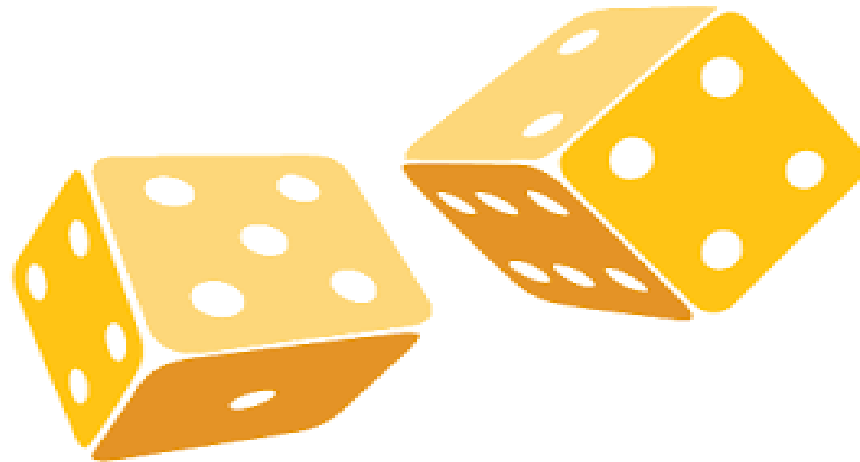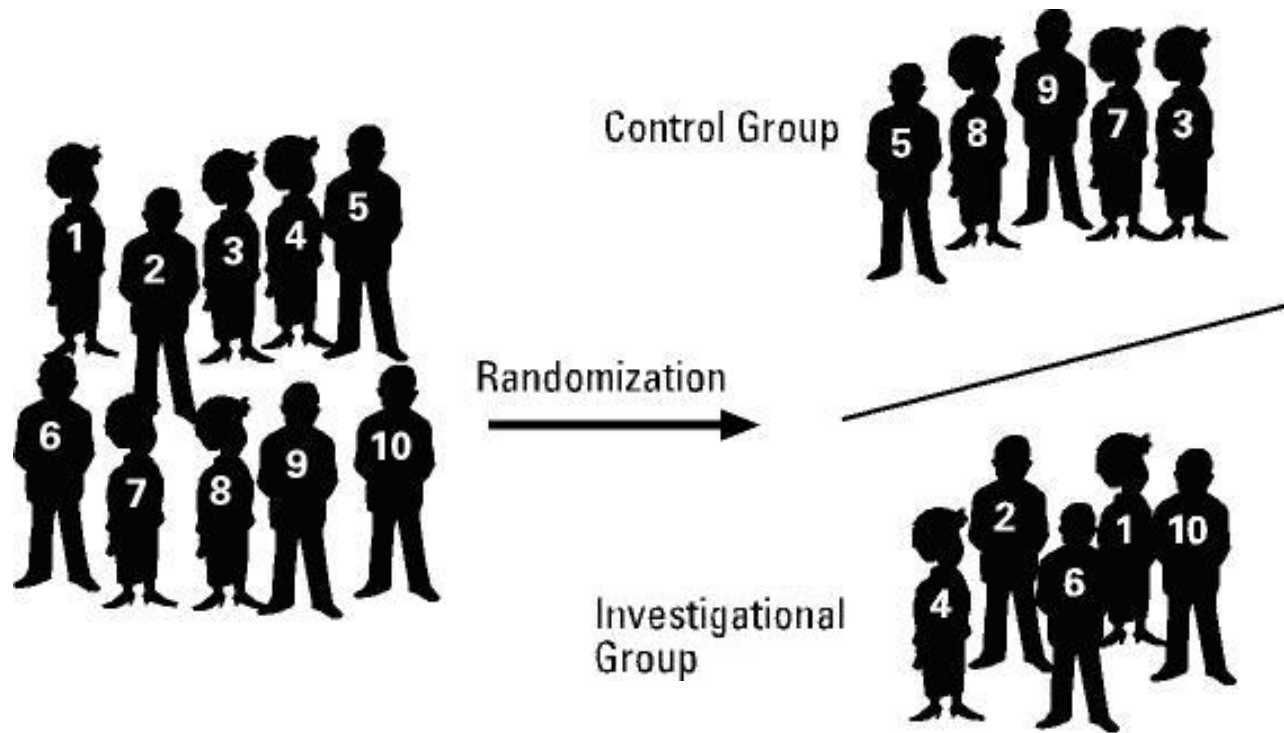بسم الله الرحمن الرحيم

روش تحقیق

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Randomization

Randomization

Concept

☐ The use of randomization can avoid subjective assignment of treatments to patients who participate in clinical trials.

