Critical analysis of the reporting quality of randomized trials within Endodontics using the Preferred Reporting Items for RAndomized Trials in Endodontics (PRIRATE) 2020 quality standard checklist.

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Abstract

Aim To critically evaluate the reporting quality of a random sample of clinical trials published in Endodontics against the PRIRATE 2020 checklist and to analyse the association between the quality of reported trials and a variety of parameters.

Methodology Fifty randomized clinical trials relating to Endodontics were randomly selected from the PubMed database from 2015 to 2019 and evaluated by two independent reviewers. For each trial, a score of "1" was awarded when it fully reported each item in the PRIRATE guidelines whereas a score of "0" was awarded when an item was not reported; when the item was reported inadequately a score of "0.5" was awarded. For the items that were not relevant to the trial, "Not Applicable (NA)" was given. Based on the interquartile range of the overall scores received, trials were categorised into "Low" (0-58.4%), "Moderate" (58.5-72.8%) and "High" (72.9-100%) quality. The associations between characteristics and quality of clinical trials were investigated. Descriptive statistics, frequency analysis and percentage analyses were used to describe the data. To determine the significance of categorical data, the Chi-Square test was used. The probability value 0.05 was considered as the level of significance.

Results Based on the overall scores, 13 (26%), 25(50%) and 12 (24%) of the reports of clinical trials were categorized as "High", "Moderate" and "Low" quality, respectively. Three items (1b, 6d, 11e) were adequately reported in all manuscripts whilst two items (5k, 5m) were scored "NA" in all the reports. The reports published from Europe had a significantly greater percentage of "High" quality scores, compared to Asia, Middle East, North America and South America (p=0.0002). The "High" quality reports were published significantly more often in impact factor journals (p=0.045). Reports of clinical trials published in journals that adhered to the CONSORT guidelines had significantly more "High" scores compared to those that did not (p=0.008). Clinical trials with protocols registered *a priori* had a significantly

greater percentage of “High” scores compared to the trials that were not registered in advance (p=0.003). No significant difference occurred between the quality of clinical trials and the number of authors, journal (Endodontic specialty vs Non-Endodontic specialty) or year of publication.

Conclusions Reports of randomized clinical trials published in the speciality of Endodontics had a substantial number of deficiencies. To create high quality reports of clinical trials, authors should comply with the PRIRATE 2020 guidelines.

Critical analysis of the reporting quality of randomized clinical trials within Endodontics using the Preferred Reporting Items for RAndomized Trials in Endodontics (PRIRATE) 2020 quality standard checklist

Introduction

Randomized clinical trials are the gold standard study design for the evaluation of health interventions and are acknowledged as the highest level of primary evidence on which to base clinical decision-making (Burns *et al.* 2011). On the other hand, incomplete or inaccurate reporting of randomized clinical trials casts doubt on the reliability of the evidence being described, the quality of the conclusions and the inferences that can be derived (MacPherson *et al.* 2010). The quality of randomized controlled trials has been reported as being sub-optimal across several specialties within Medicine (Kim *et al*. 2014, Tardy *et al*. 2018, Rikos *et al*. 2019). Similarly, an evaluation of randomized clinical trials across several Dental specialties, highlighted multiple reporting inadequacies and recommended that this was a priority area for improvement (Saltaji *et al*. 2017).

The Consolidated Standards of Reporting Trials (CONSORT) statement was developed to enhance the quality of reporting randomized clinical trials, with many journals requiring that randomized controlled trials submitted for publication conformed to its recommendations. The CONSORT statement is essentially a checklist made up of 6 sections: Title and Abstract, Introduction, Methods, Results, Discussion, and other information (Moher *et al*. 2012), that are divided into 25 individual items. It is also accompanied by a flowchart highlighting the journey of participants through the trial.

