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Full Length Research Paper

Reporting of randomised controlled trials: Before and after the advent of the CONSORT statement

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Poorly conducted randomised controlled trials and inadequate reporting are susceptible to different forms of bias, which can have a detrimental effect on the in**terpretation and application** of **clinical evidence. This study examines the effect of Consolidated Standards of Reporting Trials (CONSORT) statement on the quality of the reporting of randomised controlled trials by comparing those published before and after the advent of the CONSORT. A systematic review was performed using a MEDLINE search to find all randomised controlled trials published in JAMA and the Lancet in the years 1995, 1997 and 2002. For each trial, the quality of reporting of sample size calculation, trial period, randomisation, and blinding was assessed. There was a substantial increase in the proportion of trials reporting sample size calculation, event rates, randomisation, and blinding in the RCTs post-CONSORT. However, the improvement in the quality of those reporting appears to be slow. This increase in quantity in the post-CONSORT period may be due to reporting and publication bias, where authors are trying to comply with the CONSORT guidelines and increasingly reporting favourable results, while at the same time not clearly explaining their methodology clearly. Authors and journal editors should strictly adhere with the CONSORT guidelines to ensure transparent, unbiased, and complete reporting so that we can reap the maximum benefit from clinical trials.**

Key words: Consolidated Standards of Reporting Trials (CONSORT), sample size, randomisation, reporting, bias.

INTRODUCTION AND BACKGROUND

Randomised controlled trials (RCT) produce one of the highest levels of robust evidence available to evaluate the efficacy of health care interventions (Concato, 2000; Beller, 2002; Latronico, 2002; Piggott, 2004). Unclear or incomplete reporting makes the interpretation of randomised controlled trials difficult, even impossible in some cases, and may jeopardise an otherwise well-planned and performed trial (Beller, 2002; Latronico, 2002; Piggott, 2004; Chan, 2005; Chalmers, 2006). Inadequate reporting of results and outcomes can also have a detrimental effect on the interpretation and application of trial publications and can lead to the clinical use of harmful interventions (Djulbegovic, 2001; Chan, 2004, 2005).

The reporting of randomised controlled trials has received considerable criticism in recent years and has previously been shown in many cases to be incomplete, biased, and inconsistent with study protocols and effective reporting of findings (Latronico, 2002; Ioannidis, 2004; Altman, 2005; Chalmers, 2006). The CONSORT (Consolidated Standards of Reporting Trials) statement of 1996, and updated in 2001 and 2010, gives recommendations for reporting randomised controlled trials and is endorsed by the World Association of Medical Editors, the Council of Science Editors, and the International Committee of Medical Journal Editors (ICMJE) (Moher, 2001; Campbell, 2004; Schulz, 2010). The aim of CONSORT guidelines is to minimise those inconsistencies and bias, and guide the authors to improve the quality of reporting of their trials. Many

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journals now have adopted CONSORT as part of their author guidelines and require that reports conform to the guidelines (Piggott, 2004; Plint, 2006; Altman, 2005; Mills et al., 2005; Laine, 2007). Since the publication of CONSORT statement, several evaluations of its effectiveness have been reported (Piggott, 2004; Altman, 2005; Moher, 2001; Laine, 2007). Inconsistent, selective and incomplete reporting of methodology including sample size calculation, randomisation, and outcomes have still been reported, however insufficient data exists regarding to what extent CONSORT has achieved this goal (Piggott, 2004; Plint, 2006; Schulz, 2005).

METHODOLOGY

We compared the quality of RCTs reported before and after the advent of the CONSORT. Two high- impact and early CONSORT adopted medical journals Lancet and JAMA were selected (Rennie, 1996; McNamee, 1996). We searched the Instructions to authors of each journal to determine if adherence to CONSROT statement was required for authors reporting RCTs. Three window periods were chosen: (a) Trials performed and published pre-CONSORT (1995), (b) Trials performed pre-CONSORT but published post-CONSORT (1997), and (c) Trials performed and published post-CONSORT (2002). The years 1995, 1997 and 2002 were randomly selected from the aforementioned window periods.

