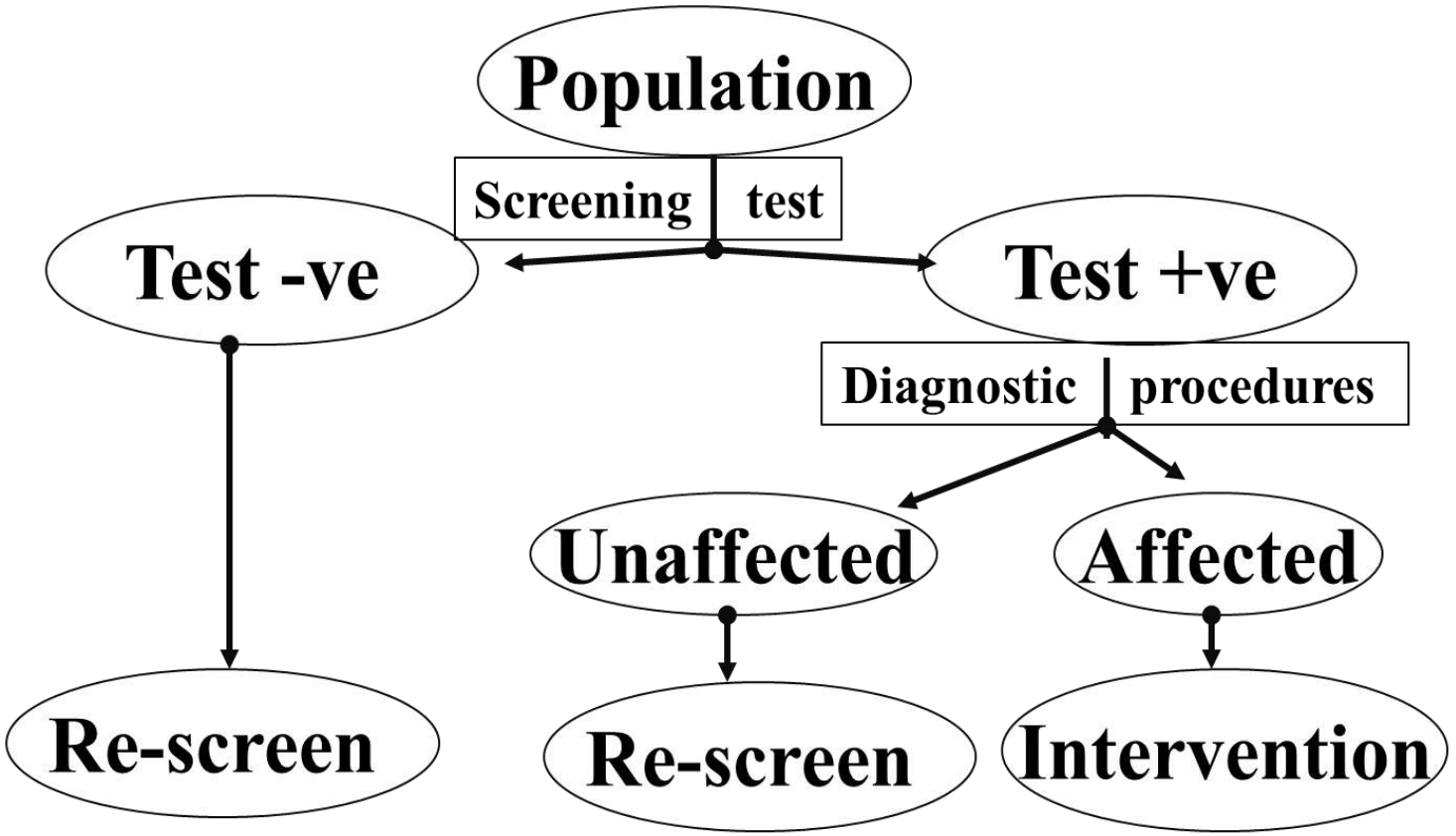
Screening

- Is the testing of apparently healthy populations to identify previously undiagnosed diseases or people at high risk of developing a disease.
- Screening aims to detect early disease before it becomes symptomatic. It is an important aspect of prevention, but not all diseases are suitable for screening.

Screening

Flow diagram for a screening program



The Principles of Screening

- The choice of disease for which to screen;
- The nature of the screening test or tests to be used;
- The availability of a treatment for those found to have the disease;
- The relative costs of the screening.

Types of screening

- **Mass** involves screening a large population (e.g., chest x-rays for TB).
- **Multiple or multiphasic *screening*** involves the use of several screening tests on the same occasion (e.g., an annual health check-up).
- **Targeted *screening*** of groups with specific exposures is often used in environmental and occupational health (e.g., battery workers).

Types of screening cont.

- **proactive or systematic screening:** population registers are used to invite members of the population at risk for screening at appropriate intervals
- **Case-finding or opportunistic** is a form of screening restricted to patients who consult a health practitioner for some other purpose (the GP may take your blood pressure when you come for your 'flu shot).

Factors appropriate for screening

- Important health problem
- High prevalence
- Natural history understood
- Long latent period
- Early detection improves prognosis

Evaluation of a screening program

- **Reliability** (consistent)
- **Feasibility**
- **Validity** (distinguishes diseased & non-diseased people)
- **Performance**
- **Effectiveness**

Reliability

- **Biological variability** (BP normally varies within an individual).
- **Instrument variability** (is the sphygmomanometer reliable).
- **Intra-observer variability** (does a given tester perform the test the same way each time).
- **Inter-observer variability** (do different teste perform the test the same way each time).

