

Guidelines for Reporting Pre-clinical In Vitro Studies on Dental Materials

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In vitro pre-clinical research is an important aspect of the development of new dental materials and techniques, because it can provide essential information for further testing of therapeutic approaches in clinical trials. These pre-clinical experiments should therefore be reported with the same rigor as studies involving humans. The objectives of this paper were twofold: (a) to search and assess existing guidelines for reporting in vitro studies in dentistry, and (b) to present a methodology for reporting these studies, based on the CONSORT checklist for reporting randomized clinical trials. After a comprehensive search in PubMed database, no guidelines for reporting in vitro studies in dentistry were found. The proposed methodology is presented and the rationale for the choice of fourteen guidelines for producing the different sections of such papers is described in detail. The assessment of a sample of in vitro studies using the proposed guidelines showed that the standards of reporting should be improved. Good standards of reporting of studies are necessary for improvement of efficiency in dental research. The guidelines presented are the first standards for reporting in vitro studies in dentistry. As with the original CONSORT document, the modified checklist is evolving. It should, therefore, be further tested by researchers and the results of these assessments should be used for further improvement of this tool.

Keywords: In vitro, Quality of reporting, Dental materials, Guidelines, Pre Clinical, CONSORT checklist.

INTRODUCTION

In vitro research for assessing potential new materials or techniques to be further tested in vivo, i.e., on animals and humans, is an important aspect of dentistry. One advantage of in vitro research is that it enables researchers to perform single-variable experiments under controlled conditions.¹ Although in vitro research can-

not reproduce a dynamic environment, for example the stomatognathic system, pre-clinical experiments can provide important information about the properties and characteristics of a new material or technique. This information is of fundamental importance when testing efficacy in more robust studies, for example randomized clinical trials. It is, therefore, necessary to conduct in vitro research of the highest possible standard. Biased information from pre-clinical experiments is likely to lead to biased clinical studies.

In restorative dentistry many studies test the biocompatibility and/or toxicity² and efficacy of dental materials, for example composites, using extracted animal or human teeth.³⁻⁶ Because systematic reviews of dental in vitro studies are becoming frequent,⁷⁻¹⁰ maximization of the output from such research is essential. Moreover, good standards in reporting are

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required to provide interested people—readers, researchers, and editors—with detailed information indicating whether the research was appropriate and which aspects might need more scrutiny.¹¹ Some efforts were made in the last years to improve the quality of reporting of scientific literature. For example, the Consolidated Standards of Reporting Trials (CONSORT) checklist was developed to assist authors in writing reports of randomized controlled trials.¹² Although the CONSORT checklist was not originally designed for designing, conducting, and analyzing trials, its use may indirectly affect their design and conduct.¹²

The objectives of the present work were twofold: (a) to critically assess the literature on guidelines on the report of *in vitro* research in dentistry. The focus was on guidelines for reporting *in vitro* studies, instead of performing some specific experiment; and (b) to describe a checklist developed for reporting pre-clinical (*in vitro*) studies of dental materials, using modified items described in the CONSORT checklist. A sample of *in vitro* studies was tested with this new methodology and the results are presented. The idea is to improve conducting and reporting of pre-clinical testing of dental materials with potential for use in clinical treatment as to possibly minimize bias and optimize efficacy for subsequent RCTs.

MATERIAL AND METHODS

Search of Guidelines for Reporting *In Vitro* Studies

On 10 August 2012 a comprehensive search of the literature was performed in the PubMed database using the following key-words: *in vitro*, *in-vitro*, *preclinical*, *pre-clinical*, *reporting*, *CONSORT*, *recommendations*, *guidelines*, *dentistry*, *dental implants*, and *teeth*. The key-words were combined using boolean operators *AND/OR*. The search was focussed only on guidelines for reporting any form of *in vitro* studies performed in teeth and dental implants. Guidelines relating to other forms of preclinical research (for example, experiments in animals) were not selected, because there are already specific guidelines for those studies.¹³⁻¹⁵

Description of New Checklist

The checklist proposed below contains 14 items enabling assessment of the standard of reporting in the different sections of a paper. See [Table 1](#):

Checklist Items

Abstract. *Item 1. Structured summary of trial design, methods, results, and conclusions*

