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Compliance to the CONSORT statement of randomized controlled trials in solid organ transplantation: a 3-year overview

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Conflicts of interest
PJM chairs a data safety committee for Bristol-Myers Squibb and has in the past received lecture fees from Novartis, Astellas, Roche and Genzyme. These were paid into the Allison Foundation to support surgical research within the Nuffield Department of Surgery of the University of Oxford.

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Summary

The Consolidated Standards of Reporting Trials (CONSORT) statement was developed to improve the reporting quality of randomized controlled trials (RCTs). Our primary aim was to assess to what extent reports of RCTs in solid organ transplantation adhere to the 2010 CONSORT statement. Secondly, we investigated the relationship between CONSORT adherence, methodological quality and some other factors. We included 290 RCTs that were published between 2007 and 2009. We examined to what extent trial reports complied with 30 items of the CONSORT statement. Methodological quality was evaluated using the Jadad scale plus allocation concealment and whether data analysis was by randomized group (intention to treat). On average, trial reports addressed 47% of the CONSORT items. Forty-three per cent of RCTs was considered to be of good quality according to Jadad scale, and the items allocation concealment and data analysis were satisfied in approximately one-third of trials. Good quality RCTs reported on more CONSORT items than poor quality trials. The methodological quality and adherence to the CONSORT statement of RCTs published in journals that endorse the CONSORT statement was superior to those in journals without CONSORT endorsement. Overall compliance with the CONSORT statement and the methodological quality of RCTs in organ transplantation remains unsatisfactory.

Introduction

Well-designed and properly conducted randomized controlled trials (RCTs) provide the most reliable evidence on the efficacy of healthcare interventions. But if the quality of RCTs is not adequate the strength of the conclusions is limited, which can further mislead decision making in health care. Accurate and complete reporting of RCTs is also critical as inadequate reporting of RCTs is associated with poor methodology [1], as such it often yields bias in estimating the effectiveness of interventions. For instance, Juni *et al.* [2] reported a trend towards larger estimates of treatment effects in publications with inappropriate or unclear reporting of the randomization method compared with those adequately reporting the randomization method. Other studies found that inadequate allocation concealment exaggerated the treatment effects [3–5].

To improve the reporting of RCTs and enable readers to understand its conduct and estimate the validity and reliability of its results, the Consolidated Standards of Reporting

Trials (CONSORT) statement was developed in 1996 and subsequently updated in 2001 and 2010 [6–8]. The CONSORT statement defines 25 criteria for adequate reporting of RCTs (www.consort-statement.org/). It provides guidance for authors on how to prepare clear, complete and transparent trial reports and aids readers to critically appraise and interpret reports of RCTs. Since its first publication in 1996, the CONSORT statement has been endorsed by many leading medical journals worldwide. Numerous studies across medical disciplines have reported the extent to which trial reports adhere to the CONSORT statement [9–14]. Brooks *et al.* [15] conducted a systematic review in paediatric kidney transplantation, in which they evaluated 27 RCTs that were published between 2000 and 2008 in peer reviewed journals and found that on average a third of the recommended 22 CONSORT items were not addressed in the trial reports. Poorly reported items included description of the method used to generate the random allocation sequence (37%) and implementation of allocation concealment (33%). Other studies showed that the reporting quality was consistently superior in RCTs that were published in journals that endorse the CONSORT endorsement [9,11,12]. While most studies found that the reporting of some CONSORT items has improved over the time, the reporting of quite a number of essential CONSORT items remains unsatisfactory and need significant improvement [16–18].

We previously assessed the quality of reporting RCTs over a 3-year period (2004–2006) in solid organ transplantation and found the quality of reporting RCTs was unsatisfactory. Only one-third of RCTs in organ transplantation published during 2004–2006 were considered to be of reasonably good quality according to Jadad scale along with allocation concealment and intention-to-treat (ITT) analysis [19]. In this overview, we sought to find out to what extent RCTs in solid organ transplantation adhere to the CONSORT statement. In addition, we aimed to explore the factors that are associated with adherence to the CONSORT statement.

