Experimental Study Design

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Steps for Conducting a Research

1) Selecting the **research topic**
2) Define the research **problem**
3) Specify the research **objectives** and **hypothesis**
4) Develop a research **design**
5) Design the **method** of collecting information
6) Manage and implement the **data collection**
7) **Analyze** and interpret the results.
8) **Write** a Final research report/manuscript

Study Designs in Health Research

What do you KNOW?

Learning Objectives

At the end of this session, you will be able to:

- ✓**Describe** RCT study design
- ✓**Explain** the advantages and disadvantages of RCT design
- ✓**Differentiate** between cohort and RCT study designs

Selection of Study Design

- There is **NO** best type of a study design.
- Choosing the study design depends on:
  - Research question and objectives
  - The knowledge already available about the problem
  - Available resources (cost, time, expertise of the researcher)
  - Ethics

2. An investigator wants to test the effectiveness of a performance-enhancing herbal supplement on students in his exercise class.

Which study design should the investigator choose?

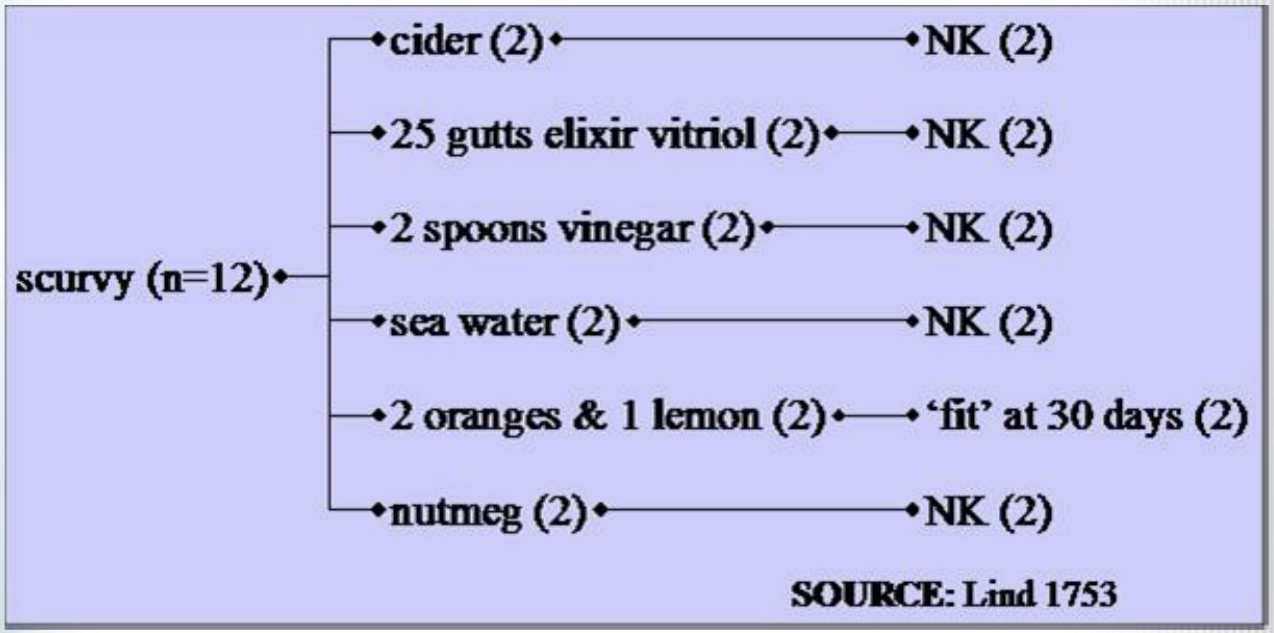
Randomized Control Trial

What are Experimental Studies?

- In an experimental study something is given or done to the experimental group but not to the control group.
- Any resulting differences in the outcome are compared.