Feasibility

- Acceptability
  - Quick
  - Easy
  - Safe

Cost effectiveness

- Screening
- Diagnosis
- Follow-up
- Intervention

Validity

- **VALIDITY** refers to what conclusions we can draw from the results of a measurement. Introductory-level definitions are "Does the test measure what we are intending to measure?", or "How closely do the results of a measurement correspond to the true state of the phenomenon being measured?

Validity of a screening test.

- This can be used to illustrate the way validity is assessed. Here, it is commonly reported in terms of sensitivity and specificity.
- **Sensitivity** refers to what fraction of all the actual cases of disease a test detects. If the test is not very good, it may miss cases it should detect. Its sensitivity is low and it generates "false negatives" (i.e., people score negatively on the test when they should have scored positive). This can be extremely serious if early treatment would have saved the person's life.

- **Specificity** refers to whether the test identifies *only* those with the disease, or does it mistakenly classify some healthy people as being sick? Errors of this type are called "false positives." This can lead to worry and expensive further investigations.

Performance

- **PV+:** Probability to be affected among test positives
- **PV-:** Probability to be unaffected among test negatives
- **PCC:** Probability to be correctly classified

Effectiveness

- **Outcome measures:**
  - Morbidity
  - Disability
  - Mortality

Bias

- **Patient self-selection**

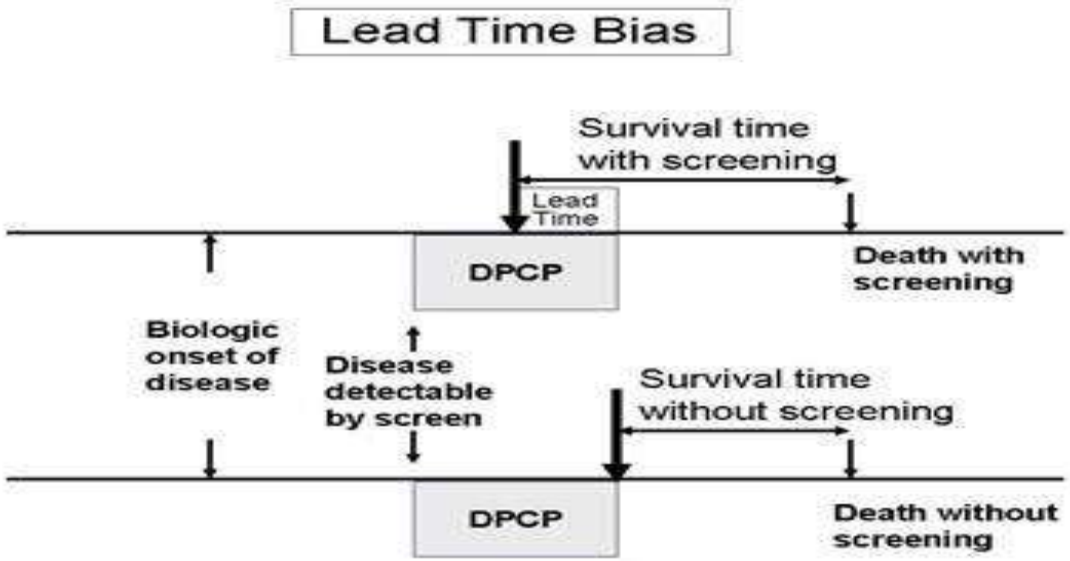
People who choose to participate in screening programs tend to be healthier, have healthier lifestyles, and they tend to adhere to therapy better, and their outcomes tend to be better because of this.

Random errors are considered part of the ***reliability*** of a measurement. **Systematic errors** are considered part of the ***validity*** of a measurement.

- **Lead time**

  The premise of screening is that it allows you to identify disease earlier, so you can initiate treatment at an early stage in order to effect cure or at least longer survival. Screening can give you a jump on the disease; this "lead-time" is a good thing, but it can bias the efficacy of screening. The two subjects to the right have the same age, same time of disease onset, the same "detectable pre-clinical phase" DPCP, and the same time of death. However, if we compare survival time from the point of diagnosis, the subject whose disease was identified through screening appears to survive longer, but only because their disease was identified earlier.

