Epidemiological Study Design

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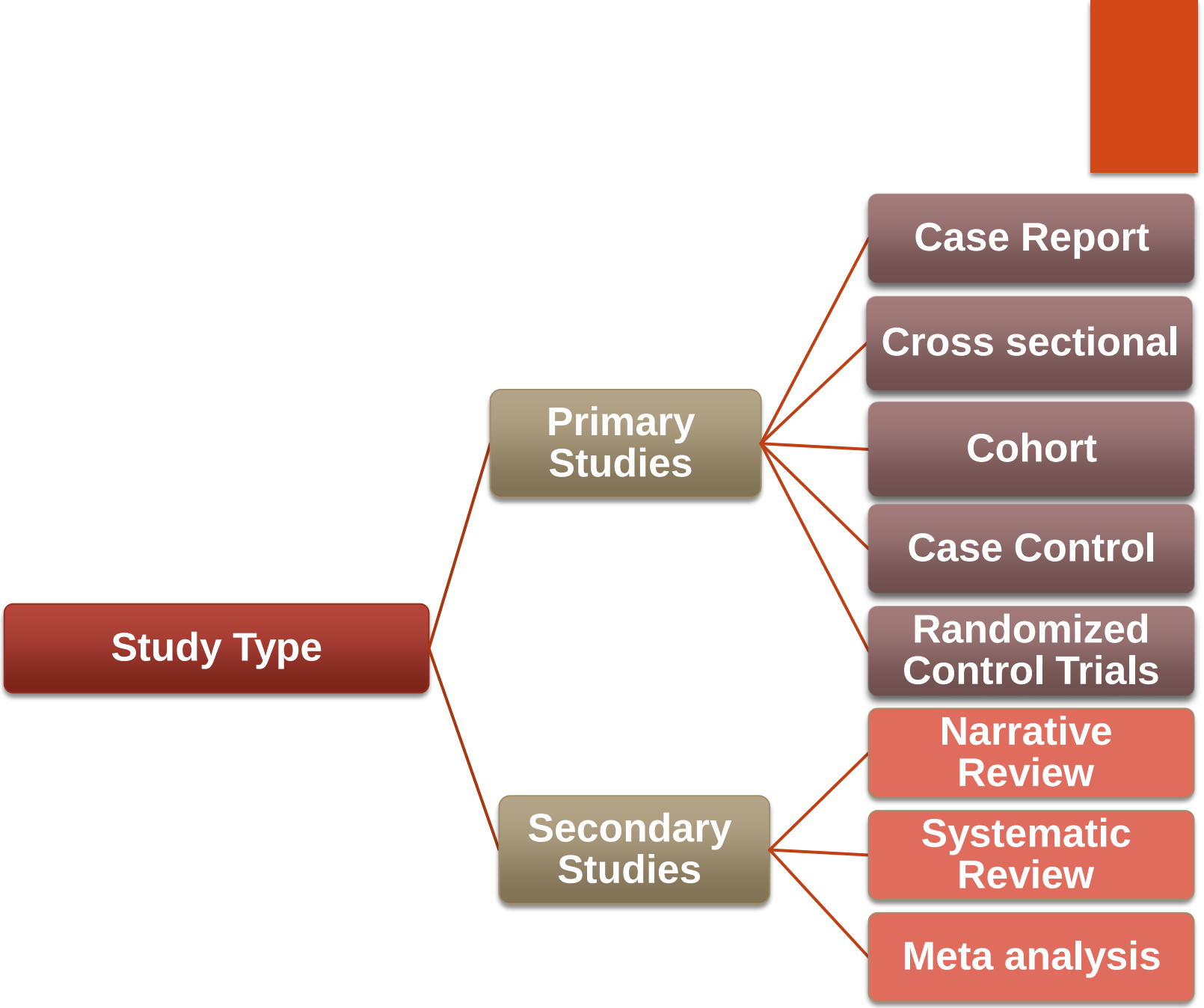
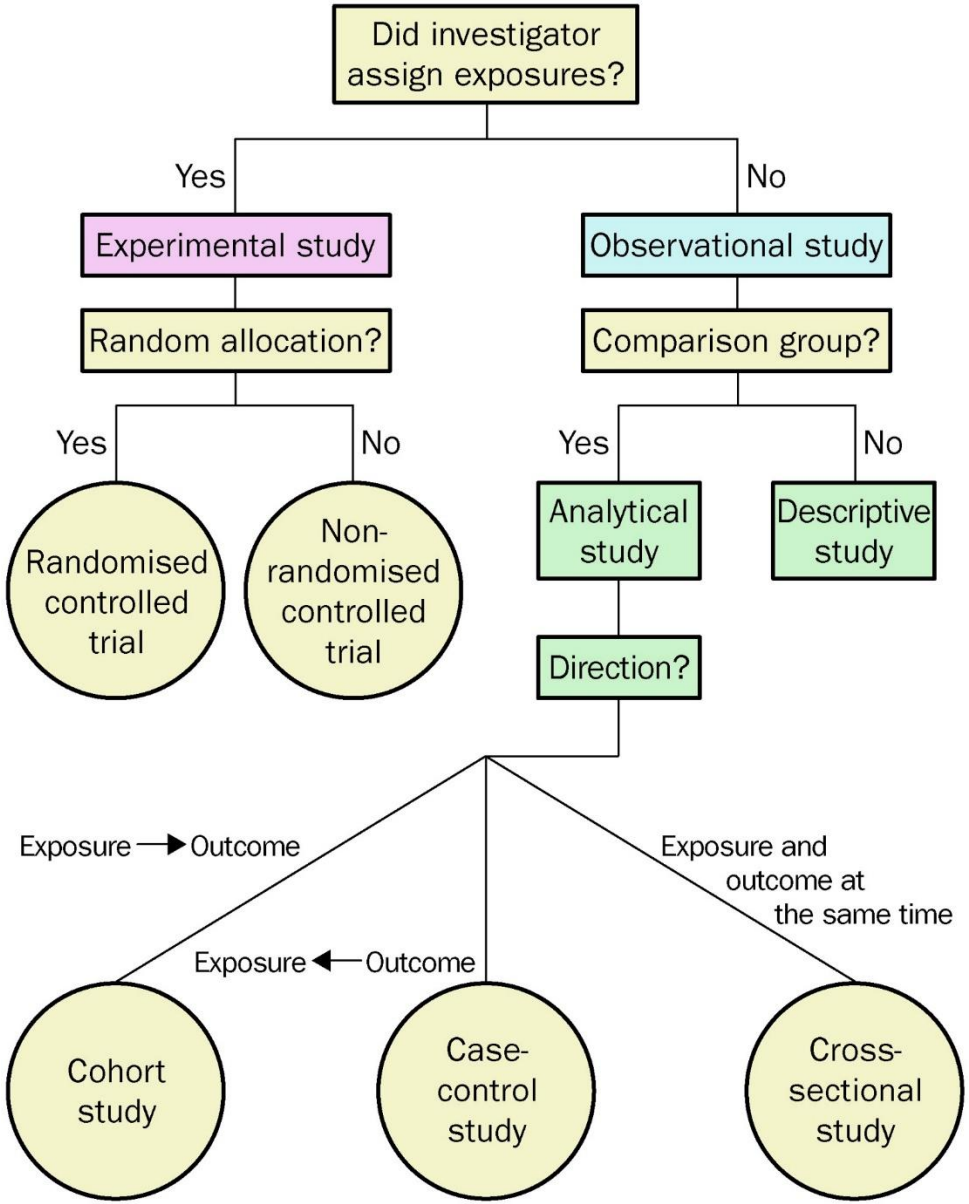

Study Type
Primary Studies
Case Report
Cross sectional
Cohort
Case Control
Randomized Control Trials
Secondary Studies
Narrative Review
Systematic Review
Meta analysis

Primary Study Design



Grimes DA and Schulz KF 2002. An overview of clinical research. Lancet 359:57-61.

