BRITISH JOURNAL OF PSYCHIATRY (1999), 175, 581-584

https://doi.org/10.1192/bjp.175.6.581 Published online by Cambridge University Press

Randomisation in clinical trials

L. O. OGUNDIPE, A. P. BOARDMAN and A. MASTERSON

Background Several studies of papers published in non-psychiatric medical journals that report on randomised controlled trials (RCTs) indicate that there is inadequate reporting of the process by which randomisation is carried out.

Aims To examine the adequacy of the reporting of the procedure of randomisation in clinical trials of parallel design published in the *British Journal of Psychiatry (BJP)* and the *American Journal of Psychiatry (AJP)*.

Method All issues of the *BJP* and the *AJP* published between January 1990 and December 1998 were surveyed, and papers that reported on RCTs were examined to judge the adequacy of the reporting of the process of randomisation.

Results We found 183 papers which claimed to report on RCTs (73 in the *BJP* and 110 in the *AJP*). Nine (8.2%) of those in the *AJP* and six (8.2%) in the *BJP* described the technique of creating the randomisation sequence. Two (1.8%) of those in the *AJP* and 11 (15.1%) of those in the *BJP* described the mechanism of allocating treatment. One paper in the *AJP* and five papers in the *BJP* described both the generation of random numbers and allocation.

Conclusions Adequate reporting of the method of randomisation was uncommon. The RCT status of some of the papers must therefore be in doubt.

Declaration of interest None.

The importance of the randomised controlled trial (RCT) is now widely acknowledged (Chalmers, 1998). The process of randomisation is important because improperly conducted random allocation risks losing the powerful effect of randomisation in eliminating systematic bias. Several authorities have recommended that authors should specify their method of randomisation (Simon & Wittes, 1985; Altman *et al*, 1989), and the recent CONSORT statement listed items that should be included in reports of randomised trials (Altman, 1996). The Vancouver Conference of the International Committee of Medical Journal Editors recommends that authors should "give details about randomisation" (*British Medical Journal*, 1991), and Bailar & Mosteller (1988) recommended that authors should "simply tell readers how the randomisation was done". To the best of our knowledge, no survey of the quality of reporting of randomisation in psychiatric journals has been conducted.

THE PROCESS OF RANDOMISATION

In a clinical trial, randomisation involves systematically assigning subjects to intervention groups. The object of randomisation is to ensure that the allocation of the treatment groups to subjects is left to chance at known, usually equal, probabilities. This removes allocation bias, and, although it does not guarantee that the groups will be identical, any differences between them are attributable to chance, and statistical methods are available to measure the probability that the observed differences in the outcome variables are due to chance. Randomisation serves two main functions: first, it generates an unpredictable assignment sequence that gives all subjects a predetermined chance of receiving any of the treatments under scrutiny, thus eliminating systematic bias; second, it lends the data to statistical analysis, because statistical methods of analysis are based on what is expected to happen in random samples, allowing useful inferences to be made from the observed data. A parallel design that employs randomisation is one of the strongest methodological designs for comparing treatment or intervention groups.

Descriptions of methods of randomisation can be found in many research textbooks (e.g. Pocock, 1983). In brief, randomisation is a two-stage process which involves the generation of the random numbers that correspond to intervention groups, for example by using random number tables or a computer-generated set of random numbers, and the allocation of these numbers to subjects by using, for example, a deck of sealed envelopes. It is good practice to adopt a well-defined routine for registering and randomising subjects and to arrange in advance the sequence of random treatment assignment. This should be done by ensuring that one person, who is independent of the clinicians, is responsible for supervising subject registration and randomisation. In the case of multi-centre studies, it is usual to do this via a central office. When a double-blind procedure is used, it is customary to use the pharmacist. The use of an independent person or process to control the randomisation procedure is an attempt to reduce the risk of having the treatment assignment manipulated by interested parties or of revealing the subjects assigned to each type of treatment ('breaking the code') and thus losing the advantage of randomisation – namely that each treatment assignment is completely unpredictable.