Explanation: the abstract should contain enough information to enable good understanding of the rationale for the approach. Because many readers do not have free access to the full text of articles to assess the validity of results,¹⁶⁻¹⁸ they may rely on reading the abstract to

make conclusions. Use of structured abstracts for reporting studies is recommended, because they enable easier access to the information reported.¹⁹

Introduction. *Item 2a. Scientific background and explanation of rationale*

Explanation: authors should provide direct and clear information about the background of the material or technique to be tested in the proposed experiment. In *in vitro* dental studies, similar previously published studies on the topic in question should be reported in detail to enable good comprehension by readers of the potential efficacy and limitations of the current experiment. The rationale for the new project should be explained in detail to avoid duplication of studies and consequent waste of resources.

Item 2b. Specific objectives and/or hypotheses

Explanation: the objective(s) of the study, with a defined hypothesis, should be reported in the introduction. The hypothesis is based on a well-developed research question (for example, use of the PICOT [population, intervention, comparison, outcomes, and time] format) and it should guide the objectives of the research.²⁰ Hypotheses are more specific than objectives and can be tested statistically to help meet the objectives of the project.²¹

Methods. *Item 3. The intervention for each group, including how and when it was administered, with sufficient detail to enable replication*

Explanation: to enable replication of the results by other interested researchers, authors should report the approach used in the experiment. Replication is regarded as one of the cornerstones of inference from experimental studies.^{22,23}

Specific information on the type of intervention performed in the control and test groups should be described in detail. For example, when testing the effect of different adhesive systems on the surface of extracted human teeth, information on how the test specimens were prepared, etching time, procedures used to apply the adhesive, polymerization time, etc., should be provided.

Item 4. Completely defined, pre-specified primary and secondary measures of outcome, including how and when they were assessed

Explanation: it is important to precisely state the primary (and secondary) outcome(s) of the proposed experiment to enable comparison with results from similar studies. The validity of a study might be questionable if it does not enable comparison, and this can be a problem when the whole body of evidence is assessed in systematic reviews with meta-analysis, for example.²⁴

Item 5. How sample size was determined

Explanation: in the planning of a randomized clinical trial, determination of the correct sample of patients enabling detection of true differences between therapies

TABLE 1. Modified CONSORT checklist of items for reporting in vitro studies of dental materials

Section/topic	Checklist item
Abstract	<ul style="list-style-type: none"> Item 1. Structured summary of trial design, methods, results, and conclusions
Introduction <i>Background and objectives</i>	<ul style="list-style-type: none"> Item 2a. Scientific background and explanation of rationale Item 2b. Specific objectives and/or hypotheses
Methods <i>Intervention</i>	<ul style="list-style-type: none"> Item 3. The intervention for each group, including how and when it was administered, with sufficient detail to enable replication
<i>Outcomes</i>	<ul style="list-style-type: none"> Item 4. Completely defined, pre-specified primary and secondary measures of outcome, including how and when they were assessed
<i>Sample size</i>	<ul style="list-style-type: none"> Item 5. How sample size was determined
<i>Randomization: Sequence generation</i>	<ul style="list-style-type: none"> Item 6. Method used to generate the random allocation sequence
<i>Allocation concealment mechanism</i>	<ul style="list-style-type: none"> Item 7. Mechanism used to implement the random allocation sequence (for example, sequentially numbered containers), describing any steps taken to conceal the sequence until intervention was assigned
<i>Implementation</i>	<ul style="list-style-type: none"> Item 8. Who generated the random allocation sequence, who enrolled teeth, and who assigned teeth to intervention
<i>Blinding</i>	<ul style="list-style-type: none"> Item 9. If done, who was blinded after assignment to intervention (for example, care providers, those assessing outcomes), and how
<i>Statistical methods</i>	<ul style="list-style-type: none"> Item 10. Statistical methods used to compare groups for primary and secondary outcomes
Results <i>Outcomes and estimation</i>	<ul style="list-style-type: none"> Item 11. For each primary and secondary outcome, results for each group, and the estimated size of the effect and its precision (for example 95% confidence interval)
Discussion <i>Limitations</i>	<ul style="list-style-type: none"> Item 12. Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses
Other information <i>Funding</i>	<ul style="list-style-type: none"> Item 13. Sources of funding and other support (for example suppliers of drugs), role of funders
<i>Protocol</i>	<ul style="list-style-type: none"> Item 14. Where the full trial protocol can be accessed, if available