Evidence pyramid

Case Report
and
Case Series

Case Report

- An article that describes and interprets an individual case, often written in the form of a detailed story. Case reports often describe:
  - Unique cases that cannot be explained by known diseases or syndromes
  - Cases that show unexpected events that may yield new or useful information
  - Cases in which one patient has two or more unexpected diseases or disorders
- The patient should be described in detail, allowing others to identify patients with similar characteristics.
  - patient's age, sex, ethnicity, race, employment status, social situation, medical history, diagnosis, prognosis, previous treatments, past and current diagnostic test results, medications, psychological tests, and clinical and functional assessments

Ecological Studies

Ecological study

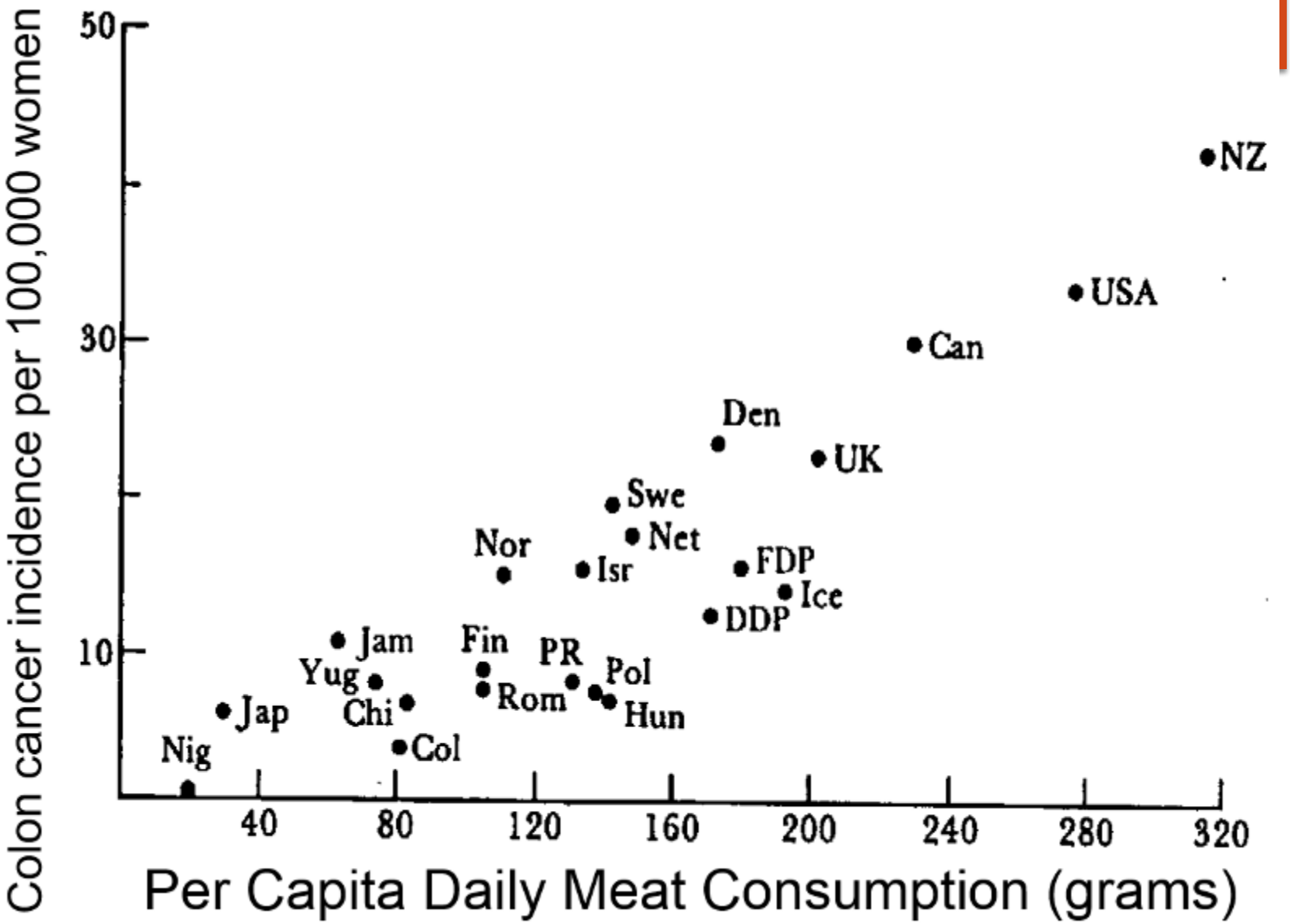
- Unit of analysis is group or population, rather than individuals (schools, factories, nations)
- Compare aggregate measure of health outcome with aggregate measure of exposure
- Generally based on existing data

Advantages

- Can be done quickly and inexpensively
- May be able to identify associations by examining a greater range in exposure

Disadvantages

- Ecological fallacy: Cannot link exposure with disease in individuals
- Difficult to control confounding factors


Colon cancer incidence per 100,000 women
50
30
10
NZ
USA
Can
Den
UK
Swe
Net
Nor
Isr
FDP
Ice
DDP
Jam
Fin
PR
Pol
Yug
Rom
Hun
Jap
Chi
Col
Nig
40
80
120
160
200
240
280
320
Per Capita Daily Meat Consumption (grams)

Cross Sectional Studies

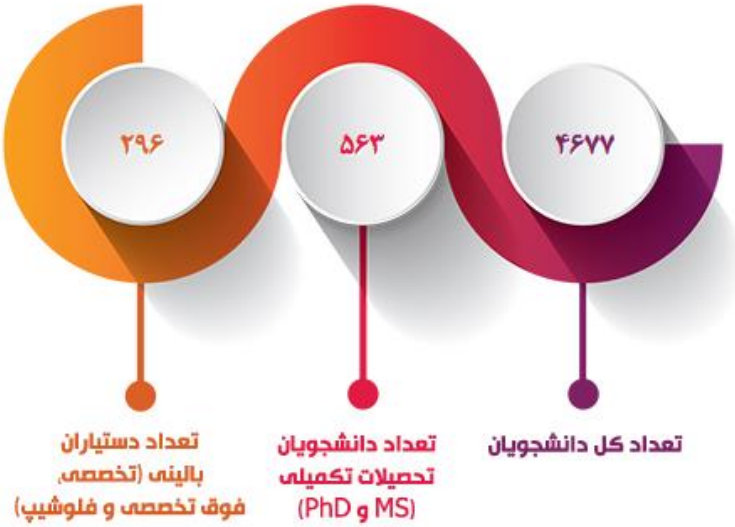
Cross Sectional Study

- Cross-sectional studies simultaneously measure the exposure and health outcome in a given population and a given geographical area at a certain time.
- Estimate prevalence or mean. (Cross-sectional studies are also called prevalence studies.)
- Determine associations: Examine characteristics associated with a condition or disease by comparing cases to non-cases

The main steps of Cross Sectional Study

Prevalence of Migraine in the Students of Zanjan University of Medical Sciences in 1402?

- ✓ **A representative sampling from the source population**
  - ➢ **Drive a sampling "frame"**
  - ➢ **Choose a sampling type**
  - ➢ **Maximize response rate**
- ✓ **Simultaneous measurement of exposure and outcome of interest**
- ✓ **Analyze and interpretation**



Number of ZUMS Students in 1402

Advantages of cross-sectional studies

- Relatively inexpensive and takes little time to conduct.
- Can estimate the prevalence of outcome of interest because the sample is usually taken from the whole population.
- Many risk factors can be assessed.
- Useful for public health planning, understanding disease etiology, and for the generation of hypotheses.
- There is no loss to follow-up.

