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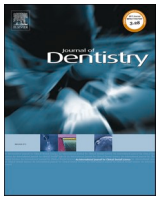

The reporting of study limitations in randomized controlled trials published in the leading dental journals: Is it sufficient?

Simone Stöckli [a], Marianna Koufatzidou [b], Jadbinder Seehra [c], Nikolaos Pandis [a,*]

[a] Department of Orthodontics and Dentofacial Orthopedics, Dental School/Medical Faculty, University of Bern, Freiburgstrasse7, CH, 3010, Bern, Switzerland
[b] Private practice, Greece
[c] Department of Orthodontics, Faculty of Dentistry, Oral & Craniofacial Sciences, King's College London, Department of Orthodontics, Floor 25, Guy's Hospital, Guy's and St Thomas NHS Foundation Trust, London, SE1 9RT, United Kingdom

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ABSTRACT

Objectives: Adequate reporting of limitations is crucial to enable clinicians to accurately interpret the clinical trial findings. This meta-epidemiological study aimed to evaluate whether study limitations are reported in full-text articles of randomized controlled trials (RCTs) published in the leading dental journals. Associations between the trial characteristics and the reporting of limitations were also explored.
Methods: RCTs published between 1st January and 31st December in the years 2011, 2016 and 2021 were identified from the 12 high impact factor dental journals (general and specialty). RCT characteristics were extracted, and reporting of limitations was recorded for the selected studies. Descriptive statistics were calculated for trial and limitations related characteristics. Univariable ordinal logistic regression models were fit to explore univariable associations between trial characteristics and reporting of limitations.
Results: Two hundred and sixty-seven trials were included and analyzed. Most RCTs were published in 2021 (40.8%), had authors based in Europe (50.2%), did not have a statistician involved (88.8%) and assessed a procedure/method intervention type (40.5%). The reporting of trial limitations was generally sub-optimal. More recent trials and studies with a published protocol were associated with better reporting of limitations. The type of journal was a significant predictor for limitation reporting.
Conclusions: Within this study, the clear reporting of study limitations in the manuscripts of dental RCTs is sub-optimal and requires improvement.
Clinical significance: The reporting of limitations should not be viewed as a weakness of a trial but due diligence, so clinicians can fully interpret the impact of these limitations on both the validity and generalisability of the results.

1. Introduction

Clinical studies such as Randomized Clinical Trials (RCTs) unavoidably may have limitations, which can influence the outcomes and conclusions of the research findings [1]. It is important to understand those limitations in order to interpret the research findings accurately and to place them in the correct context. The reporting of study limitations allows clinicians to assess potential errors and the validity and generalizability of the trial findings in order to implement them correctly in a clinical setting [2,3]. Additionally, the reporting of limitations can provide information regarding further research requirements in the respective field and possibilities for improvement of future research [1,2,4]. The reporting of study limitations is also a prerequisite of the consolidated standards of reporting trials checklist for randomized controlled trials (CONSORT) [5,6].

However, authors of clinical studies published within the medical field often fail to discuss potential study limitations and their possible influence on the interpretation of the presented results [4]. Reasons that may explain the lack of reporting of study limitations can be attributed to both the author of the study or journal. For example, a lack of awareness by authors of the relevance of certain limitations of their trial could preclude full reporting. The latter could also be influenced by the perception that transparency regarding reporting of limitations could negatively influence the acceptance of the article. At the journal level,

* Corresponding author at: Professor Nikolaos Pandis, Department of Orthodontics and Dentofacial Orthopedics, Dental School/Medical Faculty, University of Bern, Freiburgstrasse7, CH-3010, Bern, Switzerland.
E-mail address: npandis@yahoo.com (N. Pandis).

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word limitations imposed on article manuscripts could hinder the full reporting of study limitations by authors [1–3].

