**CONSORT 2010 extension checklist for within person randomised clinical trials**

*Bryan Chung,1 Nikolaos Pandis,2 Roberta W Scherer,3 Diana Elbourne,4*

1 Division of Plastic Surgery, University of British Columbia, Victoria, BC, Canada

2 University of Bern, Medical Faculty, School of Dental Medicine, Department of Orthodontics and Dentofacial Orthopedics, Bern, Switzerland

3 Johns Hopkins Bloomberg School of Public Health, Epidemiology Mailroom E6138

Baltimore, MD, USA

4 London School of Hygiene and Tropical Medicine, Department of Medical Statistics, London, UK

The aim of research is to produce valid and useful results that can ultimately improve patient care. Clinical studies should be designed, executed and communicated with the scientific community in a rigorous and unbiased manner. In the 1990s it was recognised that the reporting of clinical trials was often suboptimal, creating problems in the ability to evaluate the quality of published research. The increasing importance of systematic reviews which require synthesis of the results of existing clinical trials made it also clear that accurate and transparent reporting is vital for the clinical research to be utilised fully and correctly. Suboptimal reporting is a component of research waste with wide implications for the society (Glasziou et al. 2014). In order to improve clinical trial reporting the recommendations in the Consolidated Standards of Reporting Trials (CONSORT) statement have been drafted.

Today, a common requirement among many medical and dental journals is for randomised controlled trials (RCTs) to conform to the CONSORT statement which includes a checklist of items that should be included in the trial report. The most recent version of the CONSORT checklist, published in 2010, includes items which are based on evidence whenever possible (Moher et al. 2010). The CONSORT 2010 statement focuses mainly on two treatment groups using an individually randomised parallel group design. Most checklist items of the CONSORT statement are applicable to other RCTs designs; however, CONSORT 2010 does not cover specific areas that are inherent to designs other the 2-group parallel design. Therefore, some additional items are needed, or some existing checklist items require adaptation. Several extensions of the CONSORT statement have been recently published to address specific issues in variants of RCTs, such as cross-over (Dwan et al. 2019), non-pharmacological (Leow et al. 2016) , cluster (Campbell et al. 2012).

In some RCTs, a body part is the unit of randomization, with the assumed advantage of using paired organs or non-paired body parts or phenomena such as teeth, eyes, or warts as a means of decreasing the number of individuals required for recruitment as well as decreasing inter-individual variability. These studies do not have a uniform name, and in this extension, have been dubbed “within person” trials.  In the field of dentistry, the term “split-mouth design” has been coined where half of the mouth receives one treatment and the other half, the other treatment. The split-mouth design was used in approximately 10% of RCTs published from 1992-2012 in 8 oral health journals with high impact factors. This represents a substantial proportion of such RCTs in dentistry (Koletsi et al. 2014). Split-mouth designs include features that are not covered fully in the CONSORT 2010 statement and this together with frequent use of this design in dentistry underscore the importance of guidance in reporting of “split-mouth” designs.

The quality of these studies has not been well studied, though it has been reported that in just over half of 34 spilt-mouth trials included in the study reported an appropriate statistical method for a within-person design and only 15% of these trials commented on the potential correlation and treatment carry across effect that could occur with this study design (Lesaffre et al. 2007; Lesaffre et al. 2009).Choosing a within-person design requires careful consideration of the treatments proposed as well as the outcomes measured. The correlation that arises from the fact that both sites belong to the same individual (dependent observations) as well as the possibility that one treatment might affect a site not assigned to received it (also known as carry over effect) must be accounted for either methodologically or statistically. Justification for the use of this design type is particularly salient to allow the reader to decide whether the advantages of the design outweighs the drawbacks.

In addition to carry over effects, the main drawbacks to a within person design are:

1) Outcome measurements that are per-person (e.g. quality of life measurements) cannot be attributed to either treatment

2) Harms or unintended effects that are measured per-person (e.g. headache) cannot be attributed to either treatment

3) Interventions that have substantial carry over effects (e.g. mouth rinses where it is impossible to isolate one half of the mouth from the other) may prevent accurate measurement of the treatment effect

4) Conditions without underlying stability, which does not tend to occur in dentistry, preclude simultaneous administration of treatments

5) Conditions in which the sites for each participant are not similar in terms of baseline characteristics (e.g. endodontic treatment with different number of roots) cannot be compared accurately

6) Administration of the two interventions often makes blinding/masking impossible.

In the extension of the 2010 CONSORT Statement to within-person trials (Pandis et al. 2017), most of the baseline CONSORT statement remains the same, with the largest changes in recommended reporting being in the description of the rationale for the within-person design; greater detail in the description of interventions (including whether the treatments were administered sequentially or concurrently), greater detail in the description of outcomes, additional considerations for sample size determination, and changes to the patient flow diagram (Table 1).

Reports of RCTs should be detailed enough to allow readers to accurately interpret results as well as to enable replication. The main 2010 CONSORT statement and the extensions for specific designs such as for within person trials are useful tools for both the reporting and the design of trials and can also be used as a guide for peer-reviewers and editors. CONSORT recommendations can be found at <http://www.consort-statement.org>

**Keys words**

RCTs, Reporting Guidelines, Clinical Trials, Split-mouth, Split-face, Split-body

Author contributions

**BC** drafted the first version of the manuscript and all coauthors **NP, RS and DE** have commented, edited and approved the final version.

