Analytical Studies

Advantages and disadvantages

Advantages (Case - Control)

- Easy, inexpensive, relatively quick
- Fewer subjects
- Suitable for rare diseases
- No risk for subjects
- Simultaneous study of multiple etiological factors
- Risk factor can be identified
- No attrition problem
- Ethical problems are minimum
- Easy analysis

Disadvantages (Case - Control)

- Problem of bias specially recall bias
- Selection of controls is difficult
- Incidence can not be calculated
- Only estimation of RR
- Only disease under study is studied
- Only association is measured
- Not suitable for evaluation of therapy or prophylaxis

Advantages (Cohort)

- Incidence can be calculated
- Several possible outcomes related to the exposure can be studied simultaneously
- Provides a direct estimate of RR
- Comparison groups are formed before the development of the disease, so bias of misclassification in two groups can be minimized

Disadvantages (Cohort)

- Involves large sample
- Unsuitable for investigating uncommon ds or ds with low incidence
- Long time for completion (investigators, participants, experienced staff, funds)
- Standard methods or diagnostic procedures and criteria may change over time
- The study itself may alter people's behaviour
- Ethical issues

Experimental Epidemiology

AIM

1. To provide scientific proof of aetiological \risk factor
2. To provide a method of measuring the effectiveness & efficiency of health services for the prevention & treatment of disease & improve the health of the community.

- Animal studies
- Human experiments

Animal Studies

- Applications
- To confirm etiological hypothesis
- Testing efficacy of Preventive and Therapeutic measures
- Completing natural history of disease

Advantages of Animal Studies

- Experimental Animals can be
- Bred
- Manipulated
- Multiply Rapidly

Pasteur's vaccine (1881) for anthrax: proof of efficacy

- **Control group and experimental group**
- **Experimental sheep (25) with vaccine twice**
- **Both groups implanted with anthrax bacilli**
- **Result**
  - **All vaccinated animals healthy**
  - **All controls dead or dying**

Limitations

- Not all human diseases can be reproduced in animals
- Conclusions may not be strictly applicable to human beings

Human Experiments

- Essential for the disease that can not be produced in animal.
- Always needed to investigate the disease aetiology & to evaluate preventive & therapeutic measures