Within the literature, the failure of authors to sufficiently report study limitations has been highlighted [2,7,8]. In an assessment of orthodontic RCTs published in leading orthodontic journals, the clear reporting of trial limitations was deficient across several areas. Trials published in journals with suggested or mandatory instructions regarding a limitations section were more likely to report limitations than trials published in journals without any suggestion[7]. To our knowledge a baseline assessment of the reporting of limitations in RCTs published in general and specialty dental journals has not been previously undertaken. On this basis, the aim of this current study was to assess against a criterion developed from previous research [2,4], the reporting of study limitations in both abstracts and full-text articles of RCTs published in the leading dental journals. On an exploratory basis, associations between the reporting of limitations and study characteristics were assessed.

2. Material and methods

2.1. Eligibility criteria

In this review, nine leading dental journals representing the dental specialties (cariology, endodontology, periodontology, oral surgery/oral pathology, implantology, orthodontics, reconstructive dentistry and pediatric dentistry) and three general journals with the highest impact factor (2020) were included. RCTs published between 1st January to 31st December in each of the three years (2011, 2016 and 2021) were identified in the following journals: Journal of Clinical Periodontology (JCP) (IF, 8.728), Journal of Dental Research (JDR) (IF, 6.116), Clinical Oral Implants Research (COIR) (IF, 5.977), International Endodontic Journal (IEJ) (IF, 5.264), Journal of Prosthodontic Research (JPR) (IF, 4.642), Journal of Dentistry (JD) (IF, 4.379), Journal of Oral Pathology and Medicine (JOPM) (IF, 4.253), Caries Research (CR) (IF, 4.056), Journal of the American Dental Association (JADA) (IF, 3.634), International Journal of Paediatric Dentistry (IJPD) (IF, 3.455), European Journal of Orthodontics (EJO) (IF, 3.075) and International Journal of Oral and Maxillofacial Surgery (IJOMS) (IF, 2.789).

2.1.1. Selection and data extraction

Two authors (SS and MK) independently carried out the screening of titles and abstracts and data extraction from the included full text articles. Disagreements were discussed between both authors and resolved by a third author (NP) if required. A standardized and pre piloted data extraction form (Microsoft Excel) was employed. To ensure consistency in the interpretation of the trial variables and data extracted between both authors (SS and MK), an initial pilot calibration of ten RCTs was undertaken. 100% agreement between both authors (SS and MK) was achieved.

At the trial level the following characteristics were extracted: Journal title, trial design, year of publication (2011,2016 and 2021), journal impact factor, the continent of the corresponding author (Americas, Asia and others, and Europe), number of authors (1-3, 4-5, >6), the statistical significance of primary outcome (yes, no, or no information), ethical approval (yes or no), protocol registration (yes, no, or no information provided), trial design (parallel or split-mouth), statistical analysis undertaken by a statistician (yes or no), intervention type (material/devices, procedure/method, lifestyle, timing of procedure, drugs, behavioral/psychological, restorations and others), center (single, multi or no information), funding (university/hospital, company, self-funded, government, foundation, private dental clinic, no funding, no information provided or a combination of sources) and disclosure of any conflict of interest (yes, no, or no information provided).

In order to assess the reporting of limitations in each abstract and full-text RCT, the following criteria were developed from previously published literature [2,4]: reporting of limitations in abstract (adequate, no, or partial), reporting of limitations in the manuscript discussion section (adequate, no, or partial), a systematic approach (the examination of study limitations at each stage) in the reporting of limitations (adequate, no or partial), explanation of the implication of each limitation (adequate, no, or partial), reporting of steps taken to minimize limitations (adequate, no or partial), reporting of other methods to avoid limitations and reasons for not being chosen (adequate, no or partial) and suggestion of possible methods to avoid the reported limitations in future trials (adequate, no or partial).

Consistent with previous literature [2,4,7], to optimize the sensitivity of identifying the reporting of study limitations, the pdf article of each trial was screened for the following terms: limitation, caveat, cautio*, shortcoming(s), drawback(s) and weakness(es). Furthermore, at the journal level, submission instructions relating to the description of limitations in the article were classified as: mandatory limitation section, suggestion to include, or no reference of limitations.

