

## Chapter 880

# Randomization Lists

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## Introduction

This module is used to create a randomization list for assigning subjects to one of up to 25 treatment groups. The list can be stratified by up to 25 centers (strata) with an additional 2 stratification factors, each with up to 25 levels.

Seven randomization algorithms are available. Five of the algorithms (Block Randomization, Efron's biased coin randomization, Smith's randomization, Wei's urn randomization, and random sorting using maximum allowable % deviation) are designed to generate balanced random samples throughout the course of an experiment. The other two (complete randomization and random sorting) are less complex but have higher probabilities of imbalance. Technical details for each of these algorithms (except random sorting) as well as a discussion of randomization issues in general are given in Rosenberger and Lachin (2002), Pocock (1983), and Piantadosi (2005).

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## Why Randomize?

Random allocation has been an important part of scientific discovery since the time of R.A. Fisher. He and other scientists recognized the potential for bias in nonrandomized experiments that could compromise treatment comparisons. Randomization controls the influence of unknown factors, reducing potential bias in an experiment. Rosenberger and Lachin (2002) state on page 18 that "...the randomization of subjects between the treatment groups is the paramount statistical element that allows one to claim that a study is unbiased." The elimination of bias, however, is not the only reason for randomization. Pocock (1983) states on page 50 that randomization is used "to provide a basis for the standard methods of statistical analysis such as significance tests." Clearly, randomization is necessary in order to produce accurate and generalizable statistical conclusions.

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## Randomization in Clinical Trials

In non-clinical (or non-human) experiments, researchers often have tight control over the environment and conditions surrounding an experiment, so randomization can usually be implemented with minor difficulty. Clinical experiments, however, are quite different. Because human patients are used in clinical trials, various ethical issues must be addressed. These ethical considerations complicate the experimental design and often require adjustments in the way subjects are randomly assigned to treatments. Other factors that influence randomization in clinical trials are purely logistical. How can the investigators ensure that treatments are administered the same for all patients without the patient or the doctor knowing what treatment is being given? These and other design factors influence how randomization is administered in clinical trials.

One of the issues that arise in clinical experiments is treatment imbalance. Clinical trials are usually administered over time with patients enrolling at different time points throughout the study. It is often desirable to maintain balance in the number of patients assigned to each treatment throughout the course of the experiment. This is particularly true when time-dependent covariates influence the response or when sequential testing will be used to analyze results. Several randomization algorithms have been developed to produce lists that balance the number of patients assigned to each treatment throughout the experiment while still maintaining the randomness of the assignments. These include block randomization, Efron's biased coin randomization, Smith's randomization,

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Wei's urn randomization, and random sorting using maximum allowable % deviation. Each of these algorithms will be discussed in detail in the section that follows.

## Randomization Algorithms

Seven different randomization algorithms are available. These can be roughly divided into two categories: those that aim to produce balanced randomization lists and those that do not. The following table outlines the goal of each algorithm by the number of groups each algorithm will allow.

	Non-Balancing Algorithms	Balancing Algorithms
<b>2 Groups</b>	Complete Randomization†, Random Sorting	Block Randomization†, Efron's Biased Coin**†, Smith**†, Wei's Urn**†, Random Sorting using Maximum Allowable % Deviation
<b>k Groups</b>	Complete Randomization†, Random Sorting	Block Randomization†, Wei's Urn*, Random Sorting using Maximum Allowable % Deviation

\*These randomization algorithms have the additional restriction that unequal treatment allocation is not allowed, i.e. all groups must have the same target sample size.

†These randomization algorithms produce randomization lists in which the actual group sample size may not equal the target group sample size.

The discussion of each algorithm that follows will be based on the following scenario and notation. Suppose we have  $k$  treatments and that  $n_i$  subjects (not necessarily all equal) are to be assigned to each treatment,  $i = 1, 2, \dots, k$ . The value  $n_i$  will be referred to in discussion as the "target" sample size for each group. Let the actual sample size for each group be  $a_i$ . For some algorithms, the actual group sample size may not always equal the target sample size for all groups. The total sample size is

$$N = \sum_{i=1}^k n_i = \sum_{i=1}^k a_i,$$

and the target allocation ratio for each group is

$$R_i = \frac{n_i}{N}.$$

Define the probability of assignment of subject  $j$  to treatment  $i$  as  $p_{ij}$ .

Define the number of subjects in each group after the  $j^{\text{th}}$  subject is assigned as  $n_i[j]$ .

When the list is stratified with centers and/or additional stratification factors, randomization is completed independently within each strata combination. This is, for  $s = 1, 2, \dots, S$  strata, the total sample size ( $N$  in the notation above) within a given stratum is equal to  $N_s$ . The individual strata may have different sample sizes. All discussions that follow refer to randomization within a single stratum, but the results can be generalized to stratified randomization lists.

## Non-Balancing Algorithms

### Complete Randomization

The complete randomization algorithm is commonly referred to as a “coin flip”. For the case to two treatments, a coin is flipped each time a subject is to be randomized, determining the assignment. The probability of assignment to either treatment is 0.5 for all subjects.

The algorithm generalizes to more than two groups and allows for unequal allocation. The probability of assignment of subject  $j$  to group  $i$  is

$$p_{ij} = R_i$$

for all  $j$ . If the target sample size is the same for all  $k$  groups, then

$$p_{ij} = 1/k$$

The complete randomization algorithm proceeds by randomly assigning subjects to treatments using the above assignment probabilities. The algorithm may result in imbalances between groups even when the target group sample sizes are equal, i.e. the actual sample sizes may not always equal the target sample sizes for all groups. This algorithm is not recommended when balance is important throughout the course of an experiment.

### Random Sorting

The random sorting algorithm can be used for any number of treatment groups and any allocation ratios. The random sorting algorithm always results in randomized assignment lists in which the actual group sample sizes match the target group sample sizes, i.e.  $a_i = n_i$  for all  $i$ . The algorithm begins by creating a virtual database containing group names. Each row corresponds to one group, and the  $i^{\text{th}}$  group is represented by  $n_i$  rows. For example, if we were randomly assigning three groups (A, B, and C) with ten subjects in each group, then the database would consist of ten rows containing A's, followed by ten rows containing B's and ten rows containing C's, for a total of 30 rows. Next, a random number is assigned to each row in the database, and then the database is sorted based on the column of random numbers to place the group names in random order. The first subject is then assigned to the group in row one of the randomly sorted database, the second subject is assigned to the group in row two, and so forth. Although this algorithm always results in groups containing the target sample sizes, longitudinal imbalances among groups may still occur, therefore, this algorithm is not recommended when balance is important throughout the course of an experiment.

## Balancing Algorithms

### Block Randomization

This algorithm is designed to randomize subjects to two or more treatments and achieves balance across treatment groups over time. Predetermined blocks of set sizes containing each treatment assignment are individually randomized to keep the number of subjects assigned to each group in balance as enrollment progresses.

Block randomization is completed as follows:

For randomization of  $k$  groups, define  $r_i$  as an integer allocation ratio value for group  $i$ . For a study with 3 treatments with equal sample sizes in each group (i.e. allocation ratio = 1:1:1),  $r_i = 1$  for all  $k$ . If the allocation ratio were 1:2:2, then  $r_1 = 1$ ,  $r_2 = 2$ , and  $r_3 = 2$ . The minimum block size is equal to

$$B_{Min} = \sum_{i=1}^k r_i.$$

Thus, for a study with 3 groups,  $B_{Min} = 3$  for the case of equal group sizes, and  $B_{Min} = 5$  for 1:2:2 allocation.

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The actual block sizes used in randomization are computed as multiples of  $B_{Min}$ , using block size multipliers,  $M_b$  ( $b = 1, 2, \dots$  # of block sizes) entered by the user

$$B_b = M_b \times B_{Min}$$

If multipliers  $M_b = 1, 2,$  and  $3$  were used, then for equal allocation the block sizes would be  $3, 6,$  and  $9$ , with treatments allocated within each block according to the given ratio. For  $1:2:2$  allocation, the block sizes would be  $5, 10,$  and  $15$ . In general, the multipliers should be chosen so that the block sizes are relatively small to maintain balance, and at least two different block sizes should be selected to avoid the possibility of administrators or subjects being able to guess their treatment in a blinded study by the assignment of previous subjects. When multiple block sizes are randomly assigned, the current treatment cannot usually be guessed based solely on the previous assignments, because the block sizes are not constant.