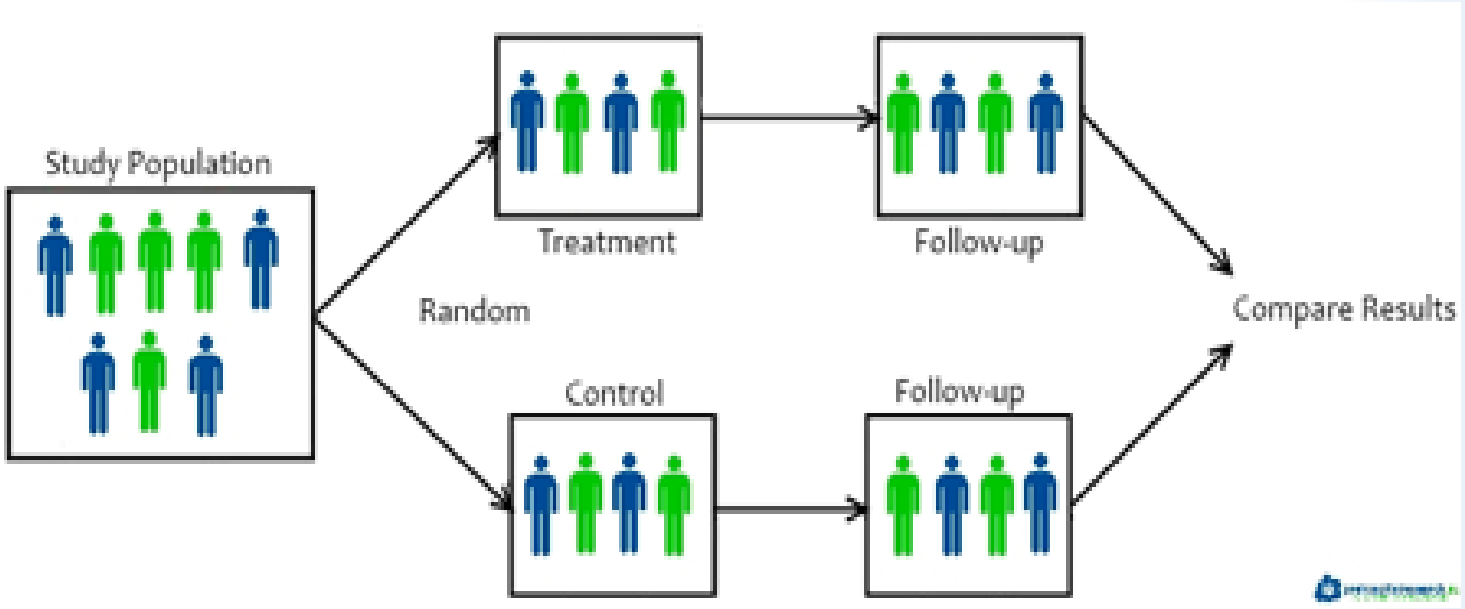
What are Experimental Studies?

The First Controlled Study?
James Lind: A Treatise of the Scurvy, 1753.



James Lind: A Treatise of the Scurvy in Three Parts. Containing an inquiry into the Nature, Causes and Cure of that Disease, together with a Critical and Chronological View of what has been published on the subject. A. Millar, London, 1753.