2.2. Statistical analysis

Descriptive statistics were calculated for general study and limitations related characteristics. Univariable ordinal logistic regression models were fit to explore univariable associations between study characteristics (publication year, continent of corresponding author, number of authors, protocol registration, ethical approval, journal impact factor) and reporting status in the main manuscript (no reporting, partial reporting, adequate reporting). A two-tailed p-value of 0.05 was considered statistically significant. All analyses were performed using Stata statistical software version 17 (StataCorp, College Station, TX, USA) and R Software version 4.0.3 (R Foundation for Statistical Computing, Vienna, Austria).

3. Results

A total of 267 RCTs were analyzed. The median impact factor was 5.165 (interquartile range: 4.024, min: 2.202, max:7.478). The number of published RCTs varied by year with the highest number published in 2021 (40.8%). The corresponding authors were mostly based in Europe (50.2%), with the number of authors often above 6 (51.7%). A parallel trial design was often employed (84.6%). However, a statistician was not commonly used (88.8%) The most common intervention type was the assessment of procedure/method (40.5%). The majority of the trials were single centered (80.1%) and were funded by a company (18.7%). In most trials, no conflict of interest was reported (67%), with 61.8% reporting statistically significant results. Almost all trials reported obtaining ethical approval (96.2%) with only 40.4% reporting a study protocol (Table 1).

Reporting of study limitations in the abstract was rarely evident (8.6%). In the full-text article adequate reporting of limitations was also uncommon (27.0%). When limitations were reported, the following were usually not described: a systematic approach (72.3%), the implication of each limitation discussed (64%), steps taken to minimize limitations reported (78.7%), reporting of other methods to avoid limitations and reasons for not being chosen discussed (85.8%) and suggestion of possible methods to avoid the reported limitations in future studies (84.7%). At the journal level, in 20.2% of journals there was no reference to reporting of limitations in the submission guidelines (IEJ, IJOMS and IJPD). The following journals: JADA, CR, JCP, JDR, JD, JOPM, JPR and COIR suggest reporting limitations in the author guidelines on their websites. EJO requires the reporting of a mandatory limitation section for all studies (Table 2).

The univariable analyses detected an association between year of publication, study protocol and journal reporting of study limitations. Trials published in 2021 (OR 8,53; 95% CI 4.43 to 16.42; $p<0.001$) and study protocol registration (OR 3,04; 95% CI 1.90 to 4.87; $p<0.001$), were more likely to better report on limitations in the main manuscript (Table 3). The type of journal was a significant predictor for limitation

Table 1
Characteristics of included RCTs.

Variables	*n (%)*
Journal	
Caries Research	11 (4.1)
European Journal of Orthodontics	31 (11.6)
International Endodontic Journal	19 (7.1)
International Journal of Oral and Maxillofacial Surgery	30 (11.2)
International Journal of Pediatric Dentistry	5 (1.9)
Journal of Clinical Periodontology	69 (25.8)
Journal of Dental Research	14 (5.2)
Journal of Dentistry	29 (10.9)
Journal of Oral Pathology and Medicine	3 (1.1)
Journal of Prosthodontic Research	1 (0.4)
Journal of the American Dental Association	6 (2.3)
Clinical Oral Implants Research	49 (18.4)
Year	
2011	73 (27.4)
2016	85 (31.8)
2021	109 (40.8)
Continent	
Americas	50 (18.7)
Asia and others	83 (31.1)
Europe	134 (50.2)
Number of Authors	
1 to 3	41 (15.3)
4 to 5	88 (33)
>6	138 (51.7)
Trial Design	
Parallel	226 (84.6)
Split-mouth	41 (15.4)
Statistician	
No	237 (88.8)
Yes	30 (11.2)
Intervention Type	
Materials/devices	78 (29.2)
Procedure/method (surgical, incl. Implants/implant parts)	108 (40.5)
Lifestyle	9 (3.4)
Timing of Procedure	4 (1.5)
Drugs (pharmacological)	43 (16.1)
Behavioral/psychological	3 (1.1)
Restorations	16 (6)
Others	6 (2.2)
Single/multicenter	
Single center	214 (80.1)
Multicenter	41 (15.4)
No information	12 (4.5)
Funding	
University/hospital	29 (10)
Company	50 (18.7)
Self-funded	22 (8.2)
Government	22 (9.2)
Foundation	50 (18.7)
No funding	34 (12.7)
No information	44 (16.5)
Private dental clinic	1 (0.4)
Combinations of the above	15 (5.6)
Conflict of Interest	
No	179 (67)
Yes	24 (9)
No information	64 (24)
Statistical Significance	
No	102 (37.8)
Yes	165 (61.8)
No information	1 (0.4)
Ethical Approval	
No	159 (59.6)
Yes	108 (40.4)
Protocol	
No	159 (59.6)
Yes	108 (40.4)
Total	**267 (100)**