After the block sizes have been determined, all possible permuted combinations of assignment sequences within each block must be calculated. For 3 groups (A, B, C) and a block size of 3, the possible block sequences are

$$ABC, ACB, BAC, BCA, CAB, CBA$$

Block sizes and sequences are chosen and randomly ordered to determine subject assignment into the treatment groups. The user can specify whether the block sizes are chosen completely at random or according to a custom block-subject allocation. The random block selection terminates when the number of subjects assigned in blocks reaches or surpasses the required sample size. It is possible for the final sample size to be larger than the target unless the block sizes are constrained to a set where the overall target sample size is achieved.

## Efron's Biased Coin Randomization

This algorithm may only be used for random assignment of subjects to two treatments. The target sample sizes must also be the same for both groups. In order to achieve longitudinal balance between groups, the algorithm dynamically changes the group assignment probabilities. The algorithm is outlined in Efron (1971).

First we define a constant probability  $p$  (called "Efron's  $p$ "), where  $0.5 < p \leq 1$ . A common value for  $p$  is  $2/3$ . Also define a difference function  $D_j = n_1[j] - n_2[j]$ . The probability of assignment of subject  $j$  to group 1 is

$$p_{1j} = \begin{cases} 1/2 & \text{if } D_{j-1} = 0 \\ p & \text{if } D_{j-1} < 0 \\ 1-p & \text{if } D_{j-1} > 0 \end{cases}$$

Efron's biased coin randomization proceeds by randomly assigning subjects to treatments using the above assignment probabilities. When group 1 has more subjects assigned than group 2, the assignment probability changes to make group 2 more probable for assignment. When group 2 has more, then group 1 becomes more probable. The algorithm may result in final imbalances between groups, but the degree of imbalance throughout the randomization process is greatly reduced.

## Smith's Randomization

This algorithm may only be used for random assignment of subjects to two treatments. The target sample sizes must also be the same for both groups. Like Efron's biased coin randomization, Smith's algorithm dynamically changes the group assignment probabilities based on the degree of imbalance to achieve longitudinal balance between groups. The algorithm is outlined in Smith (1984).

We define a positive exponent parameter  $\rho$  (called "Smith's Exponent"). The probability of assignment of subject  $j$  to group 1 is

$$p_{1j} = \frac{n_2[j-1]^\rho}{n_1[j-1]^\rho + n_2[j-1]^\rho}$$

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Smith's randomization proceeds by randomly assigning subjects to treatments using the above assignment probabilities. When group 1 has more subjects assigned than group 2, the assignment probability changes to make group 2 more probable for assignment. When group 2 has more, then group 1 becomes more probable. The algorithm may result in final imbalances between groups, but the degree of imbalance throughout the randomization process is greatly reduced.

### Wei's Urn Randomization

This algorithm may be used for random assignment of subjects to two or more treatments. The target sample sizes must also be the same for all groups. Like Smith's randomization, Wei's urn randomization algorithm dynamically changes the group assignment probabilities based on the degree of imbalance to achieve longitudinal balance between groups. Urn randomization is reviewed in Wei and Lachin (1988).

Define positive parameters  $A$  and  $B$  (called "Wei's  $A$ " and "Wei's  $B$ ", respectively). We start the algorithm by placing  $A$  balls representing each group in an urn. A single ball is then randomly chosen from the urn, recorded, and *replaced*, and then  $B$  new balls corresponding to each of the other groups are added to the urn. Therefore, when a ball from one group is chosen, the probability shifts to make the other groups more probable on the next draw. The probability of the first assignment is  $1/k$ . After that, the probability of assignment of subject  $j$  to group  $i$  is

$$p_{ij} = \frac{A + B(j-1) - Bn_i[j-1]}{kA + B(j-1)(k-1)}.$$

The algorithm continues until all subjects have been assigned to one of the groups. The algorithm may result in final imbalances between groups, but the degree of imbalance throughout the randomization process is diminished due to the shifting of probabilities toward the underrepresented groups.

### Random Sorting using Maximum Allowable % Deviation

This algorithm is equivalent to the random sorting algorithm described earlier except that a search is conducted to find a randomization list that satisfies the Maximum Allowable % Deviation criterion. The % Deviation for group  $i$  after subject  $j$  has been assigned is defined as

$$\begin{aligned} \% \text{ Deviation}_{ij} &= \left| \frac{n_i[j] - E(n_i[j])}{n_i} \right| \times 100 \\ &= \left| \frac{n_i[j] - jR_i}{n_i} \right| \times 100. \end{aligned}$$

The % Deviation measures how far the actual sample size for group  $i$  is from the expected sample size after subject  $j$  is randomly assigned. The Maximum Allowable % Deviation represents the upper bound for this measure. The search is conducted by creating an assignment list based on random sorting and then running through the assignments and calculating the maximum % Deviation for all groups after each assignment. If the maximum % Deviation is greater than the Maximum Allowable % Deviation value specified, then the list is rejected, the number of iterations is incremented, and the random sorting algorithm is started again with a new set of random numbers. The search continues until a randomization list is generated for which the criterion is satisfied for all individual assignments. Conducting a search in this manner assures a degree of balance throughout the course of the experiment.

For example, for 40 subjects to be assigned to two groups A and B with equal allocation ratios (0.5), suppose that there are 7 assigned A's and 3 assigned B's after 10 random assignments and the Maximum Allowable % Deviation is 10%. With the allocation ratio at 0.5, we would expect to have 5 A's and 5 B's ( $10 \times 0.5 = 5$ ) after 10 assignments. Therefore, the % Deviation for group A is  $|7 - 5|/20 = 10\%$  and the % Deviation for group B is  $|3 - 5|/20 = 10\%$ . Both of these are equal to the Maximum Allowable % Deviation so the next assignment would be tested. If the next assignment were to group A then the randomization list would be rejected because the %

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Deviation for group A is  $|8 - 5|/20 = 15\% > 10\%$ . A new randomization list based on random sorting would be generated and the search would continue.

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## Comparison of Balancing Properties

Rosenberger and Lachin (2002) provides a simulation comparison of the balancing properties of complete randomization, Efron's biased coin ( $p = 2/3$ ), Wei's Urn ( $A = 0, B = 1$ ), and Smith (exponent = 5). The simulation was carried out for two treatment groups with target sample sizes of 25 in each group. They found that complete randomization did not balance as well as the other three "restricted randomization" procedures. Efron's biased coin and Smith's randomization algorithms were very close in terms of bias and variability. Wei's urn was found to be slightly more variable.

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## Procedure Options

This section describes the options that are specific to this procedure. These are located on the Design, Report, and Storage tabs. For more information about the options of other tabs, go to the Procedure Window chapter.

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## Design Tab

The Design tab contains most of the parameters and options that you will be concerned with.

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## Randomization Algorithm

### Randomization Algorithm

Choose one of seven randomization algorithms. These algorithms are each described in detail in the Randomization Algorithms section above. Some of the algorithms may result in actual (final) sample sizes that are not equal to the target sample sizes. To search for a randomization list in which the final group sizes are equal to the target group sample sizes for every group, check the "Search for a randomization list..." box.

The following algorithms are available.

- **Block Randomization (Recommended)**

This algorithm results in a balanced randomization list over time and is probably the most widely used method. The user must specify block size multipliers and choose how the number of blocks of each size will be chosen (known as block-subject allocation). Because of its balancing properties, this is the method we recommend. Using this algorithm, it is possible for the final overall sample size to be larger than the target unless the block sizes are constrained to a set where the overall target sample size is achieved.

- **Complete Randomization**

This is the simplest of all randomization algorithms and is commonly known as "coin flipping". The algorithm may result in imbalances between groups even when the target group sample sizes are equal, i.e. the actual sample sizes may not always equal the target sample sizes for all groups. This algorithm is not recommended when balance is important throughout the course of an experiment.

- **Efron's Biased Coin (2 Treatments, Equal Sample Sizes)**

This algorithm may only be used for random assignment of subjects to two treatments. The target sample sizes must also be the same for both groups. In order to achieve longitudinal balance between groups, the algorithm dynamically changes the group assignment probabilities. A value for Efron's  $p$  must also be specified.

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- **Random Sorting**

The random sorting algorithm can be used for any number of treatment groups and any allocation ratio set. The random sorting algorithm always results in randomized assignment lists in which the actual group sample sizes match the target group sample sizes, i.e.  $a_i = n_i$  for all  $i$ . The random assignment is conducted by sorting a database of group labels using a column of random numbers. This algorithm is not recommended when balance is important throughout the course of an experiment.

- **Random Sorting using Max Allowable % Deviation (Search)**

This algorithm is equivalent to the random sorting algorithm except that a search is conducted to find a randomized list for which all % Deviations are less than or equal to the Maximum Allowable % Deviation specified. The search is conducted until a list is found or the maximum iterations are reached. A value for Maximum Allowable % Deviation must also be specified.

