

# 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

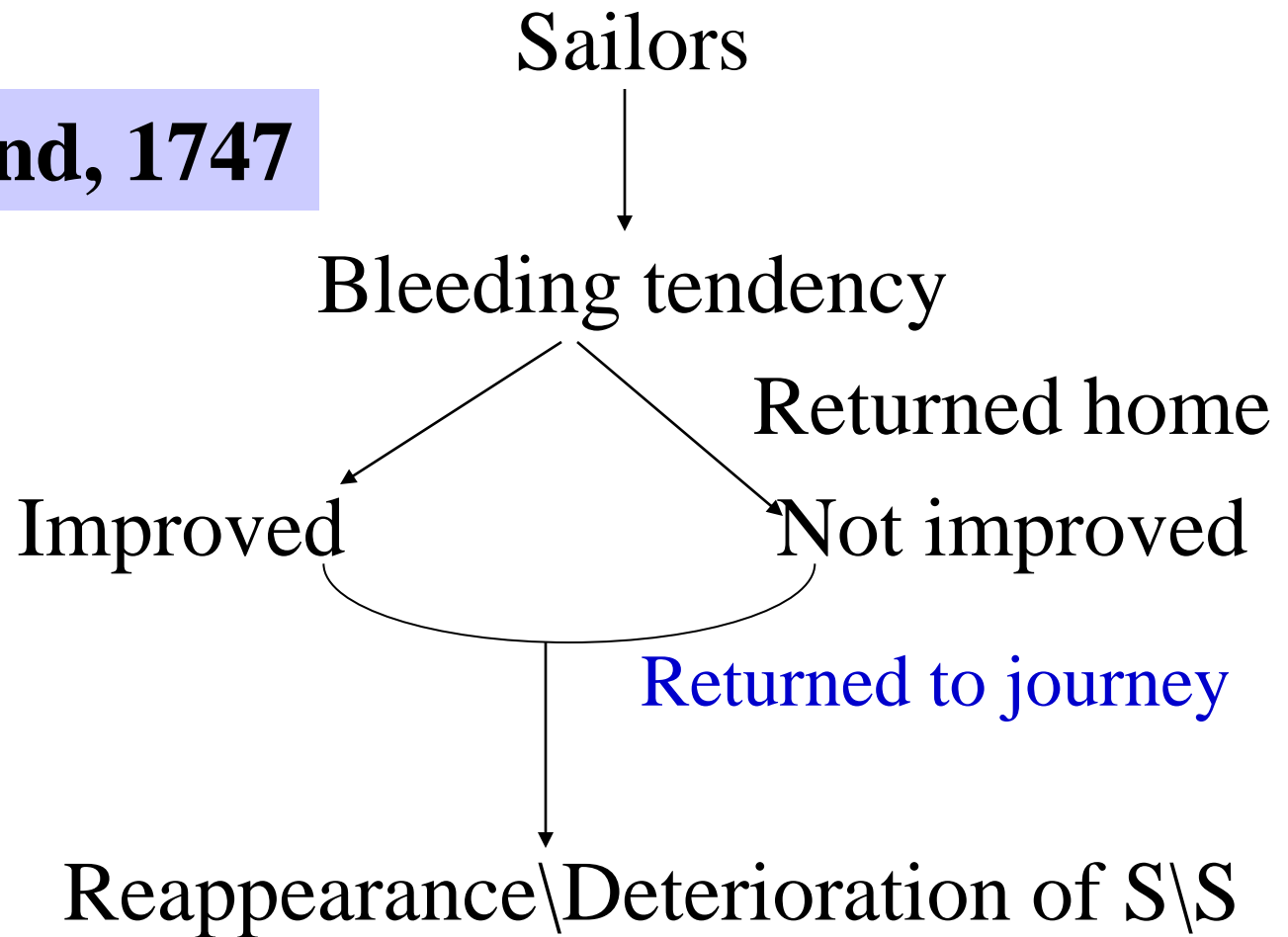
Weighing of benefits V/S risk

# Human Experiments

## Examples

- Scurvy V/S diet
- Cow-pox

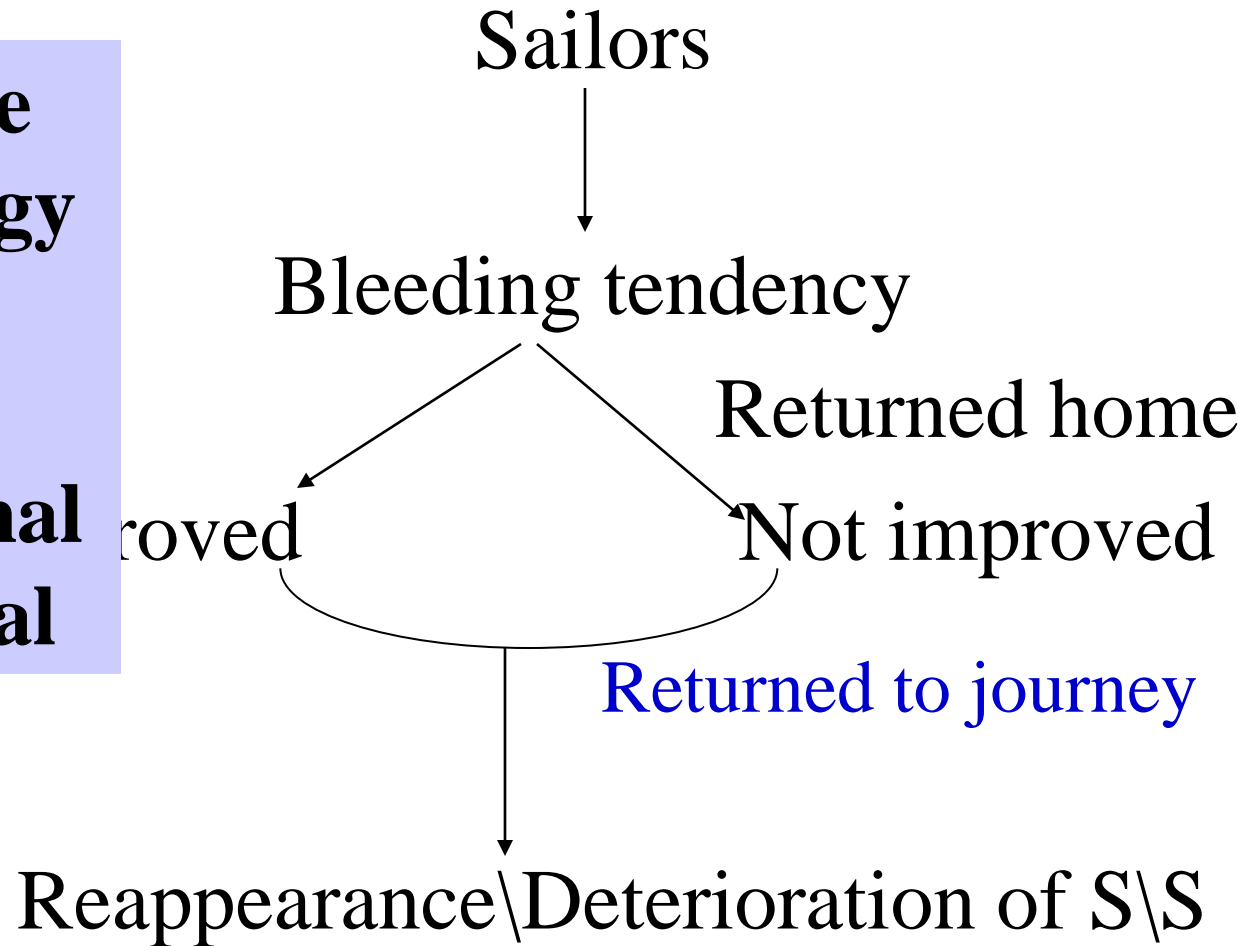