Materials and methods

Paper selection

We identified all full reports of RCTs in solid organ transplantation that were published between 2007 and 2009 using the Transplant Library (OvidSP). The Transplant Library includes all RCTs in solid organ transplantation from the earliest record to the present including conference proceedings [20]. References included in the Transplant Library are mainly sourced from MEDLINE (Ovid and PubMed), the Cochrane Central Register of Controlled Trials and hand searching. We excluded non-English trials, reports of trial protocols, pooled analyses and conference abstracts. When several reports referred to the same trial, only the major trial report was included.

CONSORT adherence

The CONSORT 2010 statement was used to assess CONSORT compliance. The CONSORT 2010 checklist consists of 25 criteria and for this study we assessed 30 individual items. A number of criteria addressed more than one component and these were split into separate items to ensure only one response per component. For example, CONSORT item 3a is defined as 'description of trial design (such as parallel, factorial) including allocation ratio' and was split into two separate items: 1) Was the trial design described, such as parallel or factorial?; 2) Was the allocation ratio reported? Each item was scored as 'yes' (score as 1) or 'no' (score as 0). A total score of reporting CONSORT items was calculated by adding up the scores of the 30 items.

Evaluation of methodological quality

Methodological quality was assessed independently by two reviewers using the Jadad score together with the items allocation concealment and whether the analysis was based on the randomized groups [19,21]. Disagreements were resolved by discussion or through consultation with a third reviewer. The Jadad score addresses the items relating to randomization, blinding and description of withdrawals and dropouts. Scores range from zero to five with trials scoring three or greater considered to be of reasonable good quality. Allocation concealment was considered adequate if patients and investigators who enrolled patients could not foresee treatment assignment. Adequate means of allocation concealment included: central randomization, pharmacy control, numbered or coded drug packs, opaque, sealed and/or sequentially numbered envelopes. 'Intention to treat' is defined as an analysis including all randomized participants based on the groups to which participants were originally randomly assigned regardless of whether they satisfied the entry criteria, the treatment actually received and subsequent withdrawal or deviation from the protocol [22]. Withdrawal or exclusion of participants is common in clinical trials and therefore a true ITT is difficult to accomplish. For this reason, we scored the analysis as analysed according to the randomized group which included strict ITT analysis, available case analysis and modified ITT analysis or per protocol analysis which was defined as only including patients who sufficiently complied with the protocol [8].

Further data extraction

We extracted the number of participants in each trial, the country or countries where the trial was conducted and whether the trial was a single or multicentre trial. We examined the journal author instructions for mention of the CONSORT statement and looked up the 2010 citation

impact factor in those journals that published at least two RCTs between 2007 and 2009. For each report, we noted the funding sources which were classified as commercial, noncommercial, mixed (commercial and noncommercial), no funding received or not described. If no information regarding funding was included but one or more authors were employees of a commercial, mostly pharmaceutical company, these trials were considered commercially funded. If there was a statement that study drugs were provided by a commercial company, then these trials were also considered commercially funded.

Statistical analysis

To explore the data we calculated descriptive statistics using the Excel 2007 and STATA version 11 for Windows (StataCorp, College Station, Texas, USA). For the comparison of continuous data between two groups, we used the *t*-test for normal distributed data. The Mann–Whitney *U*-test was used for comparison of categorical, ordinal and non-normal distributed continuous data. *P*-values were two-tailed and *P*-values <0.05 were considered statistically significant.

Univariate regression was used to identify predictors of CONSORT compliance in a sample of journals that published at least two reports between 2007 and 2009. Factors included in the model were sample size (<100 or $\geq$100), funding status (noncommercial funding, no funding received, not reported or commercial funding which included both commercial and mixed funding), Jadad score (<3 or $\geq$3), type of data analysis (per protocol or analysed by randomized group), allocation concealment (yes or no), CONSORT endorsement (yes or no) and journal impact factor (<5 or $\geq$5). Factors associated with CONSORT compliance with a probability of $P < 0.05$ were included in a multivariate regression model.