- **Smith (2 Treatments, Equal Sample Sizes)**

This algorithm may only be used for random assignment of subjects to two treatments. The target sample sizes must also be the same for both groups. Smith's algorithm dynamically changes the group assignment probabilities based on the degree of imbalance to achieve longitudinal balance between groups. A value for Smith's Exponent must also be specified.

- **Wei's Urn (Equal Sample Sizes)**

This algorithm may be used for random assignment of subjects to two or more treatments. The target sample sizes must also be the same for all groups. Wei's urn randomization algorithm dynamically changes the group assignment probabilities based on the degree of imbalance to achieve longitudinal balance between groups. Values for Wei's A and Wei's B must also be specified.

### Random Seed

Specify a numeric seed for random number generation. This value must be between 0 and 2147483647 and may be a decimal number.

### Obtaining a Computer-Generated Random Seed

Enter *Random*, 0, or leave this option blank for a randomly generated seed based on the computer's internal clock. If a randomly generated seed is used, its value will be displayed in the output.

### Using a Non-Zero Random Seed

If you enter a non-zero random seed, the same random sequence will be generated with each run and the output will not change. This is often used to replicate previous results.

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## Randomization Algorithm – Algorithm Parameters

### Block Size Multiplier(s)

*This option only appears when Randomization Algorithm = Block Randomization.*

Enter the block size multiplier(s) separated by spaces. The final block sizes used in randomization are determined by multiplying these values by the minimum possible block size, which is determined based on the treatment group sample size allocation ratio.

For example, with 3 treatment groups and equal sample size allocation and if the block size multipliers of 1, 2, and 3 were entered, the final block sizes would be 3, 6, and 9, with treatments allocated within each block according to the given ratio. For 1:2:2 allocation, the minimum possible block size is 5 and the block sizes would be 5, 10, and 15. If 2 and 3 were entered as the block size multipliers, then the final block sizes would be 10 and 15.

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In general, the multipliers should be chosen so that the block sizes are relatively small to maintain balance, and at least two different block sizes should be used to avoid the possibility of administrators or subjects being able to guess their treatment in a blinded study by the assignment of previous subjects.

### Block-Subject Allocation

*This option only appears when Randomization Algorithm = Block Randomization.*

Select how the number of subjects assigned to the list by each block size will be determined. This option effectively determines the distribution of block sizes.

The options are

- **Random**

The number of subjects assigned by each block size is determined completely at random. This will possibly result in some block sizes not being used.

- **Equal**

An equal number of subjects is assigned to the list by each block size. In some cases, the actual allocation will not be exactly equal, but as close as possible to equal.

For example, for 3 groups with equal sample size allocation, block sizes of 3, 6, and 9, and a total sample size of 100, the randomization list would be generated with a target of 33.3% of subjects assigned using a block size of 3, 33.3% using a block size of 6, and 33.3% using a block size of 9. Because sample sizes must be assigned using whole numbers, the closest allocation would be 10 blocks of size 3 (30 subjects), 6 blocks of size 6 (36 subjects), and 4 blocks of size 9 (36 subjects).

- **Custom**

Enter custom ratios separated by spaces for the relative number of subjects assigned by each block size. The first value is the ratio for the first block size, the second for the second block size, and so on. The values need not sum to one since they will be scaled to relative percentages, so for 100 subjects and to achieve 1:2:1 block-subject allocation you could enter *1 2 1*, *0.25 0.5 0.25*, or *25 50 25*. All would give the same results for the block-subject allocation percentages.

### Constrain the actual block allocation such that the total sample size matches the target (if possible)

*This option only appears when Randomization Algorithm = Block Randomization.*

In some cases (especially when using random block-subject allocation), it is possible to end up with randomization lists whose size is greater than the target sample size because of the discrete nature of the block sizes. When this option is selected, the software will trade larger blocks for smaller blocks before randomization of blocks to the sequence to achieve the overall target sample size. In some cases, it may not be possible to achieve the specified total sample size based on the underlying block sizes.

### Efron's $p$

*This option only appears when Randomization Algorithm = Efron's Biased Coin.*

Specify the probability parameter  $p$  for Efron's bias coin algorithm. This value must be greater than 0.5 and less than or equal to 1. A probability of 0.67 is often used.

### Maximum Allowable % Deviation

*This option only appears when Randomization Algorithm = Random Sorting using Max Allowable % Deviation.*

Specify a single value for the Maximum Allowable % Deviation for the random sorting using maximum allowable % deviation algorithm. You can enter the value as a percentage (e.g. 10%) or as a decimal (e.g. 0.10).



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### Smith's Exponent

*This option only appears when Randomization Algorithm = Smith.*

Specify the exponent parameter  $\rho$  for Smith's randomization algorithm. Smith (1984) favors the design with  $\rho = 5$ .

### Wei's A

*This option only appears when Randomization Algorithm = Wei's Urn.*

Specify the initialization parameter  $A$  for Wei's urn algorithm. This is the number of balls in the urn for each group when the algorithm starts. A value of 0 is often used.

### Wei's B

*This option only appears when Randomization Algorithm = Wei's Urn.*

Specify the parameter  $B$  for Wei's urn algorithm. This is the number of balls added to the other urns when a ball is selected. A value of 1 is often used. If  $B$  is 0 then Wei's algorithm is the same as complete randomization.

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## Randomization Algorithm – Search

### Search for a randomization list in which all final group sizes exactly match the target group sizes

Some of the randomization algorithms may result in actual group sample sizes that do not exactly match the target group sample sizes specified. This option forces a search to find a randomization list in which the final sample sizes match the target sample sizes for all groups.

The search is conducted by creating a randomization list using the user-specified randomization algorithm and then looking at the final sample sizes. If the sample sizes do not match the target sample sizes for all groups, then the list is discarded, and the algorithm is restarted. This continues until a list with the exact sample sizes is found.

### Maximum Search Iterations

Specify the number of iterations before the randomization list search is terminated. This option is used for the Random Sorting using Max Allowable % Deviation (Search) algorithm and in searching for a randomization list where final group sizes match the target group sizes.

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## Sample Size

### Sample Size Entry Type

Choose how to specify the target total sample size for the study. Note that some randomization algorithms may generate lists with slightly higher actual sample sizes than the target(s) entered.

The options are

- **Enter the Overall Total Sample Size for the Study**  
Enter a single number for the target overall total sample size. This number is divided among treatment groups, centers, and additional strata according to the various allocation ratios.
- **Enter Individual Treatment Group Sample Sizes**  
When this option is chosen, you will enter individual sample sizes for each treatment group (or the common group sample size for each group if they all are to be the same size). The subjects will further be divided among centers and additional strata (if applicable) according to the various allocation ratios.

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- **Enter Individual Center (Stratum) Sample Sizes**

This option only applies when randomizing by centers (strata). When this option is selected, you will enter individual sample sizes for each center (or the common sample size for each center if they all are to be the same size). The subjects will further be divided among treatment groups and additional strata (if applicable) according to the various allocation ratios.

If this option is selected and the number of centers (strata) is set to 1, you must enter the total overall sample size for the study.

### **Overall Total Sample Size**

*This option only appears when Sample Size Entry Type = Enter the Overall Total Sample Size for the Study.*

Enter a single number for the target overall total sample size for the study. Subjects are divided among treatment groups, centers, and additional strata according to the various allocation ratios.

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## **Treatment Groups**

### **Number of Treatment Groups**

Specify the number of treatment groups to which the subjects will be randomly assigned. You can randomize up to 25 treatment groups.

### **Title or Name**

Enter a name for this variable in the randomization list.

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## **Treatment Groups – Treatment Group Labels and Target Allocation**

### **Assign Equal Sample Sizes to All Treatment Groups**

Check this box if all treatment groups are to have the same target sample size.

### **Group Sample Size**

*This option only appears when Assign Equal Sample Sizes to All Treatment Groups is checked and Sample Size Entry Type = Enter Individual Treatment Group Sample Sizes.*

Specify a single target sample size to be used for each of the groups.

### **Group Label**

Specify a label or treatment name for each group. This label will be used to distinguish groups in the output and reports. Each group must have a different label.

### **Allocation Ratio**

*This option only appears when Assign Equal Sample Sizes to All Treatment Groups is unchecked and Sample Size Entry Type ≠ Enter Individual Treatment Group Sample Sizes.*

Specify the allocation ratio for the corresponding treatment group. The allocation ratios need not sum to one since they will be scaled to relative percentages.