**James Lind, 1747**





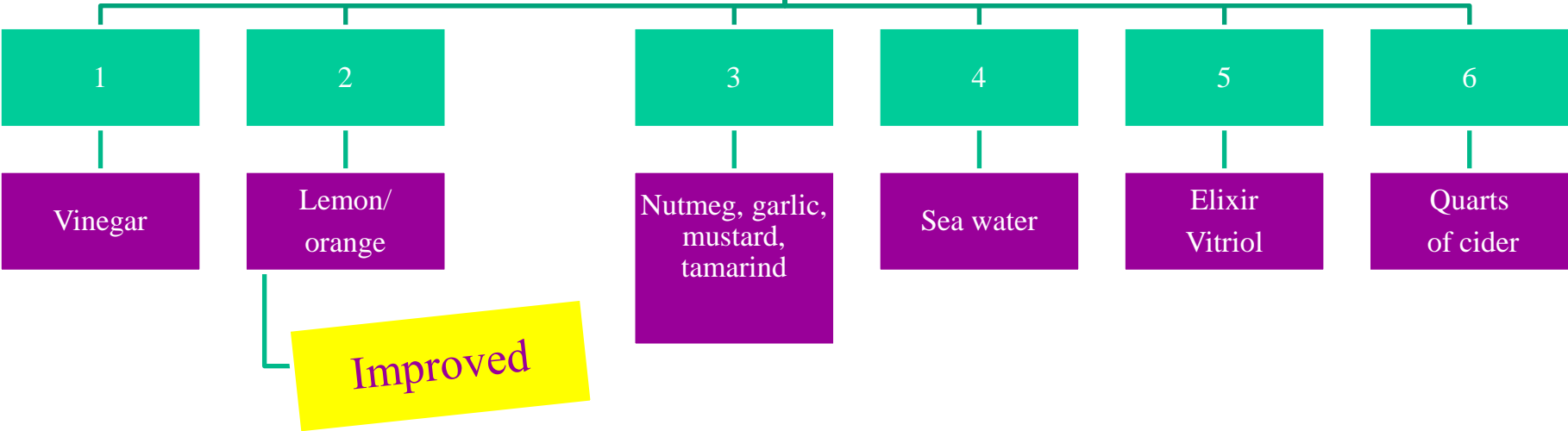
**Descriptive  
Epidemiology**

**Observational  
& Analytical**



**Hypothesis= Related to food habits**

Selected 12 patients  
(6 groups)