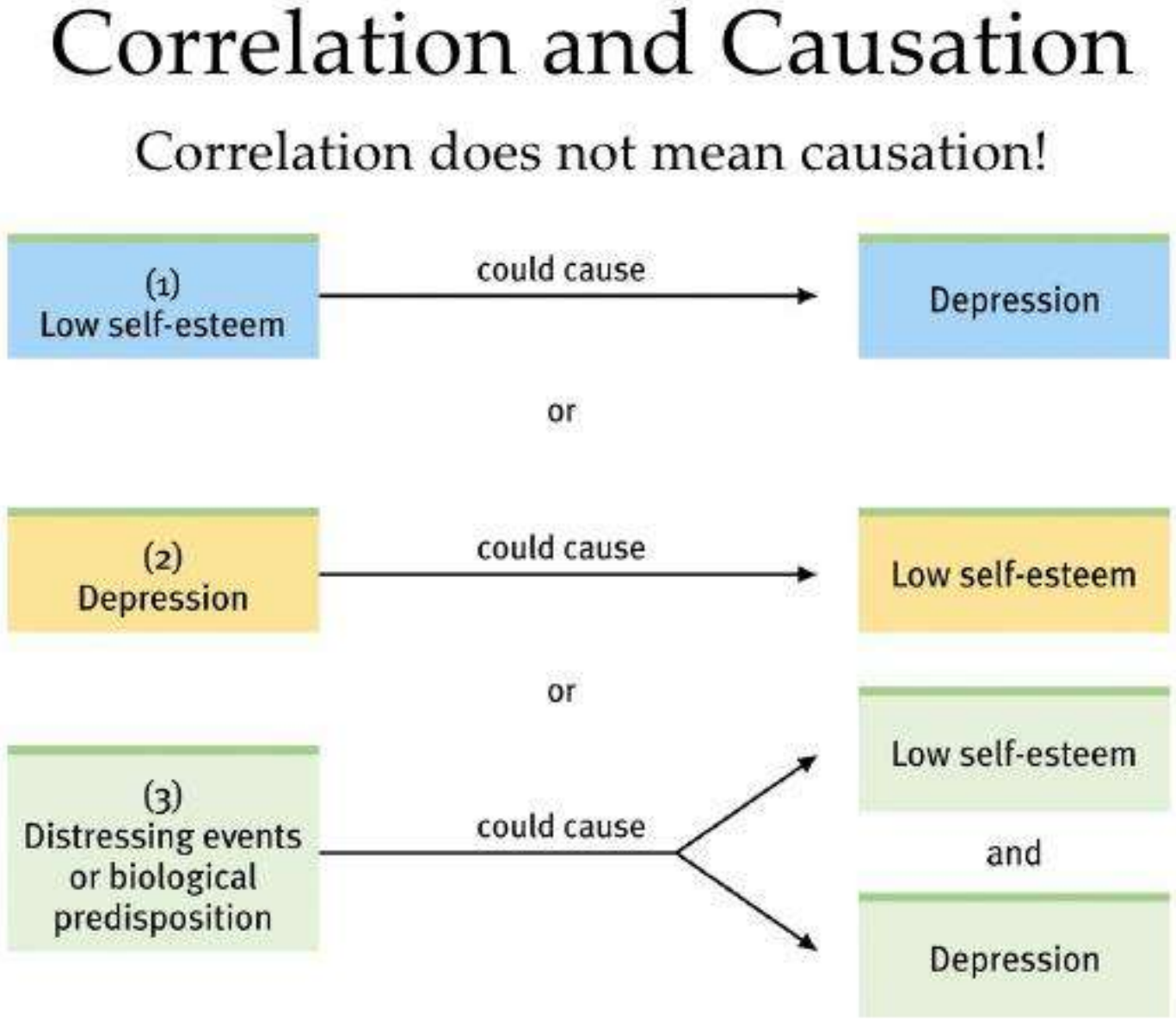
- **Length**


Lead Time Bias
Survival time with screening
Lead Time
DPCP
Death with screening
Biologic onset of disease
Disease detectable by screen
Survival time without screening
DPCP
Death without screening

Study designs for screening

- **1. Correlation Studies**
- **Use:** Description of population
- **Strength:** Suggest possibility of benefit
- **Limitation:** Can't test hypothesis