Results

Included trials

There were 1204 reports of RCTs in solid organ transplantation published between 2007 and 2009 and included in the Transplant Library. We excluded 749 congress abstracts, 24 non-English reports, 69 subsequent trials and 72 trials that were reports of study protocols, pooled analyses of several RCTs or nonrandomized trials. Therefore, the total number of RCTs analysed was 290.

Trial demographic characteristics

The 290 trials were published in 88 journals, of which 80 were specialist journals and 8 were general medicine journals. Most of the reports were on kidney transplantation (56%), followed by liver (23%), heart (10%) and lung (4%) transplantation. The number of patients per study ranged from eight to 1645 with the median being 60 participants per trial. There were 142 single centre trials, 97 multicentre trials and for 51 trials it was unclear whether the study was single or multi centred. One-third of trials (33%) were sponsored by commercial companies, 17% by noncommercial institutions, 6% received both commercial and noncommercial funding, 2% of trials declared that no funding was received, while the remaining 42% of trials did not declare the funding source in the report.

CONSORT compliance

On average, 14 out of 30 CONSORT items (range 1–26) were addressed in each trial report. Seventeen items of the CONSORT statement were addressed by <50% of trials reports (Fig. 1). For those items relating to the Title and Introduction, 38% of reports described the trial as 'randomized' in the title. Most reports provided an adequate description of the scientific background and specific objectives and hypotheses (98% and 97% respectively). For the items relating to the Methods, 17% of reports described the trial design such as parallel or factorial. Fifty-two per cent of trials prespecified primary outcomes and 42% prespecified secondary outcomes. Sample size calculation was described in 40% of reports. Only 8% of RCTs described how they dealt with missing data. For those items relating to the Results, 32% of reports included a flow chart of participants at each study stage. In those 151 (52%) reports prespecifying a primary outcome only 26 trials reported the estimated effect size and its precision. For those items relating to the Discussion and Other Information, about half of the trials (53%) discussed trial limitations and 17% of trials reported registration information. Only one trial provided information how to access the full trial protocol. CONSORT compliance was similar across the 3 years (14/30, 15/30 and 14/30, $n = 290$). RCTs published in journals that endorse the CONSORT statement in their author instructions reported on average 17 out of 30 CONSORT items whilst 11 out of 30 items were reported for those RCTs published in journals without CONSORT endorsement [mean difference (MD) 6, 95% CI, 4.2 to 6.6, $P < 0.001$].

Methodological quality assessment

The median Jadad score was two out of five and 43% of trials were considered to be of good quality (Jadad score $\geq$3). Thirty-six per cent of trials described adequate allocation concealment and 37% of trials analysed data based on the randomized groups. Analysis of the individual items of the Jadad scale showed that 36% of trials described an appropriate method to generate the randomization sequence, such as a random number table or a computer-