Human Experiments

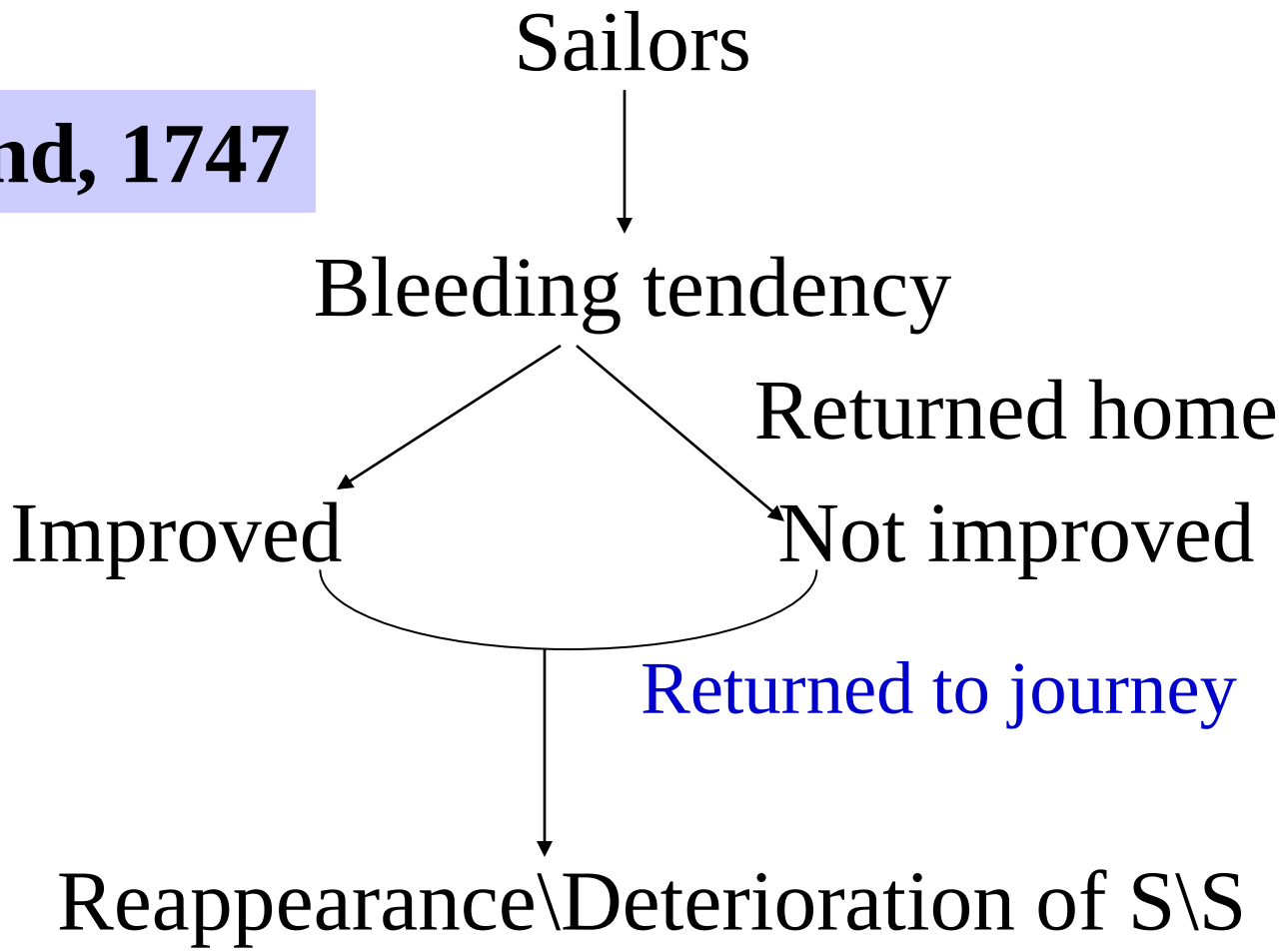
Ethical and logistic considerations

Weighing of benefits V/S risk

Human Experiments
Examples

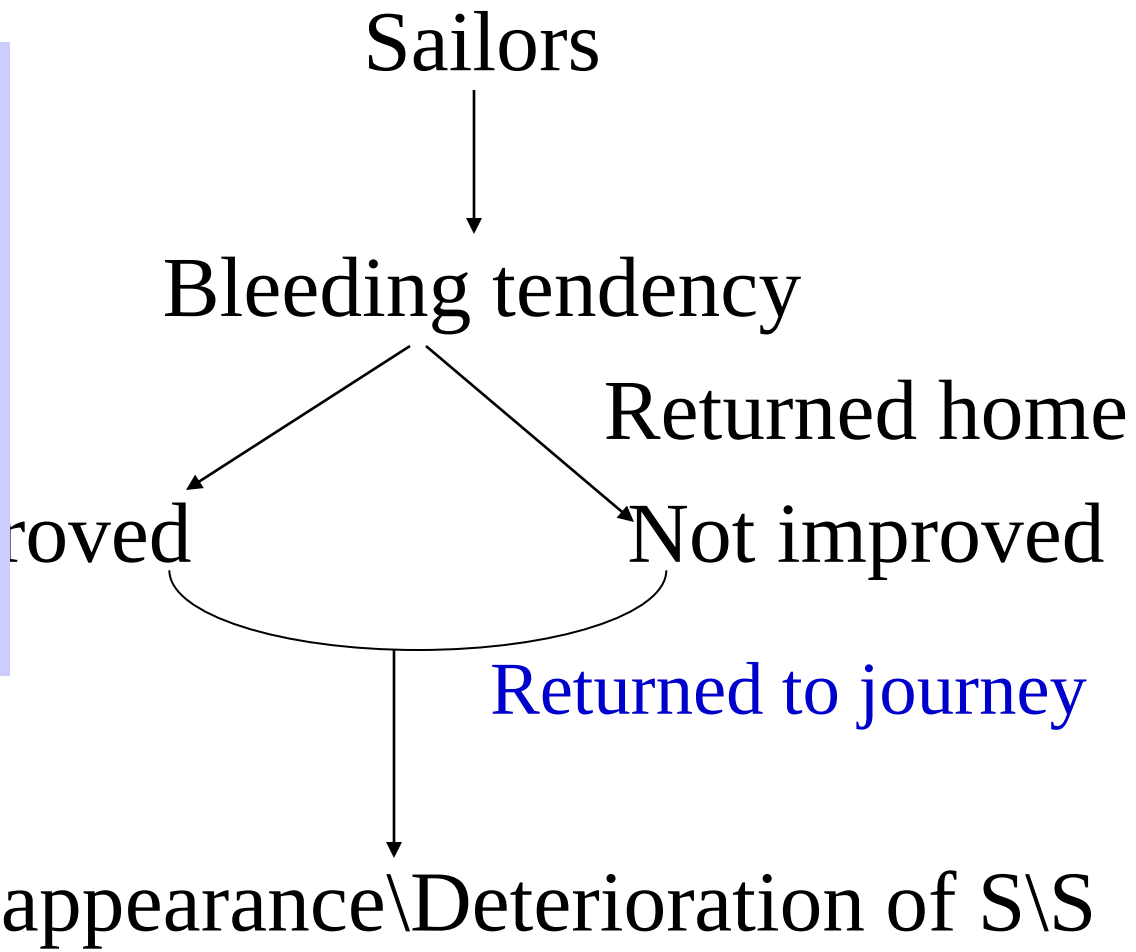
- Scurvy V/S diet
- Cow-pox

James Lind, 1747

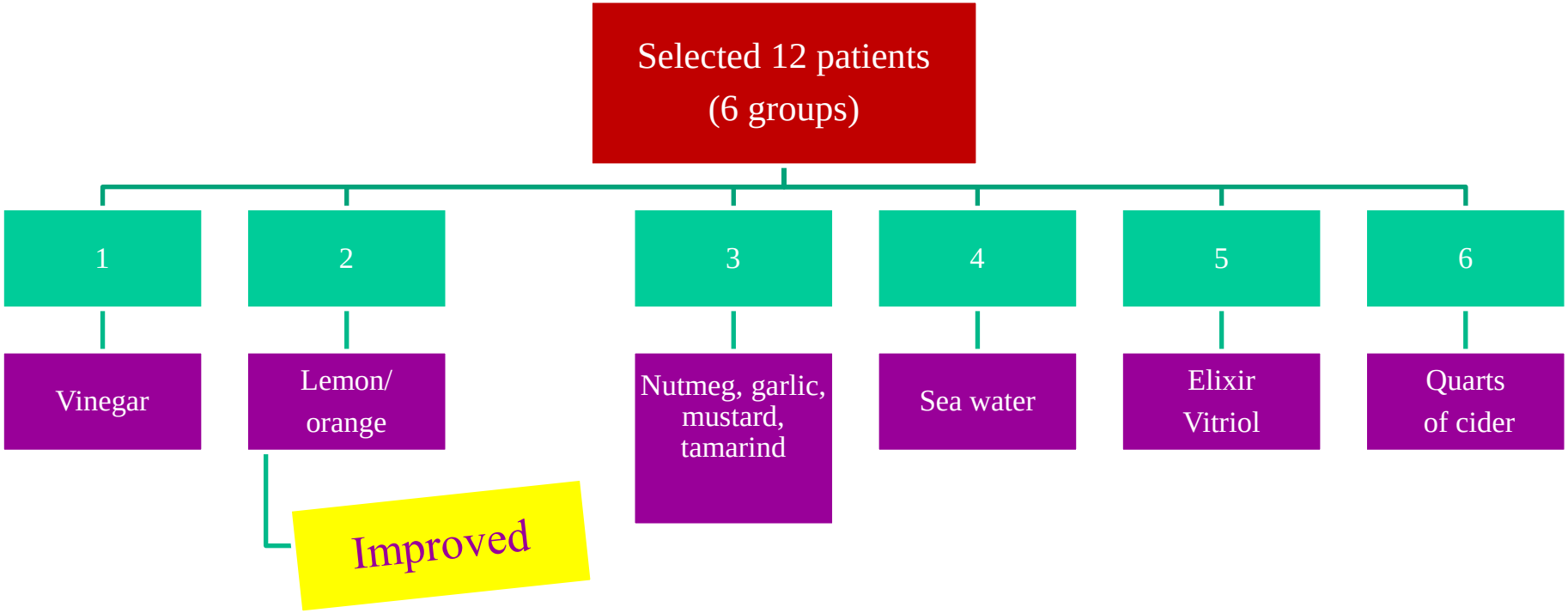


Descriptive Epidemiology

Observational & Analytical



Hypothesis= Related to food habits


Selected 12 patients
(6 groups)
1
2
3
4
5
6
Vinegar
Lemon/
orange
Nutmeg, garlic,
mustard,
tamarind
Sea water
Elixir
Vitriol
Quarts
of cider
Improved

Trial of Streptomycin in TB 1948

- **Patients randomly allocated to streptomycin or placebo**
- **Results favored streptomycin (p=0.0001)**
  - **bed rest only: 4/52 cured**
  - **bed rest + streptomycin: 28/55 cured**

Experimental Epidemiology

A-RANDOMIZED CONTROL TRIALS
(Experimental trials)

B-NON RANDOMIZED TRIALS
(Non- experimental trials)