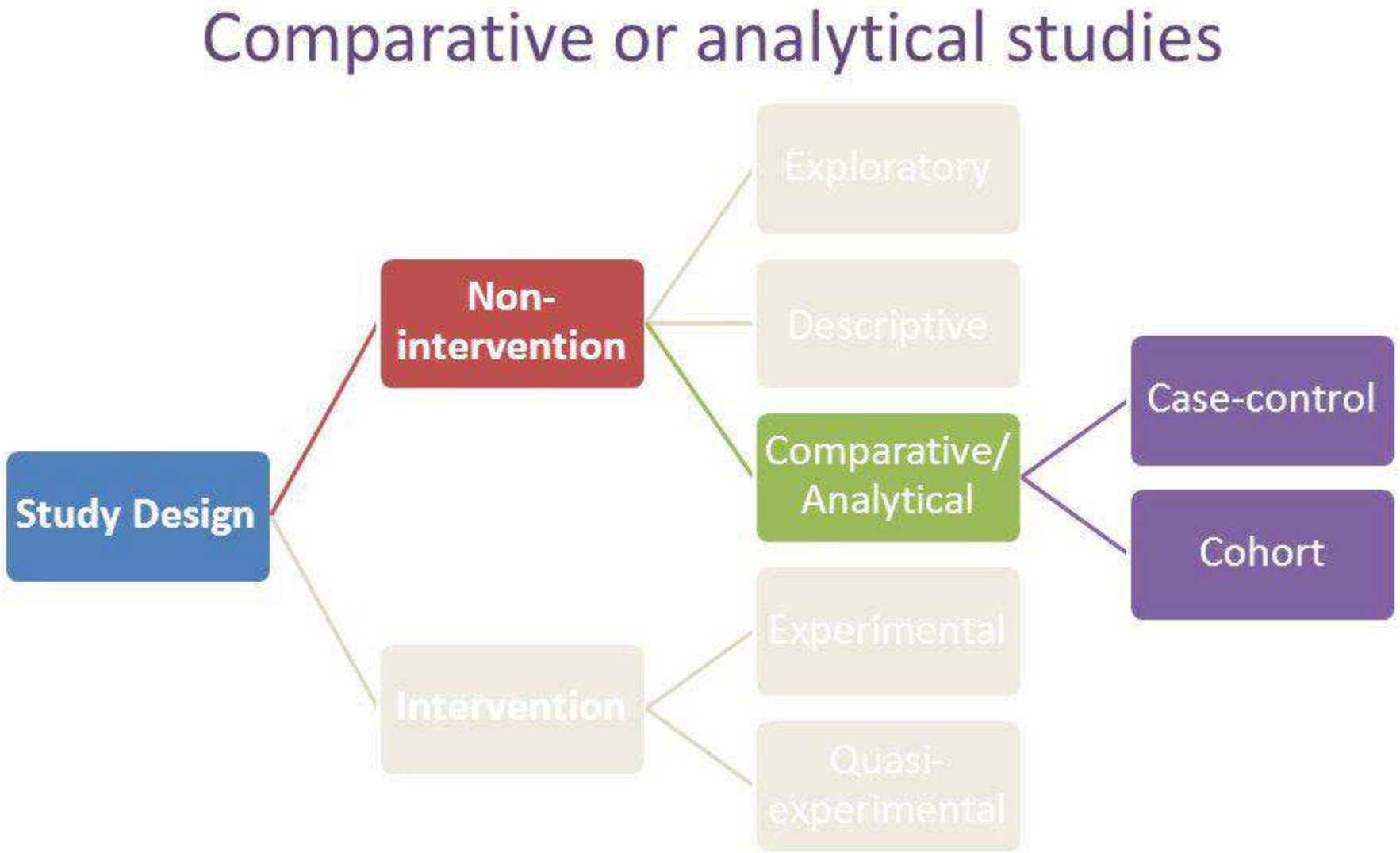
Correlation Studies



Study designs for screening

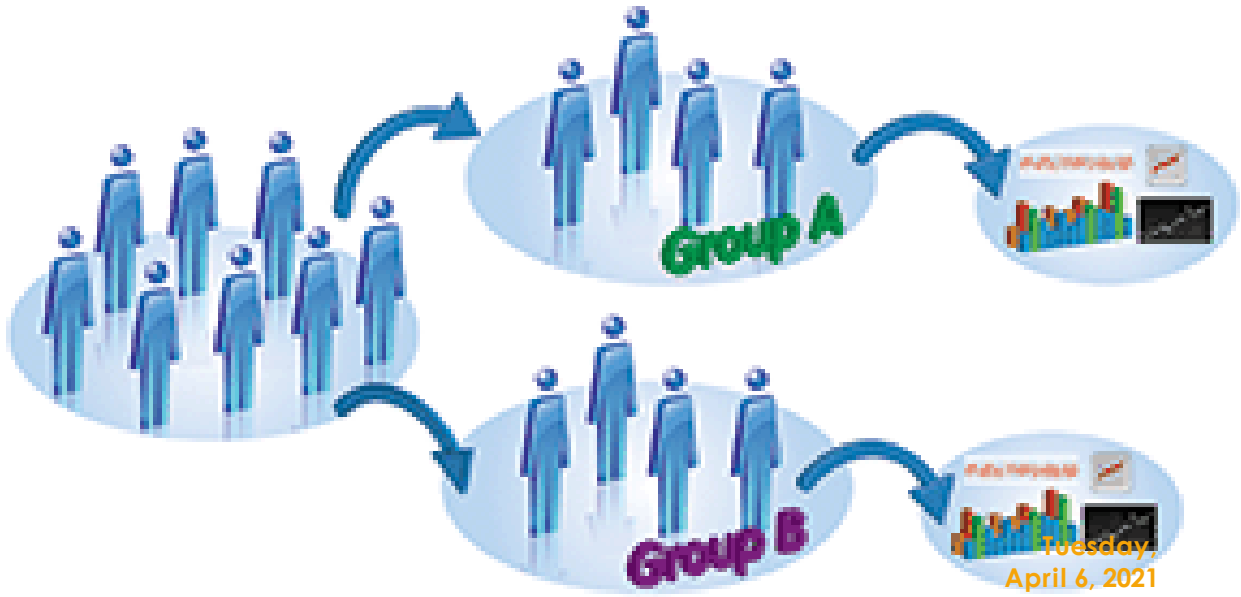
- **2. Analytical Studies**
- **Types:** Case-control and Cohorts
- **Use:** Comparison of rates
- **Advantage:** Test hypothesis
- **Limitation:** Selection, Lead time and length

- **2. Analytical Studies**



Study designs for screening

- **3. Randomized Trials**
- **Use:** Comparison of rates
- **Strength:** Most valid test of hypothesis
- **Limitation:** Cost, ethics & feasibility