Table 2
Limitations-related to descriptives of included RCTs.

Limitations	*n (%)*
Limitations in abstract	
No reporting	244 (91.4)
Partial reporting	22 (8.2)
Adequate reporting	1 (0.4)
Limitations in the manuscript	
No reporting	130 (48.7)
Partial reporting	65 (24.3)
Adequate reporting	72 (27)
Systematic approach to limitations	
No reporting	193 (72.3)
Partial reporting	52 (19.5)
Adequate reporting	22 (8.2)
Implication of each limitation	
No reporting	171 (64.0)
Partial reporting	41 (15.4)
Adequate reporting	55 (20.6)
Steps to minimize the limitations	
No reporting	210 (78.7)
Partial reporting	30 (11.2)
Adequate reporting	27 (10.1)
Other methods to avoid/minimize limitations but were not used	
No reporting	229 (85.8)
Partial reporting	17 (6.4)
Adequate reporting	21 (7.8)
Possible ways to avoid/minimize limitations	
No reporting	226 (84.7)
Partial reporting	19 (7.1)
Adequate reporting	22 (8.2)
Journal submission instruction	
No reference to limitations	54 (20.2)
Suggestion to include limitations	182 (68.2)
Mandatory limitations section	31 (11.6)
Total	**267 (100)**

Table 3
Odds ratio, 95% confidence intervals, and P values for the effect of year of publication, continent of authorship, number of authors, study protocol registration, presence of ethical approval and journal impact factor on reporting of limitations.

Predictor	*Odds ratio*	*P value*	*95% Confidence interval*
Year			
2011	Reference		
2016	3.11	0.001	1.58 to 6.11
2021	8.53	<0.001	4.43 to 16.42
Continent			
Americas	Reference		
Asia and others	0.87	0.69	0.45 to 1.71
Europe	1.43	0.25	0.77 to 2.64
Number of Authors			
1 to 3	Reference		
4 to 6	1.14	0.69	0.59 to 2.239
>6	1.84	0.10	0.89 to 3.82
Protocol			
No	Reference		
Yes	3.04	<0.001	1.90 to 4.87
Ethical Approval			
No	Reference		
Yes	2.65	0.16	0.69 to 10.19
Impact Factor (per unit)	0.91	0.16	0.80 to 1.04

reporting (p=0.02) with EJO showing the highest probability of reporting study limitations adequately (Fig. 1).

4. Discussion

It is important that trial authors report limitations of their study, which could affect the interpretation of the validity and generalisability of their reported results. The current study has highlighted that the reporting of limitations in dental RCTs is sub-optimal. Areas identified