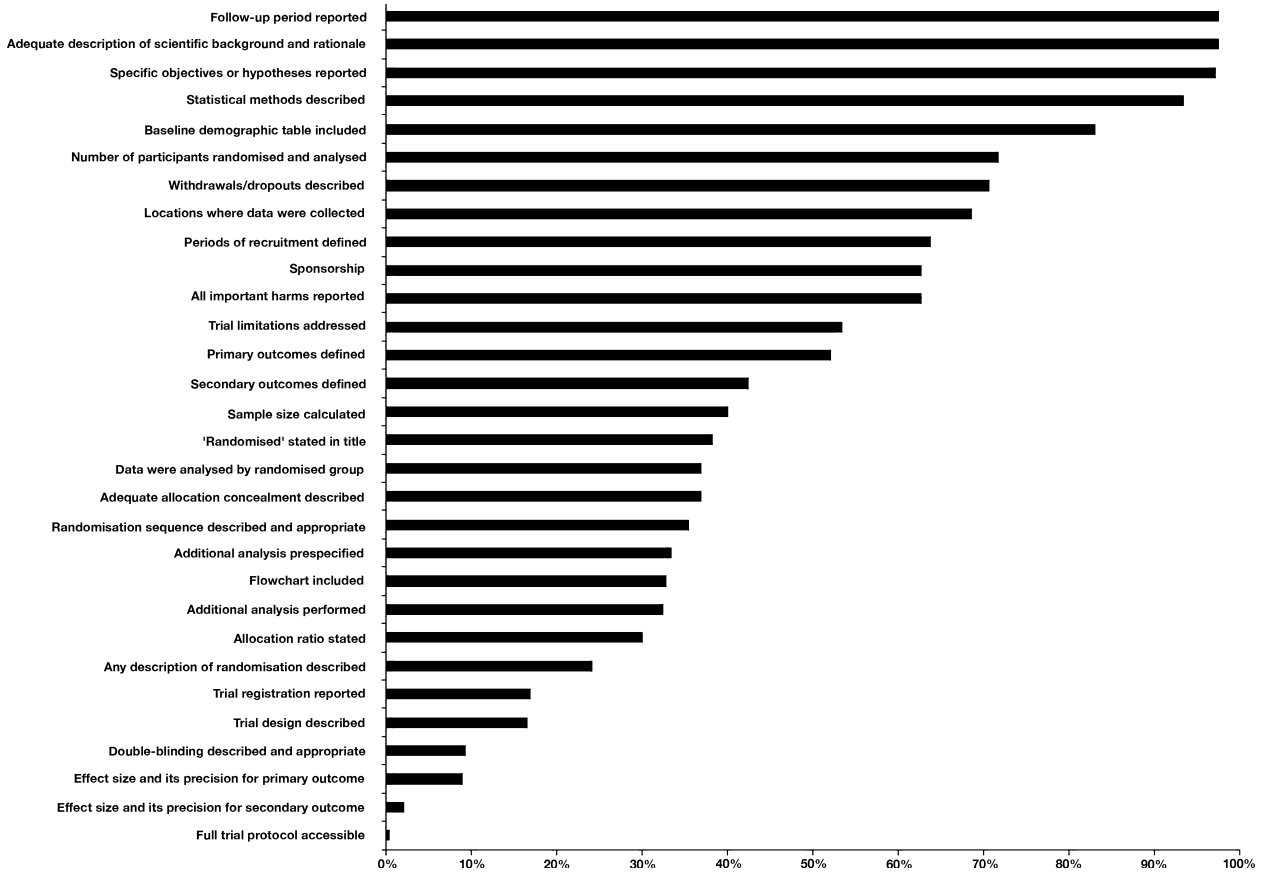

Figure 1 Compliance to the 30 items of the CONSORT statement (n = 290 trials).

generated sequence while nine reports (3%) described an inappropriate method to generate the randomization sequence, such as using alternation or patient's ID number. Forty-five reports (18%) described a double-blinded study design of which 27 reports described an appropriate method of double-blinding. The scores on any of the quality items were similar across the 3 years (Table 1).

We examined whether 31 journals that published at least two RCTs between 2007 and 2009 endorsed the CONSORT statement in their author instructions (n = 233). When we compared the quality of reports published in journals that endorse the CONSORT statement with the journals that do not endorse the CONSORT statement, we found that RCTs published in journals that endorse the CONSORT statement are of better quality according to the Jadad scale (64% vs. 27%), allocation concealment (55% vs. 23%) and data analysis according to the randomized groups (58% vs. 27%).

Good quality RCTs reported more CONSORT items than those trials with poor quality according to Jadad scale (MD 5, 95% CI: 4.4–6.5, $P < 0.001$), adequate allocation concealment (MD 6, 95% CI: 5.5–7.6, $P < 0.001$), and data analysis according to the randomized groups (MD 8, 95% CI: 0.5–8.4, $P = 0.03$).

Table 1. Quality assessment of RCTs published between 2007 and 2009.