Search strategy and study selection

We identified all RCTs published in the 2 selected journals through a MEDLINE search using the publication type limit for clinical trials and randomized controlled trials. The number of trials published in the Lancet was much greater than in JAMA. We included all articles published between in 1995, 1997, and 2002 that reported an RCT (that is, a trial in which the assignment of participants to interventions was described by the words random, randomly, randomised, or randomisation). To aid simplicity to infer sample size calculation and event rates only RCTs with primary outcomes expressed in proportion and RCTs published in the Lancet in January to June of the years previously mentioned were included in the study (Figure 1).

Study identification

Retrieved studies were included only if they were conducted on human subjects and if the study design was identified as an RCT by examining the title and the abstract. Only studies where the primary outcome event rates expressed in proportion were included. Studies were excluded from the review if they were commentaries, letters to authors or editors, or brief reports; were not RCTs; or were trials performed outside the window period. Unavailable scanned documents were also removed from the review as their full text articles were not available online via MEDLINE at the time of MEDLINE search (Figure 1).

Data extraction and analysis

For each RCT, both the authors independently extracted and analysed data on the following measures: Sample size calculation; event rates (actual, predicted, standardised difference); trial period; randomisation, and blinding.

Sample size calculation was analysed and assigned as ‘not reported/no justification’, ‘retrospective justification only’, ‘prospective justification-unclear’ or ‘prospective justification-clear’. Calculations were classified as ‘clear’ if the study included adequate justification as to how the sample size was determined, estimate outcomes in each group (control and treatment), the α (type I) error level, and statistical power or β/type II error level (Altman, 2001).

Event rates were analysed and the differences calculated. The difference between predicted and actual event rates in the control and treatment groups were standardised using the following equation: Standardised difference = $(p1 - p2) / \sqrt{[(p (1 - p)]}$: where p1 and p2 are the proportions in the two groups and p is the mean value of the two values $[(p1 + p2)/2]$ (Whitley, 2002).

The trial period was analysed and assigned as ‘reported’ or ‘not reported’, and the start and end date of the trial was recorded. Randomisation was assigned as ‘reported’ or ‘not reported’, and was allocated scores A to D, where A indicates method of randomisation adequately explained, B indicates explained but inadequate, C indicates randomisation unclear, and D indicates randomisation not truly random. Blinding was assigned as ‘reported’ or ‘not reported’. The proportions of the quality and reporting of the aforementioned measures before and after the advent of the CONSORT were compared.

RESULTS

Our MEDLINE search identified 312 randomised controlled studies published during the years 1995, 1997 and 2002, out of which 179 randomised trials from Lancet and JAMA met the inclusion criteria (Figure 1). Table 1 shows the baseline characteristics of these studies. The majority of studies were from the USA and UK and cardiology was the most popular specialty. Overall in both journals, there was an increase in the extent and quality of reporting after the advent of the CONSORT, where 99% of the studies reported their method of randomisation in 2002 when compared to 89% in the year 1995 (Table 1). The Lancet showed consistent improvement in both post-CONSORT years, whereas JAMA showed a significant increase in reporting in 2002 (Table 2).

Both journals showed increased reporting of their sample size calculations. In the Lancet, there was an improvement in the reporting of a clear prospective calculation (12% in 1995, 34% in 1997, and 61% in 2002), however in trials published in 1997 there was a significant increase in the ‘prospective’ but unclear calculations (15% in 1995, 44% in 1997, 21% in 2002) (Table 3 and Figure 2A). JAMA showed a rise in the number of retrospective sample size calculations in 1997 (12%), which then decreased in 2002 (7%). There was also an increase in the number of ‘prospective’ but unclear calculations (15% in 1995, 38% in 1997, and 39% in 2002). In the post-CONSORT period, the number of ‘prospective’ and clear calculations actually decreased in 1997 (4%) but showed improvement in 2002 (25%) (Table 3 and Figure 2B).

