# Randomization in REDCap



Adaptive randomization methods, like Pocock-Simon randomization2, determine whether there is an imbalance in some stratification factors. Randomization is then adjusted so the next patient on study is more likely to be assigned to a group that has a shortage. These adaptive randomization methods result in better balance across all of the stratification factors than basic stratified randomization. Redcap cannot do adaptive types of randomization.

Cluster randomization involves randomizing groups or sites so that each subject within a site gets the same treatment. This type of randomization is useful if there is the possibility of contamination across treatments if there were multiple treatments at the same site. There are two possible ways of doing cluster randomization in Redcap. The first method requires one Redcap database for the subject information and a second Redcap database for the cluster information. All factors needed in the randomization are contained in the Redcap cluster database, and randomization is done in this database. A second option is to only randomize one patient in each cluster. This requires keeping track of the cluster assignments so that no other subjects are randomized within that cluster.

Redcap can easily handle most of the other basic methods of randomization. These types of randomization involve creating a list of random assignments before the study opens. When a patient is randomized, Redcap goes to the list, selects the next unused arm assignment, and gives that assignment to the patient. So Redcap can handle any type of randomization where an ordered list of assignments can be created before the study starts. The types of randomization most often used in clinical trials are defined in the following sections. It is important to note that the type of randomization used on a study will have implications in the analysis of the study. It is recommended that a statistician be consulted.





*Binomial Randomization*

This randomization method is similar to flipping a coin for each patient. Every patient has an equal chance of being assigned to each arm of the study. This procedure could result in one arm having slightly more patients than another arm. For sample sizes of 200 or more, this should not affect the power of your test. However, for small sample sizes less than 200, the potential imbalance could affect the power of the study. For these small studies, it is better to make the groups more balanced using a randomization method like permuted block randomization.3,4

*Permuted Block Randomization*

This randomization method produces almost equal sample sizes for each group. For this method, group assignments are created in blocks. Each block contains the same number of assignments for each arm, but the order of the assignments within a block are random. For example, if a study has a block size of 4, there are 2 assignments for each arm within the block, but the arm assignments are arranged in a random order. The order within a block could be 1122, 1212, 1221, 2112, 2121, or 2211 (where 1 means the patient will be assigned to the first arm and 2 means the patient will be assigned to the second arm). Multiple blocks are created to reach the total sample size, with each block having a different permutation of arms. This randomization method results in the group assignments being equal at the end of each block.

It is essential that the block sizes are not known to the study team. Otherwise, at the end of a block, the study team will know the next arm to be assigned. This biases the study. One way to avoid this bias is to make the block sizes of variable length. So the first block could contain 4 patients, the next one could contain 8 patients, and so on. 5

*Stratified Randomization*

Studies are often stratified by variables that are related to the outcome of the study. In stratified randomization, separate arm assignments are created for each combination of the stratification factors. When a patient is ready to be randomized, the values of their stratification factors are assessed, then the patient is assigned the next unused arm value in that group.

In the following example, there are two stratification factors: sex (male vs. female) and age (<50 vs. >=50). If a patient going on study is a 67 year old female, Redcap will look at the fourth column of random arm numbers and assign the next unused arm to that patient.

Male/Age<50 Male/Age>=50 Female/Age<50 Female/Age>=50

1 2 2 1

2 2 2 1

2 1 2 2

1 1 1 1

2 1 1 2

1 2 1 2

The number of stratification variables should not be too large. It is recommended that the number of distinct combinations of stratification factor levels be less than the total sample size divided by two. So if there are three stratification factors like sex with 2 levels (male, female), age group with 3 levels (<50, 50-65, >65), and performance score with 3 levels (0, 1,2), then the sample size has to be at least 36. (2x3x3)\*2. If there are 50 total patients on a study, there should be no more than 25 (50/2) distinct stratification level combinations.6

*Randomization by Site*

Patients usually vary greatly between different locations. So it is usually recommended to stratify the randomization by site. Randomizing by site is the same as including site as a stratification factor. So there is a separate arm allocation ordering for each site, or for each combination of the other stratification factors within each site.



*Create the Necessary Variables*

Before setting up randomization in Redcap, create all of the variables that will be used in the randomization process. This includes variables for each of the stratification factors, variable for site, and a variable to store the results of the randomization. These variables should only have a few possible levels. They should all have field types or Yes-No, True-False, Multiple Choice-Drop-down list (Single Answer), or Multiple Choice-Radio Button (Single Answer).

The next step is to go into “Project Setup” and click on “Set up randomization”. If there is not a block listed for setting up the randomization model, you will need to enable randomization for the project (Project Setup tab 🡪 Modify project settings 🡪 Additional options). If the “Set up randomization” button is grayed out, you will need to modify the User Rights for your ID (see “*Defining User Roles in Randomization*” later in this presentation).