is important. Some believe that conducting “oversized” trials, in which there are more patients than are needed to detect a difference, and “underpowered” trials, in which there are fewer subjects than adequate, should be avoided.²⁵ The correct sample of patients is associated with the precision of results, i.e., small studies tend to result in wider confidence intervals and, consequently, imprecise results.²⁶ In in vitro studies, therefore, mainly those performed to assess the potential efficacy of

materials and techniques, statistical treatment should also be considered. Detailed reporting of the calculation of sample size is, moreover, a requirement for good comprehension of the methodology used. For example, in a study²⁷ to determine the effects of saliva contamination and cleansing solutions on the microtensile bond strengths of self-etch adhesives to dentin, microtensile bond strength was regarded as the primary outcome and the authors concluded that 75 teeth would be

required to power the study at 80%. Despite this, it is not reported in the paper how that sample size was determined (e.g., it was not reported whether the primary outcome was used as the reference for this calculation).

Item 6. Method used to generate the random allocation sequence

Explanation: in RCTs, patients should be assigned to comparison groups in the trial on the basis of a random process (chance) characterized by unpredictability.²¹ In this way, the allocation sequence would balance prognostic factors across the intervention groups and, consequently, protect against selection bias.²⁸ Similarly, in an in vitro environment, extracted teeth can provide heterogeneous conditions for generating treatment effects. For example, in an experiment in which marginal adaptation of an etch-and-rinse adhesive with a new type of solvent in class II cavities was assessed,²⁹ the authors prepared inlay cavities in 40 extracted teeth and the teeth were then randomly assigned to five experimental groups. Some might argue that teeth could have different anatomical characteristics that would be a potential confounding factor in estimation of effects (for instance, cavity architecture more prone to positive effects). Coin tossing or shuffling cards or envelopes may be a suitable means of generating the allocation sequence *before* teeth are prepared for the intervention (i.e., in the specific case cited, before the cavities are prepared).

Item 7. Mechanism used to implement the random allocation sequence (for example, sequentially numbered containers), describing any steps taken to conceal the sequence until intervention was assigned

Explanation: in clinical studies, allocation concealment may prevent selection bias by concealing the allocation sequence from those assigning participants to intervention groups until the moment of assignment.²⁸ In in vitro studies, allocation concealment could be achieved by use of, for example, sequentially numbered, opaque, sealed envelopes that would prevent investigators seeing the extracted teeth used in the experiments.

Item 8. Who generated the random allocation sequence, who enrolled teeth, and who assigned teeth to intervention

Explanation: in clinical trials randomization is achieved by use of three different steps: sequence generation, allocation concealment, and implementation.²¹ In in vitro studies all these steps would not be relevant (for example, “enrol participant”). Nevertheless, investigators responsible for allocation and its concealment should not be the same as those who implement the assignments. The idea is to try to avoid any inclusion of potential bias in the randomization process.

Item 9. If done, who was blinded after assignment to intervention (for example, care providers, those assessing outcomes) and how

Explanation: logically, some aspects of blinding in in-vitro studies are not applied (“blinding of teeth”, for example. See original checklist). Nevertheless, blinding

of investigators responsible for treatment and others responsible for assessment of outcome may be feasible. These measures could reduce the likelihood of performance, attrition, and detection bias.²⁸

Item 10. Statistical methods used to compare groups for primary and secondary outcomes

Explanation: statistical assessment in in vitro experiments should be performed with the same accuracy as that performed in clinical trials. Laboratory studies which do not involve patients should still be carefully planned. If the purpose of the study is to obtain information on efficacy that can be further used in more robust designs (in vivo, with animals, and humans), a rigorous statistical approach is essential. Information should be concisely reported, but in sufficient detail to enable understanding of the statistical approach by other researchers or interested readers.