# **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

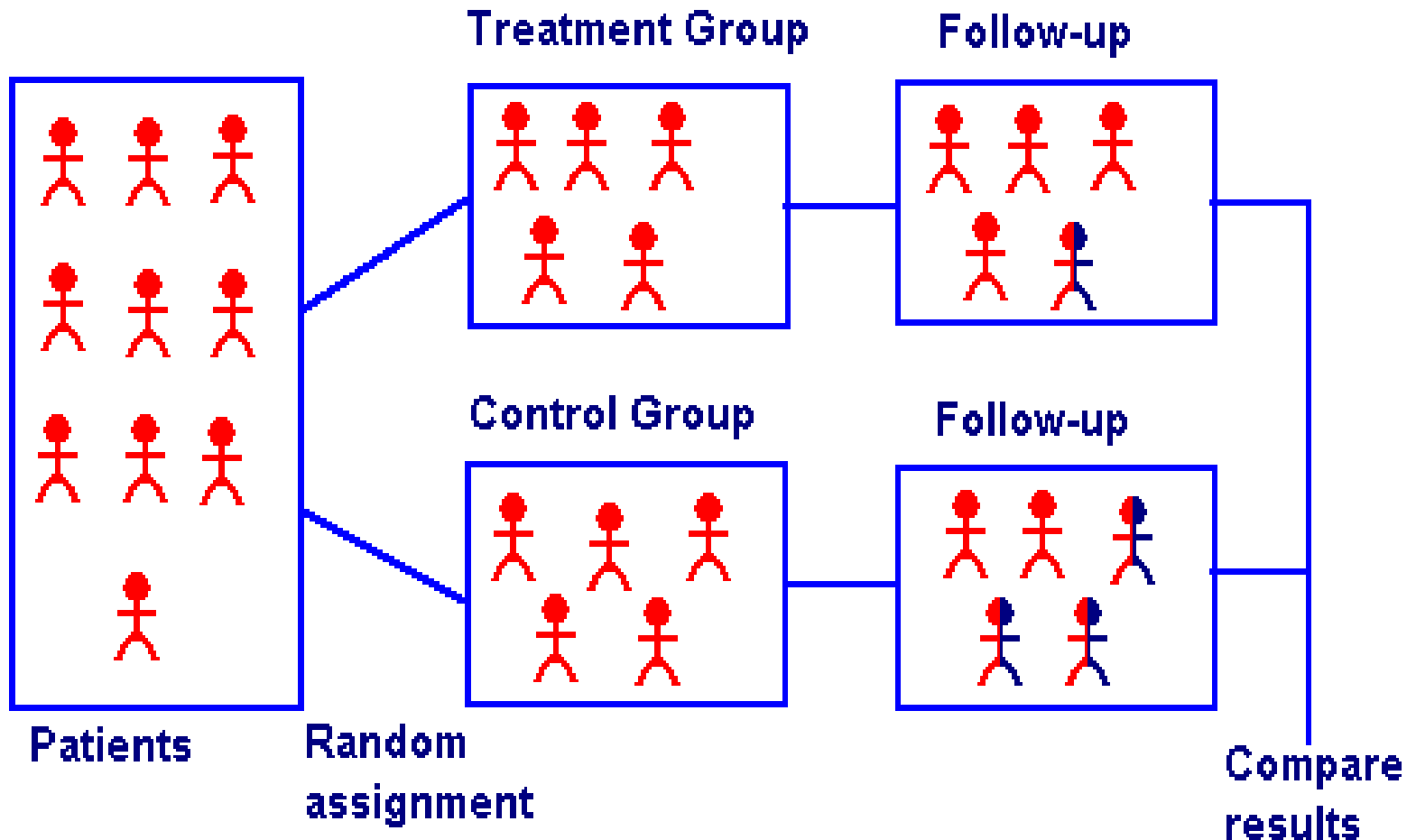
# **2- NON-RANDOMIZED TRIALS**

# Randomized Controlled Trials (RCT)

# Effectiveness of iron therapy in pregnant mothers