For most purposes a simple unrestricted method of preparing a randomisation list is employed. In cases where it is important to have approximately equal numbers of subjects in each group, methods such as random permuted blocks or replacement randomisation can be used. Methods of stratification, such as random permuted blocks within strata and minimisation, also exist to ensure that treatment groups are similar with respect to certain relevant patient characteristics.

THE REPORTING OF RANDOMISATION

Surveys of non-psychiatric medical journals show low rates of adequate reporting of the process of randomisation in studies purporting to be RCTs (Table 1). For example, DerSimonian *et al* (1982) reported that the

https://doi.org/10.1192/bjp.175.6.581 Published online by Cambridge University Press

method of randomisation was stated in only 19% of the 67 trials they investigated, although 84% claimed to use random allocation. Williams & Davies (1994) noted that certain journals reported the method of randomisation more adequately than others.

It cannot be assumed that a proper randomisation procedure was followed if, in a report of a clinical trial, randomisation is merely alluded to without being fully discussed; this implies that we cannot be certain that such a trial *was* an RCT and that the biases associated with improper randomisation were eliminated. Chalmers *et al* (1983) found such biases in trials that did not report adequate allocation concealment, while Schulz *et al* (1995) reported that the odds ratios were exaggerated by 41% for trials in which the allocation sequence was not properly concealed.

While there is no guaranteed means of ensuring the veracity of reported study methods, the reporting of methodology in scientific reports offers an open means of peer scrutiny. The present study aims to provide a quality check on the adequacy of reporting of the procedure of randomisation in clinical trials of parallel design published in the *British Journal of Psychiatry (BJP)* and the *American Journal of Psychiatry (AJP)*.

METHOD

Design

A period survey of clinical trials which claimed to be RCTs published in the *BJP* and *AJP* was carried out. All issues of the *BJP* and *AJP* published in the years 1990–98 were examined. The inclusion criteria were: being original papers in which detailed methodology was reported; the experimental and usual or placebo treatment groups having been assigned by random allocation of subjects. Parallel designs in which randomisation was not used were excluded.

The outcome measure of interest was whether or not the process of randomisation was 'adequately reported'. In the absence of an acceptable definition for adequate reporting we chose to define an adequate report as one in which the mechanism of randomisation was described in a way that would allow replication of the procedure of randomisation used in the study. The operational definition of an adequate report was one that described both the technique of generating random numbers and the method of allocating these to subjects.

Procedure

All 108 issues of the *BJP* and 108 issues of the *AJP* published between January 1990 and December 1998 were collected and searched manually. The contents tables and summaries were browsed through to identify RCTs using the following keywords: randomised, randomisation, parallel design, random allocation/assignment, RCT, placebo controlled, comparison, treatment efficacy. Whenever any of the keywords appeared in the title or abstract, the paper was selected for further analysis. In order to ensure that suitable papers were not missed the same keywords were fed into a CD-ROM database (PsychLit) in order to identify randomised controlled studies published in the *BJP* and *AJP* during the same period.

The whole of the abstract and the 'methods' section of the papers selected were reviewed. All sub-headings under 'methods' were read, paying particular attention to the 'design' and 'procedure' sections. The methods of randomisation were noted on a data collection pro forma that consisted of three questions aimed at appraising the details of the method of randomisation:

(a) whether the technique of creating the randomised sequence was described;

(b) whether the method of treatment allocation was described;

(c) whether both the technique of generating random numbers and the method of allocating these to subjects were described.

In addition, it was noted whether the procedures of weighting, stratification, blocking or minimisation were used, and what method of randomisation or treatment allocation was used.

All the papers selected were read and rated independently by the authors. Any discrepancies between raters were agreed through consensus.

