

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

إِنَّ اللَّهَ لَا يُغَيِّرُ مَا بِقَوْمٍ حَتَّىٰ يُغَيِّرَ مَا بِأَنفُسِهِمْ

The Randomization Process

- The randomized clinical trial is the standard by which all trials are judged
- In the simplest case, randomization is a process by which each participant has the same chance of being assigned to either intervention or control

Purposes of Randomization

- To generate comparative groups
- To enable valid statistical tests

Random components in RCT

- Random Sampling
- Random allocations

Bias is prevented by randomization and blindness

- Bias often occurs due to preconceived ideas or perceptions acquired during the study by:
 1. The investigator and supporting staff who might influence reporting response to therapy or adverse events
 2. The patients who might influence compliance, cooperation or provision of information

Blindness

- Open label (unblinding)
- Single blinding (patients only)
- Double blinding (patients and investigators)
- Triple blinding (patients and investigators and Monitoring investigators)

Classic classification of Randomization

- Simple
- Systematic
- Balanced block
- Stratified

Randomization methods

- Complete randomization
 - Simple randomization
- Permuted block randomization
 - Stratified randomization
 - Matched randomization
- Adaptive Randomization
 - Treatment adaptive randomization (biased coin randomization)
 - » Urn randomization
 - Covariate Adaptive randomization (minimization)
 - Response Adaptive Randomization
 - » Play-the-winner rule (without replacement)
 - » Modified Play-the-winner (deterministic)
 - » Randomized Play-the-winner

Complete randomization

(Simple randomization)

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

TABLE 7-3 ▼ A Table of Random Numbers

	00-04	05-09	10-14	15-19
00	56348	01458	36236	07253
01	09372	27651	30103	37004
02	44782	54023	61355	71692
03	04383	90952	57204	57810
04	98190	89997	98839	76129
05	16263	35632	88105	59090
06	62032	90741	13468	02647
07	48457	78538	22759	12188
08	36782	06157	73084	48094
09	63302	55103	19703	74741

Complete randomization (Simple randomization)

- Limitations:
 - Imbalanced treatment groups
 - Imbalance over time

Complete randomization

(Simple randomization)

- Random allocation

It is a form of restricted randomization

It randomly selects the $N/2$ out of a total of N patients *without replacement* and assigns these $N/2$ patients to receive the test drug and the other half to receive the placebo.

The marginal probability for assigning a patient to each of the two treatment groups is $\frac{1}{2}$ but the conditional probability for assignment of a patient given that the assignment of the previous patient is not equal to $\frac{1}{2}$.

Permuted block randomization (Balanced block randomization)

- One of the major disadvantages of simple randomization is that treatment imbalance can occur periodically
- If the demographic factors or baseline characteristics change over time, it is quite possible to have a serious covariate imbalance between treatment groups.

Treatment adaptive randomization

- The Treatment adaptive randomization adjusts for the assigning probability of the current patient with respect to the number of patients who have been randomized to each treatment group.
- Methods:
 - biased coin randomization
 - » A constant assigning probability is used during the entire course of the study
 - Urn randomization
 - » The probability of the assignment of the current patient is a function of the current treatment imbalance
 - » It requires a much more complicated analysis

Response Adaptive Randomization

Example

Modified Play-the-winner

TRT A S S F S S S F

TRT B S F

Patient 1 2 3 4 5 6 7 8 9

Generalization of RCT

- External versus internal validity
- What is the purpose of a RCT?
 - Efficacy
 - Effectiveness
 - Efficiency
- Average efficacy vs. variability of efficacy

Any Question?



Thank you