Year (n)	Jadad ≥ 3	Adequate allocation concealment	Data analysis by randomized group
2007 (111)	54/111 (49)	38/111 (34)	46/111 (41)
2008 (95)	36/95 (38)	35/95 (37)	33/95 (35)
2009 (84)	36/84 (43)	29/84 (35)	28/84 (33)
Total (290)	126/290 (43)	102/290 (35)	107/290 (37)

Values in parentheses, except the the first column, are percentages.

Factors associated with CONSORT compliance

To identify the factors that are associated with CONSORT compliance, we performed univariate and multivariate regression analyses in a subgroup of 233 reports published in journals that published at least two RCTs between 2007 and 2009. Apart from journal impact factor and noncommercial funding all significant factors included in the univariate regression analysis remained significantly associated with CONSORT compliance in the multivariate regression model (Table 2).

Table 2. Factors included in the univariate and multivariate regression models to examine which factors are associated with CONSORT compliance in a sample of journals that published at least two RCT reports between 2007 and 2009 (n = 233).

CONSORT compliance	Univariate analysis			Multivariate analysis		
Factors	Coefficient	95% CI	*P* value	Coefficient	95% CI	*P* value
CONSORT endorsement (yes, no*)	5.7	4.5–7.0	<0.0001	1.4	0.5–2.3	<0.0001
Jadad score ($\geq$3, <3*)	5.6	4.5–5.8	<0.0001	2.3	1.4–3.2	<0.0001
Allocation concealment (yes, no*)	5.8	5.7–7.9	<0.0001	2.3	1.4–3.3	<0.0001
Data analysis by randomized group (yes, no*)	7.8	6.8–8.8	<0.0001	3.9	2.9–4.8	<0.0001
2010 Journal impact factor ($\geq$5, <5*)	3.8	2.1–5.4	0.001	0.9	−0.5–1.9	0.09
Sample size ($\geq$100, <100*)	5.3	4.0–6.5	<0.0001	1.4	0.5–2.3	0.003
Commercial funding†						
Noncommercial*	3.5	1.9–5.2	<0.0001	1.1	−0.09–2.2	0.07
No funding*	2.8	−1.4–7.0	0.191	NA		
Not reported*	6.8	5.6–8.0	<0.0001	3.4	2.9–4.7	<0.0001

*Reference group; NA, not appropriate.

†Commercial funding includes commercial and mixed funding.

Discussion

Our analysis of 290 RCTs in organ transplantation published over 3 years shows considerable poor compliance to the CONSORT statement. On average, more than half of CONSORT items were not addressed in trial reports. In general, while the CONSORT items relating to the Introduction were well reported, the reporting of the Methods, Results and Discussion domains were substandard.

When we compared the methodological quality of our sample of trials with the trials published between 2004 and 2006, we found that the proportion of good quality RCTs according to Jadad scale had slightly increased (37% vs. 43%) but there was no improvement on the description of allocation concealment or the proportion of reports that analysed the data according to the randomized groups. Other studies evaluating the reporting quality in transplantation or other disciplines found similar results. For example, an evaluation of the methodological quality of trials in general surgery found that one-third of trials were of satisfactory quality according to the Jadad scale [23], while a systematic review examining 63 RCTs of immunosuppression in renal transplantation demonstrated that only 22% of trials were of good quality according to the Jadad scale [24].