Editorials published in the two leading Endodontic journals reinforces the importance of adherence to the CONSORT guidelines (Newcombe 2004, Hargreaves 2005), which helps the clinical trialist while developing the study design, conducting the clinical trial, analyzing the data and preparing the manuscript for publication (Hargreaves 2005). Despite recommendations and requirements provided by journals to the authors to adhere to the CONSORT statement, the reporting quality of

randomized trials published in the field of Endodontics has been reported to be poor (Lucena *et al*. 2017). Consequently, in an attempt to enhance the quality of randomized clinical trials published in the field of Endodontics, the Preferred Reporting Items for RAndomized Trials in Endodontics (PRIRATE) 2020 guidelines were developed through a validated consensus process (Nagendrababu *et al*. 2020). The items in the checklist were adapted and modified from the CONSORT statement (Moher *et al*. 2012) and the Clinical and Laboratory Images in Publications (CLIP) principles (Lang *et al*. 2012). The final PRIRATE checklist consists of 58 individual items under 11 sections including Title, Keywords, Abstract, Introduction, Methods, Results, Discussion, Conclusion, Funding details, Conflict of interest and the Quality of images (Nagendrababu *et al*. 2020). The PRIRATE 2020 guidelines should not only act as a template for authors when reporting randomized trials in Endodontics, but also provide journal editors and reviewers with a checklist against which they can evaluate the quality of the submitted manuscripts. As part of the process to enhance the quality of randomized controlled trial reports, it is necessary to determine how closely published randomized clinical trials adhere to the PRIRATE checklist and in addition, evaluate the association between their characteristics with the recently established reporting guidelines. Importantly, an assessment of the quality of randomized trials published in Endodontics will provide information on the items that are commonly not reported or inadequately described, which should translate into authors producing better quality reports, and eventually lead to improved clinical decision-making.

This study aims (i) to critically analyse the reporting quality of randomized trials published in Endodontics measured against the PRIRATE 2020 guidelines, and (ii) to analyse the association between the quality of reported randomized trials and the number of authors, country, journals, year of publication, Impact Factor of journal, whether the journal adhered to the CONSORT guidelines and whether the protocol had been registered in advance in a clinical trial registry.

Methods

Selection of randomized trials

Randomized clinical trials relating to Endodontics were retrieved from the PubMed database over a five-year period from January 2015 to December 2019 using the following search ((((((("randomized controlled trial") OR "randomised controlled trial") OR "clinical trial") OR "randomized clinical trial") OR "randomised clinical trial") OR "controlled clinical trial")) AND ((((((pulp) OR "root canal") OR endod*) OR "periapical surgery") OR "periradicular surgery") OR apicoectomy OR apicectomy). The publication details of each clinical trial identified from the PubMed database were exported to an Excel spreadsheet and assigned a random number to four decimal places ranging between 0 and 1. The generated random numbers were sorted in increasing order, thus randomly rearranging the retrieved publications. Thereafter, the first 50 eligible clinical trials were screened by title and abstract independently by two reviewers based on the inclusion criteria. If a selected clinical trial did not fall within the inclusion criteria the next clinical trial in the random sequence was used to replace it, until a total of 50 clinical trials were selected (n=50). Disagreements between the reviewers during clinical trial selection were resolved by a third reviewer.

Selection criteria

Randomized clinical trials related to Endodontics and published in English were included. No restriction was placed on the journal of publication. Case series, case reports, retrospective cohort studies, animal studies, laboratory-based studies and reviews were excluded.

Data extraction

A data extraction sheet was created that included: name of the first author, country of corresponding author, year the report was published, number of authors, name of the journal, Impact Factor of journal for the year in which the trial was published, whether the journal adhered to the CONSORT guidelines (yes/no) and whether the study protocol had been registered *a priori* in a clinical trial registry. Data was extracted independently by two reviewers and any disagreements between them were resolved by an independent third reviewer.

Quality assessment process using the PRIRATE 2020 checklist

Pilot study: Three out of the 50 selected randomized trials were randomly chosen and the initial scoring system piloted by two reviewers (AJ, JJ) with uncertainties and disagreements being resolved by team members (VN/HD/PD). As a result of the pilot testing, the definitive scoring system was agreed.

Main study: To assess the quality of the reports of clinical trials, the adherence of the manuscripts to each of the 58 items in the PRIRATE reporting guidelines (Nagendrababu *et al.* 2020) was scored. A score of "1" was allocated to each item when the manuscript fully satisfied the relevant criteria whereas a score of "0" was allocated when the item was not reported; when the item was reported inadequately a score of "0.5" was allocated.

