Improving the completeness and transparency of reports of randomized trials in oral health: The CONSORT Statement

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ABSTRACT: Purpose: Randomized trials provide essential evidence of the effect of interventions in oral health. Such trials need to be appraised by readers in order to decide whether to incorporate new findings into clinical practice and policy in a timely manner. The CONSORT (Consolidated Standards of Reporting of Trials) Statement is a guidance to facilitate reporting of randomized controlled trials (RCTs) and was first introduced in 1996. The purpose of this article is to highlight the importance of rigorous reporting of trials in oral health and to discuss the impact of CONSORT on trial reporting. **Results:** Empirical studies demonstrate that key aspects of trial methods influence the size of estimates of studied interventions and bias is a plausible mechanism for some of this effect. Complete and transparent reporting of these methods allows appraisal of the value of trials to be undertaken and the potential for bias to be estimated. Systematic reviews have shown that the reported quality of trials in dentistry is poor, thus hindering the understanding of the value of individual trials. Since 1996, CONSORT has been adopted by hundreds of medical journals, international editorial groups, and five dental journals. A systematic review has shown that the quality of reporting of trials improves in journals that have adopted this guidance, although with significant variation, most likely due to differing levels of editorial adherence to it. (*Am J Dent* 2008;21:7-12).

CLINICAL SIGNIFICANCE: CONSORT improves the transparency and quality of reporting of RCTs. Furthermore, it facilitates both the appraisal of the validity of trials and therefore the understanding of the potential for incorporation of findings into oral healthcare and policy. Adopting CONSORT should be considered by all oral health journals publishing RCTs together with careful planning of the editorial policies to maintain adherence to it.

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Introduction

The number of clinical trials published throughout dentistry is substantial and probably amounts to around 50 new trials published per month. Clinical trials are not the only appropriate design for clinical research but they do provide the most robust and reliable method to investigate the effect of an intervention and we should therefore be able to have confidence in their findings. Unfortunately, many investigations in medicine have shown that the quality of published trials is poor; a few studies have also looked at the quality of trials in dentistry with similar findings. In view of these results, appraising the quality of clinical trials is an essential step in making decisions on incurporating research findings into healthcare. Transparency of reporting in publications is a critical element in facilitating quality appraisal and is therefore part of the chain of processes that links clinical research with improving healthcare. Our aim with this article is to review briefly the findings from medicine and dentistry on the quality of published trials, present findings suggesting why this is important and finally to review the CONSORT Statement and why this helps to promote transparency and quality of clinical trial publications.

Quality of published trials in medicine and risk of bias

Bias - There are many dimensions to trial "quality" including aspects of generalizability. However, for this paper, the consideration of quality of clinical trials will be limited to protection from bias. Bias systematically distorts the truth, so that an estimate of the effect of the intervention (*i.e.* how different it is compared with a comparison group) will be distorted up or down in magnitude. Furthermore, bias cannot be corrected for in statistical analyses. For a reader of dental research the impact of bias might be to lose trust in what we read since the results and conclusions will not be valid and therefore cannot be applied to healthcare. Transparent reporting of trial methods is therefore important to allow evaluation of such issues.

Effect of bias – medical studies - There are many forms of bias and more detailed reviews can be found elsewhere.[1-3] However, while it seems plausible that bias can affect the results of clinical studies, there is little good evidence to support such an assertion for many types of bias. Evidence is accumulating, however, that some aspects of methodology have a demonstrable effect on the magnitude of the estimated effect of the intervention. Pioneering studies[4,5] in the mid-1990s identified poor random allocation and lack of blinding as distorting treatment effects.