RANDOMIZATION

BEST APPROACH IN THE DESIGN OF THE TRIAL

1-RANDOMIZED CONTROL TRIALS

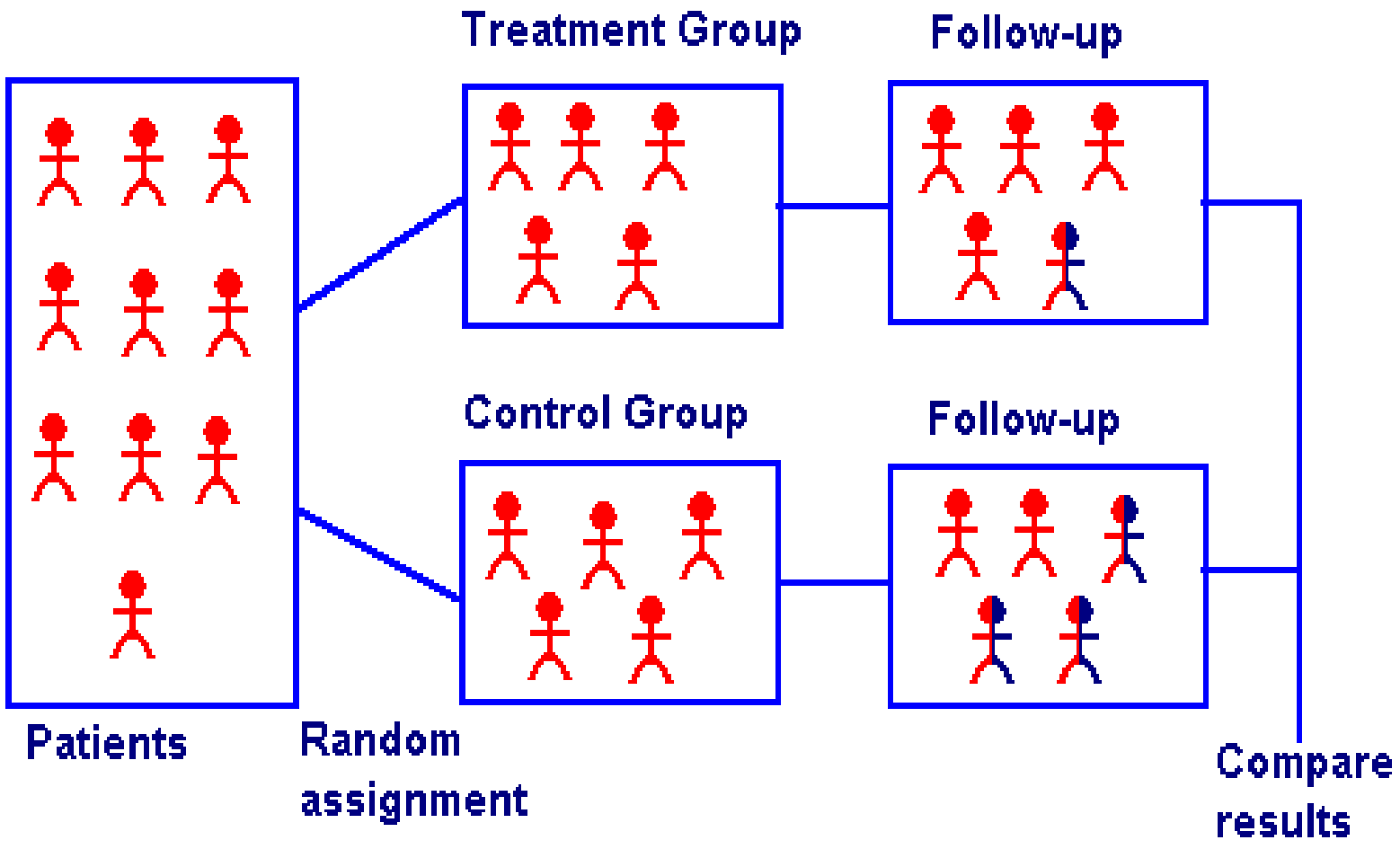
Those involving a process of random allocation

2- NON-RANDOMIZED TRIALS

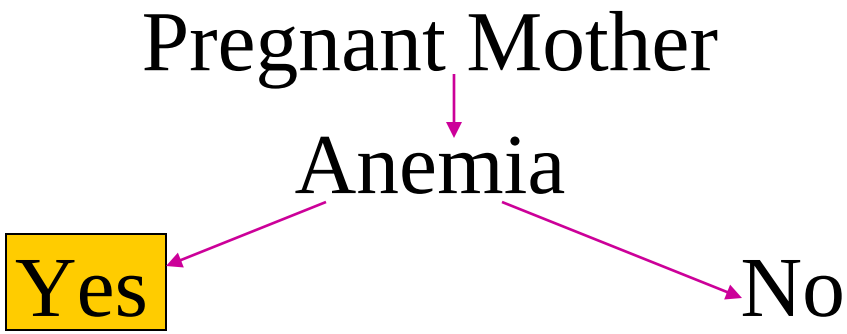
Randomized Controlled Trials (RCT)

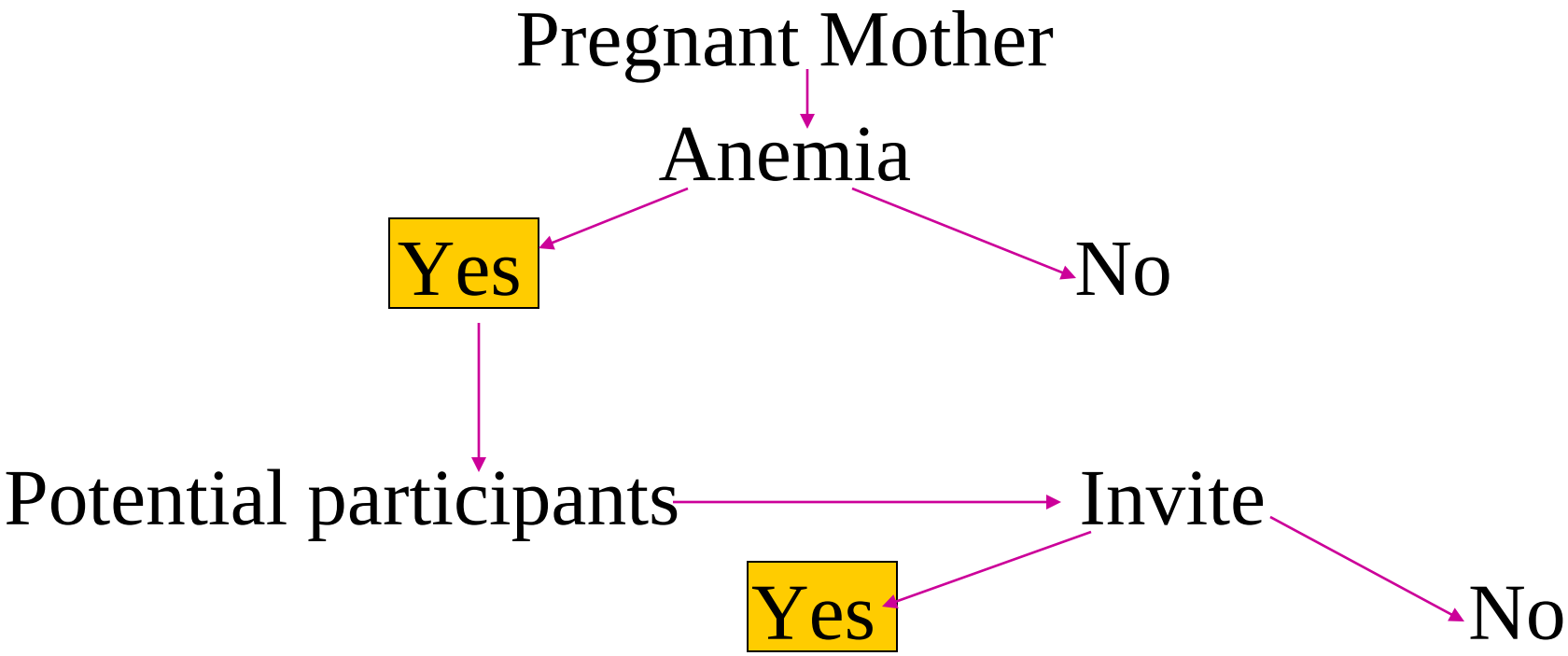
Effectiveness of iron therapy in pregnant mothers