For several items, authors were obliged to make an explicit statement that the item did not apply, e.g. Item 5b (Methods (Trial Design) – *Changes to the methodology after the trial commenced (such as eligibility criteria) must be provided along with detailed explanations*. For such items, to receive a score of "1", the authors should have mentioned explicitly there was "*no deviation/change in the methodology after the trial commenced*". If this was NOT mentioned, a score of "0" was awarded. For several other items that were not relevant to the study, "Not Applicable (NA)" was the score awarded, e.g. Item 5k (Methods (Outcomes measures) – *If primary or secondary outcomes are to be regarded as surrogate outcomes, the rationale and empirical support for the connection between surrogate(s) and the outcome(s) of clinical relevance must be provided surrogate outcomes*. To calculate the final score for each clinical trial, items awarded "NA" were excluded, with the final score being based only on the applicable items.

The final PRIRATE score for each clinical trial was calculated by adding up the assigned scores, with a total possible score of 58 (minus any "NA" awards). Based on the scores allocated to each manuscript, they were divided into three groups: low

quality (up to the 25th percentile), moderate quality (the interquartile range), and high quality (the 75th percentile and above).

Descriptive analysis and visualization

A bibliometric analysis was carried out to describe the collection of 50 selected randomized trials in terms of authorship, geographical location, journal, topics covered, and the impact factor of the journal. Depending on the completeness of the existing bibliographic details, the complete metadata of each trial was exported in plain text or BibTeX format from Web of Science, Scopus, and PubMed and imported into the R environment for statistical computing and graphics (R Core Team 2016). Due to differences between source databases and some missing information, records downloaded from PubMed were manually supplemented (e.g. affiliations of corresponding authors). To unify terms and to remove transcription or indexing errors, names of authors, institutions, and countries were also manually refined and normalized. All institutional affiliations were normalized and included on a macro level, such as universities and research centres, while micro-organisations (i.e. individual departments or research units) were discarded. Randomized trials originating from England, and Wales were recategorized as being from the United Kingdom.

A descriptive analysis of the 50 reports, as well as network extraction, were performed using R version 4.0.2 (R Core Team, Vienna, Austria) and the R package *bibliometrix* version 3.0.2 (Aria & Cuccurullo 2017). The total number of contributing authors and the frequency of their appearances (the total number of co-authors) were recorded in detail. The contribution of each author was assessed by applying the full and fractionalised counting method (Abramo *et al*. 2013), giving each contributing author a score of 1 (e.g. four authors each receive one full credit) or a fraction of one credit (e.g. four authors receive one-quarter of a credit), respectively. The “Authors per paper Index” was calculated as the ratio between the total number of authors and the total number of randomized trials, while the “Co-Authors per paper Index” was determined as the ratio between the total number of co-authors and the total number of trials. The “Collaboration Index”, that is the mean number of authors

per joint trial, was calculated as the total number of authors of multi-authored trials divided by the total number of multi-authored trials (Elango & Rajendran 2012, Koseoglu 2016). The collaboration analysis was used to identify co-authorships and determine networks of collaborating authors, institutions, and countries. Besides the "Impact Factor of the journal" in which the trial was published, the significance of each trial was measured by counting the number of times it had been cited by other publications. Citation counts for each evaluated randomized trial were retrieved from the Web of Science Core Collection (Times Cited Count). To identify and present the topical areas of the 50 selected trials, keyword analysis was performed based on a frequency distribution of keywords supplied by authors. Bibliometric networks were graphically visualized using the R packages *bibliometrix* version 3.0.2 (Aria & Cuccurullo 2017) and *wordcloud2* version 0.2.1. Geomapping of the evaluated randomized trials by country was achieved using the R package *rworldmap* version 1.3.6 (South 2011).