### **Sample Size**

*This option only appears when Assign Equal Sample Sizes to All Treatment Groups is unchecked and Sample Size Entry Type = Enter Individual Treatment Group Sample Sizes.*

Specify a target sample size for the corresponding treatment group.

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## Centers (Strata) Tab

The Centers (Strata) tab contains options for creating stratified randomization lists using centers and additional strata. Most options described below only appear if Number of Centers (Strata) > 1 or Number of Additional Stratification Factors > 0. Note that the “Center (Strata)” options may be used to specify a stratification factor that is not necessarily a center. It may be any stratification factor.

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### Centers (Strata)

#### Number of Centers (Strata)

Specify the number of centers (up to 25) for the randomization list. When the list is stratified with centers and/or additional stratification factors, randomization is completed independently within each center-stratum combination.

Enter “1 (Not Stratified)” if you do not want a randomization list stratified by centers.

#### Title or Name

Enter a name for this variable in the randomization list.

#### Assign Equal Sample Sizes to All Centers (Strata)

Check this box if all centers are to have the same target sample size.

#### Center Sample Size

*This option only appears when Assign Equal Sample Sizes to All Centers (Strata) is checked and Sample Size Entry Type = Enter Individual Center (Stratum) Sample Sizes.*

Specify a single target sample size to be used for each of the centers.

#### Center Label

Specify a label for each center. This label will be used to distinguish centers in the output and reports. Each center must have a different label.

#### Allocation Ratio

*This option only appears when Assign Equal Sample Sizes to All Centers (Strata) is unchecked and Sample Size Entry Type ≠ Enter Individual Center (Stratum) Sample Sizes.*

Specify the allocation ratio for the corresponding center. The allocation ratios need not sum to one since they will be scaled to relative percentages.

#### Sample Size

*This option only appears when Assign Equal Sample Sizes to All Centers (Strata) is unchecked and Sample Size Entry Type = Enter Individual Center (Stratum) Sample Sizes.*

Specify a target sample size for the corresponding center.

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### Additional Stratification Factors

#### Number of Additional Stratification Factors

Specify the number of additional factors on which to stratify the randomization list. The choices are 0, 1, or 2. When the list is stratified with centers and/or additional stratification factors, randomization is completed independently within each center-stratum combination.

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**Additional Stratification Factors – Stratification Factor 1, 2**

*These options only appear when Number of Additional Stratification Factors >0.*

**Number of Levels**

Specify the number of levels (up to 25) in the stratification factor.

**Title or Name**

Enter a name for this variable in the randomization list.

**Use Equal Sample Size Allocation for All Levels**

Check this box if all levels are to have the same sample size allocation.

**Level Label**

Specify a label for each factor level. This label will be used to distinguish levels in the output and reports. Each level must have a different label.

**Allocation Ratio**

*This option only appears when Use Equal Sample Size Allocation for All Levels is unchecked.*

Specify the allocation ratio for the corresponding factor level. The allocation ratios need not sum to one since they will be scaled to relative percentages.

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**List Options Tab**

The List Options tab contains options for specifying optional columns to include in the randomization list.

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**Additional Randomization List Options****Include a Column of Sequence Numbers**

Check this box to include a numeric sequence column with the randomization list.

**Include a Column of Subject ID's**

Check this box to include a column of unique Subject ID's with the randomization list.

**Restart Numbering for each Center (Stratum)**

*This option only appears when Number of Centers (Strata) > 1.*

When checked, Subject ID numbering sequences restart at 0 with each new center (stratum).

**Restart Numbering for each Additional Stratification Factor Level Combination**

*This option only appears when Number of Additional Stratification Factors >0.*

When checked, Subject ID numbering sequences restart at 0 with each new combination of additional stratification factors.

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### Subject ID Prefix

Enter a text value to be added to the beginning of each Subject ID. For example, if this value were “subj\_” then the subject ID’s would be subj\_1, subj\_2, subj\_3, etc. in the reports.

### Text Replacement Codes

The following codes are replaced by appropriate values:

{Set} by the set number.

{Code} by the combined stratification code.

{Sequence} by the sequence number.

{Center} by the center label.

{Center Code} by an abbreviated center code.

{F1} by the stratification factor 1 label.

{F1 Code} by an abbreviated stratification factor 1 code.

{F2} by the stratification factor 2 label.

{F2 Code} by an abbreviated stratification factor 2 code.

### Include a Column of Block Identifiers

*This option only appears when Randomization Algorithm = Block Randomization.*

Check this box to include a column indicating the block to which each subject belongs (i.e. by which the subject was assigned) with the randomization list.

### Include a Column of Combined Stratification Codes

Check this box to include a column of combined codes created from the corresponding strata with the randomization list.

### Use Abbreviated Codes

Check this box to generate unique and abbreviated codes for each center, stratum, and/or factor level.

### Add Code Separators

Check to include a separator between codes.

### Code Separator

Select the type of code separator to add between code values.

### Include a Column of Abbreviated Treatment Codes

Check this box to include a column of abbreviated codes corresponding to each treatment with the randomization list.

### Include a Column of Unique Randomization Codes

Check this box to include a column of unique computer-generated codes for each subject. This information can be used to blind the study and retain the information about treatments, blocks, and strata corresponding to each unique randomization code.

---

## Reports Tab

The Reports tab contains options influencing the reports.

---

### Select Report Output

#### Show Summary

Check this box to display a summary of the randomization list.

#### Show Randomization List

Check this box to display the complete randomization list.

If the randomization list is stratified, you may want to change the output page orientation to “Landscape” so that all the information fits the available width.

#### Show Randomization List Details

Check this box to display a row-by-row report with randomization list details. If the randomization list is stratified, a separate report is created for each individual center-stratum combination.

#### Show References

Check this box to display the literature reference(s) for this procedure on the report.

---

### Maximum Decimal Places for Numeric Reports

#### Percentages (%)

Specify the maximum number of decimals to display for this item on the reports. The item will be displayed with fewer decimals if the actual required number of decimals is less than this maximum.

---

## Storage Tab

The storage tab contains options for specifying data storage columns.

---

### Randomization List Storage

#### Store Randomization List

If this box is checked, then the randomization list will be written to the spreadsheet starting with the selected column. Writing the list to the spreadsheet allows you to easily store the randomization list for further use.

#### Store Randomization List Data Starting In

The first saved value is stored in this column. Each additional value that is specified is stored in the columns immediately to the right of this column.

Leave this value blank if you want the data storage to begin in the first blank column on the right-hand side of the data.

#### Existing Data Replaced

Any existing data in these columns is automatically replaced, so be careful.

#### Update Column Names

If this box is checked, the output column names in the spreadsheet will be updated to reflect the stored information.

## Example 1 – Block Randomization with Equal Allocation Ratios

A clinical researcher wishes to randomly assign 60 subjects to three treatment groups (Low, Medium, High) using block randomization with 1:1:1 allocation and block sizes of 3 and 6. The list will include sequence numbers, subject ID's, block identifiers, abbreviated treatment codes, and randomization codes.

For reproducibility, we'll use a random seed of 60502.

### Setup

This section presents the values of each of the parameters needed to run this example. First, from the data window, load the **Randomization Lists** procedure window using the Analysis menu or the Procedure Navigator. You may then make the appropriate entries as listed below, or open **Example 1** by going to the **File** menu and choosing **Open Example Template**.

<u>Option</u>	<u>Value</u>
<b>Randomization Tab</b>	
Randomization Algorithm .....	<b>Block Randomization</b>
Random Seed.....	<b>60502</b>
Block Size Multiplier(s) .....	<b>1 2</b>
Block-Subject Allocation .....	<b>Random</b>
Constrain the actual block allocation... ..	<b>Unchecked</b>
Search for a randomization list... ..	<b>Unchecked</b>
Maximum Search Iterations.....	<b>1000</b>
Sample Size Entry Type .....	<b>Enter the Overall Total Sample Size for the Study</b>
Overall Total Sample Size .....	<b>60</b>
Number of Treatment Groups.....	<b>3</b>
Title or Name .....	<b>Treatment</b>
Assign Equal Sample Sizes to All Treatment Groups .....	<b>Checked</b>
Treatment Group 1 Label .....	<b>Low</b>
Treatment Group 2 Label .....	<b>Medium</b>
Treatment Group 3 Label .....	<b>High</b>
<b>Centers (Strata) Tab</b>	
Number of Centers (Strata) .....	<b>1 (Not Stratified)</b>
Number of Additional Factors .....	<b>0</b>
<b>List Options Tab</b>	
Include a Column of Sequence Numbers.....	<b>Checked</b>
Include a Column of Subject ID's.....	<b>Checked</b>
Subject ID Prefix .....	<b>{Set}</b>
Include a Column of Block Identifiers .....	<b>Checked</b>
Include a Column of Combined Stratification Codes.....	<b>Unchecked</b>
Include a Column of Abbreviated Treatment Codes .....	<b>Checked</b>
Include a Column of Unique Randomization Codes.....	<b>Checked</b>
<b>Storage Tab</b>	
Write Randomization List to Spreadsheet .....	<b>Unchecked</b>
<b>Reports Tab</b>	
Show Summary .....	<b>Checked</b>
Show Randomization List .....	<b>Checked</b>
Show Randomization List Details .....	<b>Checked</b>
Show References .....	<b>Checked</b>

## Annotated Output

Click the Run button to perform the calculations and generate the following output.