RESULTS

The 108 issues of the *BJP* and 108 issues of the *AJP* examined contained between

Table 1 Frequency of adequate reporting of the procedure of randomisation found in some non-psychiatric medical journals

Author	Journals surveyed	Year	Assessment criteria adopted	Percentage of papers adequately reporting randomisation
Williams & Davies (1994)	Variety of journals; reports contained in bibliography of *Controlled Clinical Trials*	1980s	Process reproducible	9%
DerSimonian *et al* (1982)	*New England Journal of Medicine*	1979	Reported method of randomisation	15%
	Lancet	1979		10%
	British Medical Journal	1979		16%
	Journal of the American Medical Association	1979–80		43%
Schulz *et al* (1994)	*American Journal of Obstetrics and Gynecology*	1990–91	Both generation and concealment adequate	9%
	British Journal of Obstetrics and Gynaecology	1990–91		15%
	Journal of Obstetrics and Gynaecology	1990–91		5%
	Obstetrics and Gynecology	1990–91		7%
Altman & Dore (1990)	*Annals of Internal Medicine*	First 20 RCTs in each journal published after 1 January 1987	Both generation and concealment specified	45%
	British Medical Journal			25%
	Lancet			30%
	New England Journal of Medicine			35%

https://doi.org/10.1192/bjp.175.6.581 Published online by Cambridge University Press

them 183 papers that met our inclusion criteria – 73 from the *BJP* and 110 from the *AJP*. Papers reporting RCTs published in the *BJP* showed an increase in 1997 and 1998, when 19% and 21% respectively of the *BJP* papers on RCTs over the nine-year survey period were published. A quarter of the papers on RCTs in the *AJP* were published in 1998.

Table 2 shows the number of articles satisfying our criteria. Fifteen papers (8%) described the technique of generating a random sequence of numbers and 13 papers (7%) described the method of treatment allocation. Twenty-nine papers (16%) mentioned that a procedure such as blocking or stratification was used. The techniques of random number generation were random number tables (n=8), computer generation (n=6) and permutation (n=1). Any treatment allocation described was by use of sealed envelopes. The *AJP* and *BJP* were equally likely to contain papers describing the technique of random number generation, but the *BJP* contained more papers describing the method of treatment allocation.

Five (6.8%) of the papers in the *BJP* and one (0.9%) in the *AJP* described both the method used to generate random numbers and the allocation procedure. Only these six papers were therefore considered to contain sufficient information to make it possible for the reader to repeat the process of randomisation. These rates should be compared with those for other medical journals (Table 1).

The most common claim to randomisation, and in most cases the only indication that randomisation has been conducted, was a statement that "subjects were randomly allocated/assigned to . . .". In two of the reports, such a statement claiming randomisation was contained only in the abstract. We found one paper that claimed to be an RCT in the abstract, but whose main text reported the allocation to groups as being done by taking alternate subjects. This study was not included in the present survey. An example of a report included in the survey that contained a concise account of the generation of random numbers and the allocation procedure is van der Sande *et al* (1997).

DISCUSSION

Overall results

This study examined a series of reports of RCTs published in two major psychiatric journals from both sides of the Atlantic over the past nine years and found a similar rate of adequate reporting of the process of randomisation in the two journals. This level of reporting, although low, is comparable with the average reported for many non-psychiatric journals (Table 1).

The past nine years were chosen for the survey as, given the current emphasis on evidence-based medicine and clinical effectiveness, it was thought that this period would contain evidence of high-quality reporting of the methods employed in clinical trials, in accordance with the observation of Sonis & Joines (1994) that the year of publication was positively associated with the quality of reporting clinical trials. Although the reporting of randomisation details when describing clinical trials is recommended by the International Committee of Medical Journal Editors it appears to be uncommon in studies reported in both the *BJP* and *AJP* during the past nine years.