Disadvantages of cross-sectional studies

- Cannot tell us about cause-effect relationships (only correlation).
- Sample size requirements may be very large (especially when looking at rare outcomes or exposures).
- It evaluates prevalence rather than incidence.
- It’s not useful for rare diseases

Case-Control Studies

Case-Control Studies

- Case-control studies are observational studies, where two groups determine the level of exposure to a risk or a disease, by identifying a group of individuals with the disease and for the purpose of comparison, a group of people without the disease.
- Subjects with disease (or outcome) are called cases and subjects without disease (or outcome) are called controls.
- The investigator collects retrospective information about exposure to the risk factor from both groups.
- They are the only practical approach for identifying risk factors for rare diseases

Selecting Cases

- Select cases after the diagnostic criteria and definition of the disease is clearly established
- Study cases should be representative of all cases
- Incident cases are preferable to prevalent cases for reducing (a) recall bias and (b) over-representation of cases of long duration

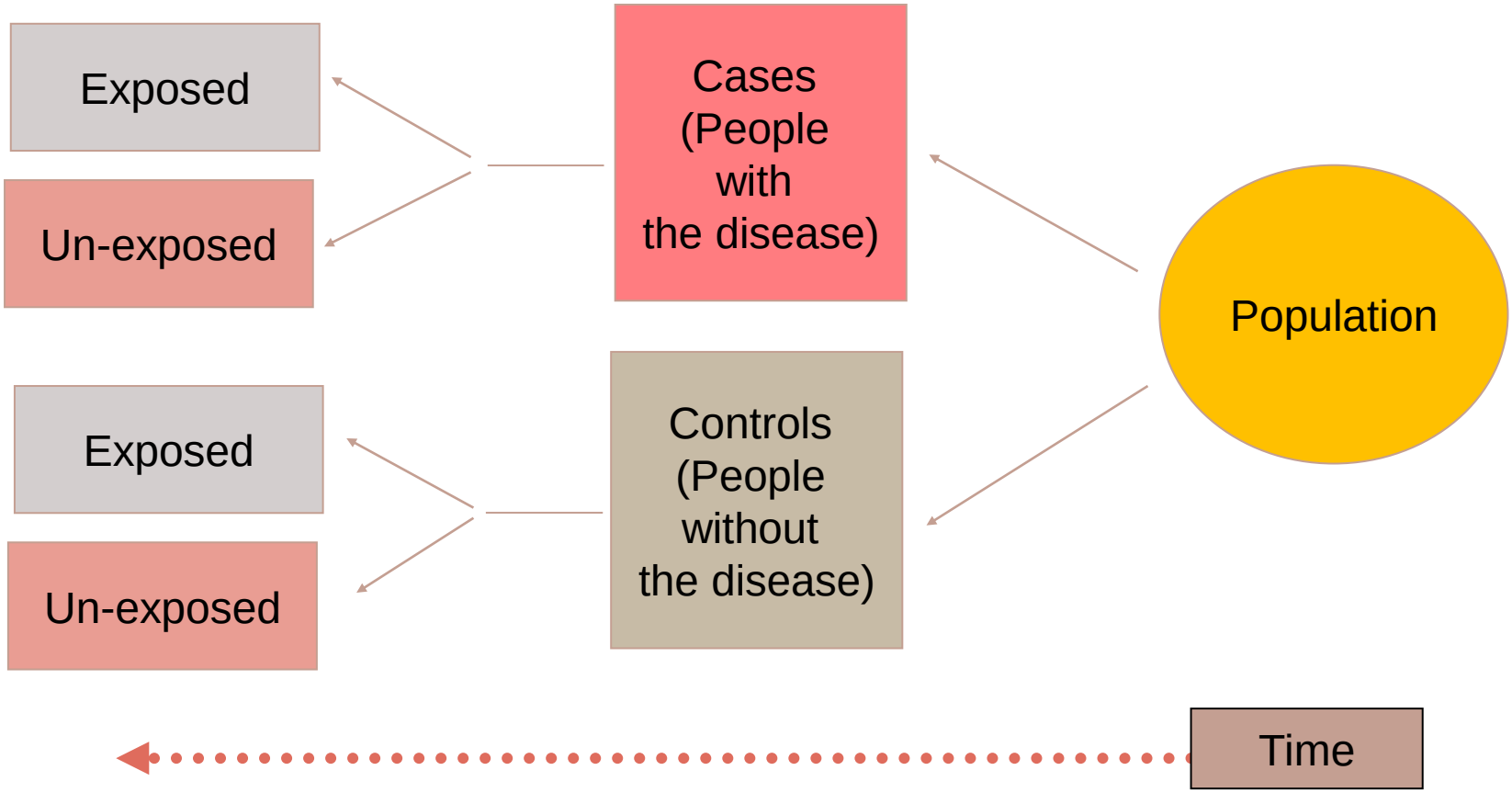
Selecting Controls

- Controls should come from the same population at risk for the disease as the cases
- Controls should be representative of the target population
- Multiple controls can be used to help add statistical power

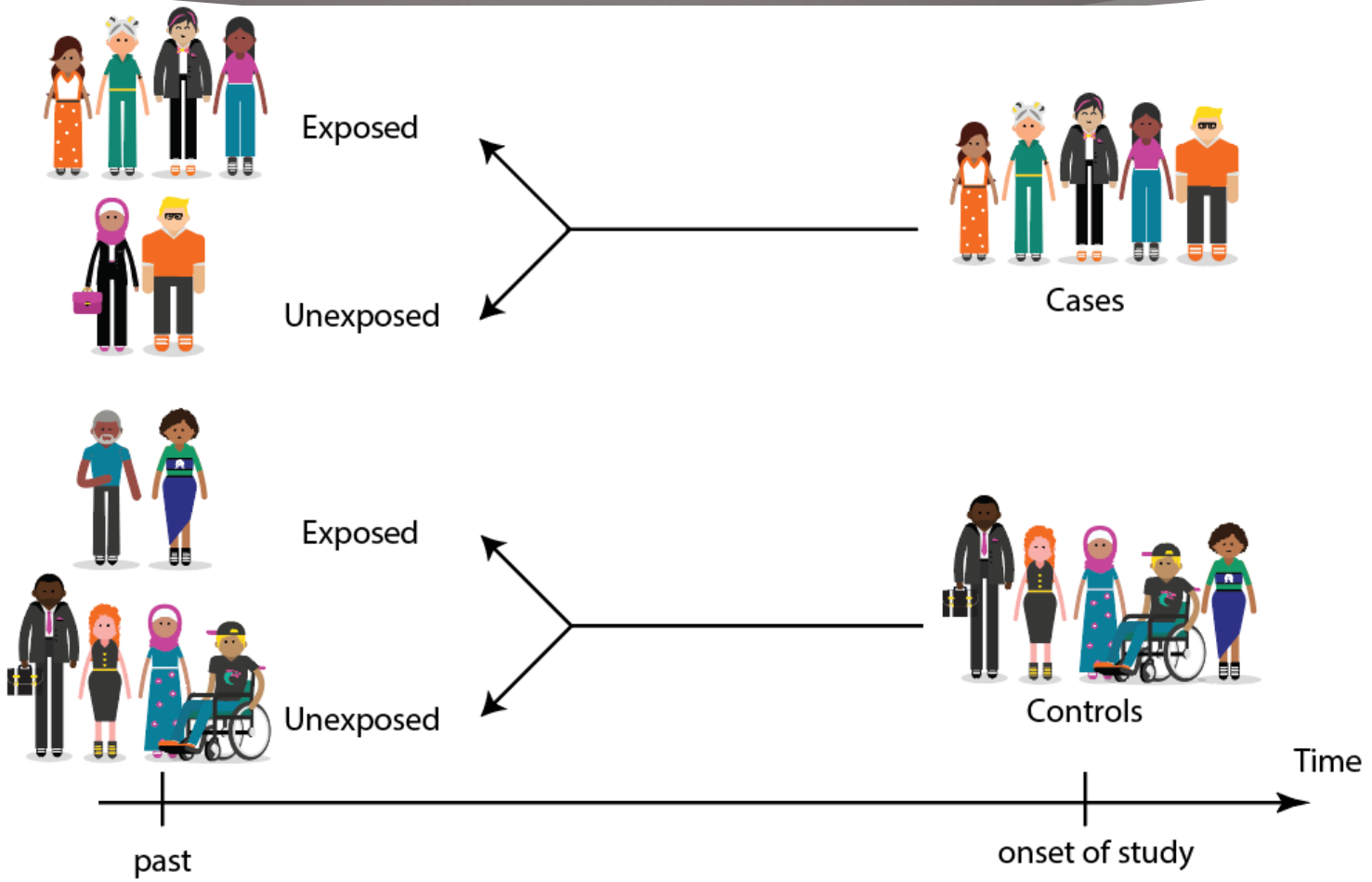
Matching

- It is a method to ensure the comparability between cases and controls.
- Each case is paired individually with a control according to background variables.
- Age, sex, race, sociocultural factors are often used to match cases and controls.
- Appropriate matching helps to reduce the confounders.
- Confounders may provide alternative explanations for any associations observed.