Two recent reviews[6,7] have synthesized all available evidence on this topic and the following conclusions can be drawn:

1. Within randomized trials, inadequate *vs.* adequate allocation concealment is associated with a 35%-40% larger estimate of treatment effect.[6]
2. Comparing high *vs.* low quality trials using a composite of methodological flaws, lower quality trials produced estimates between 55-350% larger than high quality trials of the same intervention.[6]
3. Comparing results from meta-analyses, two thirds of the conclusions that supported the superiority of an intervention lost statistical significance if only trials with adequate allo-

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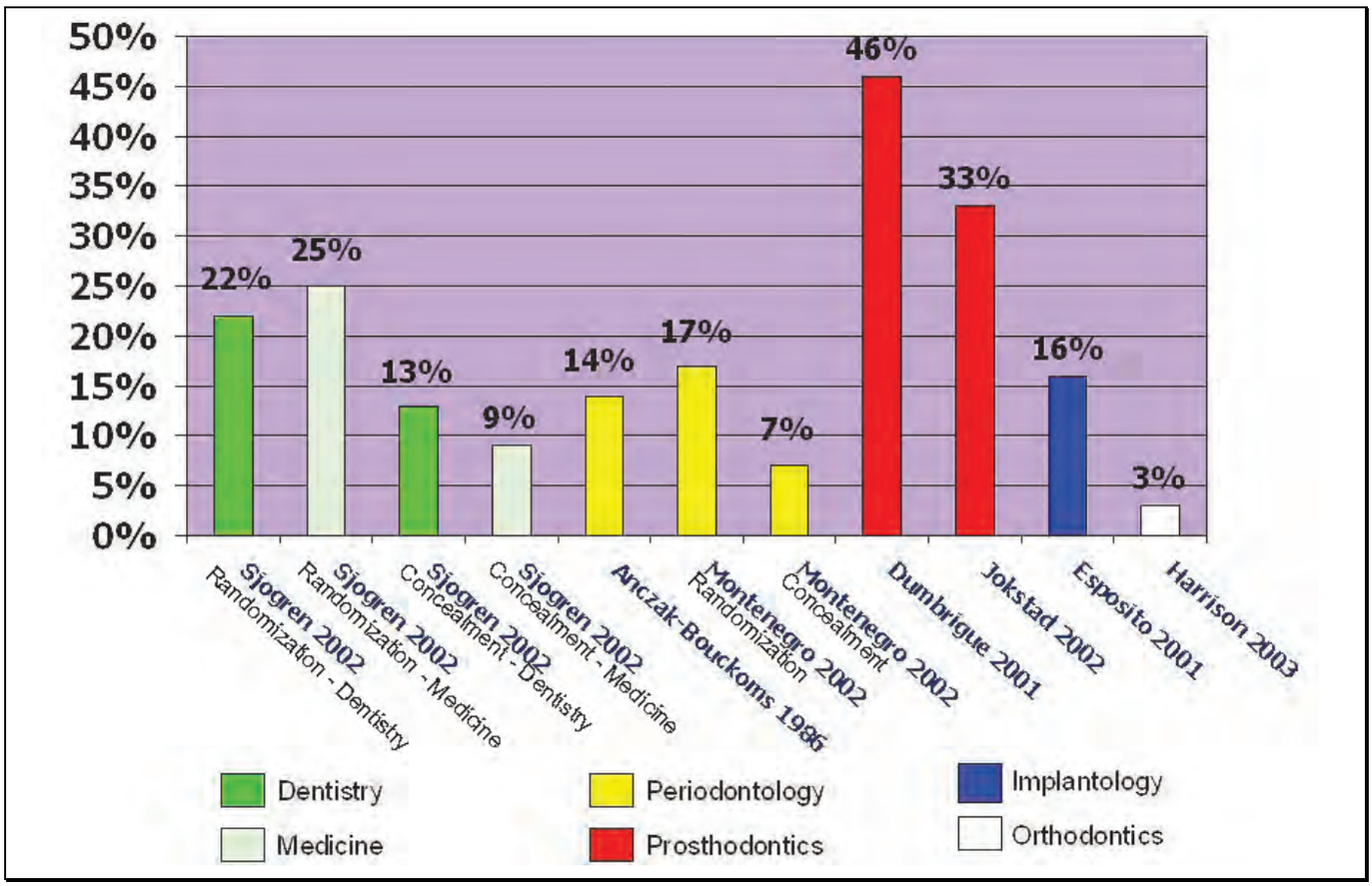