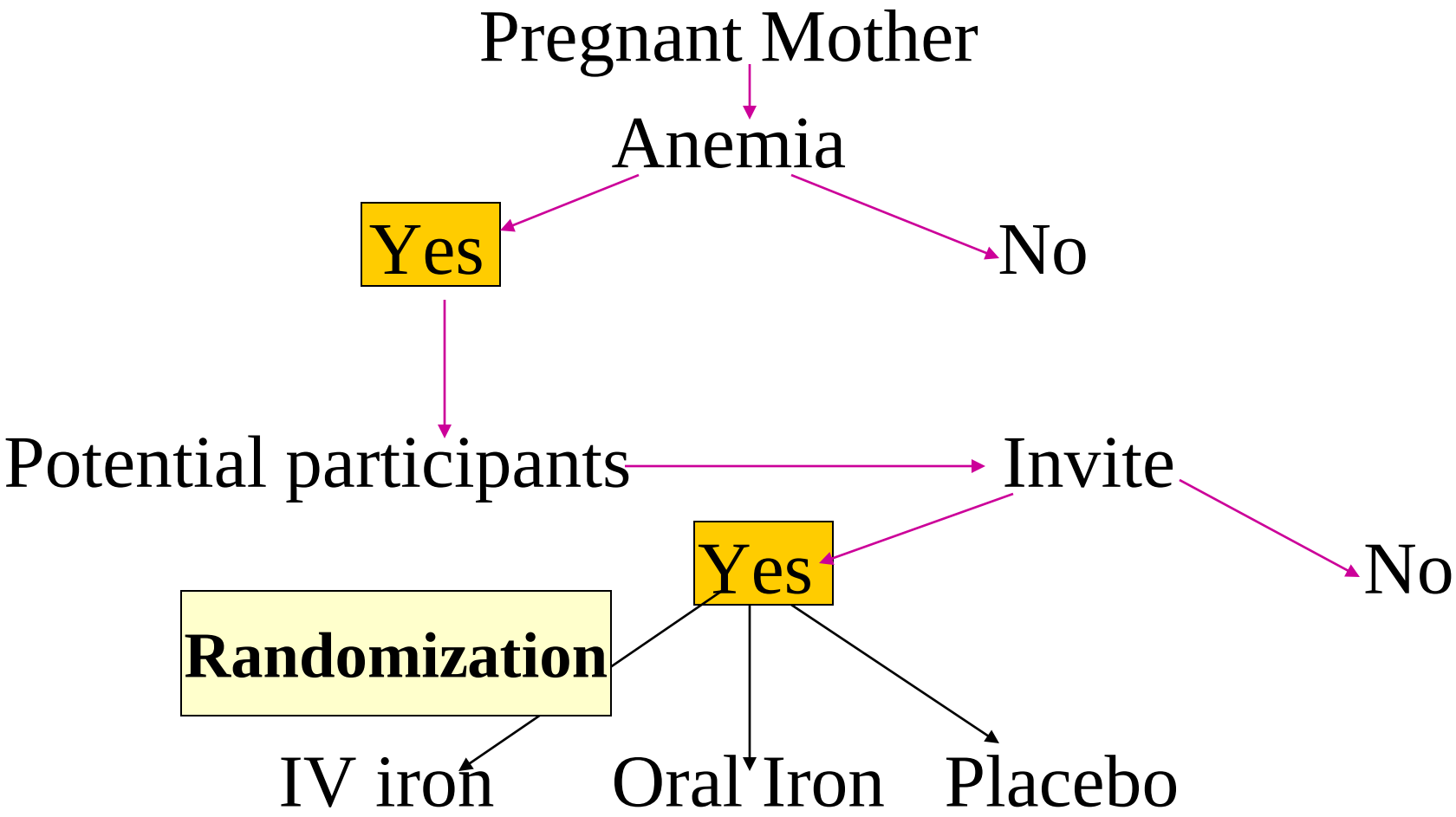
Randomized Controlled Trials

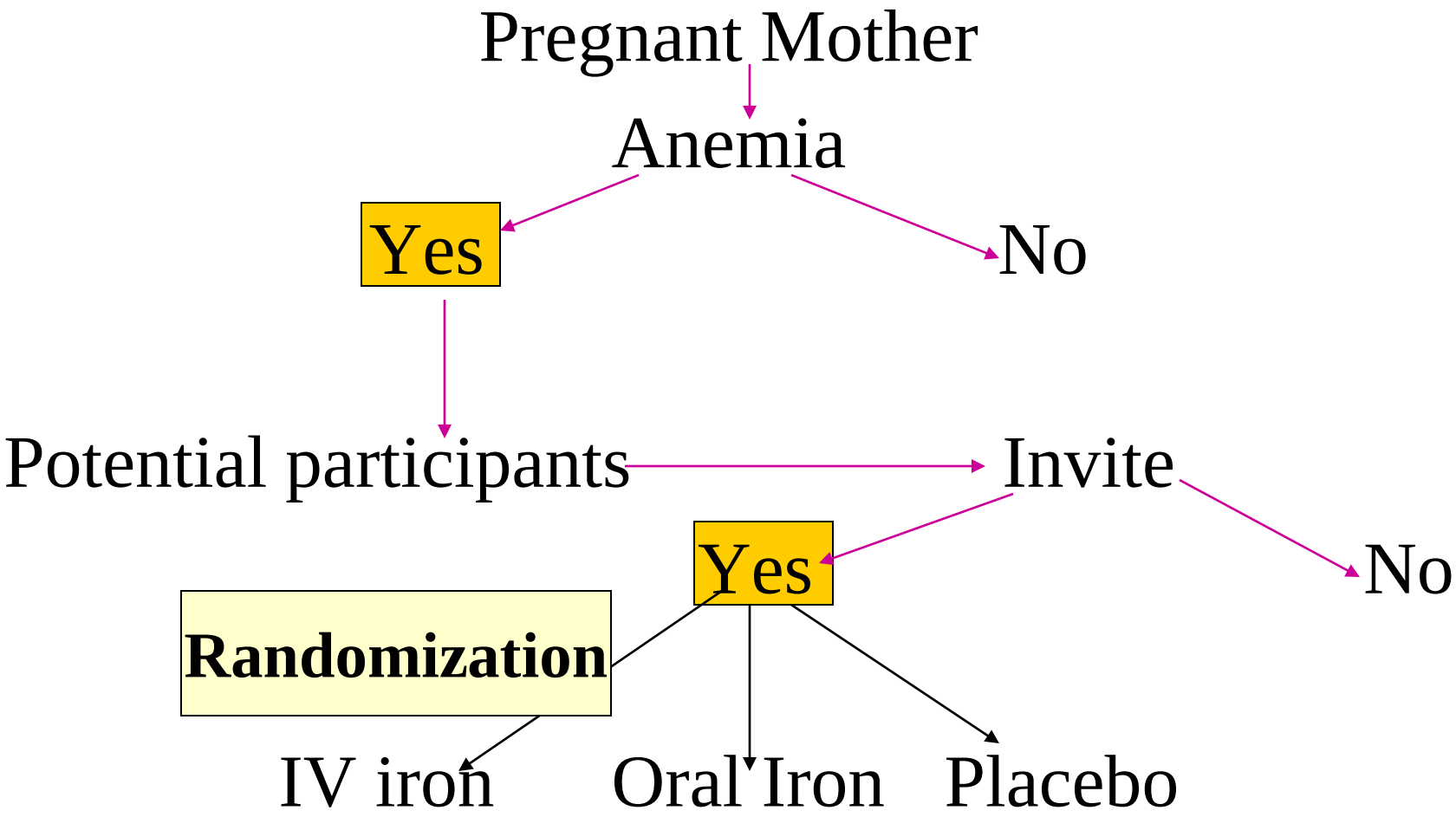


Pregnant Mother


Pregnant Mother
Anemia
Yes
No


Pregnant Mother
Anemia
Yes
No
Potential participants
Invite
Yes
No


Pregnant Mother
Anemia
Yes
No
Potential participants
Invite
Yes
No
Randomization
IV iron
Oral Iron
Placebo