Randomized Control Trial

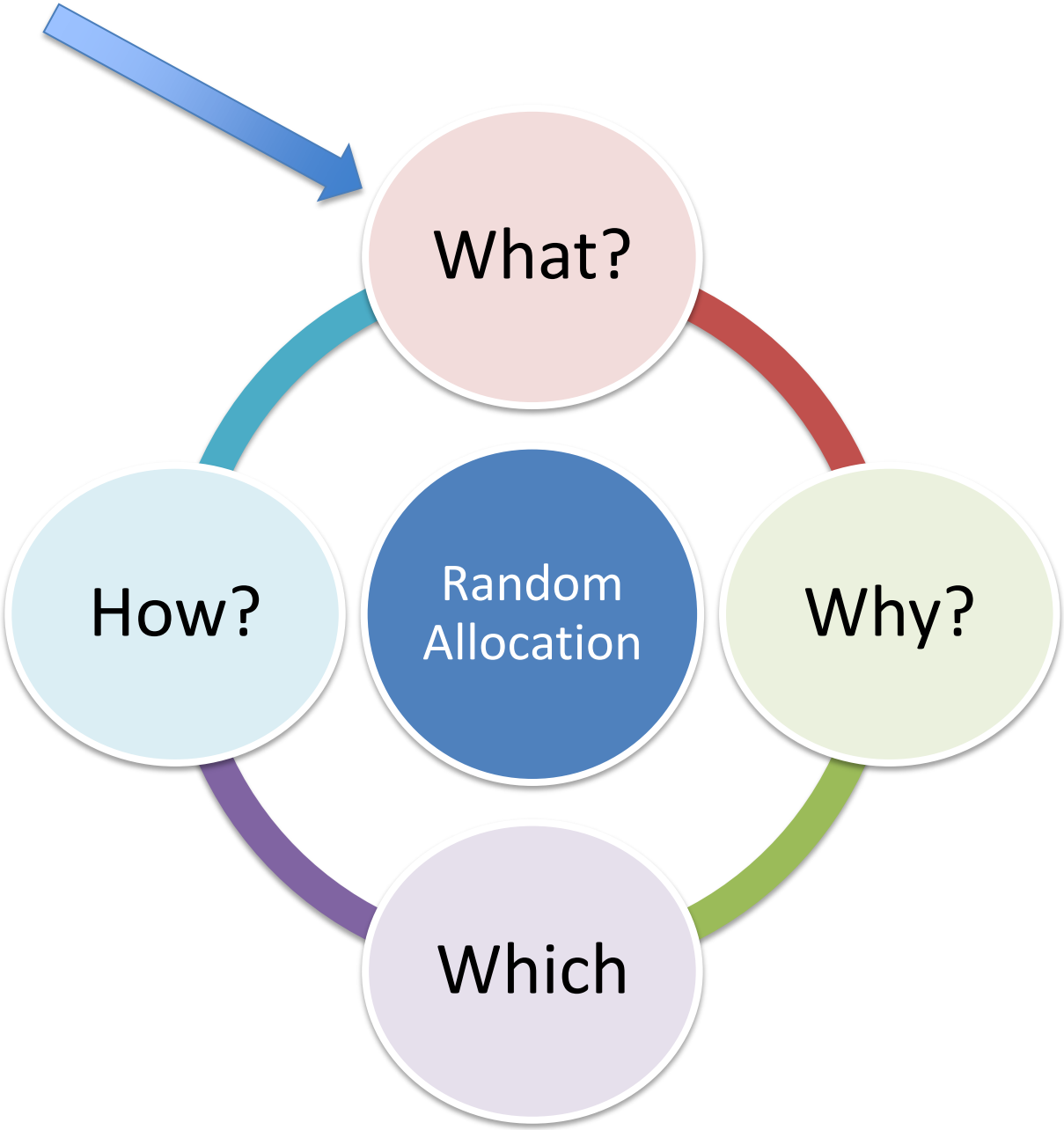


What is a randomized controlled trial?