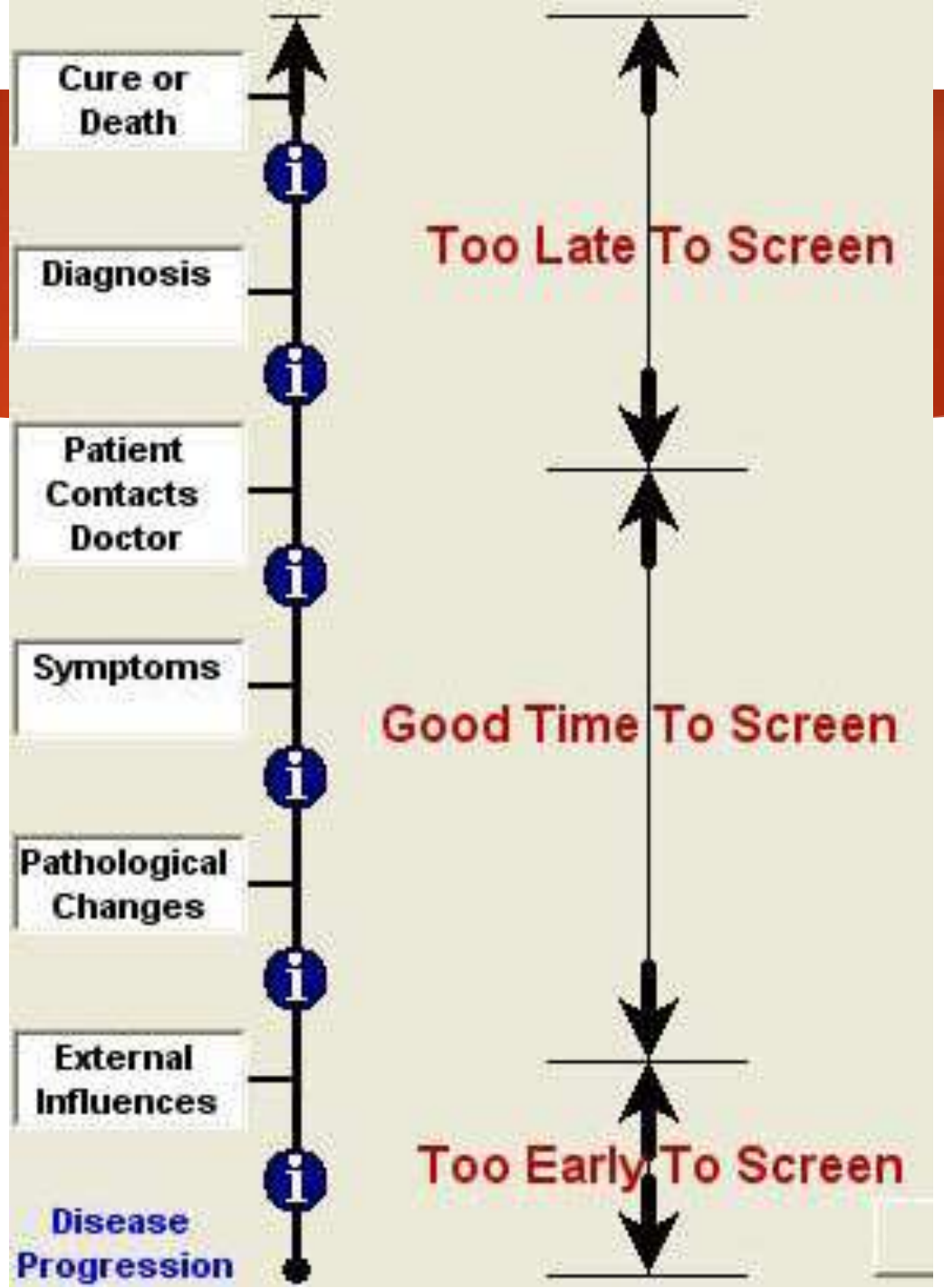


When to screen for disease?

When to screen for disease?

- The disease must be an important health problem.
- There should be a recognizable latent or early symptomatic stage.
- The natural history of the disease, including latent to declared disease, should be adequately understood.

When to screen for disease?



Test :

- **There should be a suitable test or examination.**
- **The test should be acceptable to the population.**

Screening Test	True Disease Status: Positive	True Disease Status: Negative	Total
Positive	True Positives (TP)	False Positives (FP)	TP+FP
Negative	False Negatives (FN)	True Negatives (TN)	FN+TN
Total	TP+FN	FP+TN	TP+FP+FN+TN