Assessment>> Increase Hb, Faetal outcome

Design of Randomized Controlled Trial

Select Suitable Population (Reference or Target population)

↓

Select suitable sample (Experimental or Study population)

↓

Make necessary exclusions (Those not eligible/ Those who do not give consent)

↓

RANDOMIZE

↓

Experimental group and Control Group

↓

Manipulation and follow-up in both the groups

↓

Assessment (Positive and negative results)

Basic Steps

1. Drawing up a protocol
2. Selecting reference & experimental population
3. Randomization
4. Manipulation/intervention
5. Follow-up
6. Assessment of out-come

Experimental Studies:

- The investigator controls exposure and monitors appropriate outcomes in groups of patients.
- Used for studying treatment effects, usefulness of community intervention, usefulness of diagnostic tests etc.
- A well designed clinical trial (Randomized Controlled Trial) or Community Intervention Trial (CIT) are considered as gold standards for deriving conclusions in medical research.

The Protocol

- Should specify

- Aims and Objectives
- Questions
- Criteria for selection
- Size of sample
- Allocation into Study and Control groups
- Treatment
- Standardization of procedures
- Responsibilities
- Evaluation

The Protocol
Aim

- Preventing Bias
- Reducing sources of error

(Especially when more than one centres are participating in the trial)

The Protocol

- Preliminary (Pilot) test runs
- Feasibility
- Operational efficiency
- Unknown or unexpected effects
- Acceptability
- FINAL VERSION

Selecting Reference and Experimental population

- Reference Population (Target Population) The population to which the findings of the trial, if found successful, are expected to be applicable (eg. Drug, Vaccine or other procedure)
- Experimental or Study Population : The study population is derived from reference population and it is the actual population that participates in the experimental study

Criteria to be fulfilled by Experimental population

- They must give **informed consent** (they must agree to participate in the trial after having been fully informed about the purpose, procedure and possible dangers of the trial)
- They should be representative of the population to which they belong
- They should be qualified and eligible for the trial

Randomization

- The “Heart” of a controlled trial
- Statistical procedure by which the participants are allocated in to groups usually called study and control groups, to receive or not to receive and experimental preventive or therapeutic procedure or intervention.

Randomization

- Eliminates Bias and allows comparability
- Matching : Randomization
- Stratification prior to Randomization
  (age, sex…..)

- Best done by using a table of random numbers.

Prognostic Profile at Entry

- If we know risk factor for bad outcome, we want to verify that randomization has provided reasonable similarity between the two groups in terms of these risk factors
- E.g. If age is a significant risk factor, we would want to know that randomization has resulted in groups that are comparable for age.

Manipulation

- To intervene/ manipualte the study by deliberate application/withdrawal/ reduction of exposure
- Creates an independent variable whose effect is then determined by measurement of final outcome which constitute the dependent variable.

Follow-up in Both groups

- Defined intervals of time
- Manner
- Intensity
- Circumstances
- Time Frame
- “Attrition”

Assessment

Positive results

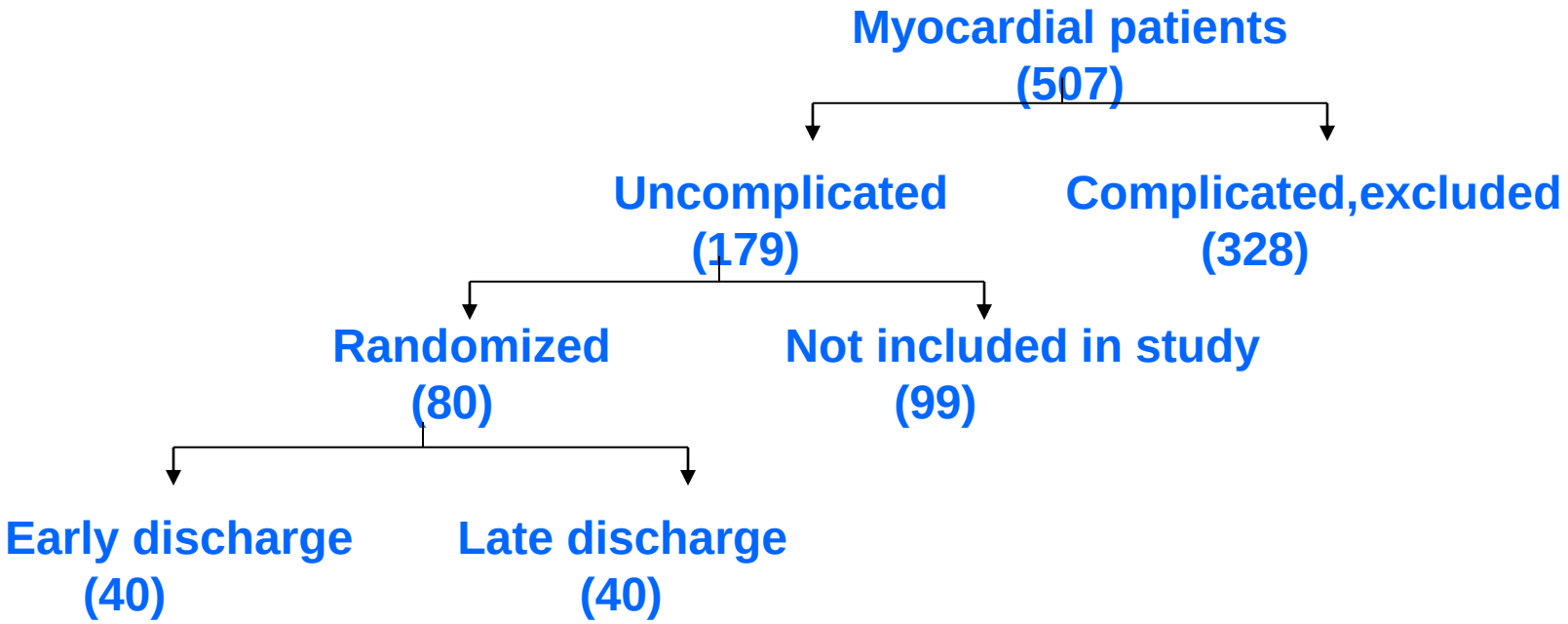
- Decrease in incidence
- Decrease in severity
- Decrease in cost of treatment

Assessment
Negative Results

- Increase in non-complience,
- Operational difficulty…
- Increase in frequency of side-effects and complications, cost….