### Randomization List Summary

Randomization List Summary				
Randomization Algorithm	Block Randomization			
User-Entered Random Seed	60502			
Block Size Multiplier(s)	1 2			
Block Size(s)	3 6			
Total Number of Blocks	12			
Overall Total Sample Size	60			
Number of Treatment Groups	3			
Treatment	Treatment Code	Sample Size	— Allocation % —	
			Actual	Target
Low	L	20	33.33%	33.33%
Medium	M	20	33.33%	33.33%
High	H	20	33.33%	33.33%

This report displays the summary of the randomization list, including block information.

#### Randomization Algorithm

States the algorithm used in randomization and any associated parameters (e.g. Block Size Multiplier(s), Block Size(s), Total Number of Blocks).

#### Random Seed

Indicates the random seed used in creating the randomization list. If the random seed was computer-generated, it will be indicated here.

#### Overall Total Sample Size

The actual sample size of the randomization list. If the sample size is different from the target, the target sample size will be indicated here.

#### Number of Treatment Groups

The treatment groups.

#### Treatment

The treatment groups.

#### Treatment Code

The abbreviated treatment group code.

#### Sample Size

The sample size for each treatment group.

#### Actual Allocation %

The actual allocation percentage achieved by each treatment group.

#### Target Allocation %

The target allocation percentage specified on the input. Note that the user input may have had integer values for the allocation ratios (e.g. 1:1:1), but they are converted to percentages in this report.



## Randomization Lists

## Randomization List

<b>Randomization List</b>					
Randomization Algorithm		Block Randomization (Block Sizes = 3 6)			
User-Entered Random Seed		60502			
Sequence	Subject ID	Block	Treatment	Treatment Code	Randomization Code
1	101	1	High	H	MW0
2	102	1	Low	L	RN7
3	103	1	Low	L	GI8
4	104	1	Medium	M	DX0
5	105	1	Medium	M	TD6
6	106	1	High	H	RN2
7	107	2	Low	L	LF5
8	108	2	Low	L	QD8
9	109	2	High	H	CZ9
10	110	2	High	H	PL6
11	111	2	Medium	M	QA4
12	112	2	Medium	M	RY0
13	113	3	Low	L	UI2
14	114	3	Low	L	BH6
15	115	3	Medium	M	BF3
.	.	.	.	.	.
.	.	.	.	.	.
.	.	.	.	.	.
46	146	9	Low	L	EG9
47	147	9	High	H	OJ4
48	148	9	Low	L	CB0
49	149	10	Low	L	GX3
50	150	10	High	H	IK6
51	151	10	Medium	M	XO1
52	152	11	Medium	M	FB6
53	153	11	High	H	ZP2
54	154	11	Low	L	XW6
55	155	12	Low	L	VA3
56	156	12	High	H	XE5
57	157	12	Low	L	LD8
58	158	12	Medium	M	BV4
59	159	12	Medium	M	FW2
60	160	12	High	H	XI6

This report shows the complete randomization list

**Sequence**

The sequence identifier.

**Subject ID**

The text identification value of the subject.

**Block**

The randomization block to which each subject belongs.

**Treatment**

The treatment group to which the subject was randomly assigned.

**Treatment Code**

An abbreviated treatment code corresponding to the treatment group.

**Randomization Code**

Unique, random, computer-generated code for each subject. This information can be used to blind the study.

## Randomization Lists

## Randomization List Details

**Randomization List Details**

Randomization Algorithm	Block Randomization (Block Sizes = 3 6)
Number of Blocks	12
Sample Size	60
Number of Treatment Groups	3

**Block-Subject Allocation**

Block Size	Number of Blocks	Subjects Assigned	— Allocation % —	
			Actual	Target
3	4	12	20%	Random
6	8	48	80%	Random

This report displays a more detailed summary of the randomization list, including block information in the Block-Subject Allocation section.

**Block Size**

The block sizes used to create the randomization list.

**Number of Blocks**

The number of blocks of each size.

**Subjects Assigned**

The number of subjects assigned to the list by blocks of the corresponding size.

**Actual Allocation %**

The actual allocation percentage achieved by each block size.

**Target Allocation %**

The target allocation percentage specified on the input. Note that the user input may have had integer values for the allocation ratios (e.g. 1:1:1), but they are converted to percentages in this report.

**Treatment Groups**

Treatment	Treatment Code	Sample Size	— Allocation % —	
			Actual	Target
Low	L	20	33.33%	33.33%
Medium	M	20	33.33%	33.33%
High	H	20	33.33%	33.33%

This section displays the same sample size information as is found in the Randomization List Summary report.

**Cumulative Details**

Sequence	Subject ID	Block	Treatment	Largest % Deviation from Target	Cumulative Sample Size (L, M, H)
1	101	1	High	3.33%	(0, 0, 1)
2	102	1	Low	3.33%	(1, 0, 1)
3	103	1	Low	5.00%	(2, 0, 1)
4	104	1	Medium	3.33%	(2, 1, 1)
5	105	1	Medium	3.33%	(2, 2, 1)
6	106	1	High	0.00%	(2, 2, 2)
7	107	2	Low	3.33%	(3, 2, 2)
8	108	2	Low	6.67%	(4, 2, 2)
9	109	2	High	5.00%	(4, 2, 3)
10	110	2	High	6.67%	(4, 2, 4)

## Randomization Lists

.	.	.	.	.	.
.	.	.	.	.	.
.	.	.	.	.	.
46	146	9	Low	3.33%	(15, 16, 15)
47	147	9	High	3.33%	(15, 16, 16)
48	148	9	Low	0.00%	(16, 16, 16)
49	149	10	Low	3.33%	(17, 16, 16)
50	150	10	High	3.33%	(17, 16, 17)
51	151	10	Medium	0.00%	(17, 17, 17)
52	152	11	Medium	3.33%	(17, 18, 17)
53	153	11	High	3.33%	(17, 18, 18)
54	154	11	Low	0.00%	(18, 18, 18)
55	155	12	Low	3.33%	(19, 18, 18)
56	156	12	High	3.33%	(19, 18, 19)
57	157	12	Low	5.00%	(20, 18, 19)
58	158	12	Medium	3.33%	(20, 19, 19)
59	159	12	Medium	3.33%	(20, 20, 19)
60	160	12	High	0.00%	(20, 20, 20)

This report shows more detailed summaries and cumulative randomization list details.

**Sequence**

The sequence identifier.

**Subject ID**

The text identification value of the subject.

**Block**

The randomization block to which each subject belongs.

**Treatment**

The treatment group to which the subject was randomly assigned.

**Largest % Deviation from Target**

The largest observed % deviation after the current assignment was made. This measures how far away the group sample sizes are from the expected sample size based on the targets. That is, this measures the degree of imbalance over time.

**Cumulative Sample Size**

The cumulative sample size total for each treatment group after the current assignment was made.

**References****References**

- 
- Piantadosi, S. 2005. *Clinical Trials - A Methodological Perspective*. John Wiley & Sons. New Jersey.  
 Pocock, S.J. 1983. *Clinical Trials - A Practical Approach*. John Wiley & Sons. New York.  
 Rosenberger, W.F., and Lachin, J.M. 2002. *Randomization in Clinical Trials - Theory and Practice*. John Wiley & Sons. New York.

This report displays the references associated with this procedure.

## Example 2 – Block Randomization with Unequal Allocation Ratios and Centers

Continuing with Example 1, suppose the researcher wants now to create a randomization list with twice as many Low treatments as the other two (allocation = 2:1:1) at 4 different centers. Each center should have 80 subjects. They want to randomize with block sizes of 4, 8, and 12 with an equal number of subjects randomized by each block size. We'll also save the randomization list to the spreadsheet.