Design of a Case - Control study



Design of a Case - Control study



Calculating the Odds Ratio

Disease Status	Exposure Status: Smoker	Exposure Status: Non-smoker
CHD cases (Cases)	112	88
No CHD (Controls)	176	224
Total	200	400

$$\text{Odds Ratio} = \frac{AD}{BC} = \frac{112 \times 224}{176 \times 88} = 1.62$$

	OR<1	OR=1	OR>1
Odds comparison between cases and controls	Odds of exposure for cases are less than the odds of exposure for controls	Odds of exposure are equal among cases and controls	Odds of exposure for cases are greater than the odds of exposure for controls
Exposure as a risk factor for the disease?	Exposure reduces disease risk (Protective factor)	Particular exposure is not a risk factor	Exposure increases disease risk (Risk factor)

Biases in case-control studies

Selection bias

Selection bias occurs when the subjects in one group are different, or the cases and controls are not comparable (other than disease). In order to prevent this bias, precise selection criteria should be defined for both cases and controls.

Ascertainment bias

It may happen because:

- Cases may recall exposure better than the controls
- Investigators may search for exposure better in cases than in control.

Limitations for recalling past events

In case-control studies much data is collected from interviews. Human beings differ in their capacity to recall information. As mentioned above, cases may have better recall than controls. It is also possible that the person may not have the information requested.

Confounding

It occurs when the observed result between exposure and disease is distorted because of the influence of the third variable.

Cohort Studies

Cohort study - Properties

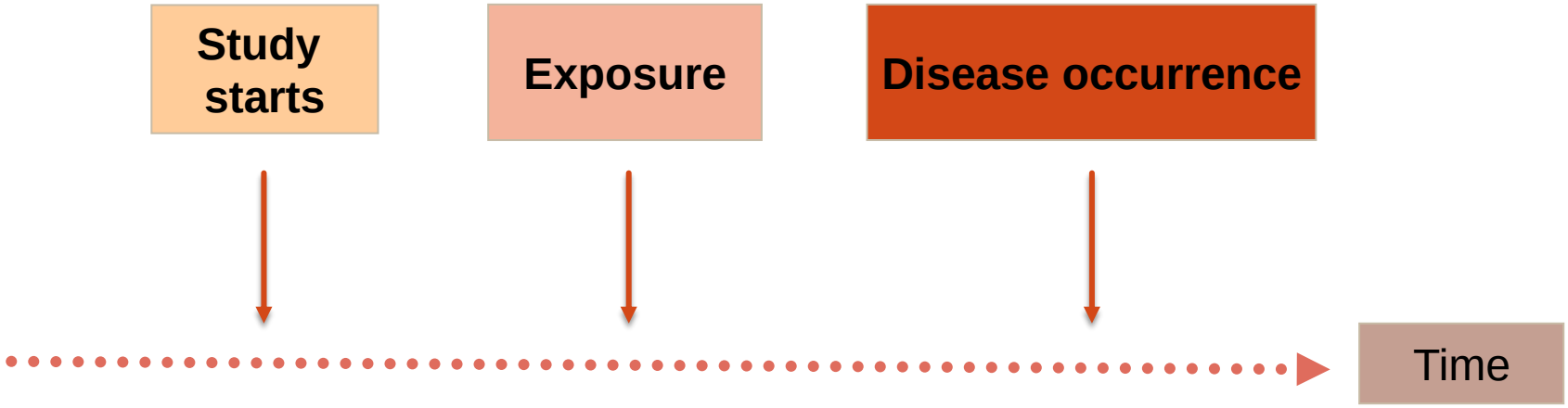
- An analytical observational study
- The most powerful observational study
- Other names:
  - Prospective study
  - Longitudinal
  - Incidence study

Type of Cohort studies

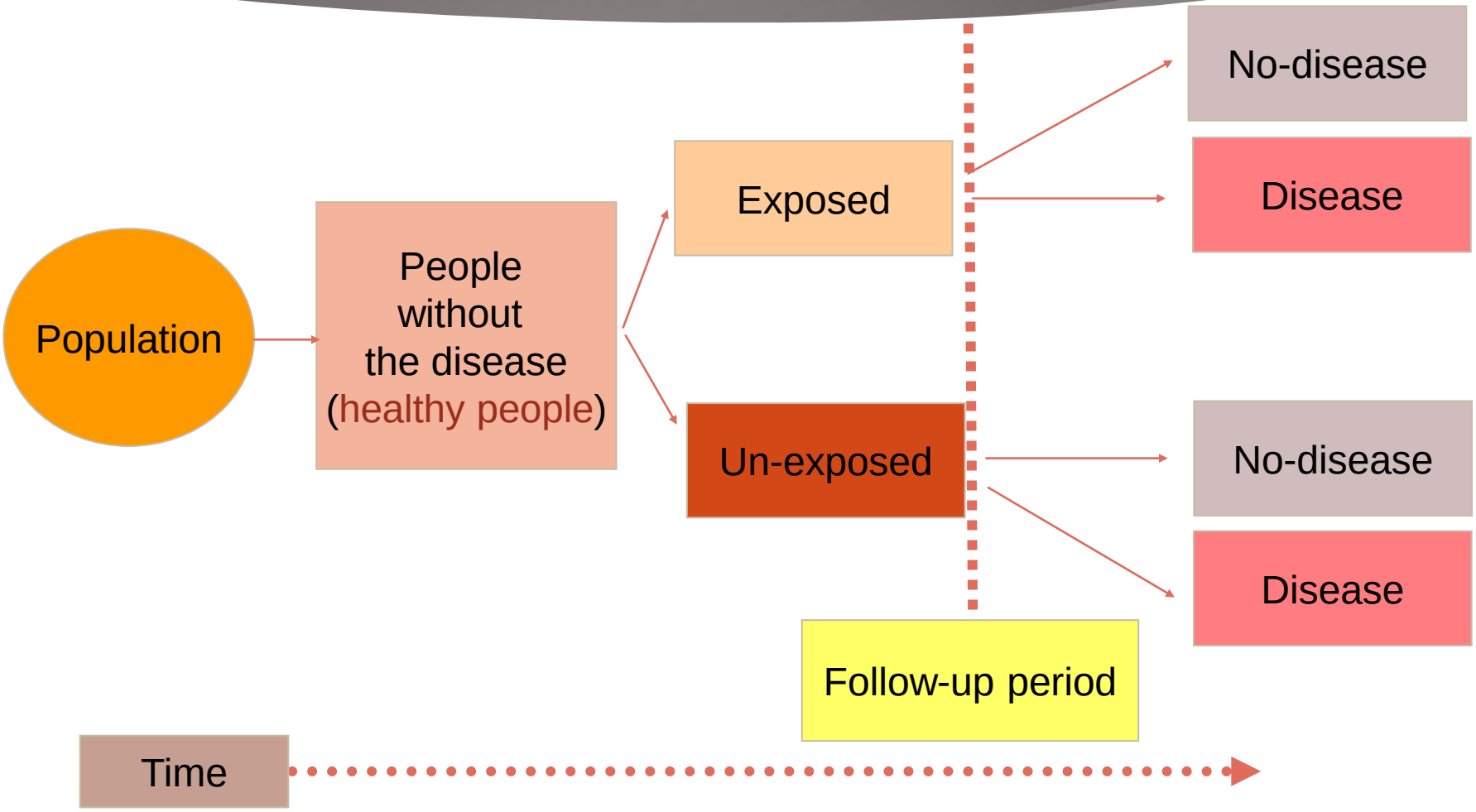
- Prospective
- Retrospective
- Retrospective-Prospective
  - In all types, subject are classified on the basis of presence or absence of exposureStart with “free of the study outcome” participants