Results. *Item 11. For each primary and secondary outcome, results for each group, and the estimated size of the effect and its precision (for example 95% confidence interval)*

Explanation: results from in vitro studies should be presented in the same way as those from clinical trials. It is important to report the precision of results as confidence intervals (CI). In contrast with *P* values, CI can provide the range of values within which the true effect is likely to reside.²⁶

These results should, moreover, be reported not only for endpoints of interest (for example, endpoints that provided positive results) but also for all endpoints that were previously reported in the material and methods section. Selective reporting of outcome, i.e., inclusion of endpoints in publication of trials on the basis of results, may generate biased results, for example overestimation of the effects of intervention in a meta-analysis.²⁸

Discussion. *Item 12. Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses*

Explanation: the discussion section should be reserved for valuable comments on the advantages and disadvantages of the approach used, not only to provide information in support of the findings. The journal *Annals of Internal Medicine* recommends that authors structure the discussion section by presenting (1) a brief synopsis of the key findings, (2) consideration of possible mechanisms and explanations, (3) comparison with relevant findings from other published studies, and (4) limitations of the study (and methods used to minimize and compensate for those limitations).¹⁵

Other Information. *Item 13. Sources of funding and other support (for example suppliers of drugs), role of funders*

Explanation: information on potential relationships between researchers and sponsors should be made clearly available to readers, to provide sufficient information on potential conflicts of interest (COI). It has been reported in the literature that trials sponsored by industry

may provide more positive results than studies not funded by industry.^{30,31} This is, therefore, an ethical issue and precise information enables readers to make their own conclusions about the effect on the results of potential COI.

Item 14. Where the full trial protocol can be accessed, if available

Explanation: information should be provided about whether the study protocol is available to the interested reader. If it is not publicly available, researchers should state explicitly that the protocol is available for detailed assessment (for example, to systematic reviewers when assessing potential threats to internal validity, for example selective outcome reporting).²⁸ Published studies which are inconsistent with their protocols may suggest unreliable and overestimated benefits of an intervention.³²

ASSESSMENT OF IN VITRO STUDIES

A second literature search was performed on 11 August 2012 to select in vitro studies published in dentistry from 01 September 2007 until 31 August 2012 and using human extracted teeth. Papers on randomized controlled trials (RCTs) were searched. The following key-words were used in the PubMed database (with RCT filter): *teeth* AND *in vitro*, *in-vitro*. After the retrieval of the literature, 10 papers were randomly selected using an available online program (randomizer.org). Finally, the proposed recommendations were applied to the sample of these studies.

The quality of reporting in in vitro studies was assessed by checking whether the 14 checklist criteria were met in the papers selected. For each item, a judgment relating to the reporting was assigned by taking into consideration a pre-specified question—was the item correctly reported?: yes (reported) or no (not reported).

RESULTS

Availability of Guidelines

The PubMed search generated 212 titles. After the assessment of titles and abstracts, no paper on guidelines for reporting in vitro studies in dentistry was found.

Report of In Vitro Studies

220 papers were initially retrieved. The results of the assessment of the 10 randomized papers are depicted in Table 2. From a total of 150 entries, 57 (38%) were correctly reported. No study reported the calculation of the adequate sample size of teeth used in the procedures. Items related to the randomization process (6, 7 and 8) were also not reported in any of the selected studies. Only two studies reported that examiners were blinded to the procedures. All studies reported correctly for items

related to the background, objectives and intervention of procedures.

DISCUSSION

The main objective of this checklist is to provide guidance for reporting in vitro studies in dentistry. The original checklist was initially developed for clinical RCTs with parallel treatment arms. In recent years, the checklist has been extended to include other types of RCT and studies not involving humans, such experiments with livestock and laboratory animal trials.¹³⁻¹⁵ It now seems reasonable to use the CONSORT concept to guide the reporting of randomized controlled trials also, at a more basic level. It is important to emphasize, nevertheless, that not all the original CONSORT items are applicable to in vitro studies. The original CONSORT checklist is reported with the proposed checklist to enable better understanding by the reader of the modifications of the items.

This checklist is a pilot proposal primarily suited to the reporting of experiments with extracted human teeth. There is a great variety of in vitro experiments in dentistry, for example tests with dental implants or cell-culture assays, and most, if not all, of the topics can also be applied to such experiments. The purpose of this checklist was to exclude topics from the original checklist that would result in heterogeneous and dubious interpretation. In contrast, items were included that the author judges to be applicable to in vitro studies and which are crucial for guiding researchers reporting their trials. Nevertheless, the tool should be further tested by researchers (by assessing the standards of reporting in published in vitro RCTs), and the results from these assessments should be used for further improvement of the tool.