# Randomized Controlled Trials



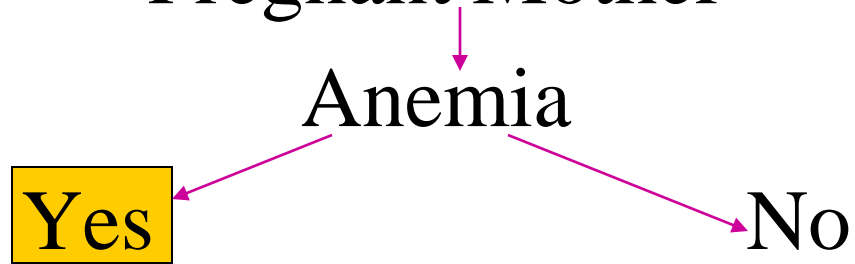
# Pregnant Mother

Pregnant Mother

Anemia

Yes

No



Pregnant Mother

Anemia

Yes

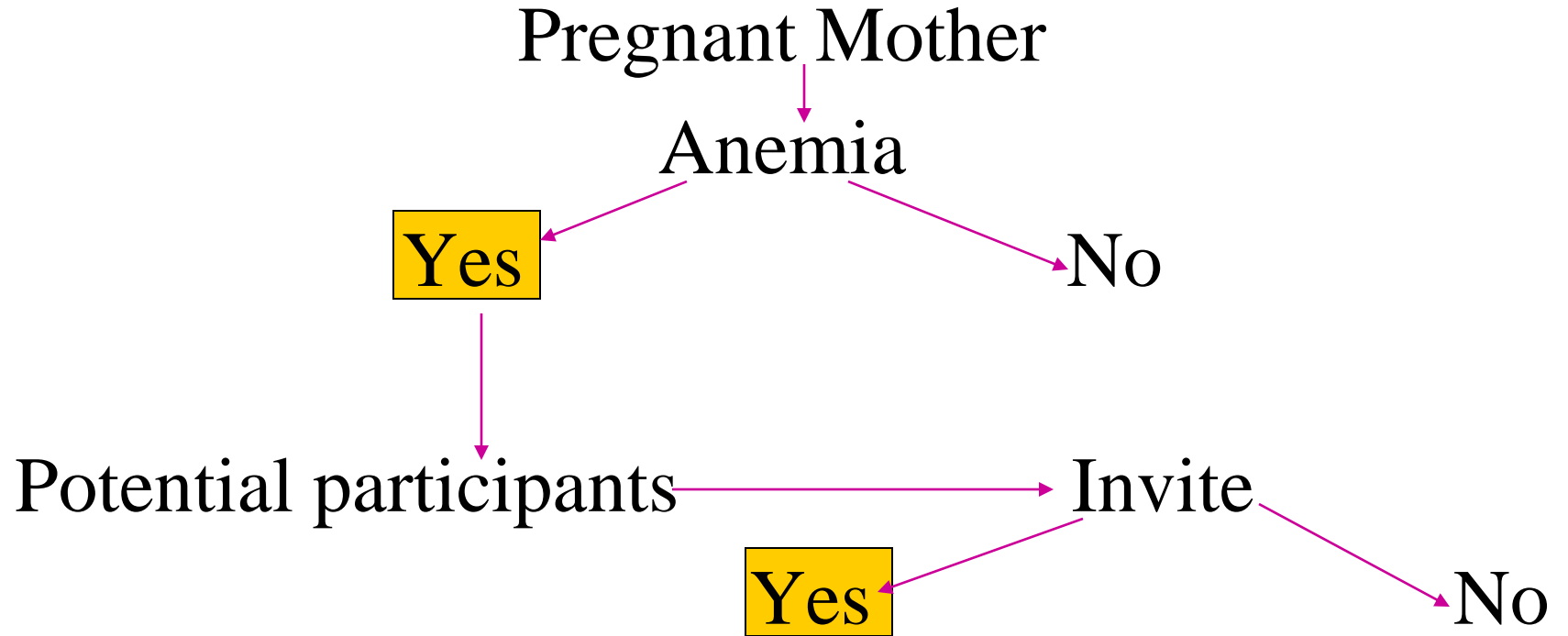
No

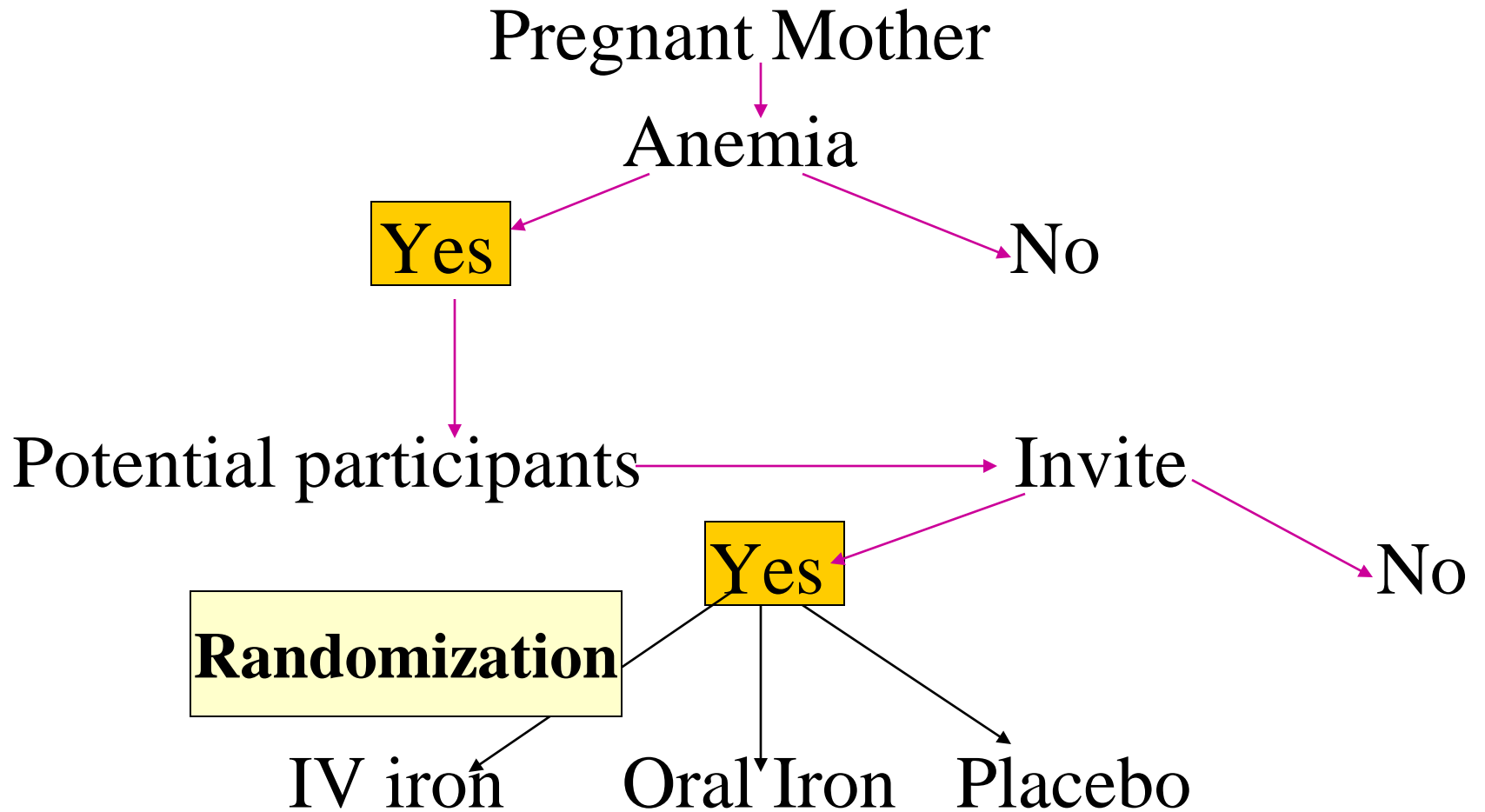