The majority of RCTs these journals reported a positive effect of the interventions. In the Lancet post-CONSORT

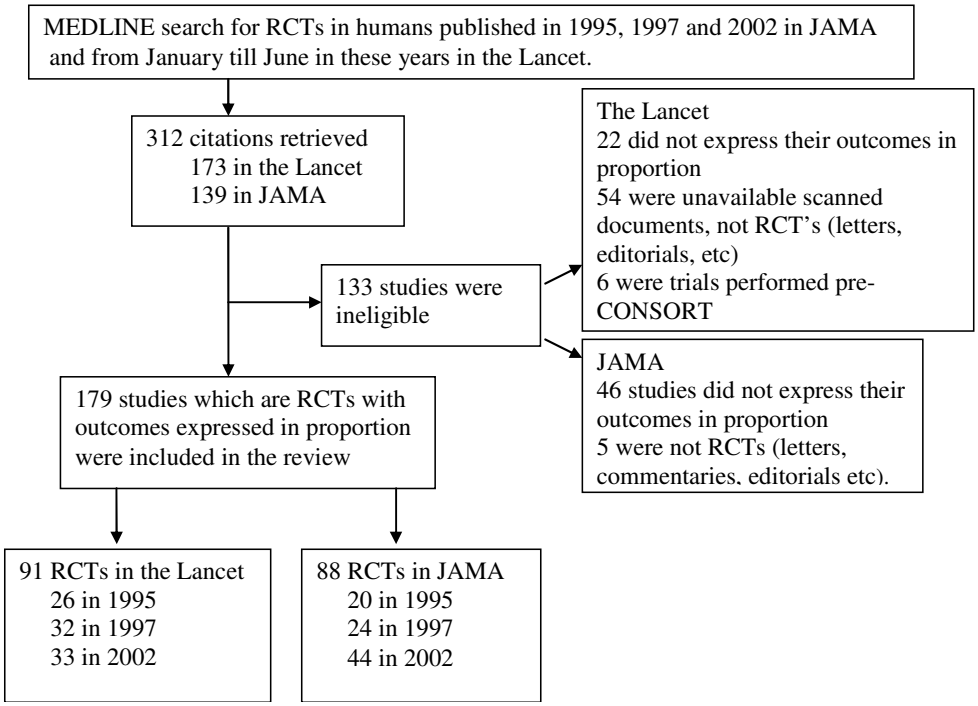

Figure 1. Selection of studies for review.

Table 1. Baseline study characteristics.

Study characteristics	1995	1997	2002
Journal: JAMA (n)	20	24	44
Journal: Lancet (n)	26	32	33
Total (n)	46	56	77
Areas of study (n)			
Cardiology	8	15	12
Oncology	7	2	10
Public health/epidemiology	4	2	9
Other medical specialties	19	26	29
Surgical specialties	8	5	10
Others	0	6	7
Country			
USA	20	25	37
Canada	3	5	3
South America	0	0	1
UK	9	11	13
Other Europe	11	11	18
Asia	2	0	1
Australia/ New Zealand	1	3	2
Africa	0	0	1
Middle-east	0	1	1
Number of sample size calculation reported	12 (26%)	38 (68%)	60 (78%)
Primary outcome-positive	36 (78%)	49 (88%)	57 (74%)
Trial period reported	20 (44%)	29 (52%)	61 (79%)
Randomisation reported	41 (89%)	53 (95%)	76 (99%)
Blinding reported	15 (33%)	33 (59%)	38 (49%)

Table 2. Reporting of trial period.

Journal/year	Trial period reported (%)
Lancet 1995 (n = 26)	14 (54)
Lancet 1997 (n = 32)	20 (63)
Lancet 2002 (n = 33)	25 (76)
JAMA 1995 (n = 20)	6 (30)
JAMA 1997 (n = 24)	9 (38)
JAMA 2002 (n = 44)	36 (84)

Table 3. Reporting and quality of sample size calculation and primary outcome.

Journal/year	n	Nothing reported(%)	Retrospective-justification(%)	Prospective justification-Not clear(%)	Prospective justification-Calculation clear(%)	Primary outcome-Positive(%)
Lancet-1995	26	19 (73)	0 (0)	4 (15)	3 (12)	22 (85)
Lancet-1997	32	6 (19)	1 (3)	14(44)	11 (34)	26 (81)
Lancet-2002	33	4 (12)	2 (6)	7 (21)	20 (61)	25 (76%)
JAMA-1995	20	15 (75)	0 (0)	3 (15)	2 (10)	15 (75)
JAMA-1997	24	11 (46)	3 (12)	9 (38)	1 (4)	23 (96)
JAMA-2002	44	13 (29)	3 (7)	17 (39)	11 (25)	32 (73)

period showed a decrease in the number of trials with a positive primary outcome. On the contrary, trials published in 1997 in JAMA showed an increase in the number of positive studies (76% in 1995, 96% in 1997, and 73% in 2002) (Table 3).