For reproducibility, we'll use a random seed of 102203.

### Setup

This section presents the values of each of the parameters needed to run this example. First, from the data window, load the **Randomization Lists** procedure window using the Analysis menu or the Procedure Navigator. You may then make the appropriate entries as listed below, or open **Example 2** by going to the **File** menu and choosing **Open Example Template**.

<u>Option</u>	<u>Value</u>
<b>Randomization Tab</b>	
Randomization Algorithm .....	<b>Block Randomization</b>
Random Seed .....	<b>102203</b>
Block Size Multiplier(s) .....	<b>1 2 3</b>
Block-Subject Allocation .....	<b>Equal</b>
Constrain the actual block allocation... ..	<b>Unchecked</b>
Search for a randomization list... ..	<b>Unchecked</b>
Maximum Search Iterations .....	<b>1000</b>
Sample Size Entry Type .....	<b>Enter Individual Center (Stratum) Sample Sizes</b>
Number of Treatment Groups.....	<b>3</b>
Title or Name .....	<b>Treatment</b>
Assign Equal Sample Sizes to All Treatment Groups .....	<b>Unchecked</b>
Treatment Group 1 Label .....	<b>Low</b>
Treatment Group 1 Allocation Ratio .....	<b>2</b>
Treatment Group 2 Label .....	<b>Medium</b>
Treatment Group 2 Allocation Ratio .....	<b>1</b>
Treatment Group 3 Label .....	<b>High</b>
Treatment Group 3 Allocation Ratio .....	<b>1</b>
<b>Centers (Strata) Tab</b>	
Number of Centers (Strata) .....	<b>4</b>
Title or Name .....	<b>Center</b>
Assign Equal Sample Sizes to All Centers (Strata).....	<b>Checked</b>
Center Sample Size.....	<b>80</b>
Center (Stratum) 1 Label .....	<b>Center 1</b>
Center (Stratum) 2 Label .....	<b>Center 2</b>
Center (Stratum) 3 Label .....	<b>Center 3</b>
Center (Stratum) 4 Label .....	<b>Center 4</b>
Number of Additional Factors .....	<b>0</b>

## Randomization Lists

### List Options Tab

- Include a Column of Sequence Numbers.....**Checked**
- Include a Column of Subject ID's.....**Checked**
  - Restart Numbering for each Center (Stratum) .....**Checked**
  - Subject ID Prefix .....{Set}
- Include a Column of Block Identifiers .....**Checked**
- Include a Column of Combined Stratification Codes .....**Unchecked**
- Include a Column of Abbreviated Treatment Codes .....**Checked**
- Include a Column of Unique Randomization Codes.....**Checked**

### Storage Tab

- Store Randomization List .....**Checked**
- Store Randomization List Data Starting In .....1
- Update Column Names .....**Checked**

### Reports Tab

- Show Summary .....**Checked**
- Show Randomization List .....**Checked**
- Show Randomization List Details .....**Checked**
- Show References .....**Checked**

## Output

Click the Run button to perform the calculations and generate the following output.

### Randomization List Summary

Randomization List Summary					
Randomization Algorithm	Block Randomization				
User-Entered Random Seed	102203				
Block Size Multiplier(s)	1 2 3				
Block Size(s)	4 8 12				
Total Number of Blocks	52				
Overall Total Sample Size	320				
Number of Treatment Groups	3				
Number of Centers (Strata)	4				
Treatments					
Treatment	Treatment Code	Sample Size	— Allocation % —		
Low	L	160	Actual	Target	
Medium	M	80	50%	50%	25%
High	H	80	25%	25%	25%
Centers (Strata)					
Center	First Subject ID	Blocks	Sample Size	— Allocation % —	
Center 1	1001	13	80	Actual	Target
Center 2	2001	13	80	25%	25%
Center 3	3001	13	80	25%	25%
Center 4	4001	13	80	25%	25%

The summary indicates that 80 subjects are randomized within each center. Randomization occurs independently within each Center.

Randomization Lists

Randomization List

<b>Randomization List</b>						
Randomization Algorithm		Block Randomization (Block Sizes = 4 8 12)				
User-Entered Random Seed		102203				
Sequence	Subject ID	Center	Block	Treatment	Treatment Code	Randomization Code
1	1001	Center 1	1	Low	L	DNC3
2	1002	Center 1	1	Medium	M	VJF1
3	1003	Center 1	1	High	H	LCD5
4	1004	Center 1	1	Low	L	NBW1
5	1005	Center 1	2	High	H	WVE1
6	1006	Center 1	2	Low	L	LSC6
7	1007	Center 1	2	Medium	M	OWK0
8	1008	Center 1	2	Low	L	UCN3
9	1009	Center 1	3	Low	L	LUS2
10	1010	Center 1	3	Low	L	GFF7
11	1011	Center 1	3	High	H	IZD1
12	1012	Center 1	3	Medium	M	GBL1
.	.	.	.	.	.	.
.	.	.	.	.	.	.
.	.	.	.	.	.	.
81	2001	Center 2	14	Low	L	MHC0
82	2002	Center 2	14	High	H	OBT8
83	2003	Center 2	14	Low	L	ETC4
84	2004	Center 2	14	Medium	M	FEC7
85	2005	Center 2	15	High	H	FKB5
86	2006	Center 2	15	Low	L	ICL4
87	2007	Center 2	15	Low	L	ZDZ9
88	2008	Center 2	15	High	H	QKM6
89	2009	Center 2	15	Medium	M	CSX4
90	2010	Center 2	15	Medium	M	CNS5
91	2011	Center 2	15	Low	L	EOQ6
92	2012	Center 2	15	Medium	M	RDY5
93	2013	Center 2	15	Low	L	UBO4
94	2014	Center 2	15	Low	L	GAE7
95	2015	Center 2	15	High	H	XIV9
96	2016	Center 2	15	Low	L	CLR4
.	.	.	.	.	.	.
.	.	.	.	.	.	.
.	.	.	.	.	.	.
161	3001	Center 3	27	Low	L	MTA2
162	3002	Center 3	27	High	H	XVZ2
163	3003	Center 3	27	Low	L	IUF0
164	3004	Center 3	27	Medium	M	IFP0
165	3005	Center 3	28	Low	L	YTJ3
166	3006	Center 3	28	Medium	M	MVC7
167	3007	Center 3	28	Low	L	TGE5
168	3008	Center 3	28	High	H	TOP5
.	.	.	.	.	.	.
.	.	.	.	.	.	.
.	.	.	.	.	.	.
241	4001	Center 4	40	Low	L	OJC6
242	4002	Center 4	40	Medium	M	LGS4
243	4003	Center 4	40	Low	L	VID5
244	4004	Center 4	40	High	H	CXU5
.	.	.	.	.	.	.
.	.	.	.	.	.	.
.	.	.	.	.	.	.
317	4077	Center 4	52	Low	L	FYT2
318	4078	Center 4	52	Low	L	TXK8
319	4079	Center 4	52	High	H	YPT8
320	4080	Center 4	52	Medium	M	FJA0

The randomization list has a length of 320 subjects with 80 each in 4 different centers. This randomization list will also have been written to the spreadsheet.

Randomization Lists

Randomization List Details

<b>Randomization List Details for Strata Combination 1 of 4</b>					
Strata Combination	Center = "Center 1"				
Randomization Algorithm	Block Randomization (Block Sizes = 4 8 12)				
Number of Blocks	13				
Sample Size	80				
Number of Treatment Groups	3				
<b>Block-Subject Allocation</b>					
	<b>Number</b>	<b>Subjects</b>	<b>— Allocation % —</b>		
<b>Block Size</b>	<b>of Blocks</b>	<b>Assigned</b>	<b>Actual</b>	<b>Target</b>	
4	8	32	40%	33.33%	
8	3	24	30%	33.33%	
12	2	24	30%	33.33%	
<b>Treatment Groups</b>					
	<b>Treatment</b>		<b>— Allocation % —</b>		
<b>Treatment</b>	<b>Code</b>	<b>Sample Size</b>	<b>Actual</b>	<b>Target</b>	
Low	L	40	50%	50%	
Medium	M	20	25%	25%	
High	H	20	25%	25%	
<b>Cumulative Details</b>					
				<b>Largest</b>	<b>Cumulative</b>
<b>Sequence</b>	<b>Subject ID</b>	<b>Block</b>	<b>Treatment</b>	<b>% Deviation</b>	<b>Sample Size</b>
				<b>from Target</b>	<b>(L, M, H)</b>
1	1001	1	Low	1.25%	(1, 0, 0)
2	1002	1	Medium	2.50%	(1, 1, 0)
3	1003	1	High	1.25%	(1, 1, 1)
4	1004	1	Low	0.00%	(2, 1, 1)
5	1005	2	High	3.75%	(2, 1, 2)
6	1006	2	Low	2.50%	(3, 1, 2)
7	1007	2	Medium	1.25%	(3, 2, 2)
8	1008	2	Low	0.00%	(4, 2, 2)
9	1009	3	Low	1.25%	(5, 2, 2)
10	1010	3	Low	2.50%	(6, 2, 2)
.	.	.	.	.	.
.	.	.	.	.	.
.	.	.	.	.	.