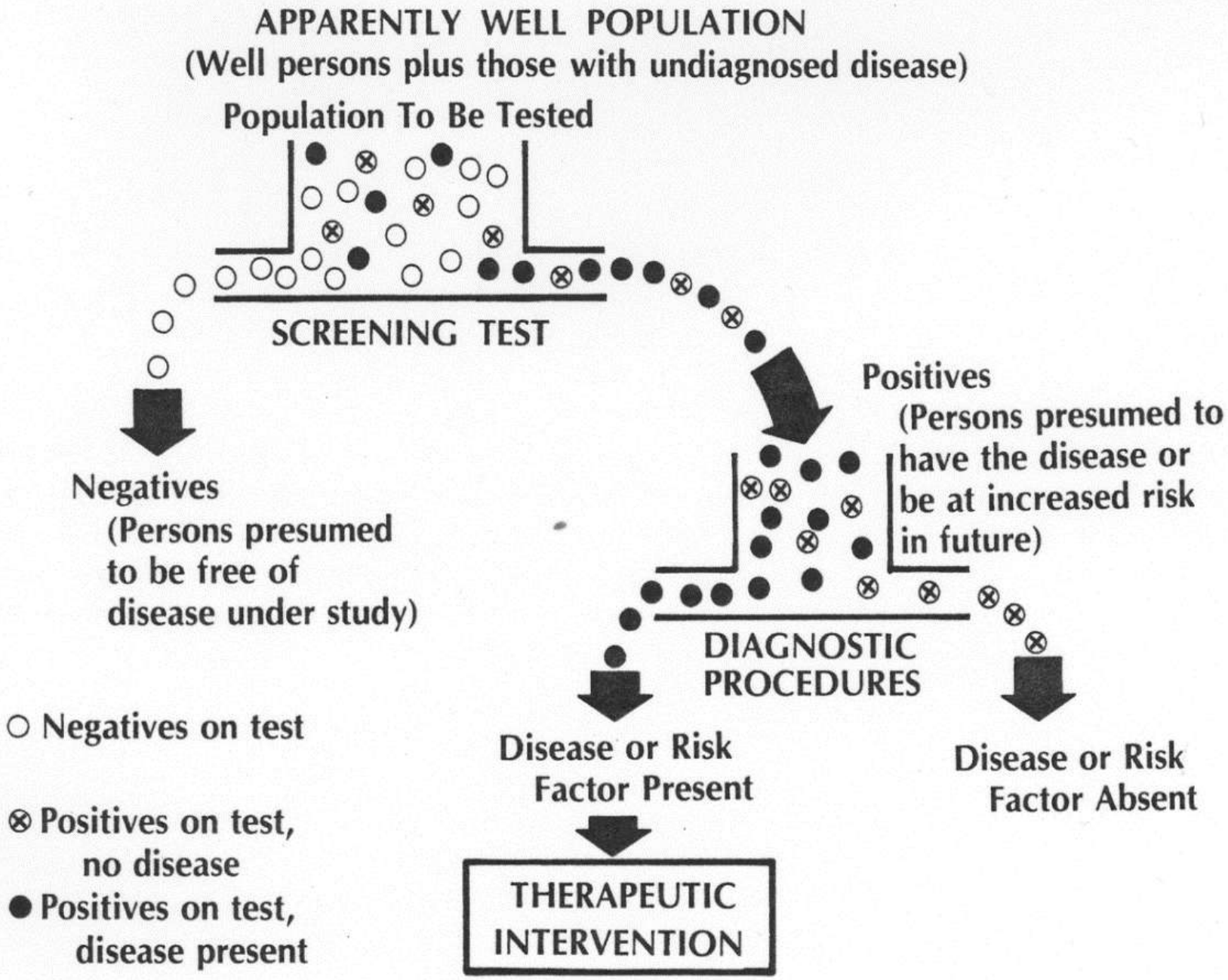
Outcomes of a Screening Test

Treatment:

- There should be an acceptable treatment for the patients with recognized disease.
- There should be facilities for diagnosis and treatment should be available.
- There should be an agreed policy on whom to treat as patients.

Costs :

- The cost of case finding (including diagnosis and treatment of patients diagnosed) should be economically balanced in relation to possible expenditure on medical care as a whole.


APPARENTLY WELL POPULATION
(Well persons plus those with undiagnosed disease)
Population To Be Tested
SCREENING TEST
Negatives
(Persons presumed
to be free of
disease under study)
Positives
(Persons presumed to
have the disease or
be at increased risk
in future)
DIAGNOSTIC
PROCEDURES
Disease or Risk
Factor Present
Disease or Risk
Factor Absent
THERAPEUTIC
INTERVENTION
○ Negatives on test
⊗ Positives on test,
no disease
● Positives on test,
disease present

Examples

Assume a population of 1,000 people

- 100 have a disease
- 900 do not have the disease
- A screening test is used to identify the 100 people with the disease
- The results of the screening appears in this table

Screening Results	True Characteristics in Population		Total
	Disease	No Disease	
Positive	80 (a)	100 (b)	180
Negative	20 (c)	800 (d)	820
Total	100	900	1,000

Calculating sensitivity and specificity

Screening Results	True Characteristics in Population		Total
	Disease	No Disease	
Positive	80 (a)	100 (b)	180
Negative	20 (c)	800 (d)	820
Total	100	900	1,000

Sensitivity = a/a+c

Sensitivity =80/80+20 = 80%

Specificity =d/d+b

Specificity = 800/800+100 = 89%

Predictive values

Positive predictive value (PPV)

- – The proportion of patients who test positive who actually have the disease

Negative predictive value (NPV)

- – The proportion of patients who test negative who are actually free of the disease

Note: PPV and NPV are not fixed characteristics of the test

Another interpretation of PPV

- If a person tests positive, what is the probability that he or she has the disease?
  „ (And if that person tests negative, what is the probability that he or she does not have the disease?)

Predictive values

- Positive predictive value $= \frac{a}{a+b} = \frac{\text{True Positives}}{\text{Test +}}$
- Negative predictive value $= \frac{d}{c+d} = \frac{\text{True Negatives}}{\text{Test –}}$

Applying concepts of predictive values to screening test

Assume a population of 1,000 people

- 100 have a disease
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Calculating Predictive Values

Screening Results	True Characteristics in Population		Total
	Disease	No Disease	
Positive	80 (a)	100 (b)	180
Negative	20 (c)	800 (d)	820
Total	100	900	1,000