- Simplest definition

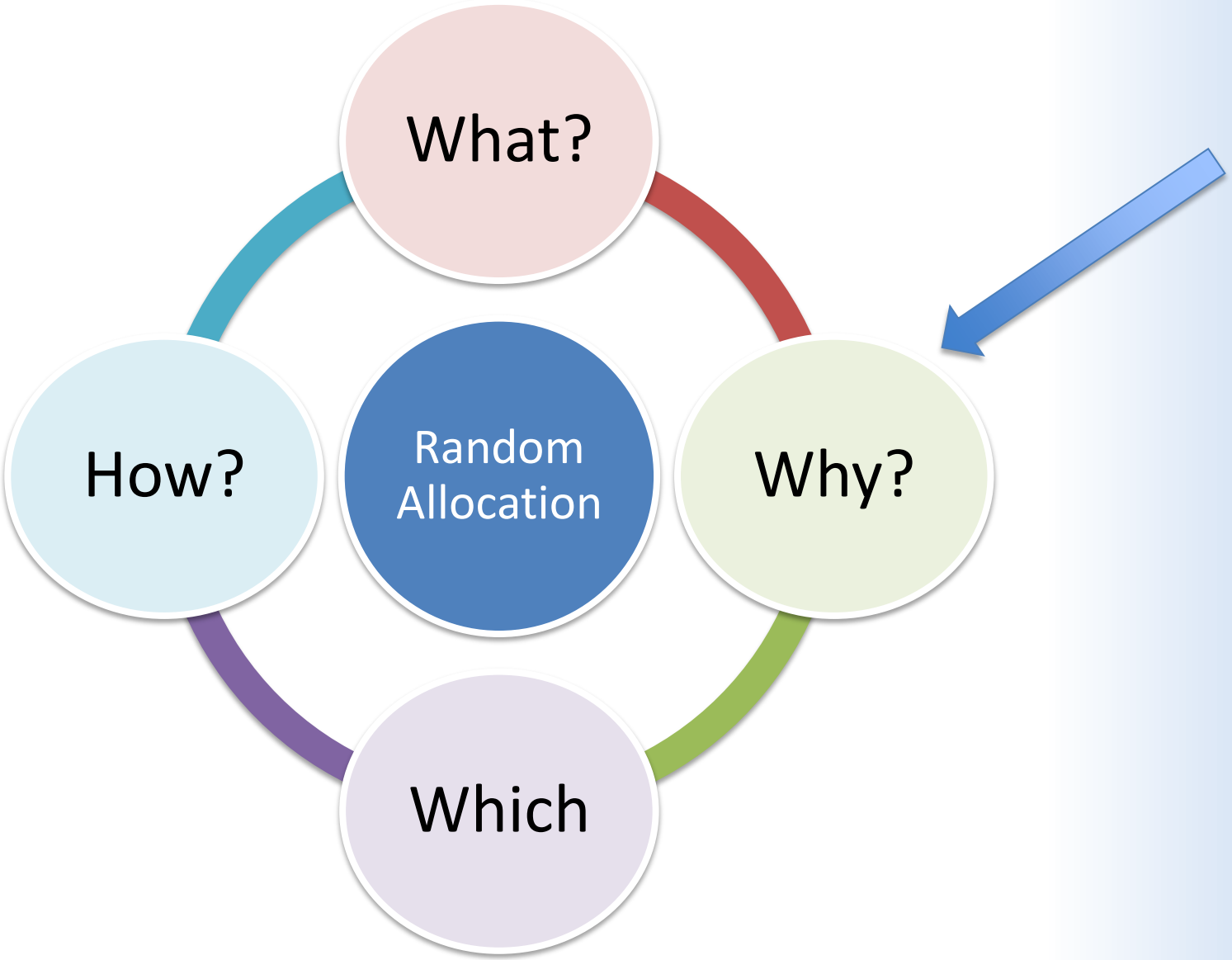
Individuals are allocated at random to receive one of several interventions (at least two total)

- RCT's are experimental—the intervention is controlled by the investigator


What?
How?
Random Allocation
Why?
Which

What is random allocation?

- Random allocation means that all participants have a defined probability of assignment to a particular intervention
  - ❖ Allocation is NOT determined by the investigator, clinicians, or participants
  - ❖ Allocation is NOT predictable based on a pattern