(Output continues with a separate Randomization List Details report for each center.)

The Randomization List Details report indicates that while it was intended to have an equal number of subjects assigned to each block size, the actual percentages were just a little off due to the discrete nature of the block sizes and total sample size.

## Example 3 – Block Randomization within Centers with Two Additional Stratification Factors

Suppose a study is to be conducted at 3 centers with randomization using 2 stratification factors: Gender (Male, Female) and Size (Small, Medium, Large). The treatment allocation will be equal among 3 groups (A, B, C) and randomized by block randomization with custom block-subject allocation such that 40% of subjects are randomized using a block size of 3 and 60% are randomized using a block size of 6. The actual block allocation will be constrained so that the total sample size matches the target if possible. We'll create a randomization list with 1000 subjects and save it to the spreadsheet.

Center 1 is expected to have half as many subjects as the other two. It is also expected that there will be a ratio of males to females of 3:2 and an equal allocation of subjects among the three sizes.

For reproducibility, we'll use a random seed of 90605.6497.

### Setup

This section presents the values of each of the parameters needed to run this example. First, from the data window, load the **Randomization Lists** procedure window using the Analysis menu or the Procedure Navigator. You may then make the appropriate entries as listed below, or open **Example 3** by going to the **File** menu and choosing **Open Example Template**.

<u>Option</u>	<u>Value</u>
<b>Randomization Tab</b>	
Randomization Algorithm .....	<b>Block Randomization</b>
Random Seed .....	<b>90605.6497</b>
Block Size Multiplier(s) .....	<b>1 2</b>
Block-Subject Allocation .....	<b>Custom</b>
Custom Block-Subject Allocation.....	<b>40 60</b>
Constrain the actual block allocation... ..	<b>Checked</b>
Search for a randomization list... ..	<b>Unchecked</b>
Maximum Search Iterations .....	<b>1000</b>
Sample Size Entry Type .....	<b>Enter the Overall Total Sample Size for the Study</b>
Overall Total Sample Size .....	<b>1000</b>
Number of Treatment Groups.....	<b>3</b>
Title or Name .....	<b>Group</b>
Assign Equal Sample Sizes to All Treatment Groups .....	<b>Checked</b>
Treatment Group 1 Label .....	<b>A</b>
Treatment Group 2 Label .....	<b>B</b>
Treatment Group 3 Label .....	<b>C</b>
<b>Centers (Strata) Tab</b>	
Number of Centers (Strata) .....	<b>3</b>
Title or Name .....	<b>Center</b>
Assign Equal Sample Sizes to All Centers (Strata).....	<b>Unchecked</b>
Center (Stratum) 1 Label .....	<b>Center 1</b>
Center (Stratum) 1 Allocation Ratio.....	<b>0.5</b>
Center (Stratum) 2 Label .....	<b>Center 2</b>
Center (Stratum) 2 Allocation Ratio.....	<b>1</b>
Center (Stratum) 3 Label .....	<b>Center 3</b>
Center (Stratum) 3 Allocation Ratio.....	<b>1</b>



**Randomization Lists**

Number of Additional Factors .....	2
<u>Stratification Factor 1</u>	
Number of Levels.....	2
Title or Name .....	Gender
Use Equal Sample Size Allocation for All Levels .....	Unchecked
Level 1 Label .....	Male
Level 1 Allocation Ratio .....	3
Level 2 Label .....	Female
Level 2 Allocation Ratio .....	2

Stratification Factor 2

Number of Levels.....	3
Title or Name .....	Size
Use Equal Sample Size Allocation for All Levels .....	Checked
Level 1 Label .....	Small
Level 2 Label .....	Medium
Level 3 Label .....	Large

**List Options Tab**

Include a Column of Sequence Numbers.....	Checked
Include a Column of Subject ID's.....	Checked
Restart Numbering for each Center (Stratum) .....	Checked
Restart Numbering for each Additional... ..	Checked
Subject ID Prefix .....	{Set}000
Include a Column of Block Identifiers .....	Checked
Include a Column of Combined Stratification Codes.....	Checked
Use Abbreviated Codes.....	Checked
Add Code Separators .....	Unchecked
Include a Column of Abbreviated Treatment Codes .....	Unchecked
Include a Column of Unique Randomization Codes.....	Unchecked

**Storage Tab**

Store Randomization List .....	Checked
Store Randomization List Data Starting In .....	1
Update Column Names .....	Checked

**Reports Tab**

Show Summary .....	Checked
Show Randomization List .....	Checked
Show Randomization List Details .....	Checked
Show References .....	Unchecked

## Randomization Lists

## Output

Click the Run button to perform the calculations and generate the following output.

## Randomization List Summary

**Randomization List Summary**

Randomization Algorithm	Block Randomization
User-Entered Random Seed	90605.6497
Block Size Multiplier(s)	1 2
Block Size(s)	3 6
Total Number of Blocks	240
Overall Total Sample Size	1017 (Target was 1000)
Number of Treatment Groups	3
Number of Centers (Strata)	3
Number of Stratification Factor 1 Levels	2
Number of Stratification Factor 2 Levels	3

**Treatments**

Group	Group Code	Sample Size	— Allocation % —	
			Actual	Target
A	A	339	33.33%	33.33%
B	B	339	33.33%	33.33%
C	C	339	33.33%	33.33%

**Centers (Strata)**

Center	Gender	Size	Stratification Code	First Subject ID	Blocks	Sample Size	— Allocation % —	
							Actual	Target
Center 1	Male	Small	1MS	10000001	10	42	4.13%	4.00%
Center 1	Male	Medium	1MM	20000001	10	42	4.13%	4.00%
Center 1	Male	Large	1ML	30000001	10	42	4.13%	4.00%
Center 1	Female	Small	1FS	40000001	6	27	2.65%	2.67%
Center 1	Female	Medium	1FM	50000001	6	27	2.65%	2.67%
Center 1	Female	Large	1FL	60000001	6	27	2.65%	2.67%
Center 2	Male	Small	2MS	70000001	19	81	7.96%	8.00%
Center 2	Male	Medium	2MM	80000001	19	81	7.96%	8.00%
Center 2	Male	Large	2ML	90000001	19	81	7.96%	8.00%
Center 2	Female	Small	2FS	100000001	13	54	5.31%	5.33%
Center 2	Female	Medium	2FM	110000001	13	54	5.31%	5.33%
Center 2	Female	Large	2FL	120000001	13	54	5.31%	5.33%
Center 3	Male	Small	3MS	130000001	19	81	7.96%	8.00%
Center 3	Male	Medium	3MM	140000001	19	81	7.96%	8.00%
Center 3	Male	Large	3ML	150000001	19	81	7.96%	8.00%
Center 3	Female	Small	3FS	160000001	13	54	5.31%	5.33%
Center 3	Female	Medium	3FM	170000001	13	54	5.31%	5.33%
Center 3	Female	Large	3FL	180000001	13	54	5.31%	5.33%

The summary lists the number of subjects randomized by each strata combination. Notice that just about twice as many subjects are assigned in centers 2 and 3 as in center 1. Also note that the ratio of males to females is about 3:2 within each center. The randomization list had to be expanded to 1017 subjects to avoid incomplete blocks.