- POSITIVE V/S NEGATIVE RESULTS

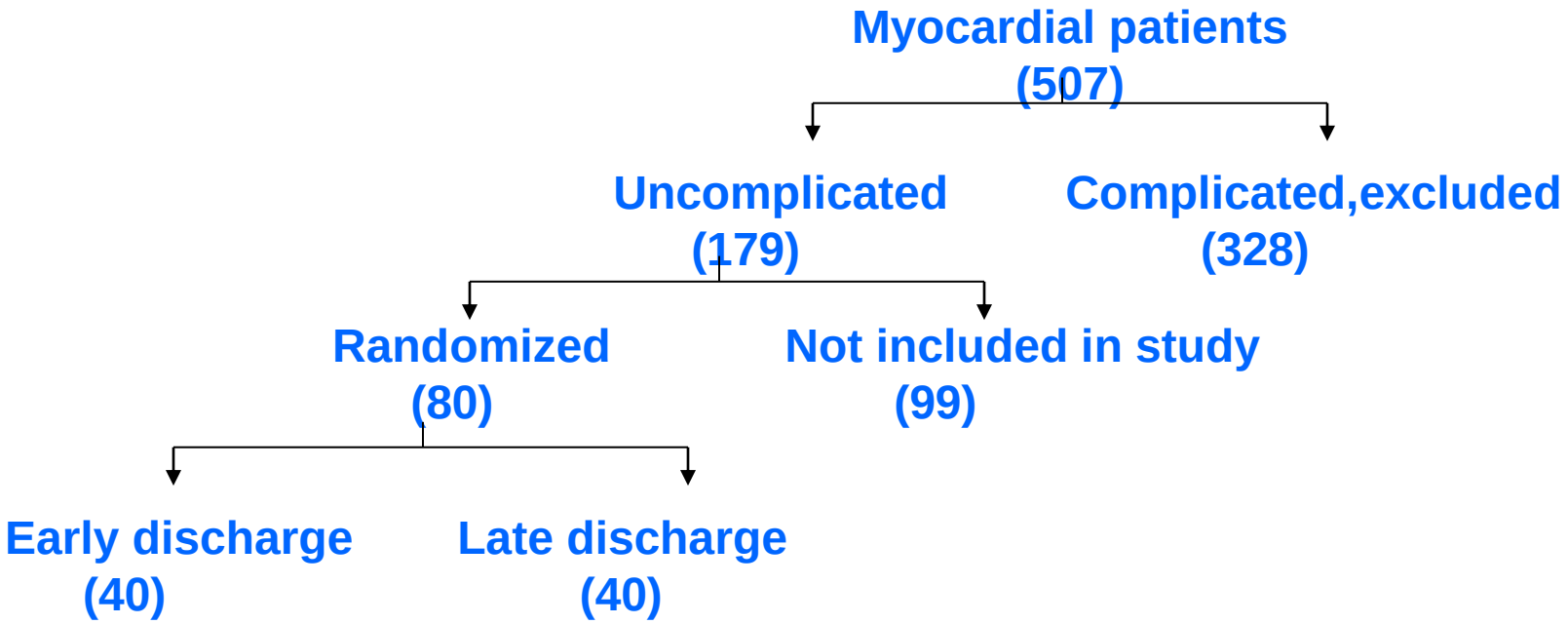
Randomized controlled trial of early hospital discharge after myocardial infarction



Outcome

Deaths
Hospital readmissions
Re-infarctions
Patients with angina

Randomized controlled trial of early hospital discharge after myocardial infarction



Outcome

Deaths
Hospital readmissions
Re-infarctions
Patients with angina

Bias

- Subject Variation
- Observer Bias
- Investigator’s bias

Blinding (Masking)

- Single blind trial
- Double blind trial
- Triple blind trial

Single Blind Trials

- We would like the subjects not to know, which group they are assigned to.
- Specially important when outcome is a subjective measure
- Using placebo (looks, tastes and smells like active agent)
- But still subjects could know which group they belong to.

Double Blind Trials

- In addition to blinding the subjects, we also want to blind or mask the data collectors and data analysts in regard to which group a patient is in.

- Institute based V/S Home based Care for MI

Triple blind trial

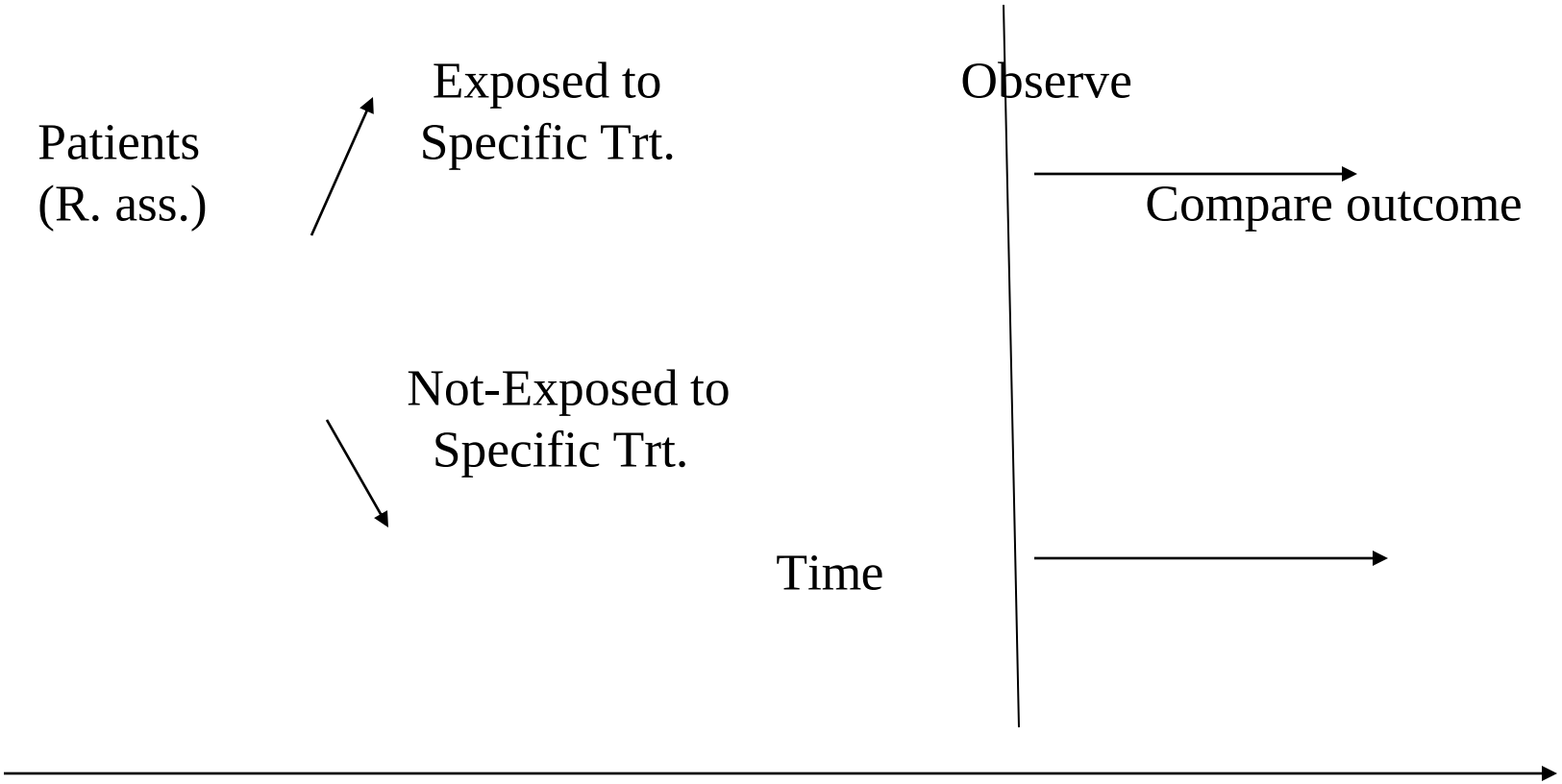
- The participant, investigator and person analyzing the data are all blinded