Inadequate reporting

There are several possible reasons for this high rate of inadequate reporting. First, it may be argued that details about randomisation will take up too much of a limited publication space. However, as randomisation is such a fundamental aspect of the methodology, at least a short paragraph needs to be devoted to explaining how it was conducted. Moreover, in the *AJP*, the 'methods' section is printed in a smaller typeface, so saving space. Second, there may be doubts about how much detail it is necessary to report. It has been suggested that the description should make clear to the reader how the procedure was performed. This can be done without resorting to lengthy descriptions; for example, the account in van der Sande *et al* (1997) was written in a short paragraph of about 100 words. Third, as Bailar & Mosteller (1988) indicate, some authors may still be using the term 'randomisation' as a synonym for 'haphazard'. Far from being haphazard, randomisation is a staged procedure that needs to be incorporated into the protocol of all RCTs. Sacket *et al* (1991) warned us to "beware of look-alikes to randomisation", but unfortunately many authors (the majority in our survey) make no effort to convince readers that their RCTs are not 'look-alikes'.

We agree with DerSimonian *et al* (1982) that an author's assurance that randomisation was performed is not convincing unless the method used is discussed. Randomisation is crucial in controlled clinical trials and its reporting should leave no doubts as to how it was done. The corollary is that the absence of its reporting suggests that it was not done properly, if done at all. Altman & Dore (1990) found that when a methodological procedure is not reported in a paper, the bulk of the missing data are due to a failure to perform the procedure, rather than underreporting.

Study considerations

Perhaps the main limitation of our study is the operational definition of 'adequate

Table 2 Adequacy of reporting of the process of randomisation in two psychiatric journals

Criterion	Articles surveyed satisfying adopted criteria					
	British Journal of Psychiatry (n=73)		*American Journal of Psychiatry* (n=110)		Total (n=183)	
	n	%	*n*	%	*n*	%
Was the technique of creating the randomisation sequence described? (e.g. random numbers table, tossing coin, die)	6	8.2	9	8.2	15	8.2
Was the method of allocating treatment to the experimental and control groups described?	11	15.1	2	1.8	13	7.1
Were both the generation of the random sequence and the allocation described?	5	6.8	1	0.9	6	3.3
Was a procedure such as stratification, blocking or minimisation used?	11	15.1	18	16.4	29	15.8

https://doi.org/10.1192/bjp.175.6.581 Published online by Cambridge University Press

reporting' of randomisation. In the absence of a generally accepted instrument, we have employed a pragmatic definition based on reproducibility. The advantages of this approach are that the randomisation procedure carried out is unambiguous and open to critical scrutiny by members of the scientific community. It is also in line with the CONSORT statement that aims to improve the quality of reporting of RCTs (Altman, 1996). The work reported here may be extended by surveying other psychiatry journals, perhaps as a continuous process in order to monitor any changes over time. In addition, it may be informative to survey the authors of reports of clinical trials in order to determine the actual method they employed in randomising their subjects. Liberati *et al* (1986) conducted a telephone survey of authors and reported a rise from 32% to 43% in the proportion of RCTs in which a proper randomisation was conducted, thus indicating that the majority of studies that claimed to have carried out randomisation were not in fact RCTs but mere 'look-alikes'.

Improving the quality of RCT reporting

There is a need to establish standards of reporting through the acceptance of what constitutes an adequate report of the process of randomisation (Altman, 1996). One possibility is to submit all reports of parallel controlled studies to statisticians for preview. In the absence of sufficient numbers of statisticians, however, journal editors may ask assessors to comment specifically on the method of randomisation, perhaps using a predetermined check-list for reports of randomised trials that employs an accepted definition of adequate reporting. Finally, authors should be encouraged to indicate in the title of their report that they have conducted an RCT, in order to make it easier for their paper to be so identified and correctly compiled in electronic databases.

CLINICAL IMPLICATIONS

- Authors should convince assessors and readers that randomisation was properly conducted; without proper reporting of the randomisation procedure, the evaluation of a randomised controlled trial (RCT) is difficult and may be misleading.
- An acceptable check-list to judge the reporting of the process of randomisation is required.
- All reports of RCTs should indicate in the title or keyword list that the study was designed as an RCT.