It is clear with the assessment of the present sample of studies that the randomization process is not reported in detail to the reader. Important phases of randomization process (sequence generation, allocation concealment and implementation) should be performed to reduce the risk of biased results and increase our confidence on the reported estimates. Similarly, sample size calculation was not reported in any of the studies assessed. An inadequate sample of teeth or dental implants may generate incorrect results which could be used to guide further research in the form of animal experiments or clinical trials. Ethical concerns may arise when the experiment is not properly conducted.

Because all phases of the research process are connected, proper conducting and reporting may have positive consequences in the development of dental materials and therapeutic approaches. First, the decision to test a new composite for dental restorations in clinical trials may be made based on its performance in in vitro environments. If this phase in the research process is well conducted and reported, it is likely that the information

TABLE 2. Results of the assessment of in vitro studies by the use of the modified CONSORT checklist

Item	Studies										
	Aschenbrenner et al ³³ 2012	Gupta ³⁴ 2011	Arnaud et al ³⁵ 2010	Behnan et al ³⁶ 2010	Catalbas et al ³⁷ 2009	Inan et al ³⁸ 2009	Mohammadi ³⁹ 2009	Poggio et al ⁴⁰ 2009	Murray et al ⁴¹ 2008	Yamada et al ⁴² 2008	
1	No	No	Yes	Yes	Yes	Yes	No	Yes	No	Yes	
2a	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	
2b	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	
3	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	
4 ^a	No	No	No	No	Yes	No	No	No	No	No	
5	No	No	No	No	No	No	No	No	No	No	
6	No	No	No	No	No	No	No	No	No ^f	No	
7	No	No	No	No	No	No	No	No	No ^f	No	
8	No	No	No	No	No	No	No	No	No ^f	No	
9	No	Yes ^b	No	No	No	No	No	No	No	Yes	
10 ^c	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	
11	Yes	No ^c	No ^c	Yes	No ^c	No ^c	No ^c	No ^c	No ^c	No ^c	
12	Yes	No	No	Yes	No	Yes	No	No	No	Yes	
13	Yes	No	No	No	No	Yes ^d	No	No	No	Yes	
14	No	No	No	No	No	No	No	No	No	No	

^aThis item received a yes only when authors explicitly described the words measure of outcome. When more than one measure of outcome was used, authors should explicitly describe primary and secondary measures.

^bThe examiner was blinded to the test.

^cNo confidence interval presented.

^dAuthors report no financial interests in any company manufacturing the types of products mentioned in the article.

^eThis item received a yes if there is the description of the statistical method used to compare the samples.

^fIt is not reported whether the teeth were randomized before the tests were performed.

obtained from in vitro experiments is reliable and will lead to more reliable clinical research. Second, high standards of reporting provide more reliable information for assessment of the whole body of evidence by use of the systematic approach of reviewing the literature.

In summary, this paper presented a tool based on the CONSORT checklist that might be useful for improving the reporting of in vitro experiments in dentistry. The present initial findings demonstrated that there is room for improvement of the quality of this reporting. The checklist should be applied to more samples of studies to confirm the present findings.

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CONFLICT OF INTEREST

The author declares he has no conflicts of interest.

Supplementary data

Supplementary data related to this article can be found online at <http://dx.doi.org/10.1016/j.jebdp.2012.10.001>.