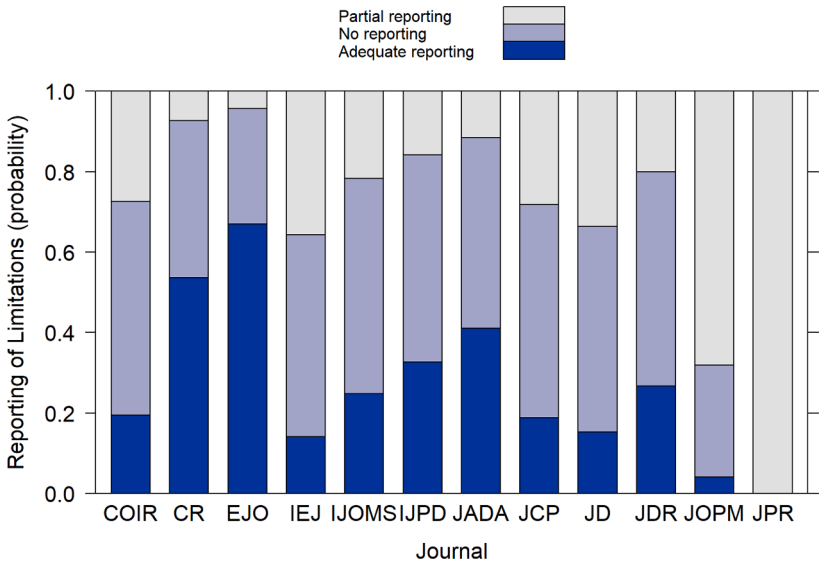

Fig. 1. Predicted probabilities calculated from the univariable logistic regression of reporting limitations in the manuscript by journal.

that require improvement include: a report of limitations in the abstract, a systematic approach to reporting limitations, the implication of each limitation discussed, steps taken to minimize limitations reported, reporting of other methods to avoid limitations and reasons for not being chosen discussed and suggestion of possible methods to avoid the reported limitations in future trials. An association between the year of publication and study protocol registration and reporting of trial limitations was evident. Trials published in 2021 were more likely to report trial limitations compared to those published in 2016 and 2011. Additionally, the type of a journal was a significant predictor for trial limitation reporting.

The reported findings mirror the results of previous investigations [2, 7]. In the assessment of orthodontic RCTs published in five leading orthodontic journals published between 2011-2021, a report of limitations in the abstract, a systematic approach to reporting limitations, the implication of each limitation discussed, steps taken to minimize limitations reported, reporting of other methods to avoid limitations and reasons for not being chosen discussed and suggestion of possible methods to avoid the reported limitations in future trials were infrequently reported [7]. In a review of studies published in six most cited journals and two open access journals less than 20% used at least one word referring to limitations of the presented work with only 1% of studies referring to limitations in the abstract section[2].

The type of journal was a significant predictor for trial limitation reporting. This is consistent with previous literature [7]. It can be expected the presence of suggested or mandatory instructions for trial limitation reporting within journal instructions would influence this outcome. Of the twelve included journals, in three journals there was no reference to reporting of limitations in the submission guidelines. In eight journals the reporting limitations was suggested in the author guidelines on the respective websites. Predictably, the only journal (EJO) requiring the reporting of a mandatory limitation section for all studies had a higher probability of reporting study limitations adequately.

It is not uncommon that a failure to discuss how a limitation could affect the trial results and conclusions is present in the study manuscripts [2]. Study weakness related to methodology and generalisability are not routinely reported by authors with limitations commonly omitted [9]. However, when limitations are reported they tend to conflict with the contributing authors' opinions [9]. For instance, in a trial investigating the efficacy of ondansetron in patients with an eating disorder, weaknesses published in the manuscript were self-reporting of symptoms and the risk of higher motivation to succeed among study participants. In contrast when the study contributors were directly questioned, weakness cited were small sample size, limited follow-up period and poor generalisability [9].

The apparent reluctance to report study limitations by authors could be attributed to the belief that the chances of article acceptance and publication are higher if limitations are omitted [1,4]. However, the inclusion of the term "limitation" in both abstracts and full-text articles does not necessarily mean they are reported in the correct context [2]. There is a tendency for authors to downplay the presence of limitations and incorporate terminology which highlights the importance of their work [2]. For instance, both estimates of random and systematic error are reported without discussion of the implication of these on the reported findings and generalisability of any inferences [2]. A lack of clear reporting of limitations can be dictated by the editorial policy of the journal, which may not advocate the use of specific sub-headings.