Potential participants

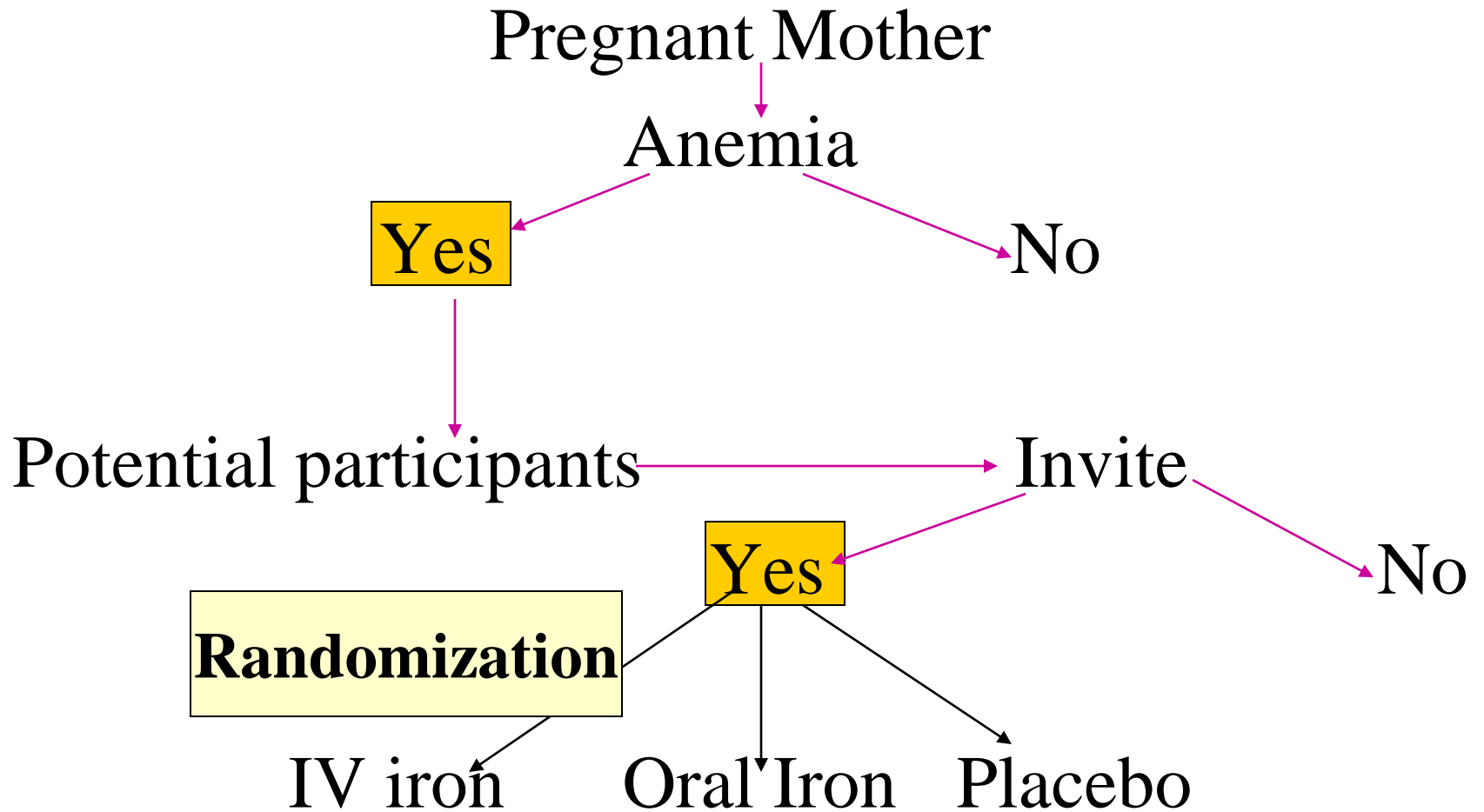
Invite

Yes

No







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/ manipulate 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

