STANDARD OPERATING PROCEDURE

RANDOMISATION SOP
S65

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DISCLAIMER

This generic R&D Standard Operating Procedure (SOP) must be followed unless;

- A study specific SOP exists
- A departmental SOP dictates a different working practice

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VERSION HISTORY LOG

This area should detail the version history for this document. It should detail the key elements of the changes to the versions.

VERSION	Reviewer	Date Implemented	Details of significant changes
1.0	Rohan Chauhan, NHS Research Advisor	14 November 2014	
1.1	Lisella Wilkinson, Quality Assurance Coordinator, R&D	22 September 2016	• Copyright symbol removed • Updated link to online SOPs on the new Hub Intranet, live from August 2016

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1 BACKGROUND

Randomisation is often used in trials to allocate eligible and consenting patients to the treatment options under investigation. A **randomisation list** is usually produced electronically. As patients are recruited to the trial they are assigned the next treatment allocation and unique study identification number on the list. In some cases (**minimisation**) the lists are not predetermined but depend on the characteristics and allocations of previously recruited patients. Details of how the randomisation list/system is used and how allocation is concealed will be detailed in the trial protocol.

2 PURPOSE

This Standard Operating Procedure (SOP) has been written to describe the procedure for producing and handling randomisation lists for randomised trials. This document is for use by the statistician(s) in R&D Department of the RD&EFT.

Study teams should receive randomisation training if involved in the randomisation process.

3 SCOPE

This SOP applies to generation of randomisation lists and schemes for all randomised trials where members of the RD&EFT are the main trial statistician. Details of how the randomisation list/system is used and how allocation is concealed will be detailed in the trial protocol.

4 RESPONSIBILITIES

The trial statistician and programmer of the randomisation system should follow this SOP.

5 PROCEDURES

6.1. Type of randomisation to be used

The type of randomisation suitable for a trial should be carefully considered to ensure good balance is achieved on patient characteristics between randomised groups. In particular:

- For large sample sizes (greater than around 200) simple randomisation can be appropriate.

- For smaller sample sizes blocking should be used to ensure similar numbers in the randomised groups. Random permuted blocks (e.g. blocks of sizes 4 and 6) help maintain blinding and concealed allocation.

- Stratification or minimisation should be used to ensure balance between randomised groups for important prognostic factors (particularly in smaller studies) such as sex and age group. The number of strata must be limited to ensure reasonable sample sizes in each (often only 2 or 3 factors are possible, strata sizes of less than about 20 are not recommended). Strata chosen must be independent so that they can be adjusted for in the final analysis. Where there are several important prognostic factors minimisation should be preferred.

- For multicentre trials it may be appropriate to stratify by centre

- In blinded studies the clinical staff involved should not be informed of the details of stratification / minimisation variables or block sizes unless absolutely necessary.

6.2 Creating the randomisation list

The randomisation list should be obtained in a way that is reproducible. A record should be made of the seed used for computer generated lists. The randomisation list / scheme should provide an associated unique study identification number.

- Blocking and stratification can be carried out using the user written Stata[1] command *ralloc.*

For example:

ralloc block size treat, seed(654) sav(allocation) ns(50) init(4) osiz(2) ntreat(2) trtlab(intervention, control)

This code randomises 50 patients to 2 treatment groups with 2 block sizes, starting at block size 4 (ie sizes 4 and 6). It is important to set the seed here to ensure the list is reproducible.

- To carry out minimisation a secure programme for use during the randomisation process will need to be produced.

If the Stata package is unavailable, blocking and stratification can be achieved using other statistical packages such as StatsDirect for which the RD&E Trust has a site licence.

6.3 Handling the randomisation list / minimisation programme

- Randomisation lists should be saved as a document in a format which assigns appropriate identifiers to the study subjects and which clearly shows the treatment

allocation in words rather than symbols. This document should be carefully and securely kept by the statistician along with a log of the code used to generate the list.

- To preserve blinding and concealed allocation, the randomisation list or minimisation programme should be sent to a carefully chosen person (e.g. pharmacist). The investigators or those recruiting and caring for the patients should not see the randomisation list during the running of the trial.

- Concealment means that the process of allocation of the participants in the trial is concealed from the investigators and the people conducting the trial. This means that the next participant should be read from the randomisation list by somebody independent of the investigators e.g. a pharmacist or a medical secretary. To assist concealment the list can be used to create opaque sequentially numbered envelopes containing a slip of paper indicating the allocation (e.g. control or intervention).

6 FURTHER READING

Dawn-Marie Walker (Editor). *An introduction to Health Services Research*. 2014. Sage. 362pp.

Pocock SJ, Simon R. Sequential treatment assignment with balancing for prognostic factors in the controlled clinical trials. *Biometrics* 1975;31:103-115.↩

StataCorp. 2007. Statistical Software: Release 10.0. College Station, TX: Stata Corporation.

Taves DR. Minimization: a new method of assigning subjects to treatment and control groups. *Clin Pharmacol Therapeut.* 1974;15:443-453.↩