REFERENCES

1. White DJ. The application of in vitro models to research on demineralization and remineralization of the teeth. *Adv Dent Res* 1995;9:175-93.
2. Polyzois GL. In vitro evaluation of dental materials. *Clin Mater* 1994;16:21-60.
3. Ibarra G, Vargas MA, Geurtsen W. Interfacial and surface characterization of two self-etching adhesive systems and a total-etch adhesive after bonding to ground and unground bovine enamel – a qualitative study. *Clin Oral Investig* 2006;10:331-41.
4. Frankenberger R, Lohbauer U, Schaible RB, Nikolaenko SA, Naumann M. Luting of ceramic inlays in vitro: marginal quality of self-etch and etch-and-rinse adhesives versus self-etch cements. *Dent Mater* 2008;24:185-91.
5. El Zohairy AA, Saber MH, Abdalla AI, Feilzer AJ. Efficacy of microtensile versus microshear bond testing for evaluation of bond strength of dental adhesive systems to enamel. *Dent Mater* 2010;26:848-54.
6. DüNDAR M, Özcan M, Cömlekoglu ME, Sen BH. Nanoleakage inhibition within hybrid layer using new protective chemicals and their effect on adhesion. *J Dent Res* 2011;90:93-8.
7. Abduo J, Lyons K, Swain M. Fit of zirconia fixed partial denture: a systematic review. *J Oral Rehabil* 2010;37:866-76.
8. Finnema KJ, Ozcan M, Post WJ, Ren Y, Dijkstra PU. In-vitro orthodontic bond strength testing: a systematic review and meta-analysis. *Am J Orthod Dentofacial Orthop* 2010;137:615-22.
9. Laaksonen M, Sorsa T, Salo T. Emdogain in carcinogenesis: a systematic review of in vitro studies. *J Oral Sci* 2010;52:1-11.
10. Archambault A, Lacoursiere R, Badawi H, Major PW, Carey J, Flores-Mir C. Torque expression in stainless steel orthodontic brackets. A systematic review. *Angle Orthod* 2010;80:201-10.

11. Egger M, Altman DG, Vandembroucke JP, STROBE Group. Commentary: strengthening the reporting of observational epidemiology the STROBE statement. *Int J Epidemiol* 2007;36:948-50.
12. Schulz KF, Altman DG, Moher D, CONSORT Group. CONSORT 2010 statement: updated guidelines for reporting parallel group randomised trials. *PLoS Med* 2010;7:e1000251.
13. Kilkenny C, Browne WJ, Cuthill IC, Emerson M, Altman DG. Improving bioscience research reporting: the ARRIVE guidelines for reporting animal research. *PLoS Biol* 2010;8:e1000412.
14. Faggion CM Jr, Giannakopoulos NN, Listl S. Risk of bias of animal studies on regenerative procedures for periodontal and peri-implant bone defects – a systematic review. *J Clin Periodontol* 2011;38:1154-60.
15. O'Connor AM, Sargeant JM, Gardner IA, et al, Steering Committee. The REFLECT statement: methods and processes of creating reporting guidelines for randomized controlled trials for livestock and food safety. *J Vet Intern Med* 2010;24:57-64.
16. Can OS, Yilmaz AA, Hasdogan M, et al. Has the quality of abstracts for randomised controlled trials improved since the release of Consolidated Standards of Reporting Trial guideline for abstract reporting? A survey of four high-profile anaesthesia journals. *Eur J Anaesthesiol* 2011;28:485-92.
17. Chen Y, Li J, Ai C, et al. Assessment of the quality of reporting in abstracts of randomized controlled trials published in five leading Chinese medical journals. *PLoS One* 2010;5:e11926.
18. Faggion CM Jr, Giannakopoulos NN. Quality of reporting in abstracts of randomized controlled trials published in leading journals of periodontology and dental implantology: a survey. *J Periodontol* 2012;83:1251-6.
19. Haynes RB, Mulrow CD, Huth EJ, Altman DG, Gardner MJ. More informative abstracts revisited. *Ann Intern Med* 1990;113:69-76.
20. Farrugia P, Petrisor BA, Farrokhyar F, Bhandari M. Practical tips for surgical research: research questions, hypotheses and objectives. *Can J Surg* 2010;53:278-81.
21. Moher D, Hopewell S, Schulz KF, et al. CONSORT 2010 explanation and elaboration: updated guidelines for reporting parallel group randomised trials. *Br Med J* 2010;340:c869.
22. Hackam DG, Redelmeier DA. Translation of research evidence from animals to humans. *J Am Med Assoc* 2006;296:1731-2.
23. Faggion CM Jr, Schmitter M, Tu YK. Assessment of replication of research evidence from animals to humans in studies on peri-implantitis therapy. *J Dent* 2009;37:737-47.
24. Higgins J, Thompson S, Deeks J, Altman D. Statistical heterogeneity in systematic reviews of clinical trials: a critical appraisal of guidelines and practice. *J Health Serv Res Policy* 2002;7:51-61.
25. Charles P, Giraudeau B, Dechartres A, Baron G, Ravaud P. Reporting of sample size calculation in randomised controlled trials: review. *Br Med J* 2009;338:b1732.
26. Montori VM, Kleinbart J, Newman TB, et al, Evidence-Based Medicine Teaching Tips Working Group. Tips for learners of evidence-based medicine: 2. Measures of precision (confidence intervals). *Can Med Assoc J* 2004;171:611-5.
27. Sheikh H, Heymann HO, Swift EJ Jr, Ziemiecki TL, Ritter AV. Effect of saliva contamination and cleansing solutions on the bond strengths of self-etch adhesives to dentin. *J Esthet Restor Dent* 2010;22:402-10.
28. Higgins JPT, Altman DG, Sterne JAC, eds. Chapter 8: Assessing risk of bias in included studies. In: Higgins JPT, Green S, eds. *Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0* (updated March 2011). The Cochrane Collaboration; 2011. Available from www.cochrane-handbook.org.
29. Manhart J, Trumm C. Marginal adaptation of an etch-and-rinse adhesive with a new type of solvent in class II cavities after artificial aging. *Clin Oral Investig* 2010;14:699-705.