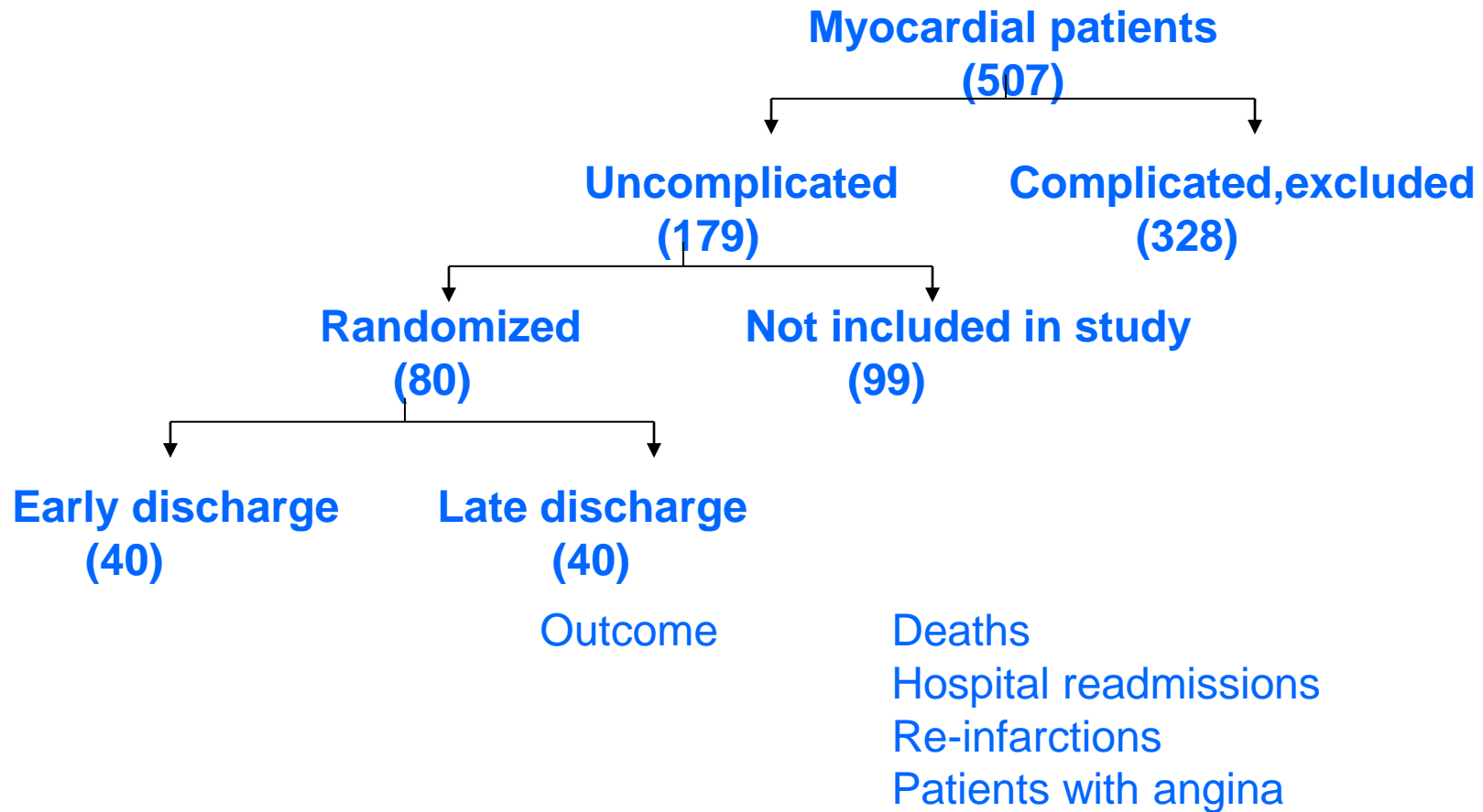
- Decrease in incidence
- Decrease in severity
- Decrease in cost of treatment

# Assessment

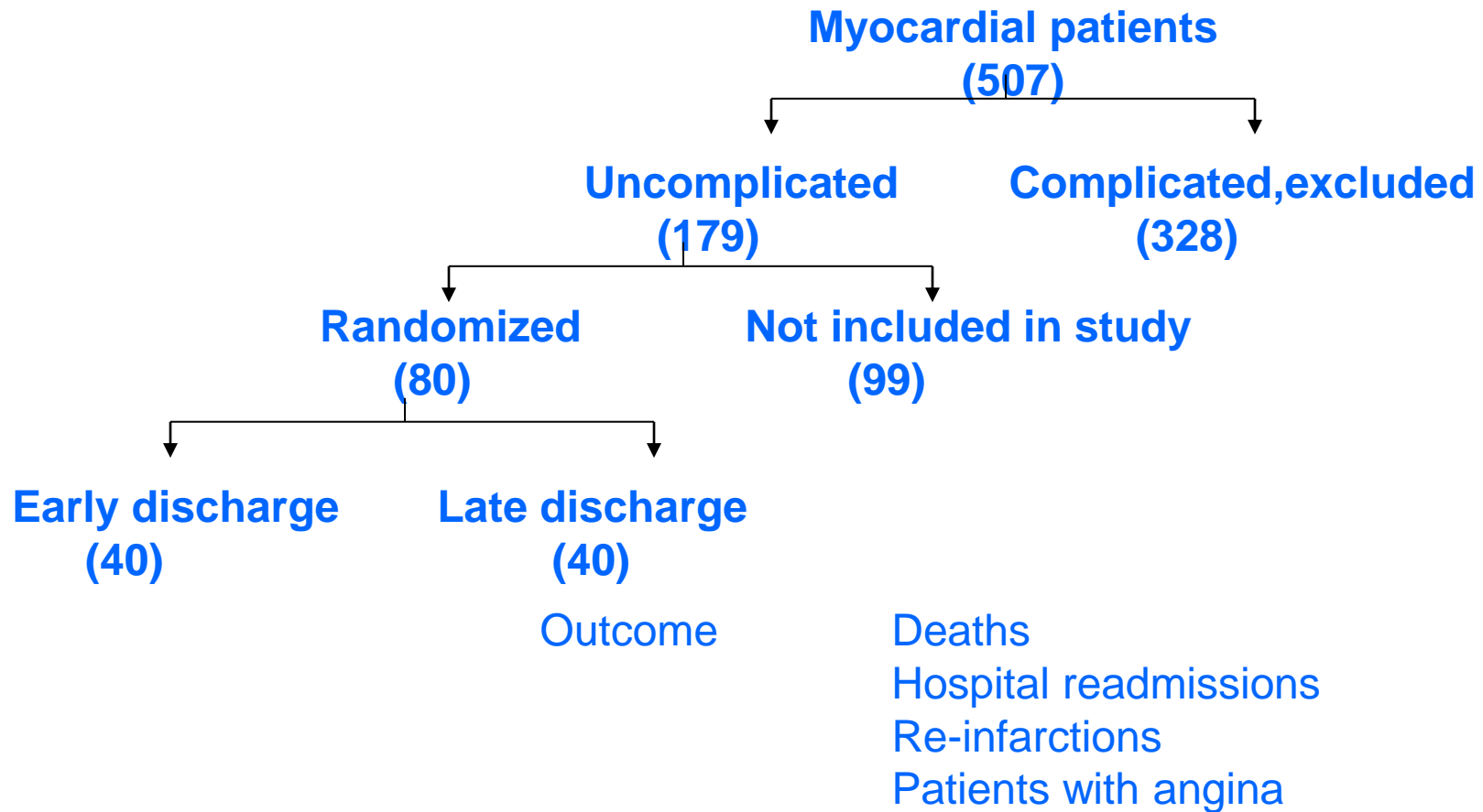
## Negative Results

- Increase in non-compliance,
  - 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