Design of a Prospective Cohort

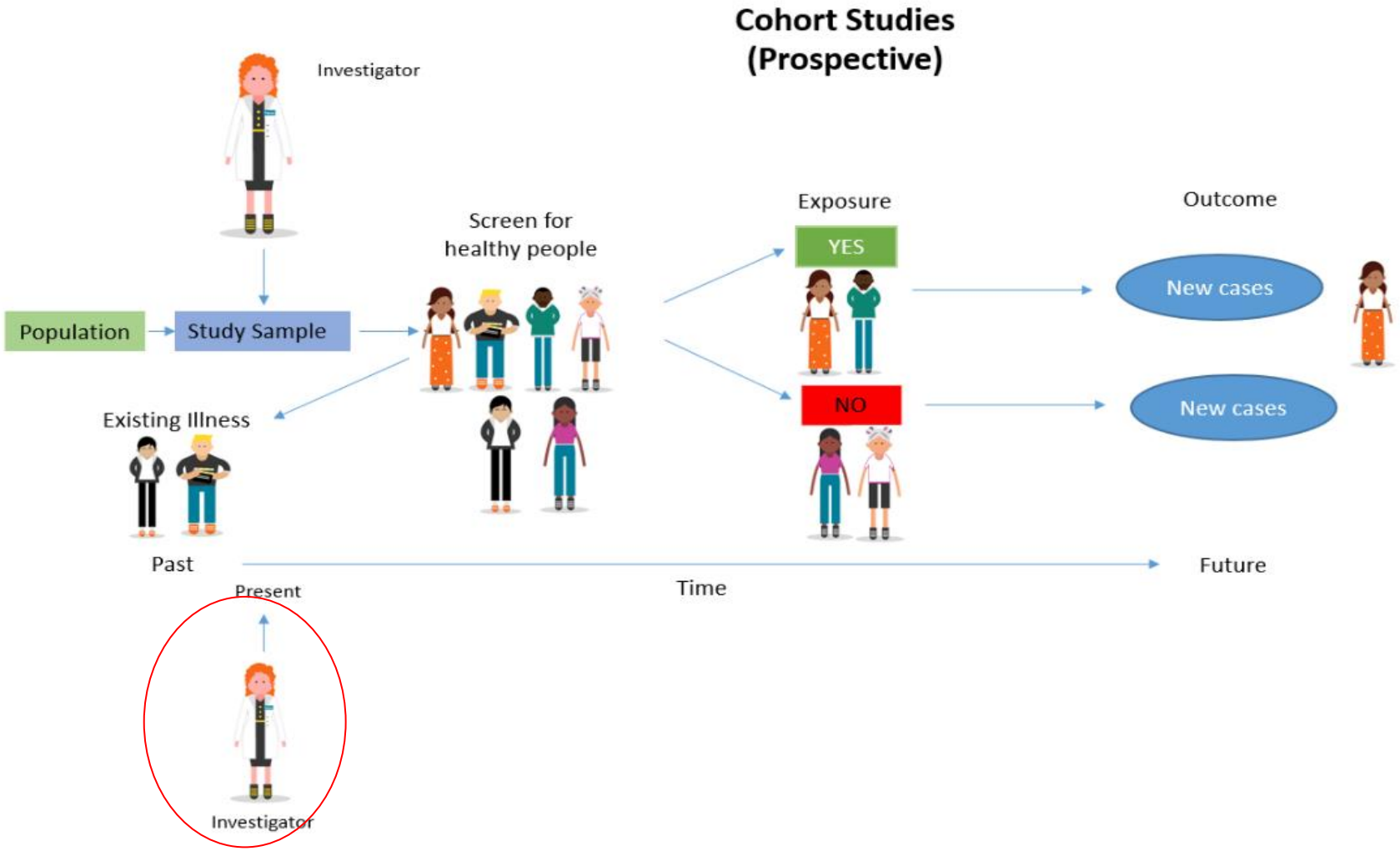
- At the time of study, the outcome have certainly not yet occurred.