What?
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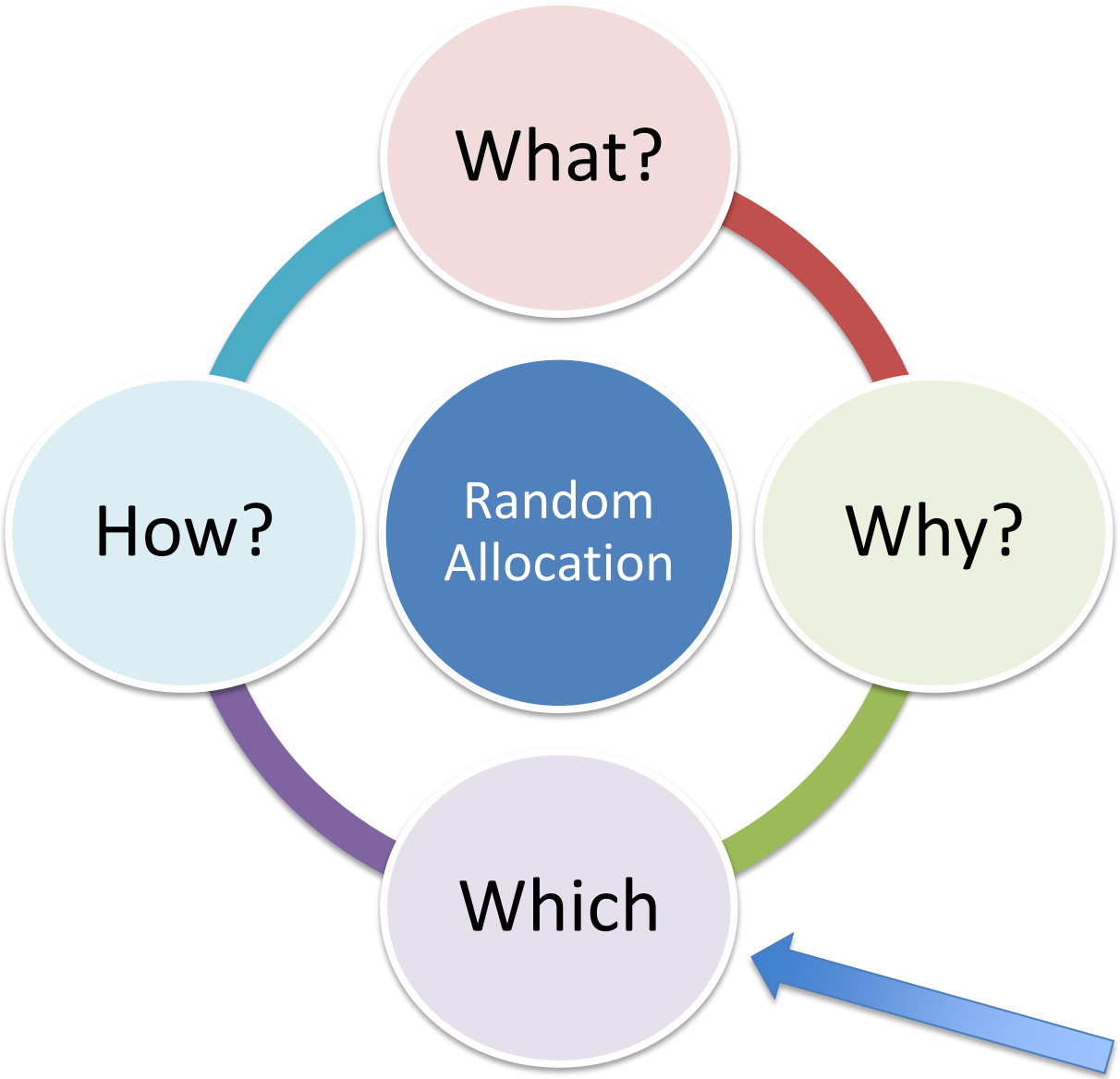
What purpose is served by random allocation?