In the post-CONSORT period, there was an increase in the reporting of randomisation (Table 4). The Lancet showed an increase in the number of trials with score-A (randomisation adequately explained) and score-B (explained but inadequate). Trials with score-C (unclear) and score-D (not truly random) showed a decrease in the post-CONSORT period (Figure 3A). In JAMA, although there was an increase in the number of trials with score-B and a decrease in score-C and D in the post-CONSORT period surprisingly in 2002, there was a decrease in the number of trials with the score-A (Table 4 and Figure 3B).

Reporting of blinding has improved in the post-CONSORT period in these journals. In the Lancet 2002, there was a decrease in the reporting (31% in 1995, 59% in 1997, and 36% in 2002), whereas JAMA showed a steady increase in reporting in the post-CONSORT period (35% in 1995, 58% in 1997, and 59% in 2002) (Table 5).

DISCUSSION

We found that RCTs published in both journals post-CONSORT showed significant improvement in reporting. Both Lancet and JAMA showed an increase in the number and quality of explanation of the sample size calculation in the post-CONSORT period. Studies where the trials performed pre- CONSORT but published post-CONSORT in 1997 showed a marked increase in prospective reporting and explanation of the sample size calculation in both journals. However, most calculations were unclear with inadequate justification as to how their sample size was determined, the estimates of outcome in each group, and statistical power. There was also an increase in the oxymoronic retrospective sample size calculation reporting in the post-CONSORT period in both journals. This shows that CONSORT had a positive impact on the reporting of sample size calculation. Sample size projection is vital and must be planned and calculated to ensure that research time, patient and researcher's effort and costs invested in a clinical trial are not wasted. An adequate sample size is important to control the probability of a real difference in an outcome being overlooked by chance alone. Therefore, RCTs must be adequately powered to achieve their aims, and appropriate sample size calculations should be carried out at the design stage of any study (Altman, 2001; Whitley, 2002; Schulz, 2005).

In the post-CONSORT period, there has been an improvement in the number of trials reporting predicted and actual event rates in each group. Overall, more studies in the Lancet reported their event rates than studies in JAMA. Studies published pre-CONSORT in 1995 showed poor reporting but accurate event rates in each group but with inadequate justification. In the studies, where the trials performed post-CONSORT, the difference in event rates between each groups are

