

WOMBAT

Perinatal Trials Toolkit

How to generate a randomisation sequence

Simple randomisation

Simple randomisation is analogous to repeated fair coin tossing

- preserves complete unpredictability of each intervention assignment
- best achieved using a random numbers table or a computer generated random number sequence
- other manual methods such as coin-toss, dice throw, card shuffling are acceptable methods but can be subverted, cannot be audited and can be difficult to implement in practice

How to use a random numbers table:

- decide where to start reading the table
- decide which direction the table will be read
- decide which numbers will represent treatment A and which treatment B
e.g. odd numbers treatment A, even numbers treatment B
OR treatment A – all numbers 0-20 B 21 – 40 (any other numbers ignored)

02 31 10 88 97	54 99 58 45 66
12 58 55 46 84	98 74 87 65 54
54 94 49 52 52	44 80 94 98 87
78 61 68 31 62	78 51 65 87 94
52 07 64 48 65	91 34 25 54 67
11 06 32 45 87	51 01 23 12 91
54 25 54 26 96	45 30 24 20 67
98 87 69 64 65	64 55 58 64 98
64 95 87 48 48	94 60 11 66 13
03 63 74 97 45	10 44 22 45 30
63 94 45 45 20	61 99 95 97 51
78 87 98 61 12	32 77 87 22 58
56 59 16 24 02	20 51 46 11 45
94 64 54 03 05	58 84 91 36 69
23 12 99 90 94	54 62 34 45 45

Where to find a random numbers table:

- Excel, statistical textbooks, EpiInfo
- www.randomization.com is a free web-based randomization program

Problems with simple randomisation

“No other allocation generation approach, irrespective of its complexity and sophistication, surpasses the unpredictability and bias prevention of simple randomisation.”

Schulz & Grimes 2006

- for small sample sizes can be quite imbalanced between the randomised treatment groups (over time if the sample is large enough this will even out)
- if recruitment is over a long period simple randomisation could lead to imbalances in baseline characteristics of the treatment groups if the type of patients being enrolled changes over time and a long series of assignments to one treatment occurs

Blocking (random permuted blocks)

Blocking is a method to deal with the imbalances caused by simple randomisation. It is one form of restricted randomisation which aims to create unbiased comparison groups of about the same size throughout the trial.

- block sizes can vary from 2 to 20 (the smallest block size is determined by adding up the allocation ratio e.g. 1:1 ratio = block size of 2; 2:2:1 ratio = block size of 5)
- smaller block sizes can be susceptible to subversion of the randomisation sequence because it is possible to guess future allocations on the basis of past allocations
- it is recommended that the block sizes used are randomly varied to avoid this problem especially if the trial has limited blinding (randomly permuted blocks)

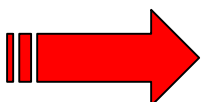
Blocking Example: Block size of 6

Block 1: AAABBB	Choose a block at random and the first 6 treatments are allocated according to the permutations in that block Then a new block is chosen at random and the next 6 treatments are allocated according to that block. Keep going until the required sample size is recruited
Block 2: BBBAAB	
Block 3: AABBAB	
Block 4: BBAABA	
Block 5: ABABAB	
Block 6: BABABA	
Block 7: ABAABB	
Block 8: BABBAA	

Stratification

Stratification involves dividing the sample to be studied according to prognostic factors.

- stratification aims to control for imbalances in baseline characteristics between the treatment groups
- stratification can only be used with restricted randomisation schemes (usually blocking) not with simple randomisation
- only variables observed and recorded before randomisation can be used for stratification
- it is generally only practical to include at most two or three stratification variables
- variables used for stratification should be easy to observe and reasonably free of measurement error
- by reducing imbalances on prognostic factors stratification can increase the statistical power and precision of small trials but with samples of 50 per group the statistical gain will be minimal
- stratification is recommended for multicentre trials with the trial centre used as the stratification variable – this will control for differences in the study population due to environmental, social, demographic and other factors related to the clinic or centre



[See related toolkit - Randomisation services in Australia](#)

This toolkit was prepared by Rebecca Tooher and Philippa Middleton.

References:

Meinert CL. Clinical Trials. Design, Conduct and Analysis. New York: Oxford University Press, 1986.
Schulz K, Grimes D. The Lancet Handbook of Essential Concepts in Clinical Research, Philadelphia: Elsevier Ltd. , 2006

Last revised: December 28, 2007.