In terms of adherence to the CONSORT statement, we found that on average less than half of the CONSORT items were addressed in a trial report. Fritsche and colleagues conducted a systematic review, and analysed 63 large multicentre RCTs published between 1987 and 2003 evaluating immunosuppressive regimens in de novo kidney transplantation. They found that trial reports addressed on average 69% of the CONSORT criteria [24]. However, those 63 RCTs were selected on the basis of being multicenter studies and the sample sizes of at least 50 patients per arm. It has been previously shown that larger and multicentre trials are of better reporting quality than smaller, single centre trials [19]. Similarly, Brooks *et al.* [15] carried out a systematic review of 27 RCTs of paediatric kidney transplantation and demonstrated that RCT reports addressed on average 67% (15/22) of the CONSORT criteria for trials including children only and 66% (14.5/22) for trials including a mixed population of adults and children. Although they reported a slightly higher percentage of CONSORT items addressed in trial reports, their review only included a relatively small number of RCTs and was restricted to kidney transplantation alone. In contrast, our study evaluated 290 RCTs with a sample size ranging from 8 to 1645 across all types of solid organ transplantation. We believe that our findings present the average reporting quality of all types of RCTs in solid organ transplantation. Indeed, our findings were in good agreement with similar analyses in other specialties in the literature: For example, Smith *et al.* [9] examined 96 RCTs in nursing published between 2002 and 2005 and found that 52% of CONSORT items were reported. Likewise, Agha *et al.* [25] demonstrated that on average 50% of CONSORT items were reported in 90 urological RCTs involving a surgical procedure that were published between 2000 and 2003.

We found that the number of CONSORT items reported was greater in journals with CONSORT endorsement than those without. Among the 31 journals that we examined in this study, 12 mentioned the CONSORT statement in their author instructions and more items were reported in RCTs published in journals endorsing the CONSORT statement compared with journals not endorsing the CONSORT statement. These results should be interpreted with a certain amount of caution, because there is a time lag in our study between the time of publication (2007–2009) and assessment of journal author instructions (2011). However, similar results were found by others. For example, Hopewell and

colleagues examined all RCTs indexed in PubMed between 2000 and 2006 to determine whether the quality of reporting RCTs has been improved since the publication of the 2001 CONSORT statement [11]. They concluded that some selected key methodological CONSORT items were more often addressed in reports published in journals endorsing the CONSORT statement as opposed to nonendorsing journals. Even though journals that endorse the CONSORT demonstrate superior reporting of RCTs, still a significant number of the CONSORT items are not addressed.

One of the limitations of our study was the exclusion of non-English language literature. It has been previously shown that trials reported in languages other than English are of lower methodological quality [26]. This means that if non-English literature was included CONSORT compliance and methodological quality would have been even poorer. Another limitation is that we assessed the published report. We are aware that journal restrictions often require that the methodology sections are shortened hence it is possible that not all information regarding the quality items is included in the report. In addition, in our review some CONSORT items were not included because they did not apply to organ transplantation trials such as the item relating to settings where data were collected or because we felt that items were very subjective such as the items generalizability or interpretation. Finally, all 30 CONSORT items were given equal weight when calculating the total CONSORT score for each report. One may argue that some items are more important than others when evaluating the quality of reporting, but there is not enough evidence for the importance of the individual items of the CONSORT statement and therefore all items were given equal weight.

In conclusion, the majority of trials in solid organ transplantation that show poor adherence to the CONSORT statement continue to be of inadequate methodological quality. Despite the development of guidelines to improve the reporting of RCTs, both authors and journal editors show insufficient commitment to using the guidelines. As publications are the primary link between trials and medical decision-makers, every effort should be made to produce complete and transparent trial reports and the responsibility lies with all involved, from authors to peer reviewers and editors. To improve the reporting quality of trial reports all journals should include the CONSORT statement in their author instructions but also implement editorial processes to ensure that trial reports adhere to the statement.

To help the transplantation community find high quality evidence the Centre for Evidence in Transplantation (www.transplantevidence.com) has developed the Transplant Library, an electronic database that includes all RCTs and selected systematic reviews in solid organ transplantation. However, relevant to the context of this report is that the Transplant Library also includes an assessment of the reported methodological quality of RCTs published from 2004. This quality assessment helps readers to judge the potential value of a trial as evidence. Major defects in the trial quality indicate that trial results should be interpreted with caution.

Authorship

LQL: extracted data, analysed data and wrote the paper. LHMP: designed the study, extracted data, analysed data and wrote the paper. PJM: designed the study, analysed data and wrote the paper.

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