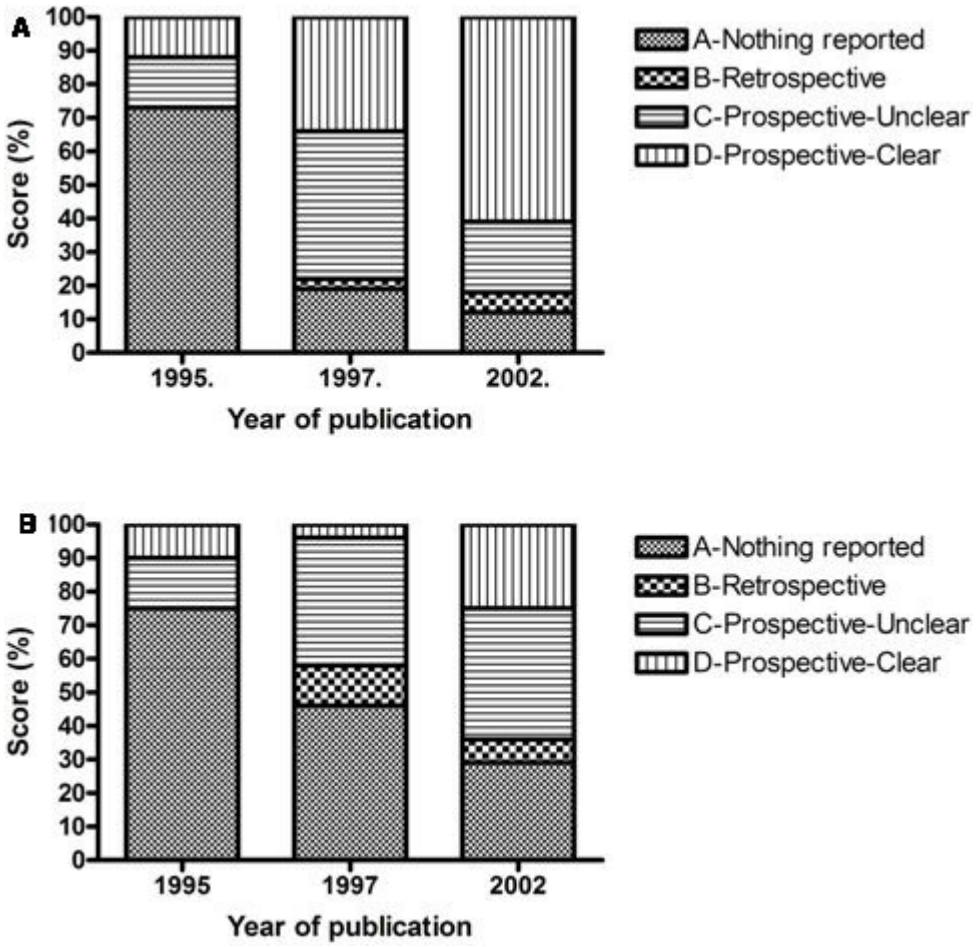

Figure 2. Reporting and quality of sample size calculations. (A) Reporting and quality of sample size calculations-The Lancet. (B) Reporting and quality of sample size calculations-JAMA.

Table 4. Reporting and quality of randomisation.

Journal/year	n	Number reported(%)	Score-A(%)	Score-B(%)	Score-C(%)	Score-D(%)
Lancet-1995	26	23 (89)	0 (0)	7 (27)	13 (50)	6 (23)
Lancet-1997	32	32 (100)	10 (31)	9 (28)	12 (38)	1 (3)
Lancet-2002	33	33 (100)	13 (39)	16 (49)	4 (12)	0 (0)
JAMA-1995	20	18 (90)	2 (10)	7 (35)	9 (45)	2 (10)
JAMA-1997	24	21 (88)	6 (25)	11 (46)	4 (17)	3 (12)
JAMA-2002	44	43 (98)	8 (18)	23 (52)	9 (21)	4 (9)

Table 5. Reporting of blinding.

Journal/Year	n	Blinding reported (%)
Lancet-1995	26	8 (31)
Lancet-1997	32	19 (59)
Lancet-2002	33	12 (36)
JAMA-1995	20	7 (35)
JAMA-1997	24	14 (58)
JAMA-2002	44	26 (59)