Association between characteristics and quality of clinical trials

The following characteristics were investigated:

1. Number of authors (1-2 *vs* 3-4 *vs* 5-6 *vs* >6),

2. Geographical source of reports in terms of the continent of the corresponding author (North America and Canada *vs* South America *vs* Europe *vs* Asia *vs* Oceania *vs* Middle East),

3. Journal (Endodontic specialty *vs* Non-Endodontic specialty journals),

4. Published in a journal with an Impact Factor (yes/no),

5. Year of publication (2015 *vs* 2016 *vs* 2017 *vs* 2018 *vs* 2019),

6. Journal adhered to the CONSORT guidelines (yes/no), and

7. Protocol had been registered in advance in a clinical trials registry (yes/no).

Statistical analysis

The collected data were analysed with SPSS statistics software (version 23.0; IBM Corp, Armonk, NY, USA). To describe the data, descriptive statistics, frequency analysis and percentage analysis were used. The Chi-Square test was used to determine the significance of categorical data. The probability value 0.05 was considered as the level of significance.

Results

Characteristics of included trials

Table 1 shows the characteristics of the studies entered in the analysis, including first author, country of principle affiliation of the corresponding author, year published, number of authors, journal name, Impact Factor for the year in which the trial was published, whether the journal adhered to the CONSORT guidelines (Yes/No) and whether the protocol had been registered *a priori* in a clinical trials registry. The literature search yielded 827 articles, which fitted the inclusion criteria, from this 50 clinical trials were randomly selected. Supplemental Table 1 shows the list of 50 trials included. Supplemental Table 2 demonstrates the Impact factor of the journal for the year in which the clinical trial was published, the impact factor of the journal based on the current release of Journal Citation Reports (JCRs) (2019), its five-year impact factor and data on the quartile ranking and JCR category for the 50 trials. In addition to journals with an impact factor, journals that are not indexed on the JCR list also appear in the present study. Among them, three are indexed in the Clarivate Analytics' Emerging Sources Citation Index and two indexed in MEDLINE.

The reports of the 50 randomized clinical trials were authored or co-authored by 220 individuals and published in 25 journals between 2015-2019 (Table 2). The number of randomized clinical trials published in 2015, 2016, 2017, 2018 and 2019 were 8, 5, 13, 12 and 12 respectively. Of the 50 randomized clinical trials, one (Botero *et al*. 2017) was published in the supplement of the *Journal of Endodontics* as a 'proceedings' paper (Proceedings of the Pulp Biology and Regeneration Group

Satellite Meeting: Dental Regenerative Medicine and Functional Dental Longevity: June 26-28, 2016; Nagoya, Japan. Edited by Anibal Diogenes). The 50 trials were published in 25 journals (Table 3) with 36 being published in the most relevant journals, referenced in the JCR.

Among the included trials, the most productive individual authors are presented using a full counting, as well as a fractional counting method (Table 4). The ranking of authors were based on their total (TRCTs) and adjusted frequency (TRCTsF) that reflects randomized clinical trials with multiple authors (for instance, if a randomized clinical trial is published by two authors, each receives half a credit). The top four most prolific authors who appear in three randomized clinical trials are Beck M, Drum M, Nusstein J, and Reader A, affiliated to Ohio State University, USA, while their fractionalised frequency is equal to 0.51 when the number of co-authors is taken into account. The most productive author with a fractionalised frequency of 0.833 is Arslan H (Ataturk University, Turkey), followed by Sangwan P (College in Rohtak, India), Topçuoğlu G (Oral and Dental Health Hospital, Kayseri, Turkey; Erciyes University, Turkey), and Topçuoğlu HS (Erciyes University, Turkey), whose fractionalised frequency is 0.533.

The authors were associated with 84 institutions and the 20 most frequently stated affiliations are presented in Table 5. The 50 trials were published by authors from 22 countries or regions (Table 6). Figure 1 provides a representation of frequently used keywords supplied by authors (as a word cloud), where the size of the displayed keyword is proportional to its frequency (Interactive version – Supplementary Figure 1). Given the size of the keyword presented in the figure, such as postoperative pain, it is clear that it is an important keyword that most often appears among the keywords used, and that a large number of the studies dealt with postoperative pain following root canal treatment. The efficacy of several local anaesthetics, such as Articaine or Lidocaine, and various injection techniques (e.g. IANB, Gow-Gates, Vazirani-Akinosi) were also highly prevalent topics (n=11, 22%). Furthermore, the keyword analysis also highlighted regenerative endodontics, bacterial reduction in canals, and the efficacy of calcium hydroxide and mineral

trioxide aggregate (MTA) in apexification, as topics covered within the trials (n=9, 18%).