Design of a Prospective Cohort

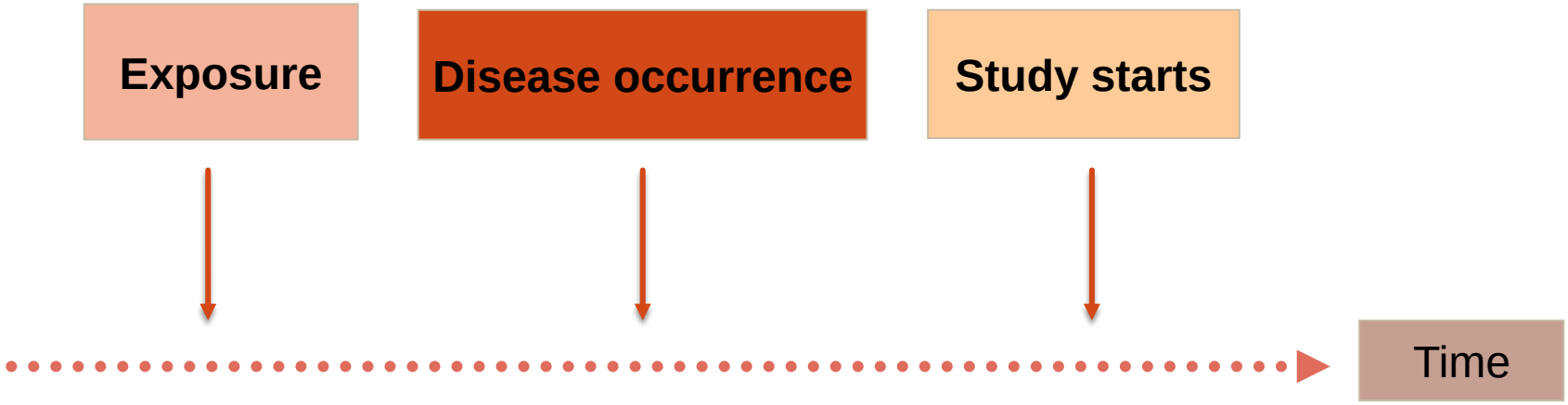


Prospective Cohort

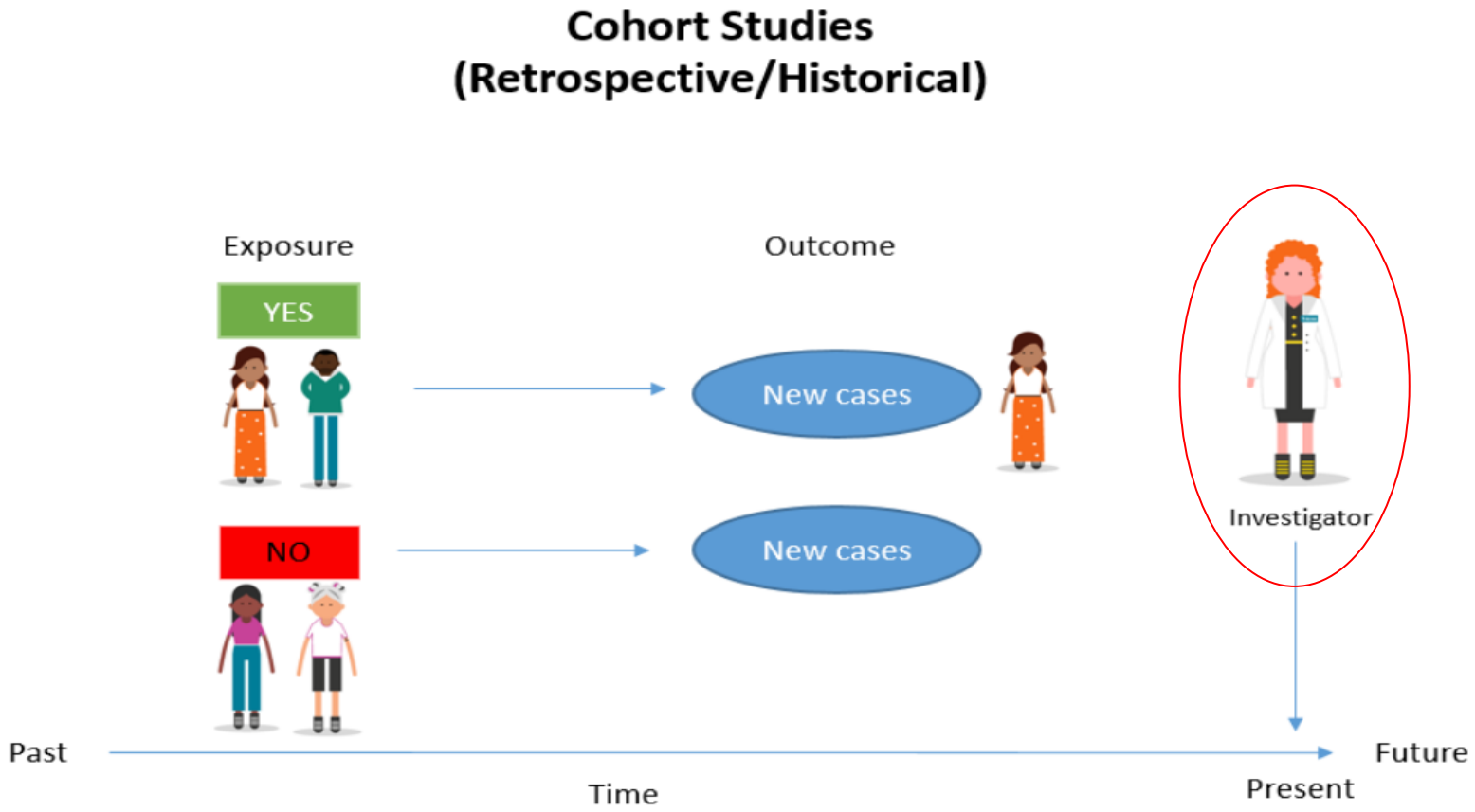


Design of a Retrospective Cohort

- Both the exposure and outcome of interest had already occurred when the study was initiated.
- **Example**: Industrial worker cohort



Retrospective Cohort

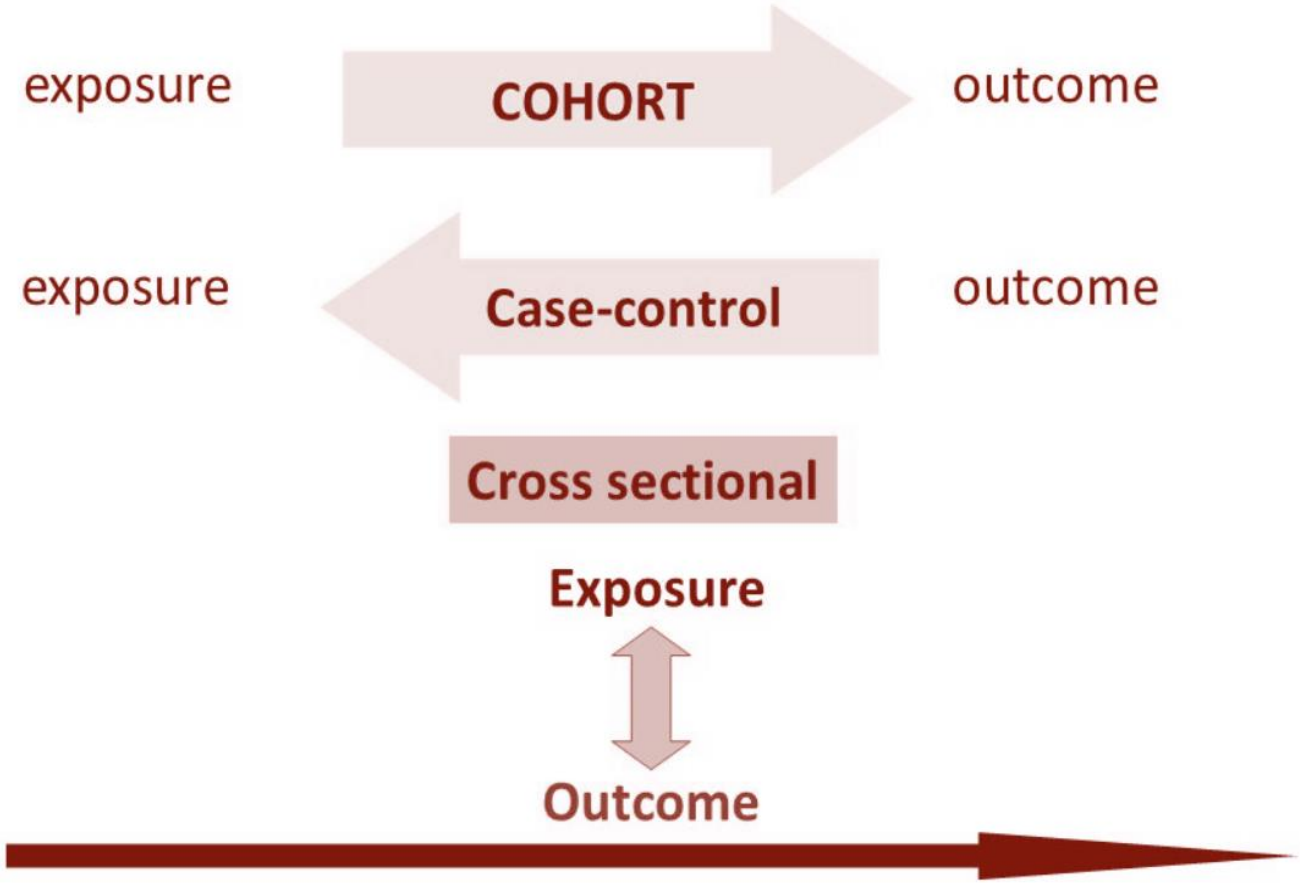


Main difference between both designs

- **Case control:** The study begins with diseased (cases) and non-diseased (control) people

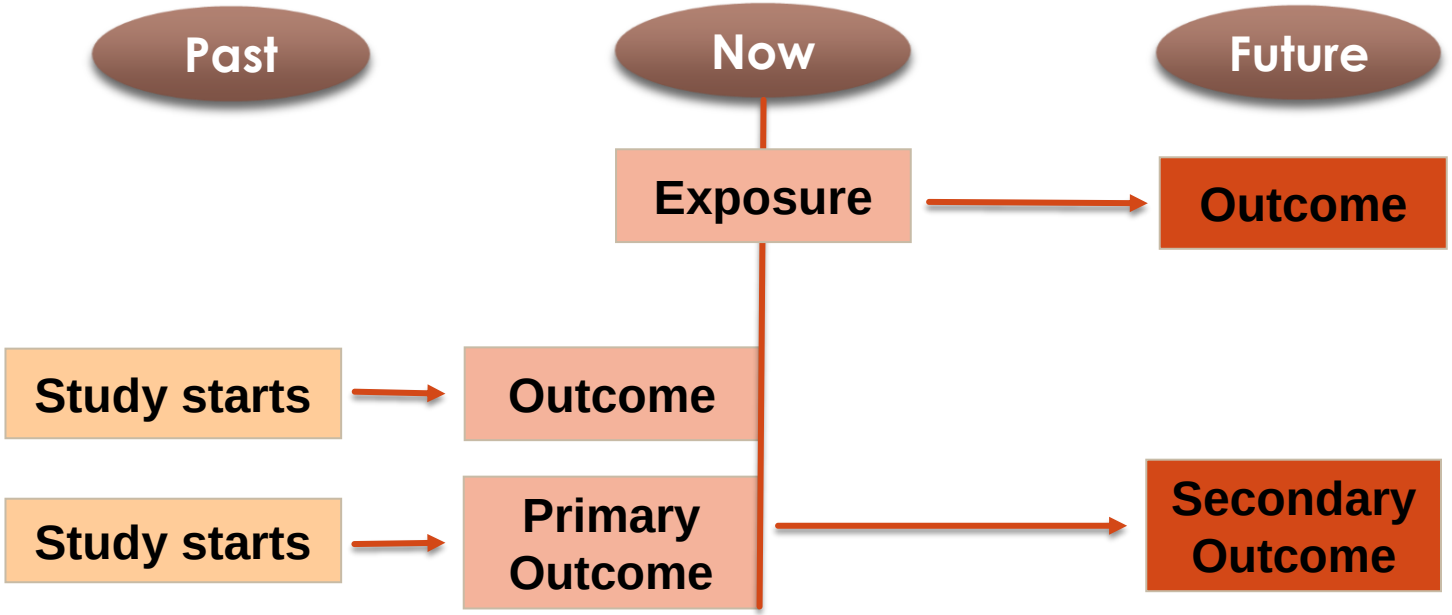
- **Cohort study:** The study begins with exposed and non-exposed people