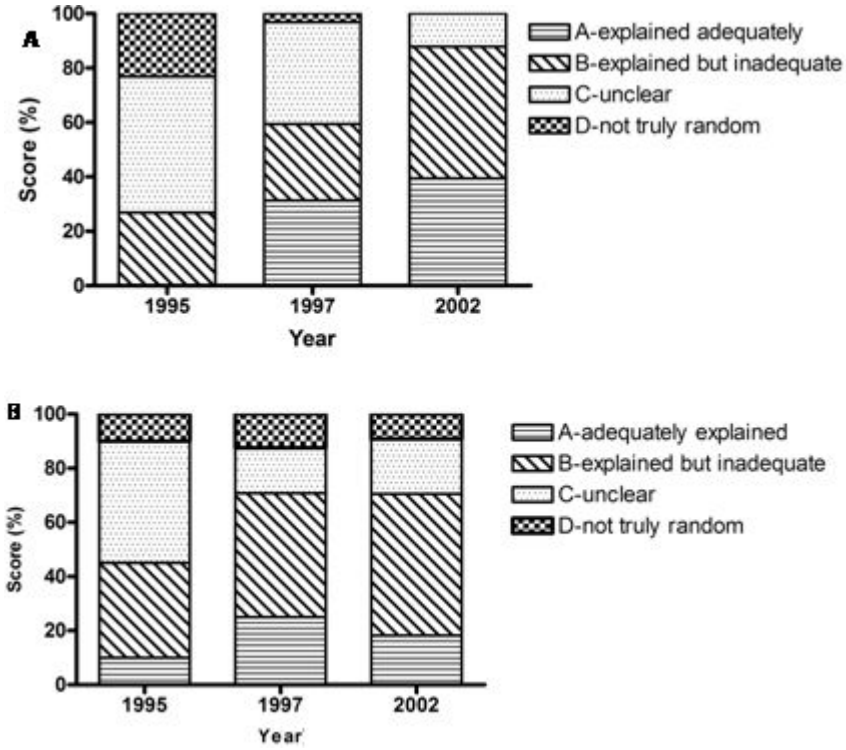

Figure 3. Reporting and quality of randomisation of: (A) The lancet. (B) JAMA.

variable when compared to studies where the trials were performed pre-CONSORT. Although during the post-CONSORT period, there has been an improvement in reporting and the quality of the predicted and actual event rates in both of these journals, the proportion of the trials reporting their predicted event rates are nevertheless still very low. Predicted event rates must be reported so the readers can determine if the study has the power to detect a clinically relevant and statistically significant difference in the outcome as a result of an intervention. This effect could be due to reporting and publication bias in 1997 where trials with similar predicted and actual event rates get reported more often than studies with a wider difference in their event rates. However, the small number and poor quality of reporting has made it difficult to more clearly infer bias.

The main aim of randomisation is to avoid bias by randomly distributing the factors that may influence outcome between the groups so that any difference in outcome can be explained only by the intervention (Altman, 2001; Beller, 2002; Schulz, 2002). Both journals showed an increase in the number of reporting and quality of randomisation. In the post-CONSORT period, the Lancet showed a consistent improvement in the number of trials with randomisation score 'A' (0% in 1995, 31.3% in 1997, and 39.4% in 2002). Conversely, in 1997 JAMA showed an increase in trials with score-A, which then dropped in 2002 (10% in 1995, 25% in 1997, and 18% in 2002). JAMA also showed a higher proportion of trials with a randomisation score of 'D', indicating that the randomisation methodology was not truly random (9% in 2002); compared to the Lancet (0% in 2002). This trend may be due to greater CONSORT compliance of reviewers and editors in the Lancet when compared to JAMA.

Both journals showed increase in reporting of blinding in the post-CONSORT period. JAMA showed a consistent improvement in the reporting of the blinding compared to Lancet. Nevertheless, the proportion of the trials reporting blinding is still low. CONSORT recommends that the authors should report blinding and explicitly detail how blinding was maintained for patients, investigators or clinicians and outcomes assessment committees (Moher, 2001; Altman, 2001; Schulz, 2002). Failure or inability to blind people to the intervention could potentially introduce biases. These include reporting bias, assessment bias, and associated treatment bias by either the patient or investigator. These biases contribute to differences between groups other than those resulting from the allocated study treatment and can makes those results unreliable (Schulz, 2002; Chan, 2004, 2005; Forder, 2005).

This study has several limitations. Firstly, due to statistical constraints and simplicity to infer sample size calculation and event rates only studies which expressed their event rates in proportion (%) are included in this review. Second, we only looked at RCTs published in JAMA and Lancet, which are of higher quality; we would

expect that any CONSORT related improvements would be seen first in these journals. Therefore generalisation of the findings from this study may be limited.

Conclusion

Our study suggests an increase in the reporting of sample size calculation, event rates, randomisation, and blinding in the RCT's post-CONSORT. However, the improvement in the quality of those reporting appears to be slow. This increase in quantity in the post-CONSORT period may be due to reporting and publication bias, where authors are trying to comply with the CONSORT guidelines and increasingly reporting favourable results, while at the same time not clearly explaining their methodology clearly. However, in order to guide clinical decision-making and improve the qualities of the RCTs, future studies need to improve the quality of their reporting by adhering to the CONSORT statement. To limit reporting and publication bias, researchers should ensure that complete data are provided for all trial outcomes; independent of their results. Prior to publishing, journal editors and reviewers should strictly comply with the CONSORT guidelines and scrutinise the studies to ensure transparent, unbiased, and complete reporting so that the scientific community and the patients can reap maximum benefit from clinical trials.

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