Positive predictive value = a/a+b 80/100+80 = 44%

Negative predictive value = d/d+c 800/800+20 = 98%

PPV primarily depends on

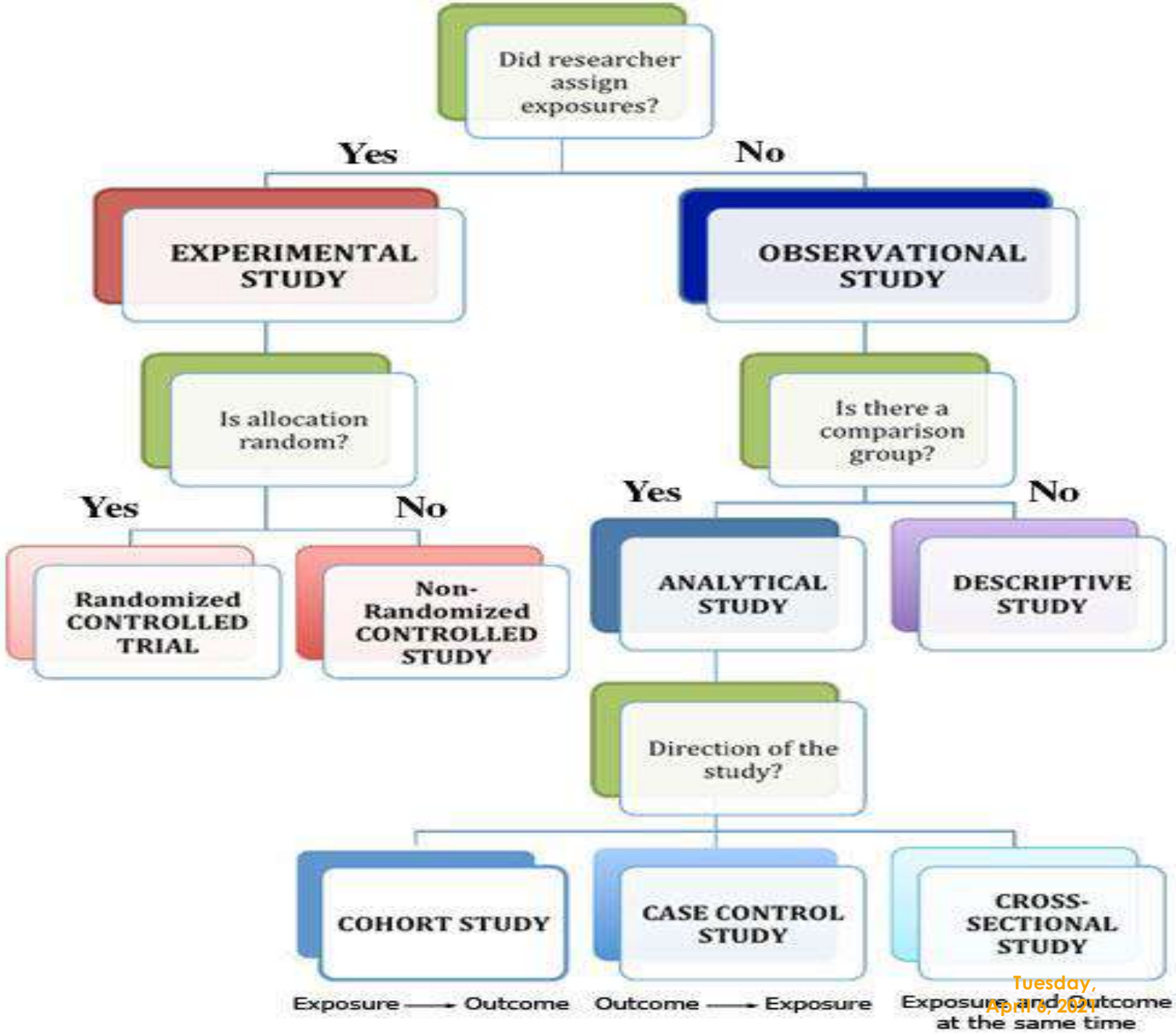
- The prevalence of the disease in the population tested, and the test itself (sensitivity and specificity)
- In general, it depends more on the specificity (and less on the sensitivity) of the test (if the disease prevalence is low)

Epidemiology

Epidemiology

- Is the study of the distribution and determinants of health-related states. or events (diseases) in specified populations and the application of this study to the control of health problems.

Types of Epidemiological Studies:



Observational Studies: Descriptive & Analytical Types

- **Observational studies** involve no intervention other than asking questions and carrying out medical examinations and simple laboratory tests or X-ray examinations.
- **In epidemiology**, observational studies are more common than experimental ones, particularly if an investigator wants to determine whether an agent or exposure causes cancer in humans.

Descriptive Studies

Descriptive studies are observational studies which describe the patterns of disease occurrence in relation to variables such as person, place and time. They are often the first step or initial enquiry into a new topic, event, disease or condition.

Descriptive Studies cont.

Descriptive studies do not have a comparison (control) group which means that they do not allow for inferences to be drawn about associations, casual or otherwise. However, they can suggest hypotheses which can be tested in analytical observational studies.

Descriptive Studies

- **Descriptive studies** tend to be simpler and easier to conduct than analytical or experimental studies but they are nonetheless quite important.
- **Descriptive studies** can provide the background from which analytical studies emerge.
- They help to generate hypotheses, as opposed to testing them.

Descriptive Studies

Advantages:

- A large range of outcomes because no subgroups are studied
- A large range of potential predictors again because no subgroups are studied

Descriptive Studies cont.

Disadvantages:

- Not possible to study subgroups
- No control for confounding as data is in aggregate form
- Not able to reproduce/replicate results as data was not collected in an experiment with defined perimeters.

Cross-Sectional Comparison Studies: "Am I like my neighbors?"

- **Cross-sectional studies** compare data that are combined from smaller groups as opposed to very large descriptive studies. These studies focus on observations made at only one point in time so they are quickly completed and relatively inexpensive. But they cannot reveal a sequence of events over time since they sample data only once.

Cross-Sectional Comparison Studies:

- Advantages
  - They cut across the general population, not simply those seeking medical care.
  - Good for identifying prevalence of common outcomes, such as arthritis, blood pressure or allergies.

- Limitations
  - Cannot determine whether exposure preceded disease.
  - It considers prevalent rather than incident cases, results will be influenced by survival factors.

Correlation (Ecologic) Studies: "What if I am exposed to this?"

- Ecologic studies look at diet and cancer at the population level, think of this as the view from 30,000 feet. These types of studies represent a transition to analytical studies since they compare cancer rates of populations in relation to risk factors.
- They do not include outcome so they aren't considered analytical.

Correlation (Ecologic) Studies:

Most epidemiological investigations of etiology are **observational**. They look for associations between the occurrence of disease and exposure to known or suspected causes. **In ecological studies** the unit of observation is the population or community.

Why do ecologic studies?

- Low cost and convenience.
- Some measurements cannot be made on individuals.
- Ecologic effects are the main interest (at the population level).
- Simplicity of analyses and presentation.
- Often helpful for generating new hypotheses for further research.

Correlation (Ecologic) Studies: "What if I am exposed to this?"

Examples:

- The diet-cancer correlation.
- Following populations as they migrate to compare cancer rates.

Correlation (Ecologic) Studies: "What if I am exposed to this?"