Figure 2 shows the contribution of each country (Figure 2a - country of the corresponding author based on the total number of studies; Figure 2b – country of each author based on the frequency of stated institutions). A full collaboration network among countries is presented in Figure 3. Most of the clinical trials (72%) were conducted by authors from a single country, with India (n=8) and Turkey (n=7) followed by the USA (n=5) and Iran (n=5) being the countries with the largest number of trials in the selection. Thirteen trials were the result of international cooperation between two countries, mostly USA and Iran (n=4), while only one trial reflected cooperation between the authors of three different countries, namely the USA, UK and Iran (Ghabraei *et al*. 2019). The relationship among the most prolific countries, authors and journals in which clinical trials were published are illustrated in a Sankey plot (Figure 4) (Interactive version – Supplementary Figure 2). The line in the plot connecting a country and author represents the frequency of institutions of all co-authors, while the line between an author and a journal reflects the number of randomized clinical trials published by that author in that journal. The top of Figure 4 reveals that the four most prolific authors were Beck M, Drum M, Nusstein J, and Reader A, affiliated to Ohio State University, USA who published trials in the *Journal of Endodontics.*

Quality of included trials assessed using the PRIRATE 2020 guidelines

The overall percentage scores for trials analysed against the PRIRATE 2020 guidelines are shown in Table1. A graphical representation of the overall results related to the individual PRIRATE items are provided in Figure 5. Among 50 clinical trials, one (Ali *et al.* 2018) published in the *Journal of Dental Research* had the greatest (85%) overall percentage score, followed by Rajasekharan *et al.* (2017) published in the *International Endodontic Journal* (82%). Based on the interquartile range (IQR) of the overall scores, 13 (26%), 25 (50%) and 12 (24%) of the 50 randomized clinical trials were categorized as “High”, “Moderate” and “Low” quality, respectively.

The scores for individual PRIRATE items is presented in Table 7. Several items were adequately reported in all the clinical trials, these included: Item 1b - *Details of the specific area(s) of interest using words and phrases that identify the clinical problem and the intervention(s) must be provided*; Item 6d - *Reason(s) for any early termination of the trial must be described*; and Item 11e - *Patient(s) identifiers (names, patient numbers) must be removed to ensure they are anonymized*. Two items were scored "NA" for all the included trials: Item 5k - *If primary or secondary outcomes are to be regarded as surrogate outcomes, the rationale and empirical support for the connection between surrogate(s) and the outcome(s) of clinical relevance must be provided*; and Item 5m - *Any interim analyses and stopping guidelines must be described, when applicable*.

Relationship between characteristics of the trials and their quality (Table 8)

i) *Number of authors*: No significant difference was observed between the number of authors and the quality of the manuscripts reporting the clinical trials. However, 3-4 authors were associated with the greatest percentage (46%) of "High" quality trials compared to 1-2 (0 %), 5-6 (31%) and >6 (23%).

ii) *Continent of corresponding author*: A significant difference (p=0.0002) was observed among the various continents. The clinical trials published from Europe were associated with the greatest percentage (58 %) of "High" quality trials, compared to Asia (17%), Middle East (8%), North America (0 %) and South America (17 %). Two trials (Alzahrani *et al*. 2018, Ghabraei *et al.* 2019) had two corresponding authors from different continents and were excluded from the analysis.

iii) *Journal (Endodontic specialty vs Non-Endodontic specialty journals):* No significant difference was observed between the Endodontic specialty and Non-Endodontic specialty journals in terms of the quality of the reporting of clinical trials. Non-endodontic speciality journals (62%) were associated with the greatest percentage of "High" quality clinical reports compared to Endodontic speciality journals (38%). In contrast, among the "Moderate" quality manuscripts, Endodontic speciality

journals (64%) were associated with the greatest percentage compared to Non-Endodontic speciality journals (36 %).