Fig. 1. Percentage of trials with adequate reported randomization methods in dental and medical research.

cation concealment were included.[7] This effect appeared to be due both to a loss of statistical power in the analysis and to a reduction in the beneficial effect of the treatment.

Mechanism of effect of bias - Allocation concealment is important in order to protect a trial from selection biases that may operate when selecting individuals for a clinical trial. Knowledge of which group a participant will be allocated to can influence those enrolling them (consciously or not). This might lead to participants being preferentially allocated to one intervention group over another based on how likely they are to respond to treatment.[8] For instance, in a study of a new periodontal intervention, current smokers might be systematically allocated to a control group with non-smokers allocated to the experimental group. As a result, the control group would perform less well and this difference would be unrelated to the intervention under investigation. Checking baseline characteristics of major prognostic factors such as age, gender, smoking *etc.* (often presented as Table 1 in a publication) can help to assess the similarity of groups and therefore possible risk of such bias. Formal testing is generally not however recommended.[9,10] A better safeguard is having a detailed explanation in the publication of exactly how the allocation process operated. Regrettably, that key information is often missing.

To protect from bias, allocation must be entirely unpredictable requiring both the generation of a true random number sequence and its subsequent concealment until the point of group assignment. An excellent random sequence results from a computer generated random number sequence.[11,12] Concealment can be achieved though a central facility that maintains the sequence and is remote from the trialists and all others participating in the study or by using truly opaque, sequentially numbered envelopes or identical coded containers for pharmacy preparation.[13] Examiner blinding (masking) is thought to be important when the measurement of the outcome involves subjectivity and can therefore be affected by knowledge of the study group. Blinding is therefore important in stages after the recruitment/selection phase. Subjective outcome measures might include visual color assessments and periodontal probing. Objective outcomes which would be difficult to bias would include tooth survival/loss. In such outcomes, examiner blinding might be unimportant.[5,14]

Effect of bias – dental studies - There has been little formal evaluation of the effect of bias in dentistry. In a recent Cochrane review of the effect of guided tissue regeneration (GTR) surgery,[15] sensitivity analyses suggested indirect evidence. When all 16 studies were included in the meta-analysis, the difference between GTR and access flap surgery was highly statistically significant at 1.22 mm greater gain in clinical attachment favoring GTR (95% CI: 0.80, 1.64). When studies were excluded without examiner or operator blinding the estimate became less pronounced: 0.41 mm (95% CI: -0.33 to 1.08) and was no longer statistically significant. In addition,[15] these authors reported that a previous meta-analysis of GTR which included both randomized and non-randomized trials[16] calculated a difference of 2.7 mm gain in attachment compared with the 1.22 mm estimate when only randomized controlled trials were included in the Cochrane

Table. CONSORT Statement 2001 – Checklist. Items to include when reporting a randomized trial.