- Covariates are distributed equally across the groups at baseline

- Affects both measured and, more importantly, unmeasured variables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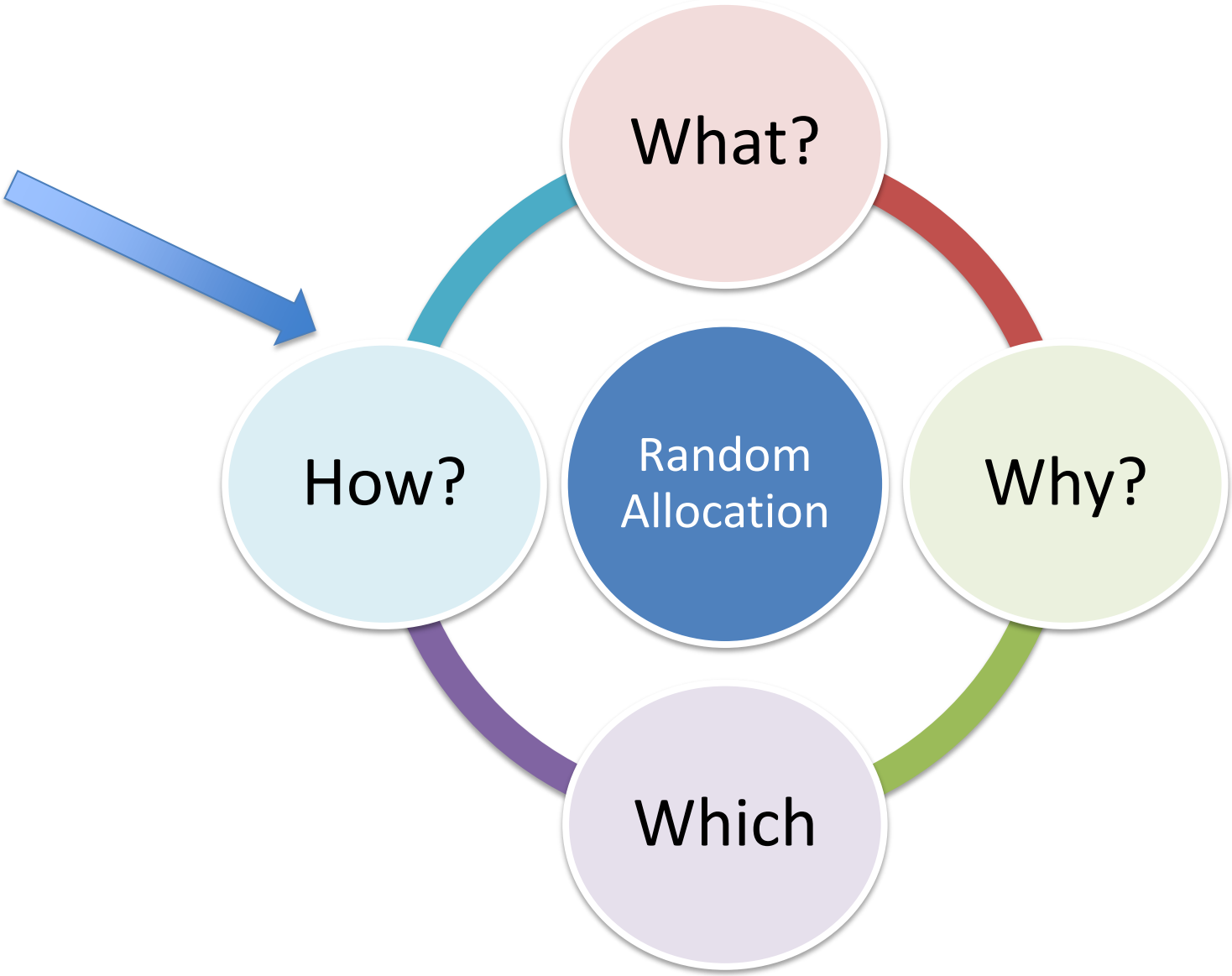
Methods of Randomization

- Date of birth (odd to group 1; even to group 2)
- Hospital record number (last digit; odd to group 1, even to group 2)
- Day of enrollment (Monday=Rx, Tues=Placebo, etc)
- Alternating (first person=Rx, second person=placebo, etc)

What elements of a trial can be randomized?

- Most common unit is individual patient
- Sometimes groups are randomized = **cluster randomization**
  - Examples: families, schools, towns, hospitals, communities
  - Worry about contamination in cluster randomization
  - Special statistical techniques needed to cope with the loss of independence of the individual units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How is randomization achieved?

- Two steps involved:
  - ❖Generation of allocation sequence
  - ❖Implementation of allocation (concealment of allocation)

Generation of allocation sequence

- Simple randomization
  - Analogous to a repeated fair coin tossing
- Restricted randomization

Blocking

  - Done to ensure equal balance of arms throughout all portions of the study
  - For example, blocks of six would have 3 active/3 control
  - Block size itself can/should vary
- Stratified randomization
  - Individuals are identified based on important covariates (sex, age, etc.) and then randomization occurs within the strata