# Randomized controlled trial of early hospital discharge after myocardial infarction





# 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

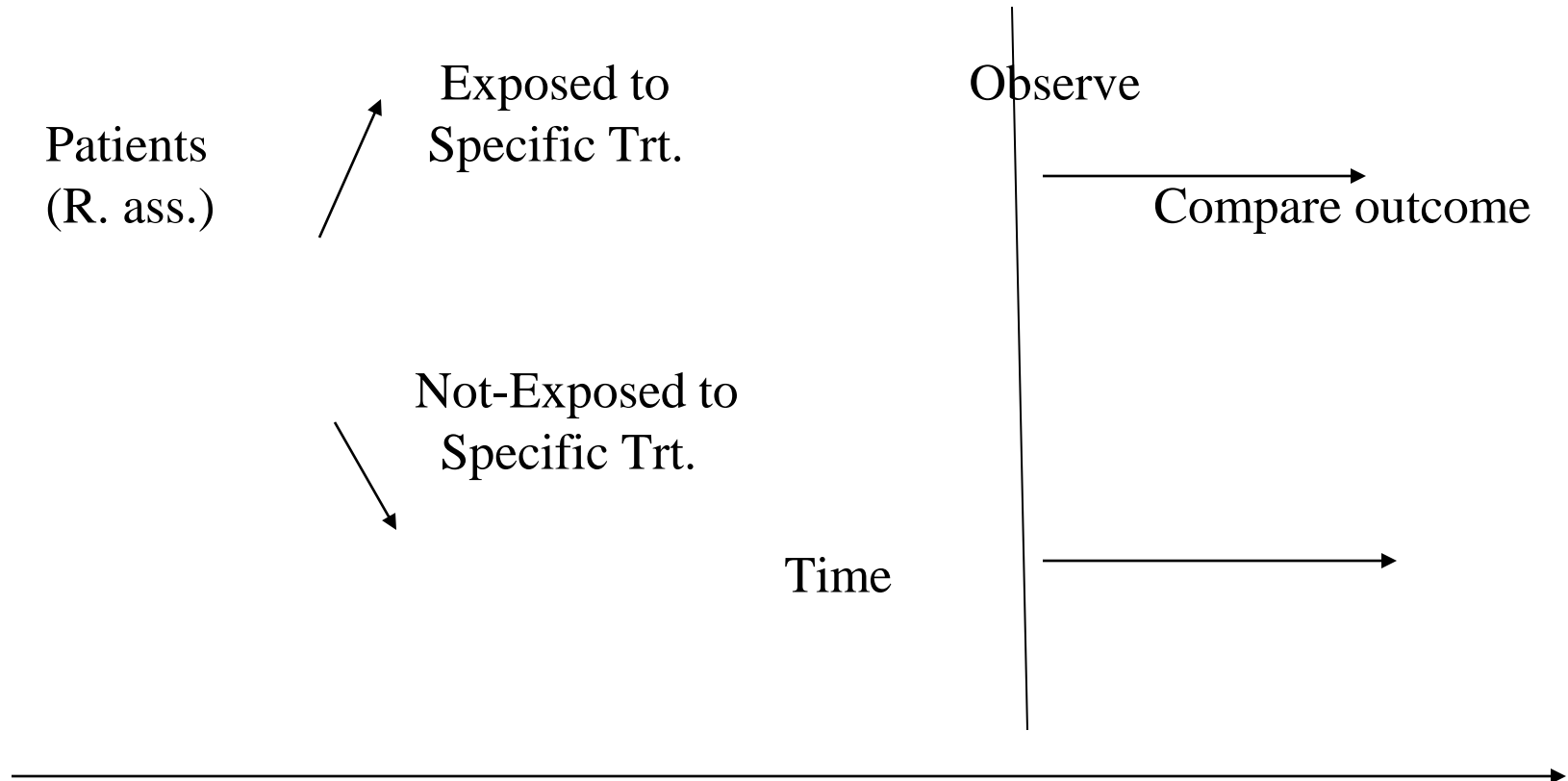
# Triple blind trial

- 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**

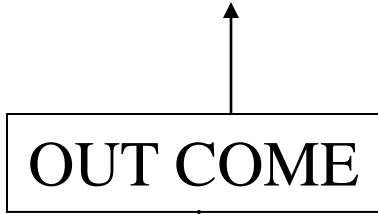
Therapy Y ----->

Therapy X ----->