Randomization Lists

Randomization List

Randomization List							
Randomization Algorithm		Block Randomization (Block Sizes = 3 6)					
User-Entered Random Seed		90605.6497					
Sequence	Subject ID	Center	Gender	Size	Stratification Code	Block	Group
1	10000001	Center 1	Male	Small	1MS	1	A
2	10000002	Center 1	Male	Small	1MS	1	B
3	10000003	Center 1	Male	Small	1MS	1	C
4	10000004	Center 1	Male	Small	1MS	1	A
5	10000005	Center 1	Male	Small	1MS	1	C
6	10000006	Center 1	Male	Small	1MS	1	B
7	10000007	Center 1	Male	Small	1MS	2	B
8	10000008	Center 1	Male	Small	1MS	2	A
9	10000009	Center 1	Male	Small	1MS	2	C
.	.	.	.	.	.	.	.
.	.	.	.	.	.	.	.
.	.	.	.	.	.	.	.
3	20000001	Center 1	Male	Medium	1MM	11	A
44	20000002	Center 1	Male	Medium	1MM	11	C
45	20000003	Center 1	Male	Medium	1MM	11	B
46	20000004	Center 1	Male	Medium	1MM	12	C
47	20000005	Center 1	Male	Medium	1MM	12	A
48	20000006	Center 1	Male	Medium	1MM	12	A
49	20000007	Center 1	Male	Medium	1MM	12	B
50	20000008	Center 1	Male	Medium	1MM	12	B
51	20000009	Center 1	Male	Medium	1MM	12	C
.	.	.	.	.	.	.	.
.	.	.	.	.	.	.	.
.	.	.	.	.	.	.	.
127	40000001	Center 1	Female	Small	1FS	31	C
128	40000002	Center 1	Female	Small	1FS	31	B
129	40000003	Center 1	Female	Small	1FS	31	A
130	40000004	Center 1	Female	Small	1FS	31	B
131	40000005	Center 1	Female	Small	1FS	31	C
132	40000006	Center 1	Female	Small	1FS	31	A
133	40000007	Center 1	Female	Small	1FS	32	C
134	40000008	Center 1	Female	Small	1FS	32	A
135	40000009	Center 1	Female	Small	1FS	32	B
.	.	.	.	.	.	.	.
.	.	.	.	.	.	.	.
.	.	.	.	.	.	.	.
208	70000001	Center 2	Male	Small	2MS	49	C
209	70000002	Center 2	Male	Small	2MS	49	A
210	70000003	Center 2	Male	Small	2MS	49	B
211	70000004	Center 2	Male	Small	2MS	49	C
212	70000005	Center 2	Male	Small	2MS	49	A
213	70000006	Center 2	Male	Small	2MS	49	B
.	.	.	.	.	.	.	.
.	.	.	.	.	.	.	.
.	.	.	.	.	.	.	.
613	130000001	Center 3	Male	Small	3MS	145	C
614	130000002	Center 3	Male	Small	3MS	145	B
615	130000003	Center 3	Male	Small	3MS	145	B
616	130000004	Center 3	Male	Small	3MS	145	A
617	130000005	Center 3	Male	Small	3MS	145	C
618	130000006	Center 3	Male	Small	3MS	145	A
.	.	.	.	.	.	.	.
.	.	.	.	.	.	.	.
.	.	.	.	.	.	.	.
1015	180000052	Center 3	Female	Large	3FL	240	B
1016	180000053	Center 3	Female	Large	3FL	240	A
1017	180000054	Center 3	Female	Large	3FL	240	C

The randomization list has a length of 1017 subjects with 339 in each group. Randomization occurred independently within each strata combination. The randomization list will also have been written to the spreadsheet.

Randomization Lists

Randomization List Details

Randomization List Details for Strata Combination 1 of 18

Strata Combination	Center = "Center 1" Gender = "Male" Size = "Small"
Randomization Algorithm	Block Randomization (Block Sizes = 3 6)
Number of Blocks	10
Sample Size	42
Number of Treatment Groups	3

Block-Subject Allocation

Block Size	Number of Blocks	Subjects Assigned	Allocation %	
			Actual	Target
3	6	18	42.86%	40%
6	4	24	57.14%	60%

Treatment Groups

Group	Group Code	Sample Size	Allocation %	
			Actual	Target
A	A	14	33.33%	33.33%
B	B	14	33.33%	33.33%
C	C	14	33.33%	33.33%

Cumulative Details

Sequence	Subject ID	Block	Group	Largest % Deviation from Target	Cumulative Sample Size (A, B, C)
1	10000001	1	A	4.76%	(1, 0, 0)
2	10000002	1	B	4.76%	(1, 1, 0)
3	10000003	1	C	0.00%	(1, 1, 1)
4	10000004	1	A	4.76%	(2, 1, 1)
5	10000005	1	C	4.76%	(2, 1, 2)
6	10000006	1	B	0.00%	(2, 2, 2)
7	10000007	2	B	4.76%	(2, 3, 2)
8	10000008	2	A	4.76%	(3, 3, 2)
9	10000009	2	C	0.00%	(3, 3, 3)
10	10000010	3	A	4.76%	(4, 3, 3)
11	10000011	3	C	4.76%	(4, 3, 4)
12	10000012	3	B	0.00%	(4, 4, 4)
13	10000013	4	B	4.76%	(4, 5, 4)
14	10000014	4	A	4.76%	(5, 5, 4)
15	10000015	4	C	0.00%	(5, 5, 5)
.	.	.	.	.	.
.	.	.	.	.	.
.	.	.	.	.	.

(Output continues with a separate Randomization List Details report for each strata combination.)

The Randomization List Details reports indicate the allocation within each strata combination. The number of male subjects with Size = Small in Center 1 is 42. Note that the number of subjects randomized using each block size matches closely our specified percentages of 40% and 60%.

## Example 4 – Complete Randomization and Imbalance

In this example we'll demonstrate the imbalance that can occur when using complete randomization by generating a simple randomization list with 20 subjects and 2 treatment groups, A and B.

For reproducibility, we'll use a random seed of 60608.

### Setup

This section presents the values of each of the parameters needed to run this example. First, from the data window, load the **Randomization Lists** procedure window using the Analysis menu or the Procedure Navigator. You may then make the appropriate entries as listed below, or open **Example 4a** by going to the **File** menu and choosing **Open Example Template**.

<u>Option</u>	<u>Value</u>
<b>Randomization Tab</b>	
Randomization Algorithm .....	<b>Complete Randomization</b>
Random Seed.....	<b>60608</b>
Search for a randomization list... ..	<b>Unchecked</b>
Maximum Search Iterations .....	<b>1000</b>
Sample Size Entry Type .....	<b>Enter the Overall Total Sample Size for the Study</b>
Overall Total Sample Size .....	<b>20</b>
Number of Treatment Groups.....	<b>2</b>
Title or Name .....	<b>Treatment</b>
Assign Equal Sample Sizes to All Treatment Groups .....	<b>Checked</b>
Treatment Group 1 Label .....	<b>A</b>
Treatment Group 2 Label .....	<b>B</b>

### Output

Click the Run button to perform the calculations and generate the following output.

#### Randomization List Summary

Randomization Algorithm Complete Randomization  
User-Entered Random Seed 60608

Overall Total Sample Size 20  
Number of Treatment Groups 2

Treatment	Treatment Code	Sample Size	— Allocation % —	
			Actual	Target
A	A	7	35%	50%
B	B	13	65%	50%

#### Randomization List

Randomization Algorithm Complete Randomization  
User-Entered Random Seed 60608

Sequence	Subject ID	Treatment
1	101	B
2	102	A
3	103	B
4	104	A
5	105	B
6	106	B
7	107	B
8	108	A

Randomization Lists

9	109	B
10	110	A
11	111	B
12	112	B
13	113	A
14	114	B
15	115	B
16	116	B
17	117	B
18	118	B
19	119	A
20	120	A

The randomization list generated using complete randomization has nearly twice as many subjects assigned to group B as A. The actual randomization is imbalanced between groups even though the target was to assign equal sample sizes to both treatment groups.

To search for a balanced randomization list, check **Search for a randomization list...** or open **Example 4b**.

<u>Option</u>	<u>Value</u>
<b>Randomization Tab</b>	
Search for a randomization list...	<b>Checked</b>

Click the Run button to perform the calculations and generate the following output with balanced groups

---

**Randomization List Summary**

Randomization Algorithm	Complete Randomization
User-Entered Random Seed	60608
Overall Total Sample Size	20
Number of Treatment Groups	2

  

Treatment	Treatment Code	Sample Size	Allocation %	
			Actual	Target
A	A	10	50%	50%
B	B	10	50%	50%

  


---

**Randomization List**

Randomization Algorithm	Complete Randomization
User-Entered Random Seed	60608

  

Sequence	Subject ID	Treatment
1	101	B
2	102	A
3	103	B
4	104	A
5	105	A
6	106	B
7	107	A
8	108	A
9	109	B
10	110	B
11	111	A
12	112	B
13	113	A
14	114	A
15	115	B
16	116	B
17	117	A
18	118	B
19	119	B
20	120	A

  

Note: This list was generated by searching for a randomization list in which the final group sizes exactly match the target group sizes. One or more generated lists did not meet the required criteria and were discarded. The number of search iterations to obtain this list was 3.