Study Designs



Retrospective - Prospective Cohort

- Initiated in the past and extended into the future.
- Most useful for exposures having both short-term and long-term effects.
- Example: A chemical that may increase the risk of birth defects within a few years of exposure as well as cancer risk after one or two decades.



Advantage of Cohort Studies

- Can determine incidence rates and risk
- Can be efficient for studying rare exposures (Nuclear bomb, radiation for enlarged thymus, Chernobyl nuclear accident, Minamata, toxic chemical (methyl isocyanides) from industry such as Bhopal, India)

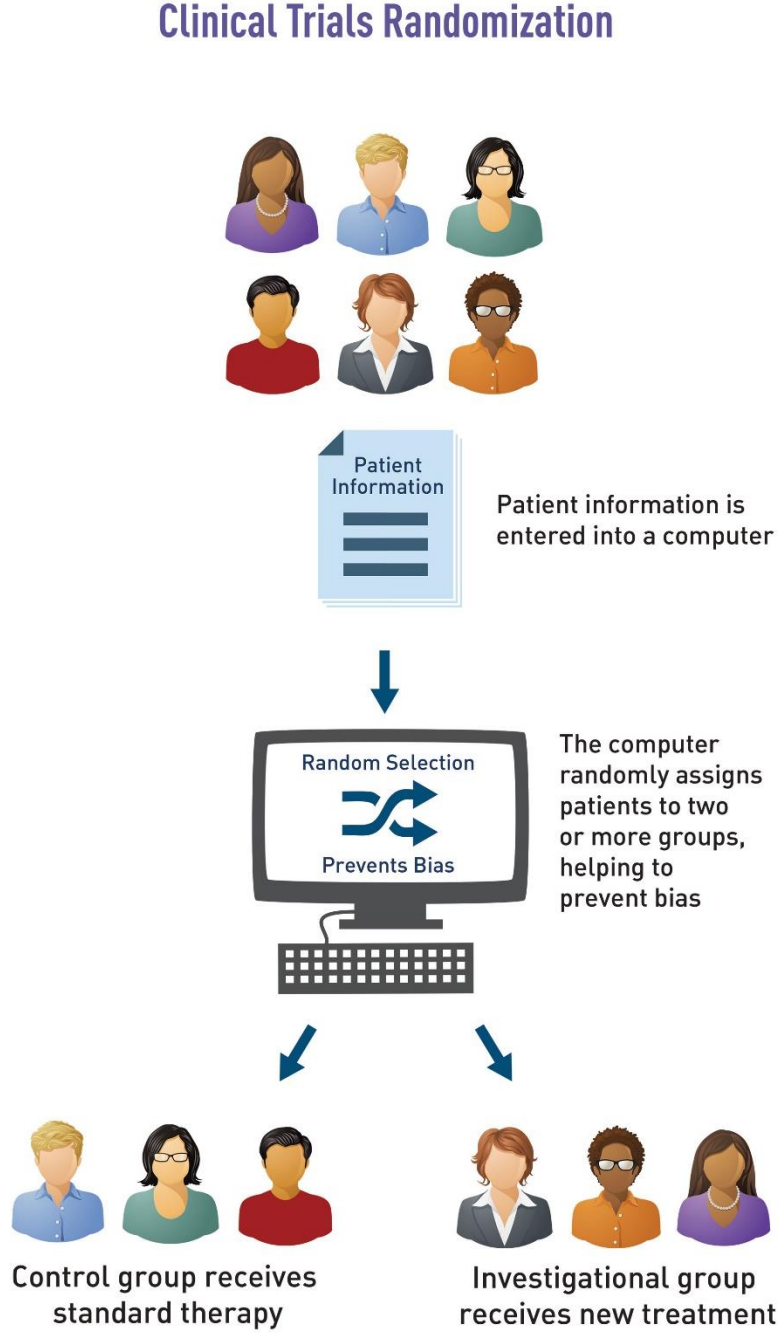
Disadvantage of Cohort Studies

- Expensive
- Results are not available for a long time
- Bias due to attrition and loss to follow-up

Randomized Clinical Trial

Randomized Clinical Trial

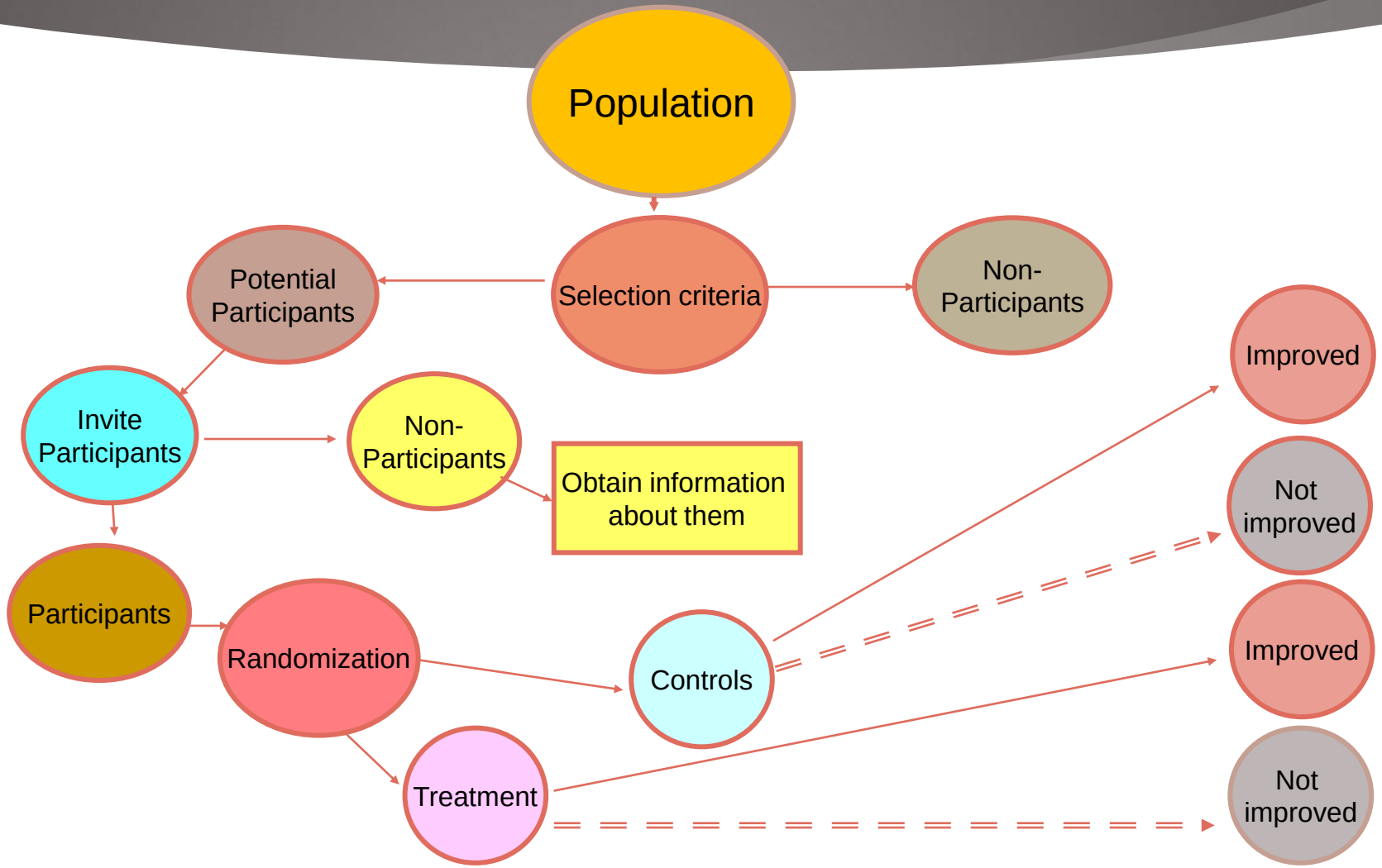
- RCT has become the accepted standard for evaluating therapeutic efficacy.
- The outstanding feature of such trials is the use of randomization to help prevent bias in the assignment of subjects to specific intervention groups.
- If randomization is carried out properly, differences in outcome that are observed among treatment groups tends to result from treatment effects and not from inherent differences among the groups.