- Usually RCTs are double blind studies

Some Study Designs

- Concurrent Parallel Study Design
- Cross-over type of Study Design

Concurrent Parallel Study Design



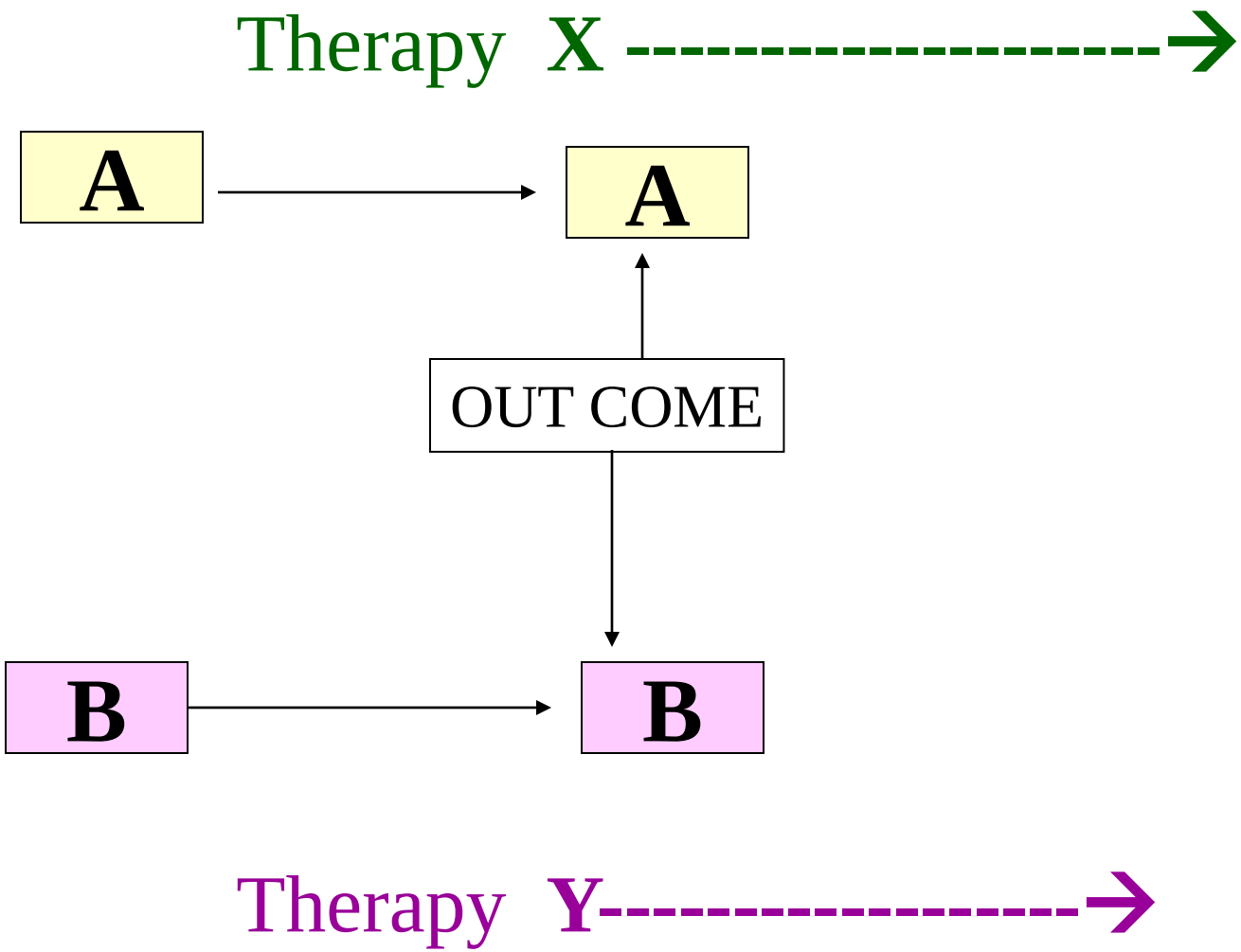
Cross- over type of Study Design

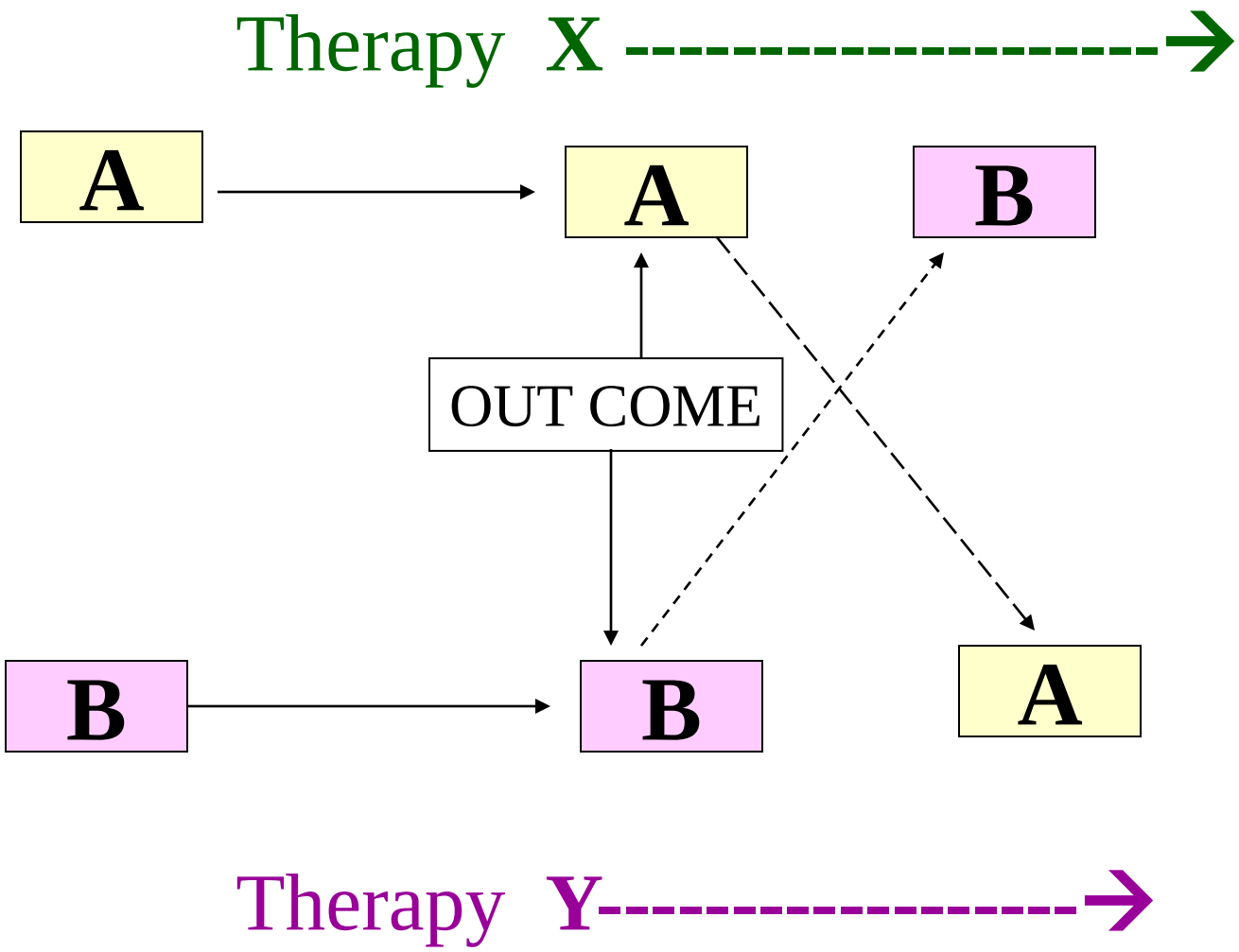
Therapy **X** ----------→

A

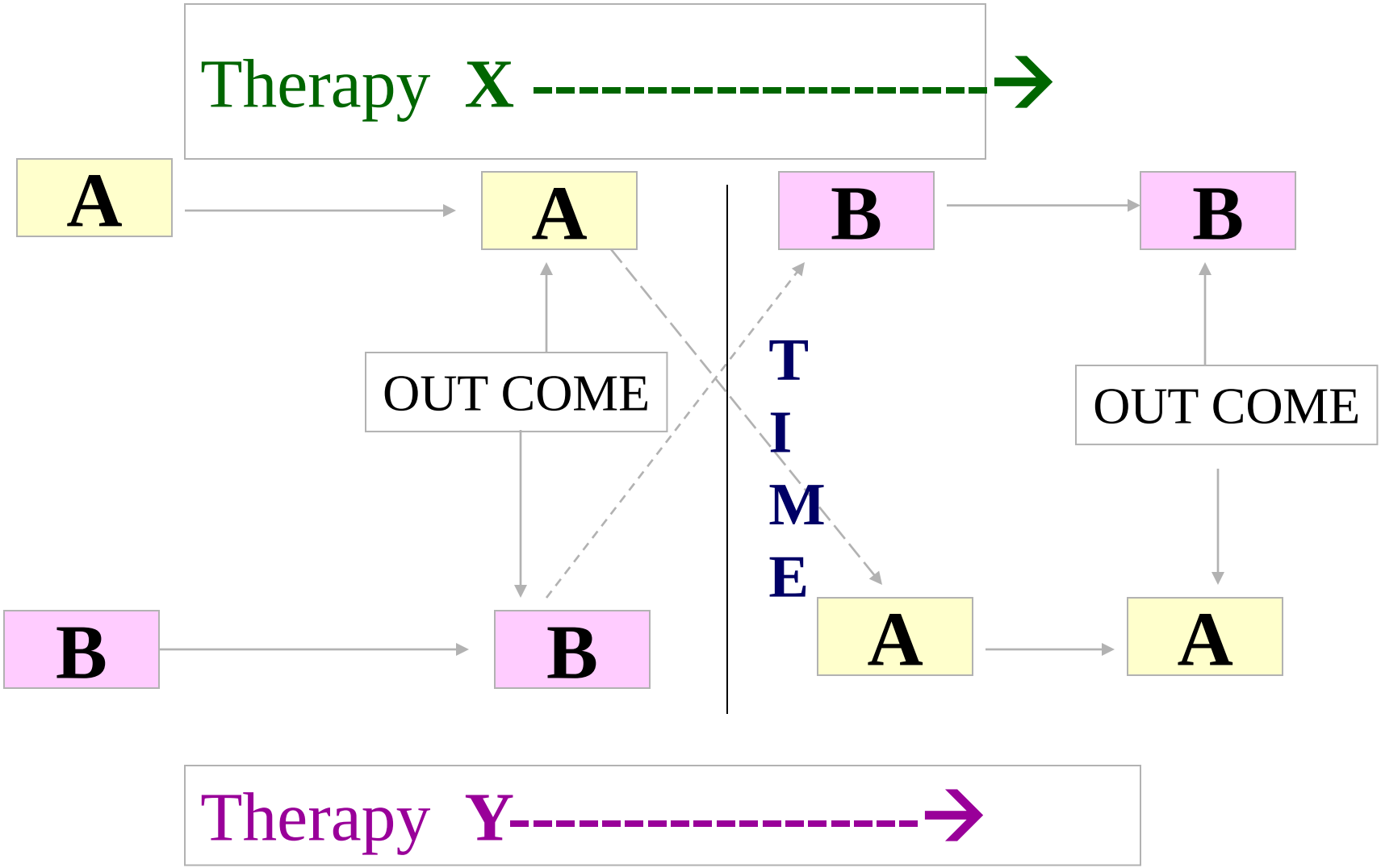
B

Therapy **Y**----------→


Therapy X
A
A
OUT COME
B
B
Therapy Y


Therapy X
A
A
B
OUT COME
B
B
A
Therapy Y

Cross- over type of Study Design



- Advantages
  - All patients (Both group) receive therapy
  - Economic (no. of patients, time)
- Not suitable
  - If drug cures
  - Disease changes

THANK YOU

Cohort Studies V/S Randomized Trials

- Both compare exposed with non-exposed group
- Randomization in Cohort Study can not be carried out and is unethical
- Exposure in RCT is often therapeutic or preventive measure whereas in CS it is possibly toxic or carcinogenic
- Absence of Randomization in Cohort Studies

Results of trial of BCG Vaccine

Group	No. of children	No. of deaths due to TB	%
Vaccinated	445	3	0.67
Controls	545	18	3.30

Non-compliance

- After randomization patient may not comply to the assigned treatment
- Overt or Covert
- Overt (Articulate their refusal called Drop-outs)
- Covert (Without disclosing any body stop taking drugs)

Problem of Drop-in

- The patient in one group may take agent assigned to other group
- Net effect will be that in study group there will be some persons not taking assigned treatment and vice versa.
- Two steps to avoid this problem
- Provide the list of over the counter available drugs having same composition and asking them to avoid them
- Perform test to check compliance periodically in both the groups

Limitation

- Randomization may not be appropriate or ethical in certain settings.
- Bias could occur if the investigators are not blinded to exposure and outcome
- Expensive, difficult to execute, requires close monitoring.
- Appropriate sample sizes are a prerequisite or else one may end up with false negative conclusions.

STUDY QUESTIONS AND APPROPRIATE DESIGNS

Type of Question	*Appropriate Study Design*
Burden of illness	
- Prevalence	Cross Sectional Survey
- Incidence	Longitudinal survey
Causation, Risk & Prognosis	Case Control Study, Cohort study
Occupational risk, Environmental Risk	Ecological studies
Treatment Efficacy	Randomized Controlled study
Diagnostic Test Evaluation	Randomized Controlled study
Cost Effectiveness	Randomized Controlled study

Evidence Pyramid

Thank You