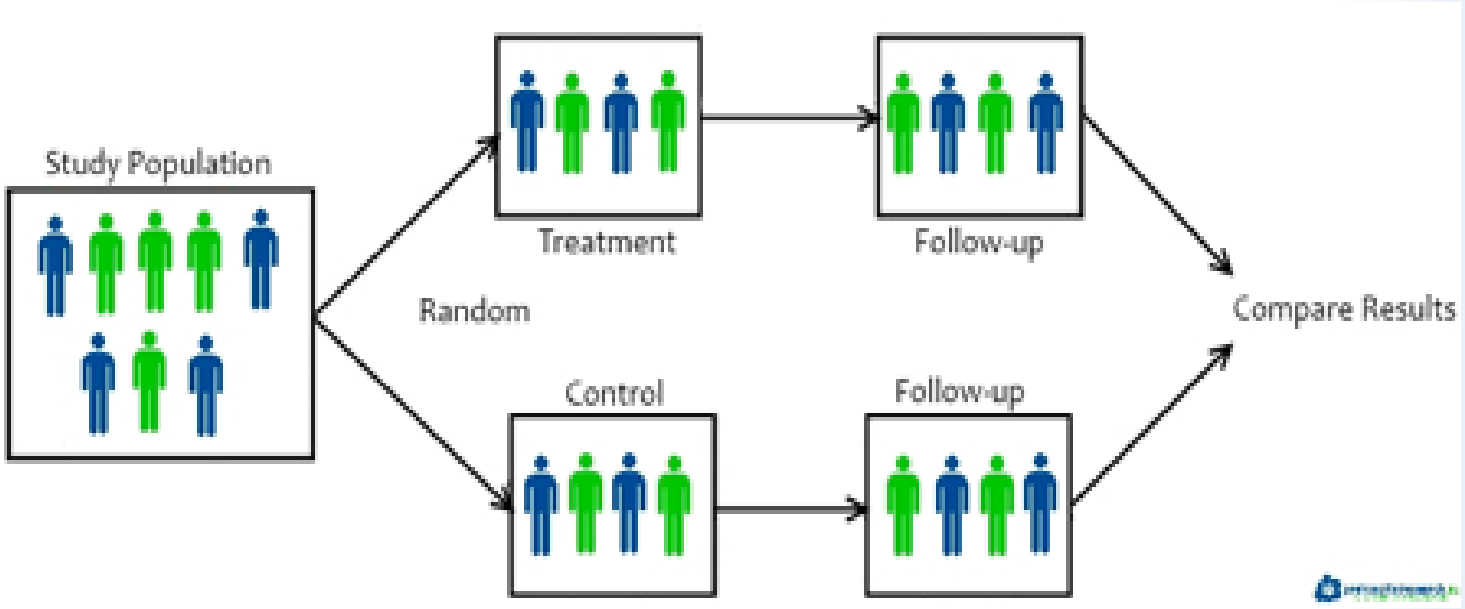
Concealment of allocation

Concealing the allocation sequence from those assigning participants to the intervention groups, until the moment of assignment.

→ it prevents researchers from (unconsciously or otherwise) influencing which participants are assigned to the intervention or control group.

- If those making the decision about patient eligibility are aware of the arm of the study to which the patient will be allocated --if randomization is unconcealed--they may systematically enroll sicker--or less sick--patients to either treatment or control groups.
- This will defeat the purpose of randomization and the study will yield a biased result.

Randomized Control Trial



Blinding (Masking)

- Process that attempts to keep the group (e.g. active drug or placebo) to which the study subjects are assigned not known or easily ascertained by those who are “masked.”

- Relevant groups who may/may not have knowledge of treatment assignments
  1. Participants
  2. Investigators/clinicians administering intervention
  3. Investigators assessing outcomes
  4. Data analyst(s)