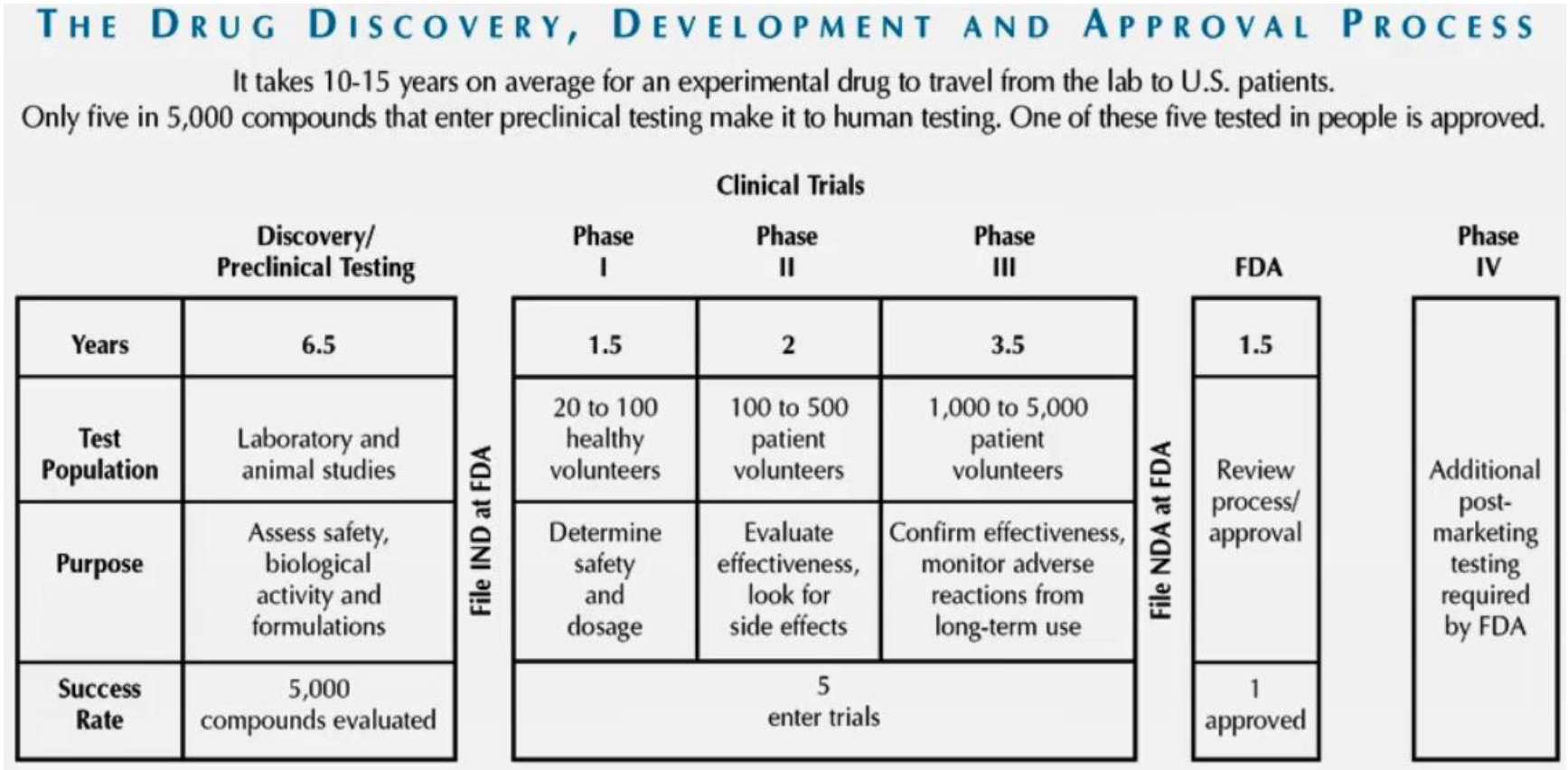
Randomized Clinical Trial

- RCTs are often difficult to conduct. Many clinicians and patients are reluctant to accept randomization, especially if one of the proposed interventions is particularly desirable or undesirable.
- This may be an ethical consideration.
- Furthermore, large numbers of patients may be required if the disease prevalence is low.
- This may necessitate the involvement of multiple institutions, which may increase its complexity and cost.

Randomized Clinical Trials



Clinical Trials - Phases



THE DRUG DISCOVERY, DEVELOPMENT AND APPROVAL PROCESS

It takes 10-15 years on average for an experimental drug to travel from the lab to U.S. patients.
Only five in 5,000 compounds that enter preclinical testing make it to human testing. One of these five tested in people is approved.

	Discovery/ Preclinical Testing	File IND at FDA	Clinical Trials: Phase I	Clinical Trials: Phase II	Clinical Trials: Phase III	File NDA at FDA	FDA	Phase IV
Years	6.5		1.5	2	3.5		1.5	
Test Population	Laboratory and animal studies		20 to 100 healthy volunteers	100 to 500 patient volunteers	1,000 to 5,000 patient volunteers		Review process/ approval	Additional post-marketing testing required by FDA
Purpose	Assess safety, biological activity and formulations		Determine safety and dosage	Evaluate effectiveness, look for side effects	Confirm effectiveness, monitor adverse reactions from long-term use			
Success Rate	5,000 compounds evaluated		5 enter trials				1 approved	

Narrative reviews

Narrative reviews

- Summarize in general what is in the literature on a given topic.
  - **Often written by experts in a given field**
  - **A good source for background information**

- Do not follow strict systematic methods like the other literature review designs.
  - Therefore, they are **prone to bias**
  - **Lower in the hierarchy of evidence**

Narrative reviews

- They do not employ many of the **safeguards needed to control against bias**.
  - **Authors may be selective** as to which articles are included.
  - They may **include articles that support their hypothesis** and exclude those that do not.
  - **Rigorous appraisal methods are not used** to evaluate included articles.

The Concept of a Systematic Review

Differences between narrative and systematic reviews

Feature	Narrative Review	Systematic Review
Topic	Typically broad-scoped	Focused research question
Data sources and search strategy	The search strategy and databases that were used may not be provided	The search strategy is explicit and comprehensive with a list of all databases that were utilized
Authorship	A recognized expert(s) on the topic	A team of experts having methodologic and clinical expertise
Article selection criteria	Typically not specified	Consistently applied inclusion and exclusion criteria
Searching	May be extensive, intended to locate literature on the topic area in question	Extensive, intended to locate all primary studies on a particular research question
Appraisal of included articles	Indefinite, may be variable	Critical appraisal is meticulous, typically involving the use of data extraction forms
Synthesis	A qualitative summary is usually provided	A qualitative summary is provided, quantitative when the data can be pooled
Inferences	Sometimes evidence-based	Usually evidence-based


THANK YOU
FOR YOUR
ATTENTION