30. Als-Nielsen B, Chen W, Gluud C, Kjaergard LL. Association of funding and conclusions in randomized drug trials: a reflection of treatment effect or adverse events? *J Am Med Assoc* 2003; 290:921-8.
31. Bhandari M, Busse JW, Jackowski D, et al. Association between industry funding and statistically significant pro-industry findings in medical and surgical randomized trials. *Can Med Assoc J* 2004; 170:477-80.
32. Chan AW, Hróbjartsson A, Haahr MT, Gøtzsche PC, Altman DG. Empirical evidence for selective reporting of outcomes in randomized trials: comparison of protocols to published articles. *J Am Med Assoc* 2004;291:2457-65.
33. Aschenbrenner CM, Lang R, Handel G, Behr M. Analysis of marginal adaptation and sealing to enamel and dentin of four self-adhesive resin cements. *Clin Oral Investig* 2012 Feb;16(1):191-200.
34. Gupta R. In vitro evaluation of effect of different finish lines on marginal adaptation in metal-ceramic restorations under thermo-mechanical loading. *Indian J Dent Res* 2011 Jul-Aug;22(4): 608-10.
35. Arnaud TM, de Barros Neto B, Diniz FB. Chitosan effect on dental enamel de-remineralization: an in vitro evaluation. *J Dent* 2010 Nov;38(11):848-52.
36. Behnan SM, Arruda AO, González-Cabezas C, Sohn W, Peters MC. In-vitro evaluation of various treatments to prevent demineralization next to orthodontic brackets. *Am J Orthod Dentofacial Orthop* 2010 Dec;138(6):712.e1-712.e7. discussion 712-3.
37. Catalbas B, Ercan E, Erdemir A, Gelgor IE, Zorba YO. Effects of different chlorhexidine formulations on shear bond strengths of orthodontic brackets. *Angle Orthod* 2009 Mar;79(2):312-6.
38. Inan U, Aydin C, Tunca YM, Basak F. In vitro evaluation of matched-taper single-cone obturation with a fluid filtration method. *J Can Dent Assoc* 2009 Mar;75(2):123.
39. Mohammadi Z. In vitro evaluation of apical extrusion of bacteria following use of new rotary instrumentation system. *N Y State Dent J* 2009 Apr;75(3):28-30.
40. Poggio C, Lombardini M, Dagna A, Chiesa M, Bianchi S. Protective effect on enamel demineralization of a CPP-ACP paste: an AFM in vitro study. *J Dent* 2009 Dec;37(12):949-54.
41. Murray PE, Farber RM, Namerow KN, Kuttler S, Garcia-Godoy F. Evaluation of *Morinda citrifolia* as an endodontic irrigant. *J Endod* 2008 Jan;34(1):66-70.
42. Yamada Y, Hossain M, Shimizu Y, Kimura Y, Masuda Y, Nakamura Y, Matsumoto K. Analysis of surface roughness and microleakage of fissure sealants following organic debris removal with Carisolv. *J Dent* 2008 Feb;36(2):130-7.