☐ Randomization tends to

  ■ Produce study groups comparable with respect to known and unknown risk factors.

  ■ Removes investigator bias in the allocation of participants.

  ■ Guarantees that statistical tests will have valid significance levels.

Difference Between Two Concepts

- Random selection (Sampling)

- Random allocation

Pseudo randomization

- Some systematic unacceptable methods for assignment

  - Assignment of patients to treatment according to the order of enrollment (every other patient is assigned to one group).

  - Assignment of patients to treatment according to patient's initial.

  - Assignment of patients of treatment according to patient's birthday.

  - Assignment of patients according to the dates of enrollment.

Randomization Methods

- Types of randomization methods
  - Complete (simple) randomization
  - Restricted randomization
    - The permuted-block randomization
    - Stratified randomization
  - The adaptive randomization

Complete Randomization

☐ Also known as **Simple Randomization.**

☐ No restrictions are enforced on the nature of randomization sequence except for the number of patients required.

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Complete Randomization(Cont.)

- □ Properties
  - ■ The chance that a patient receives either the test drug or the placebo is 50%.
  - ■ Randomization of assignments is performed independently for each of the N patients.

- □ The randomization codes can be generated either by the table of random numbers or by a software.

Complete Randomization(Cont.)

- ☐ It is possible that a trial will end up with an unequal number of patients in each treatment group.
- ☐ One of the major disadvantages of simple randomization is that treatment imbalance can occur periodically.
  - ■ The randomization is performed within each center and the number of patients to be enrolled at each center is usually few.
  - ■ Most clinical trials recruit patients sequentially: demographic factors or baseline characteristics change over time.

Permuted-Block Randomization

◻ In addition to the assurance of treatment balance, the permuted-block randomization can account for a possible time-heterogeneous population by forcing a periodic balance.

Permuted-Block Randomization(Cont.)

□ First divide the whole series of patients into blocks with appropriate (typically equal) blocking sizes.

□ Then randomize the patients within each block to ensure that an equal number of patients will be assigned to each group.

Balanced Block Randomization

1.	AABB	1	3	2	9	1
2.	ABAB	6	4	3	8	7
3.	ABBA					
4.	BBAA	3	1	2	5	8
5.	BABA	2	4	1	7	3
6.	BAAB	4	5	3	9	6

Balanced Block Randomization(Cont.)

1. AABB	1	3	2	9	1
2. ABAB	6	4	3	8	7
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B	A	A	B	B	B	A	A
A	B	B	A	A	B	B	A
A	A	B	B	A	B	A	B
B	A	B	A	A	B	B	A
B	B	A	A	A	A	B	B
A	B	B	A	B	B	A	A
B	A	B	A	A	B	B	A
B	A	A	B	A	A	B	B

Stratified Randomization

- Ensure balance in treatment assignments within subgroups defined before Randomization.
  - Clinic, gender, risk level
- Subgroup should be related to outcome—strong confounder or effect modifier.
- Requires a separate set of treatment assignments schedules for each category of each stratum.

Masking

- Synonymous with blinding.

- Treatment assignment is not known after randomization.

  - Patient, clinic personnel, evaluators, data processors, analyst, independent review committee, sponsor . . .

  - Single, double, triple, quadruple . . .

  - protects against information bias

- Not the same as concealment of treatment assignment prior to randomization.

  - Concealment protects against selection bias

Definition

□ Any attempt to make the various participants in a study unaware of the assigned treatment, so that they should not be influenced by their knowledge or preconception in their report, assessment, recording, analysis and interpretation.

Level of Masking

☐ Unblended or Open label

☐ Single blind

☐ Double blind

☐ Triple blind

Level of Masking

- ◻ Single
  - ∎ Participant is masked
- ◻ Double
  - ∎ Participant and clinical investigator are masked
- ◻ Triple
  - ∎ Participant and clinical investigator and "others" are masked
    - ◻ Others: outcome evaluators, data analysts, data monitoring committees, sponsors . . .

Allocation Concealment (Randomization Blinding)

□ Efforts made to generate unpredictable and unbiased sequences are likely to be ineffective if those sequences are not protected by adequate concealment of the allocation sequence from those involved in the enrolment and assignment of participants.

Allocation Concealment (Randomization Blinding)

☐ **Concealment of allocation sequence** shields those who admit participants to a study from knowing the upcoming assignments.