*Defining the Randomization Scheme*

ThisRedcap screen will ask if there are stratification factors, whether you want to randomize by group/site, and where you want to store the results of the randomization. When you select any of these fields, you will be given a drop down menu to select the variable names. The following example shows a study that is stratified by sex and ps (performance score), is randomized by site, and the arm assignments will be stored in the Redcap variable called arm.



*Creating a Randomization List*

You then need to create a CSV file that contains the random arm assignments. On the next Redcap screen, you can download examples of how the CSV file should look for your study.

WARNING: DO NOT USE THESE FILES DIRECTLY FROM REDCAP! These files are not correctly randomized. These files can be modified to include random arm assignments and then uploaded back into Redcap.

WARNING: Setting up the allocation file incorrectly may result in not being able to randomize patients, may result in an invalid randomization, and may bias your study results. It is HIGHLY recommended that a statistician be consulted to set up this file!

The arm allocation files need to be CSV files. The first line will contain Redcap variable names. There should be one column containing the random arm assignments. If the study is stratified, there should be one column for each Redcap stratification variable. If the randomization is done by site, there should also be a column for the site variable. This file will contain all possible combinations of stratification factors and site, with the combinations repeated multiple times. This CSV file can be created easily using SAS. (See example in Appendix A)

*Uploading the CSV File*

Once the CSV file is created, you can upload it into Redcap on the next screen. It is recommended that one CSV file should be created for testing during development, and a new CSV file (with different random values) be created for production.



Defining User Roles in Randomization

Each user of the Redcap database needs to be granted randomization authorizations. The three different randomization roles are Setup, Dashboard, and Randomization. Redcap users with Setup authorization can define the randomization criteria, define the randomization variables, and can create and upload the CSV file. Users with ‘Randomization’ authorization can randomize patients. Users with Dashboard authorization can see the number of randomization slots that have been used and how many slots are still available to be assigned. An example of the dashboard is shown.



Maintaining Blinding

In most studies the arm assignments are blinded or double-blinded. This means the arm assignments are not known to the patient or to the medical personnel. It is imperative that the patient and medical personnel not have access to any information about arm assignments. This includes having access to the dashboard. Randomization should also not be done by anyone associated with patient interactions.

Emergency Unblinding

There may be situations where the arm assignments need to be unblinded for certain patients. An example would be if a patient had emergency health issues and the medical staff needed to know the arm assignment for safety reasons. There should always be a process in place to handle these emergency unblinding situations. This includes having someone always available to access the arm information. There should also be a place in Redcap to note when and why a patient was unblinded.

Blinding Arms For DSMB Reporting

DSMB reports often require analyses done by arm. But most DSMB committees want to be blinded to the arm assignments. For these reports, a new arm variable needs to be created that is a blinded version of the original arm variable. If a statistician is creating the DSMB report, they can easily create the blinded arm value. Otherwise, create a new blinded arm variable in Redcap that equals some is a transformation of the original arm values. For example, arm 1 might be changed to ‘X’ and arm 2 might be changed to ‘Y’.



How to Randomize a Patient?

To randomize a new patient, log into Redcap, select the project, enter the ID number for the new patient and hit Enter.

Enter the other patient information and hit ‘Randomize’.

You will then get a screen showing all of the randomization information. If a patient is missing any of this information, they cannot be randomized. Make sure that all of the information on this screen is correct. Once the patient is randomized, none of this information can be changed. If all of the information looks correct, hit ‘Randomize’.

Once you hit ‘Randomize’, the randomization is complete and the arm assignment is stored in Redcap.



How to Randomize a Patient (continued)

You will then get a screen showing all of the randomization information. If a patient is missing any of this information, they cannot be randomized. Make sure that all of the information on this screen is correct. Once the patient is randomized, none of this information can be changed. If all of the information looks correct, hit ‘Randomize’.

Once you hit ‘Randomize’, the randomization is complete and the arm assignment is stored in Redcap.



Limitations

There are several very important things to consider when setting up randomization in Redcap. First, the randomization allocation file (the CSV file) cannot be modified once the study is moved from a testing environment to production. This means that stratification factors cannot be changed. It also means if the study is stratified by site, no new sites can be added to the study. One possible solution to this problem is to always include a site called ‘Other’ and create randomization data for it. If new sites are added later, the new sites would be randomized in this other group.

Once a patient is randomized, none of stratification or arm variables can be changed. It is very important to check the stratification and site values before hitting ‘Randomize’. If stratification factors do change, the arm cannot be changed.