To allow clinicians to interpret limitations within the study which can impact their interpretation of the results and generalisability of the findings, the clear and transparent reporting of study limitations manuscripts (abstract and full text) of articles is encouraged [1,2,4]. Identification of study weaknesses can also be beneficial to inform both future research hypothesis and study designs [2]. So, what measures can be implemented to improve trial limitation reporting? A key stakeholder in this process should be the authors of studies who should be able to identify limitations and not just the variation in random errors, which could influence the direction of the reported effects [4]. However, acknowledging limitations can be a subjective process [2,4]. To circumvent this, guidance to improve the reporting of study limitations is suggested in Table 4. The discussion section of articles is considered the weakest part of the paper [10], with often a lack of appraisal of the methods and results present [10]. Indeed, as a result of biased presentation of results, the inferences drawn can differ independently [11]. The use of a structured discussion section with sub-headings (strengths and weaknesses in relation to other studies, study question, study design, data collection, analysis and interpretation and differences in results compared to previous studies) can also be beneficial [9,12]

An improvement in both journal and peer-review practice is also required to facilitate better reporting of study limitations [9]. This is highlighted by the fact that in this study, in a quarter of journals, there was no reference to the reporting of limitations in the manuscript in the journal submission instructions. This is also a common finding in the medical literature where authors are encouraged to highlight importance, novelty, and lack of error rather than limitations [2]. Journal editors should enforce the clear reporting of limitations in manuscripts

Table 4
Recommendations to improve the reporting of study limitations [4].

Section of manuscript	Recommendations
Abstract	At the end of the results section add one sentence highlighting the one or two main limitations of the study
Discussion (Full text)	Report on all limitations that may have affected the quality of the evidence being presented, including aspects of study design and implementation. Give the authors' view on how the limitations impact on the quality of the evidence and discuss the direction and magnitude of bias Do not restrict the discussion of limitations to aspects of internal validity and discuss where the limits of applicability of the results may lie Discuss the strengths of the study that may counterbalance or outweigh (some of) the limitations. Provide suggestions for future research specifically overcoming the limitations of the current study. Provide suggestions for future research specifically overcoming the limitations of the current study.

and in certain cases make a final editorial decision based on the thoroughness with which these are discussed [4]. To facilitate this, instructions and guidance for peer reviewers regarding the reporting of limitations should be provided. It is suggested article word limits also hinder the reporting of study limitations [3,9]. This can be addressed by increasing article word limits [9] and considering online publication which may have less restrictions regarding space compared to print journals [9].

RCTs were sourced from the websites of each journal. As hand-searching of each printed journal edition was not performed this may have resulted in a degree of selection bias attributed to non-identification of potentially relevant trials. Methods used to reduce other sources of bias include screening, selection of trials and data extraction undertaken in duplicate and independently and pre-piloting and calibration prior to data extraction. Almost two hundred and seventy trials representing the various dental specialities were assessed in this study, which provides a baseline indication of the issue of reporting trial limitations. In some of the journals, like the JPR and JOPM, the number of included studies was low, however, this does not affect the overall conclusion. The findings of this study should be weighed against the fact that the reporting of limitations can be a subjective process. To limit any subjective judgements, a criterion based on published literature in the field of reporting study limitations [2,4,7] was used. However, this criterion only allowed an assessment of the reporting of limitations rather than whether the authors of a trial have fully understood their trial's limitations. As part of the study methodology, RCTs were selected from three calendar years. Up to date trials published in 2022-23 were not included. However, the selected time periods in this investigation allowed an assessment of the trends of reporting limitations in RCTs, following the introduction of the updated CONSORT guidelines in 2010 [6].

5. Conclusions

Within this study, the clear reporting of study limitations in the manuscripts of dental RCTs is sub-optimal. The reporting of limitations should not be viewed as a weakness of a trial but due diligence, so clinicians can fully interpret the impact of these limitations on both the validity and generalisability of the results.

Declaration of Competing Interest

The authors received no financial support and declare no potential conflicts of interest with respect to the authorship and/or publication of this article.

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