

## Understanding Randomization Trials

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**Abstract:** RCT's has been recognised as the standard method for rationalising treatment outcomes in medical literature. However, many researchers are still unfamiliar with how to properly randomize the study, and it has been shown that there are limitations in studies due to inaccurate performance of the randomization, leading to errors in results, even though they published in indexed International journals. This review on randomization trials, help researchers to develop the skills for critically analysing RCT's in terms of methodology, magnitude and precision of treatment.

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### I. Introduction

The randomised controlled trial (RCT) provides the most accurate and reliable evidence on the effectiveness of interventions, as the process used during the random allocation minimise the risk of confounding factors. Due to this, the findings generated by RCTs are likely to be closer to the true effect than the findings generated by other research methods [1]. The term "RCT" and randomised trial are sometimes used synonymously, but the methodologically sound practice is to reserve the "RCT" name only for trials that contain control groups, in which the groups receiving the experimental treatment are compared with control groups receiving no treatment. The term "randomised trials" omits mention of controls and can describe studies that compare multiple treatment groups with each other (in the absence of control groups) [2].

The first published RCT in medicine appeared in 1948 paper entitled "Streptomycin treatment of pulmonary tuberculosis", which described a Medical Research Council investigation. One of the authors of that paper was Austin Bradford Hill, who is credited as having conceived the modern RCT [3]. By the late 20<sup>th</sup> century, RCT's were recognised as the standard method for "rational therapeutics" in medicine. To improve the reporting of RCT's in the medical literature, an international group of scientists and editors published Consolidated Standards of Reporting Trials (CONSORT) statements in 1996, 2001 and 2010, and these have been widely accepted [4].

### Random allocation

Random allocation is a technique that chooses individuals for treatment groups and control groups entirely by chance with no regard to the will of researchers or patient's preferences. This allows researchers to control all known and unknown factors that may affect the results in treatment groups and control groups. Many researchers are still unfamiliar with how to do randomization, and it has been shown that there are limitations in many studies due to inaccurate performance of the randomization and that some studies are reporting incorrect results, even though they published in International journals of repute. Thus, the ideal way of balancing limitations is to apply accurate randomization technique in the initial stage of clinical research instead of using it in post data collection period.

When you are reading and analysing a RCT based study, the answer to few questions will help you to decide whether you can trust the results of the study/ or you can apply the results to your patients. Issues to consider when reading a RCT may be condensed into three important areas [5].

- The validity of the trial methodology
- The magnitude and precision of the treatment effect
- The applicability of the results to your patient or population

### Categories of Randomization

Many procedures have been proposed for the random assignment of participants to treatment groups in trials. In this article, common randomization techniques are reviewed. It is very important to select a method that will produce interpretable and valid results for your study.

### Simple Randomization:

Thus is commonly used and intuitive procedure, similar to "repeated fair coin-tossing". For example, with two treatment groups (control versus treatment), the side of the coin (i.e, heads- controls, tails- treatment) determines the assignment of each subject. Even though this is the most basic way, if the total number of

samples is small, sample numbers are likely to be assigned unequally. It is therefore recommended only for RCT's with over 100 subjects.

### **Block Randomization**

It can ensure balance in the number of patients allocated to each of the groups in the trial. Patients are considered in blocks, which keeps the number of subjects in each group similar at all times. The block is determined by researcher and should be a multiple of the number of groups (i.e., with two treatment groups, block size of either 4,6 or 8). After determining the block size, all possible balanced combinations with the blocks must be calculated. For example, using a block size of four for two treatments arms (A&B) will lead to six possible arrangements of two A's and two B's (blocks): AABB, BBAA, ABAB, BABA, ABBA, BAAB. Any of the randoms can be used to start allocation order for the first four subjects. However, there is a disadvantage, that the executes can predict the next assignment and groups may be generated that are rarely comparable in terms of certain covariates [6]. Website, [www.randomization.com](http://www.randomization.com) can do block randomization for upto 4 kinds of block sizes and it is very easy to use.

### **Stratified Randomization**

This method balances the influence of covariates.it can achieve balance in groups in terms of subjects baseline characteristics (covariates). It is achieved by generating a separate block for each combination of covariates, and subjects are assigned to the appropriate block of covariates. After identifying and assigning into blocks, simple randomization is performed. But it has certain limitations like, it is difficult to implement if many covariates exists and all subjects should be identified before group assignment, which is difficult.

### **Covariate adaptive Randomization**

For small to moderate clinical samples, using previous methods may result in imbalance of the important covariates among groups. Covariates adaptive randomization uses the method of minimisation by assessing the imbalance of sample size among several covariates. It is not routinely used method. Using online randomization softwares [www.graphpad.com/quickcalcs/index.cfm](http://www.graphpad.com/quickcalcs/index.cfm), [www.randomization.com](http://www.randomization.com) one can generate randomization plan for treatment assignment to patients. These online softwares are very simple and easy to implement.

### **Reporting of randomization procedures**

It has been reported that in some articles published in indexed journals, randomization was not completely done and results were not properly reported [8]. It would be helpful to look at CONSORT checklist ([http://www.consort\\_statement.org](http://www.consort_statement.org)).

Allocation concealment is the technique that is used to help prevent selection bias by concealing the allocation sequence from those assigning participants to intervention groups, until the moment of assignment. Best way is to seal each individual assignment in envelop. Knowledge of treatment received could also influence management of patients during the trial, and this can be a source of bias. To control this, "blinding" may be undertaken. It is a practice of preventing study participants, health care professionals, and those collecting and analysing data from knowing who belongs to experimental group and who is in control group.

## **II. Conclusion**

RCT is the most rigorous scientific method for evaluating the effectiveness of health care interventions. However, bias could arise when there are flaws in selecting patients to a particular treatment method. Simple randomization works well for the large clinical trials (n>100). For small to moderate clinical trials (n<100) without covariates, use of block randomization helps to achieve the balance and those with covariates, adaptive randomization is useful. Readers must try to develop the skills for critically analysing RCT's in terms of methodology, magnitude and precision of treatment.

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