**Acknowledgments**

Not applicable

**Competing interests:** None to declare

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**Table 1: Checklist for reporting within-person trials**

| **Section/Topic** | **Item no.** | **Standard CONSORT Checklist item** | **Extension for within-person trials** |
| --- | --- | --- | --- |
| **Title and abstract** | | | |
|  | 1a | Identification as a randomised trial in the title | Identification as a within-person randomised trial in the title |
| 1b | Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts (Hopewell et al. 2008)) | Specify a within-person design and report all information outlined in table 1 |
| **Introduction** | | | |
| Background and objectives | 2a | Scientific background and explanation of rationale |  |
| 2b | Specific objectives or hypotheses |  |
| **Methods** | | | |
| Trial design | 3a | Description of trial design (such as parallel, factorial) including allocation ratio | Rationale for using a within-person design and identification of body sites |
| 3b | Important changes to methods after trial commencement (such as eligibility criteria), with reasons |  |
| Participants | 4a | Eligibility criteria for participants | Eligibility criteria for body sites |
| 4b | Settings and locations where the data were collected |  |
| Interventions | 5 | The interventions for each group with sufficient details to allow replication, including how and when they were actually administered | Whether interventions were given sequentially or concurrently |
| Outcomes | 6a | Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed | Outcomes should be clearly defined as per-site or per-person |
| 6b | Any changes to trial outcomes after the trial commenced, with reasons |  |
| Sample size | 7a | How sample size was determined | Report the correlation between body sites |
| 7b | When applicable, explanation of any interim analyses and stopping guidelines |  |
| Randomisation: | | | |
| Sequence generation | 8a | Method used to generate the random allocation sequence |  |
| 8b | Type of randomisation; details of any restriction (such as blocking and block size) | Methods used to determine the allocation sequence of body sites and treatments within an individual (e.g. how first site to be treated was decided) |
| Allocation concealment mechanism | 9 | Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned |  |
| Implement-ation | 10 | Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions | Replaced by 10a |
|  | 10a |  | Who generated the random allocation sequence, who enrolled participants, and who assigned body sites to interventions |
| Blinding (masking) | 11a | If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how |  |
| 11b | If relevant, description of the similarity of interventions |  |
| Statistical methods | 12a | Statistical methods used to compare groups for primary and secondary outcomes | Statistical methods appropriate for within-person design |
| 12b | Methods for additional analyses, such as subgroup analyses and adjusted analyses |  |
| **Results** | | | |
| Participant flow  (a diagram is strongly recommended) | 13a | For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome | Number of participants and number of body sites at each stage |
| 13b | For each group, losses and exclusions after randomisation, together with reasons | Number of participants and number of body sites lost or excluded at each stage, with reasons |
| Recruitment | 14a | Dates defining the periods of recruitment and follow-up |  |
| 14b | Why the trial ended or was stopped |  |
| Baseline data | 15 | A table showing baseline demographic and clinical characteristics for each group | Baseline characteristics for site and individual participants as applicable |
| Numbers analysed | 16 | For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups | Number of randomised body sites in each group included in each analysis |
| Outcomes and estimation | 17a | For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval) | Observed correlation between body sites for continuous outcomes and/or and tabulation of paired results for binary outcomes |
| 17b | For binary outcomes, presentation of both absolute and relative effect sizes is recommended |  |
| Ancillary analyses | 18 | Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory |  |
| Harms | 19 | All important harms or unintended effects in each group (for specific guidance see CONSORT for harms) | Harms or unintended effects reported by participant and by body site |
| **Discussion** | | | |
| Limitations | 20 | Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses |  |
| Generalisability | 21 | Generalisability (external validity, applicability) of the trial findings |  |
| Interpretation | 22 | Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence |  |
| **Other information** | | | |
| Registration | 23 | Registration number and name of trial registry |  |
| Protocol | 24 | Where the full trial protocol can be accessed, if available |  |
| Funding | 25 | Sources of funding and other support (such as supply of drugs), role of funders |  |

Table 2. Information to include in the abstract of a report of a within-person randomised trial: extension of CONSORT for abstracts checklist

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| --- | --- | --- |
| **Item** | **Standard CONSORT Checklist item**[3] | **Extension for within-person trials** |
| Title | Identification of study as randomised | Identification of study as a within-person trial (or an alternative within-specialty accepted term) |
| Trial design | Description of the trial design (e.g. parallel, cluster, non-inferiority) |  |
| Methods |  |  |
| Participants | Eligibility criteria for participants and the settings where the data were collected | Eligibility criteria for body sites |
| Interventions | Interventions intended for each group | Intervention timing: sequential or concurrent |
| Objective | Specific objective or hypothesis |  |
| Outcome | Clearly defined primary outcome for this report |  |
| Randomisation | How participants were allocated to interventions | How body sites were allocated within a single participant |
| Blinding(masking) | Whether or not participants, care givers, and those assessing the outcomes were blinded to group assignment |  |
| Results |  |  |
| Numbers randomised | Number of participants randomised to each group | Number of body sites randomised to each group |
| Recruitment | Trial status |  |
| Numbers analysed | Number of participants analysed in each group | Number of body sites analysed in each group |
| Outcome | For the primary outcome, a result for each group and the estimated effect size and its precision |  |
| Harms | Important adverse events or side effects | For participants and for body sites |
| Conclusions | General interpretation of the results |  |
| Trial registration | Registration number and name of trial register |  |
| Funding | Source of funding |  |