A

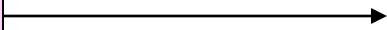


A



OUT COME

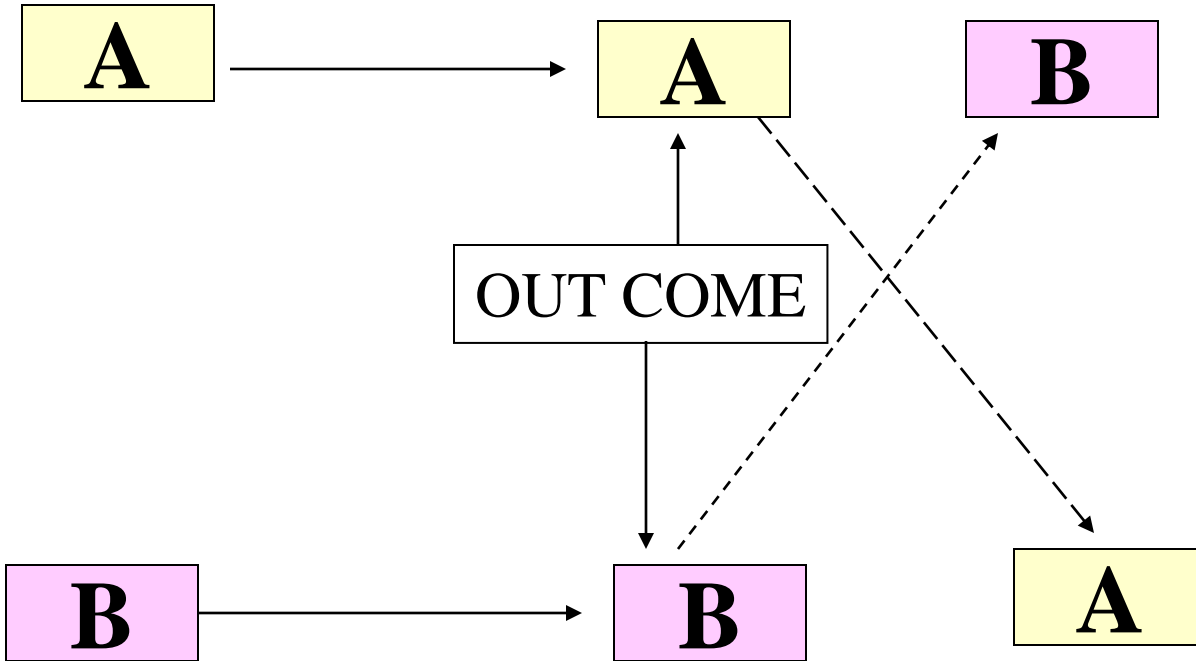
B



B

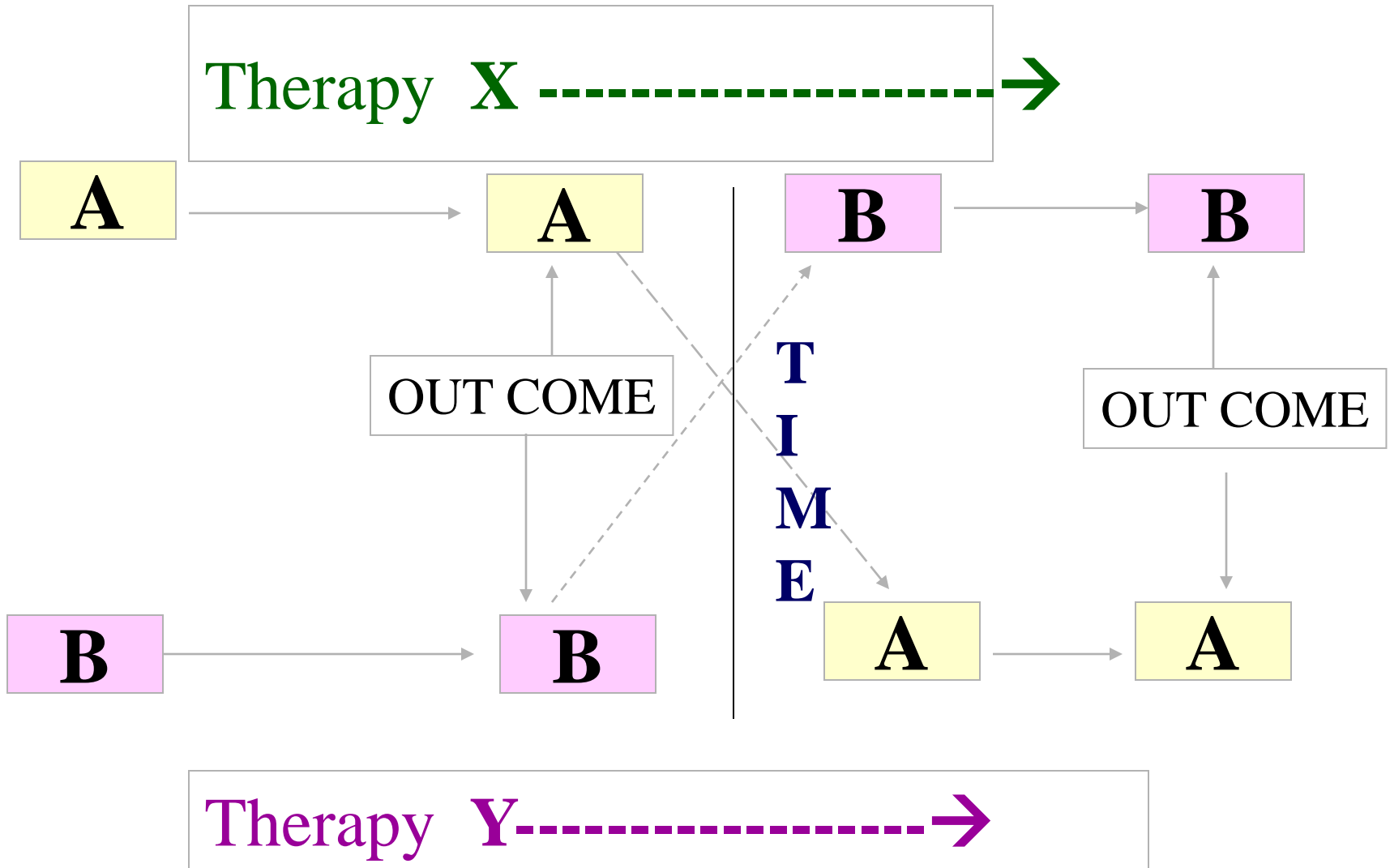
Therapy Y ----->

Therapy X ----->



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
- Incidence

Cross Sectional Survey

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