Concealment of Allocation vs. Blinding

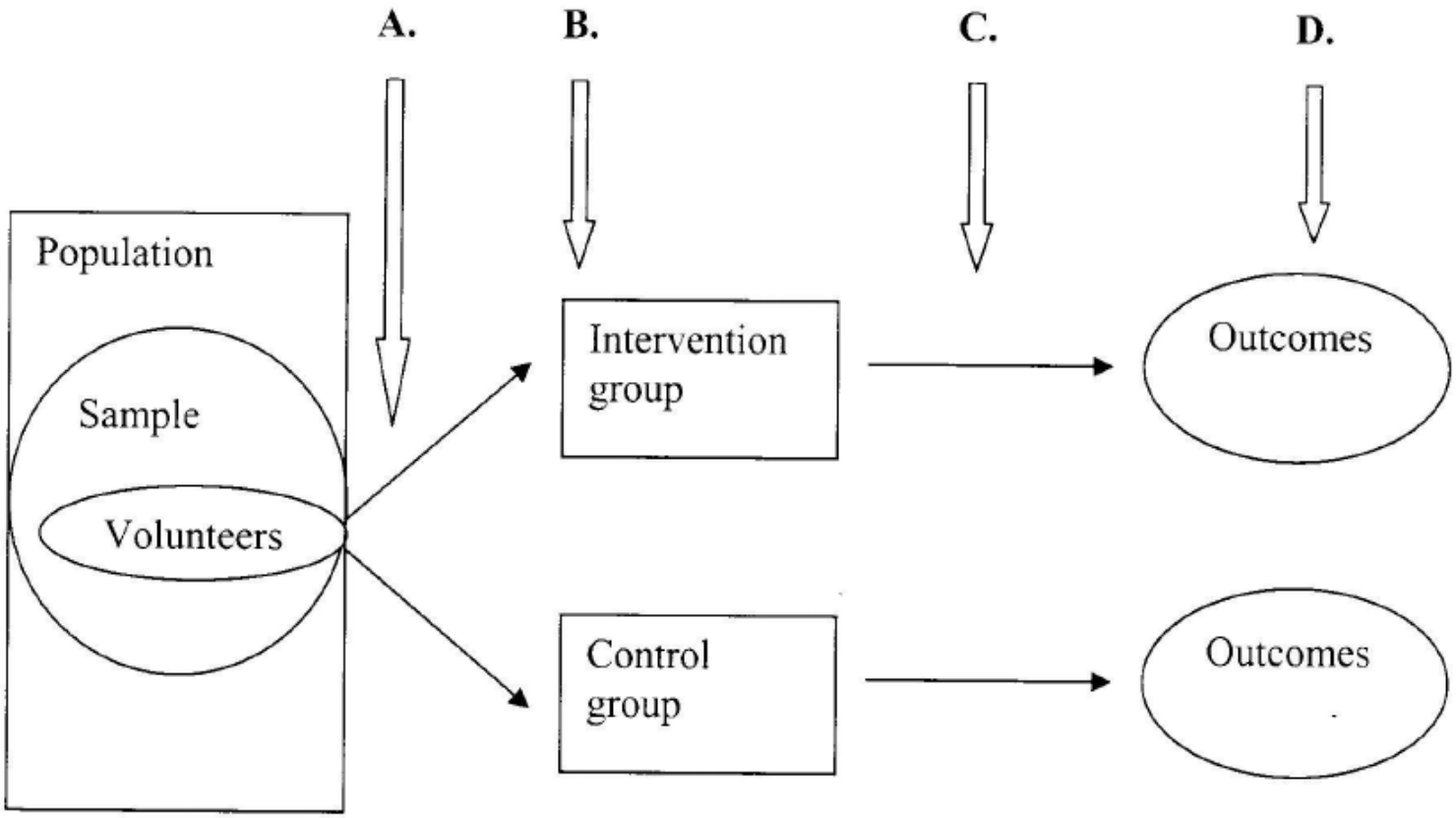
Concealment of allocation:

- Procedure to protect the randomization process **before** the subject enters the trial
- Concealment of allocation is ALWAYS feasible
- If not done, results in selection bias (randomization benefits are lost, and treatment assignment is no longer truly random)

Blinding:

- Masking of the treatments **after** randomization (once trial begins)
- Blinding is not always feasible
- If not done, can result in patients biasing their responses because of their knowledge of treatment; can also lead to biased outcome assessment because investigators have knowledge of treatment

General Design of a Randomized Controlled Trial



A. Randomization and allocation concealment
B. Actual assignment that can be followed by masking subjects as to their assigned group
C. Prospective evaluation period during which health care providers, investigators, and/or external monitoring committees (eg, data safety monitoring board) can be masked as to the subjects' assigned group
D. Outcome evaluation or adjudication during which outcome asessors can be masked as to the subjects' assigned group

Reference: Viera A and Bangdiwala S, Eliminating Bias in Randomized Controlled Trials:Importance of Allocation Concealment and Masking, Fam Med 2007;39(2):132-7

Strengths and Limitations

- **Strengths**
  - One treatment is directly compared to another to establish superiority.
  - This study design can make causal inferences, i.e. it is the strongest empirical evidence of a treatment's efficacy
  - Minimum bias
- **Limitations**
  - Resource, expensive
  - Results may not mimic real life application
  - Ethical implications: denying treatment to one group, ability to provide informed consent


thank
you!