Paper section and topic	Item	Descriptor	Reported on page #
Title & Abstract	1	How participants were allocated to interventions (*e.g.*, "random allocation", "randomized", or "randomly assigned").	
Introduction			
Background	2	Scientific background and explanation of rationale.	
Methods			
Participants	3	Eligibility criteria for participants and the settings and locations where the data were collected.	
Interventions	4	Precise details of the interventions intended for each group and how and when they were actually administered.	
Objectives	5	Specific objectives and hypotheses.	
Outcomes	6	Clearly defined primary and secondary outcome measures and, when applicable, any methods used to enhance the quality of measurements (*e.g.*, multiple observations, training of assessors).	
Sample size	7	How sample size was determined and, when applicable, explanation of any interim analyses and stopping rules.	
Randomization -- Sequence generation	8	Method used to generate the random allocation sequence, including details of any restrictions (*e.g.*, blocking, stratification)	
Randomization -- Allocation concealment	9	Method used to implement the random allocation sequence (*e.g.*, numbered containers or central telephone), clarifying whether the sequence was concealed until interventions were assigned.	
Randomization -- Implementation	10	Who generated the allocation sequence, who enrolled participants, and who assigned participants to their groups.	
Blinding (masking)	11	Whether or not participants, those administering the interventions, and those assessing the outcomes were blinded to group assignment. If done, how the success of blinding was evaluated.	
Statistical methods	12	Statistical methods used to compare groups for primary outcome(s); Methods for additional analyses, such as subgroup analyses and adjusted analyses.	
Results			
Participant flow	13	Flow of participants through each stage (a diagram is strongly recommended). Specifically, for each group report the numbers of participants randomly assigned, receiving intended treatment, completing the study protocol, and analyzed for the primary outcome. Describe protocol deviations from study as planned, together with reasons.	
Recruitment	14	Dates defining the periods of recruitment and follow-up.	
Baseline data	15	Baseline demographic and clinical characteristics of each group.	
Numbers analyzed	16	Number of participants (denominator) in each group included in each analysis and whether the analysis was by "intention-to-treat". State the results in absolute numbers when feasible (*e.g.*, 10/20, not 50%).	
Outcomes and estimation	17	For each primary and secondary outcome, a summary of results for each group, and the estimated effect size and its precision (*e.g.*, 95% confidence interval).	
Ancillary analyses	18	Address multiplicity by reporting any other analyses performed, including subgroup analyses and adjusted analyses, indicating those pre-specified and those exploratory.	
Adverse events	19	All important adverse events or side effects in each intervention group.	
Discussion			
Interpretation	20	Interpretation of the results, taking into account study hypotheses, sources of potential bias or imprecision and the dangers associated with multiplicity of analyses and outcomes.	
Generalizability	21	Generalizability (external validity) of the trial findings.	
Overall evidence	22	General interpretation of the results in the context of current evidence.	

www.consort-statement.org

review. This finding suggests that including non-randomized studies in summaries of the treatment of effect of GTR can lead to a larger estimate of treatment effect. Such a finding is consistent with those from the medical literature discussed above.

Summary

Study quality and in particular, protection from bias, has been shown to affect the size of the treatment effect of an intervention. This is generally in the direction that makes the estimate of effect appear to be larger. The impact of bias emphasizes the need to be able to critically appraise the publication and underlines the importance of transparency to permit appraisal. Therefore, a related question to ask is what is the reported quality of clinical trials in oral health research?

The reported quality of oral health clinical trials in relation to protection from bias

While there is little direct assessment of study quality, there are a number of investigations of the reported quality of trials in dentistry. Seven studies have been published (Fig. 1), including more than 500 trials across dentistry generally[17] and the specialties of periodontology,[18,19] prosthodontics,[20,21] implantology,[22] and orthodontics.[23] While the methodology varies a little from one study to another, a number of conclusions can be drawn; Firstly, the reported quality of trials in dentistry generally and in the above four specialties in dentistry is inadequate. In relation to reported quality of randomization methods, of the seven studies, four found adequate methods in less than one in five publications (range: 3%-46%). Secondly, in periodontology, where investigations were published both in 1986[18] and 2002,[18] there was no real improvement in quality over time. Thirdly, comparing RCT reports in medicine and dentistry, there was no difference in reported quality.[17]