LIMITATIONS

- We did not carry out a survey of the authors to enquire whether an adequate randomisation procedure was employed.
- A widely accepted manner of reporting is currently lacking, and adequate reporting may be difficult to judge.
- Further studies are required to examine the relations between inadequate reporting and the estimates of treatment effects.

LOAFE OGUNDIPE, MRCPsych, Department of Psychiatry, School of Postgraduate Medicine, Keele University, Staffordshire; ANTHONY P. BOARDMAN, MRCPsych, AMY MASTERSON, BA, Academic Department of Psychiatry, The Guy's, King's College and St Thomas' Hospitals' Medical and Dental School, London

Correspondence: Dr A. P. Boardman, Academic Department of Psychiatry, The Guy's, King's College and St Thomas' Hospitals' Medical and Dental School, Guy's Campus, 5th Floor, Thomas Guy House, Guy's Hospital, London SE1 9RT

(First received 12 November 1996, resubmitted 20 January 1999, accepted 9 June 1999)

REFERENCES

Altman, D. G. (1996) Better reporting of randomised controlled trials: the CONSORT statement. *British Medical Journal*, **313**, 570–571.

—, Gore, S. M., Gardner, M. J., *et al* (1989) Statistical guidelines for contributors to medical journals. In *Statistics with Confidence* (eds M. J. Gardner & D. G. Altman), pp. 83–100. London: BMJ Press.

— & Dore, C. J. (1990) Randomisation and baseline comparisons in clinical trials. *Lancet*, **335**, 149–153.

Ballar, J. C. & Mosteller, F. (1988) Guidelines for statistical reporting in articles for medical journals. *Annals of Internal Medicine*, **108**, 266–273.

***British Medical Journal* (1991)** Uniform requirements for manuscripts submitted to biomedical journals. *British Medical Journal*, **302**, 338–341.

Chalmers, I. (1998) Unbiased, relevant and reliable assessments in healthcare. *British Medical Journal*, **317**, 1167–1168.

Chalmers, T. C., Celano, P., Sacks, H. S., *et al* (1983) Biases in treatment assignment in controlled clinical trials. *New England Journal of Medicine*, **309**, 1358–1361.

DerSimonian, R., Charette, L. J., McPeer, B., *et al* (1982) Reporting on methods in clinical trials. *New England Journal of Medicine*, **306**, 1332–1337.

Liberati, A., Himel, H. N. & Chalmers, T. C. (1986) A quality assessment of randomised controlled trials of primary treatment of breast cancer. *Journal of Clinical Oncology*, **4**, 942–951.

Pocock, S. J. (1983) *Clinical Trials. A Practical Approach*. Chichester: John Wiley & Sons.

Sackst, D. L., Haynes, R. B., Guyatt, G. H., *et al* (1991) *Clinical Epidemiology. A Basic Science for Clinical Medicine* (2nd edn). Boston, MA: Little Brown.

Schulz, K. F., Chalmers, I., Grimes, A., *et al* (1994) Assessing the quality of randomisation from reports of controlled clinical trials published in obstetrics and gynaecology journals. *Journal of the American Medical Association*, **272**, 125–128.

—, Chalmers, I., Hayes, R. J., *et al* (1995) Empirical evidence of bias. Dimensions of methodological quality associated with estimates of treatment effects in controlled trials. *Journal of the American Medical Association*, **273**, 408–412.

Simon, R. & Wittes, R. E. (1985) Methodological guidelines for reports of clinical trials. *Cancer Treatment Reports*, **69**, 1–3.

Sonis, J. & Joines, J. (1994) The quality of clinical trials published in the *Journal of Family Practice*. *Journal of Family Practice*, **39**, 226–235.

van der Sande, R., van Rooijen, L., Buskens, E., *et al* (1997) Intensive in-patient and community intervention versus routine care after attempted suicide. A randomised controlled intervention study. *British Journal of Psychiatry*, **171**, 35–41.

Williams, H. & Davies, C. (1994) Reporting of assignment methods in clinical trials. *Controlled Clinical Trials*, **15**, 294–298.