Advantages:

- Ecologic studies can provide powerful clues pointing in a particular direction, especially when they compare large populations with different diets.

Correlation (Ecologic) Studies: "What if I am exposed to this?"

Disadvantages:

- Ecologic studies can't prove cause and effect.
- Scientists need more evidence from other studies to help prove the connection that ecologic studies point to.

Analytical Studies

- **Analytical studies** measure both disease-related outcomes and risk factors. The vast majority (>99%) of all epidemiological studies in the medical literature fall into this category.
- **The advantages and disadvantages** of these types of studies are the converse of those listed for descriptive studies.

Analytical Studies

Advantages:

- The ability to focus on subgroups
- The ability to control for confounding
- Possible to reproduce/replicate results

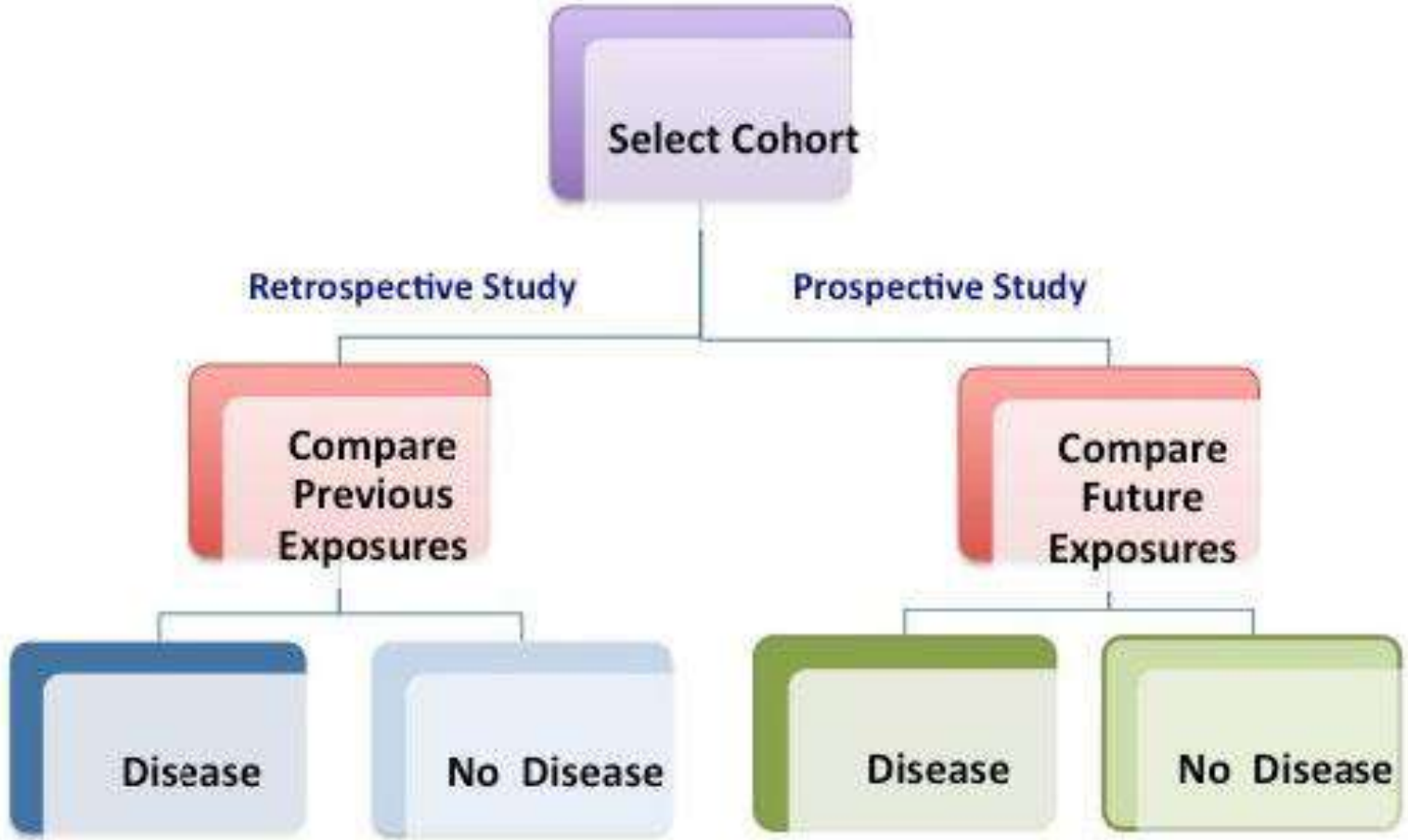
Disadvantages:

- Limited variability in disease rates
- Narrow range of potential predictors

Cohort Studies:
"What will happen to me"?

- **In cohort studies** investigators compare populations that are assumed to be similar except that they have different exposures to factors of interest (e.g., diet, exercise, sun, asbestos, cigarette smoke), and determine whether or not the prevalence (likelihood) of getting the disease varies with exposure.

Cohort Studies:
"What will happen to me"?



Cohort Studies:
"What will happen to me"?

- **Prospective studies** begin prior to the exposure and study the population over time.

Cohort Studies: "What will happen to me"?

- **Epidemiologists** then looked at the lifestyle data gathered to determine whether there were any factors that were different among those who did versus did not develop the disease.
- **Historical or retrospective studies** look back in time for patterns of exposure that may have differed among the groups.

Cohort Studies:
"What will happen to me"?

- These studies look at groups of people who have or have not developed a disease and compare them. When these studies rely on health or occupational records they can be very useful. However, when they are based on subjects' memories, they may be less reliable.