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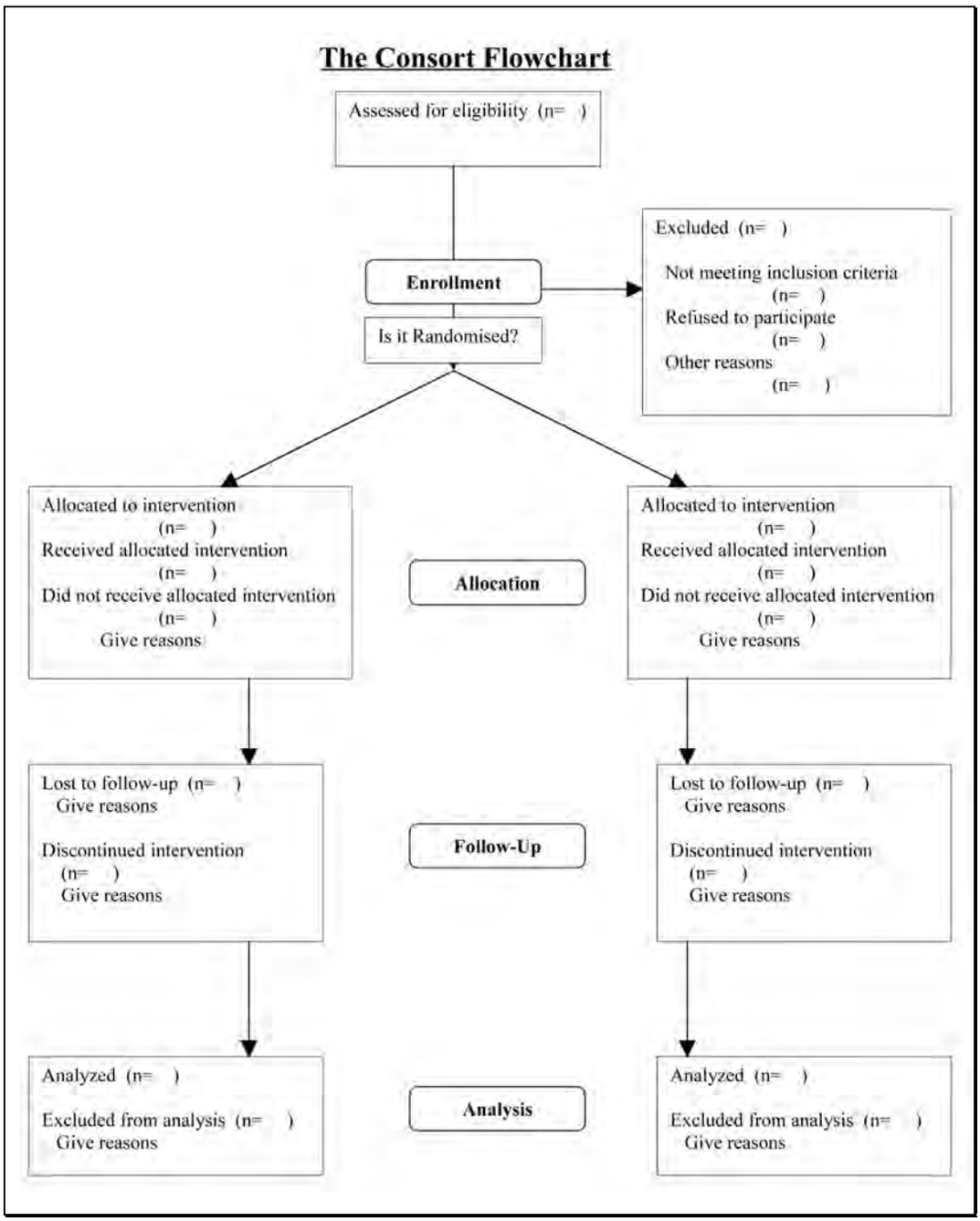

Fig. 2. The CONSORT flowchart.

Clearly, reported quality might not mirror actual study conduct. Lack of awareness of the importance of publishing full methodological details coupled with limitations of space could have resulted in under reporting of such information. Further research is needed to determine whether these data represent actual study flaws. However, without complete reporting, a reader is prevented from adequately appraising the quality of the study, increasing the uncertainty of whether the results can be applied to healthcare. Since clinical trials involve patient participation and are expensive to conduct, being unable to use the results in healthcare is somewhat of a moral issue and undermines the basis of undertaking clinical research. Solutions to promote transparency of reporting should therefore be considered a priority to adopt.

CONSORT

The CONSORT (Consolidated Standards of Reporting of Trials) Statement was proposed in 1996 as one possible solution to encourage more complete study reporting[24] and was updated in 2001[10,25] (www.consort-statement.org, accessed 14 October 2007). It has gained wide acceptance by most major medical journals and international editorial groups. The British Dental Journal was the first journal in oral health to adopt this guidance.[26] CONSORT was designed to encourage the transparent and complete reporting of randomized controlled trials and through such an objective, to facilitate peer review. Initially designed for two-group, parallel-arm studies, extensions to it

have been adapted for the following trial designs; cluster-randomized, non-inferiority and equivalence; CONSORT for pragmatic trials is under development. Other CONSORT extensions have been developed for non-pharmacological treatments, and herbal interventions. There is also an extension to strengthen the reporting of harms, and CONSORT for abstracts has been recently completed.

CONSORT consists of two elements; first, a 22-item checklist (Table) to guide the author through thorough trial reporting and second, a flow chart (Fig. 2) to account for all study participants throughout the trial. The checklist is intended to be both a guide for authors and helpful for journal peer reviewers and editors and is not intended to be published, whereas the flow chart should form part of the final publication. The items in the checklist are based as far as possible on those with evidence of an effect on study validity. Readers should be aware that a third version is likely to appear in 2008; they should consult the website for the latest version. Reporting standards for other research designs have been published and these include: systematic reviews (QUOROM, to be renamed PRISMA), observational studies (STROBE) and studies of diagnostic accuracy (STARD). These, and other reporting guides, can all be downloaded from the EQUATOR Network website (www.equator-network.org).

Does adopting CONSORT improve reporting of trials?

In a recent systematic review, the authors located and reviewed all studies that had investigated the effect of journal adoption (and non-adoption) of the CONSORT Statement on the quality of reporting of RCTs.[27] In summary, the findings were that there was better quality of reporting of RCTs both in CONSORT *vs.* non-CONSORT adopting journals and within journals, comparing publications following CONSORT adoption with the same journal prior to this change. What was also clear ironically was that the evidence regarding the impact of CONSORT was not strong as there was much variability in the findings. Much of the variability in improvement in CONSORT adopting journals would seem to be due to a lack of adherence to the guideline following its adoption by a journal. The authors found that some journals were using the obsolete 1996 checklist compared with the current (2001) version. Therefore, in addition to adopting CONSORT, it is important to train editorial staff and referees in how to use it and also to institute systems to check that it is being used. Several journals have now partially addressed this issue in their electronic submission process and manuscripts will be automatically returned unless the checklist and figure are included. However, maintaining adherence will need close control of the editorial process.

In summary, there is good evidence that bias affects the estimate of effect of an intervention in clinical research. Determining whether a trial is at risk of such bias and therefore whether to introduce new research findings into oral healthcare is dependent on transparent reporting of clinical trial methods and findings. Currently, there is a problem in that the reported quality of randomized trials in dental journals is poor. To address this, the CONSORT Statement should be used by journals to assist authors and editorial processes to produce more complete and higher quality trial publications. Where necessary, some detail might be reserved for online appendices should page space be an issue.

The era of electronic publishing offers great opportunities to improve both the quality of publications and access to new findings with potential to improve oral healthcare. All of us involved in clinical research have a responsibility to try to ensure that important research findings are communicated in such a way as to allow their early adoption. Initiatives that have evidence of improving transparency of reporting, such as the CONSORT Statement, will facilitate such an important aim.

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