iv) Impact Factor: A significant difference was observed between the impact factor and non-impact factor journals (p=0.023) with "High" quality reports associated only with journals with an impact factor (100%).

v) Year of publication: No significant difference was observed between the year of publication. Reports of clinical trials published in 2019 (31%) had the greatest percentage of "High" quality trials compared to 2015 (23), 2016 (8%), 2017 (23%) and 2018 (15%).

vi) *Adherence to the CONSORT guidelines*: A significant difference (p=0.008) was observed between journals that adhered to the CONSORT guidelines and those that did not. The journals that adhered to the CONSORT guidelines had the greatest percentage (85%) of "High" quality reports compared to journals that did not adhere to the CONSORT guidelines (15%).

vii) A priori protocol registration: A significant difference (p=0.003) was observed between those studies where the protocol was registered and without registration. Registered clinical trials had the greatest percentage of "High" scores (77%) compared to trials without protocol registration (23%).

Discussion

Randomized clinical trials are considered to be the highest level of primary research evidence and are essential to support clinical decision-making (Burns *et al.* 2011). However, incomplete or inaccurate reporting of trials has a negative impact on their reliability and any inferences that can be drawn (MacPherson *et al.* 2010). Clearly, it is important to evaluate reports describing randomized clinical trials in Endodontics, not only to provide evidence of their quality but also to allow a better understanding

on whether recommendations made to change clinical practice can be done with confidence. The present study is the first to assess the quality of reporting randomized clinical trials in Endodontics using the PRIRATE 2020 checklist (Nagendrababu *et al*. 2020). Among the random selection of 50 trials included in the study, 13 (26%), 25 (50%) and 12 (24%) were categorized as "High", "Moderate" and "Low" quality respectively, which confirms previous reports that highlighted concerns in the reporting of randomized trials in Dentistry (Saltaji *et al*. 2017).

The present study generated a substantial volume of information related to the 58 items in the PRIRATE 2020 guidelines. Overall, the items that were poorly reported included:

Title

The PRIRATE checklist has two items within the Title domain. For Item 1a, 78% of the trials reported it adequately whilst all reported Item 1b adequately. The deficiency in reporting Item 1a reflects the fact that a substantial number of reports did not mention the term "Randomized clinical trial" or "Randomized controlled trial" in the title, which is considered essential for readers to appreciate the type of study being reporting as well as to facilitate indexing in databases and literature searches.

Keywords

Only 48% of reports adequately described the most appropriate keywords (Item 2a). To address this deficiency, future reports should include keywords from the Key Medical Subject Headings (MeSH), which has the added benefit of aiding indexing in search databases as well as facilitating literature searches.

Abstract

The Methodology section in an Abstract provides essential reproducible information on the manner in which a clinical trial was conducted. It was concerning that only 2% of trials adequately reported all the elements of Item 3c (Methodology), with 98% of trials only partially reporting these elements. Item 3c demands authors describe the design of the trial, the selection criteria for participants, trial setting(s),

intervention(s) under investigation, criteria for outcome measure(s), how participants were allocated to groups, as well as the blinding process and data analysis. These essential elements in manuscripts were generally poorly reported suggesting that authors in future should focus on these critical elements when writing manuscripts.

None of trials adequately reported all the sections within Item 3d (Results), with 98% only partially reporting these items. It is essential that authors provide information for every treatment outcome in each experimental group(s), clearly indicating the direction of the treatment effect as well as the effect size along with the confidence intervals and P-values.

Overall, only 2% of the clinical trials adequately reported Item 3f (Registration and Funding). It is recommended by many journals that authors must ensure they register their trial protocol *a priori* in an accessible database because it pre-specifies the methodology before the trial commences. This is important to ensure that the chances of selective outcome reporting and/or any inappropriate *post-hoc* changes to methodology or outcome measures are minimized. In the Abstract, authors should state any sources of funding to allow readers to evaluate the potential influence of the funder on the findings of the clinical trial (Hopewell *et al*. 2008).

Introduction

Overall, in the Introduction, 90% and 94% of the reports adequately described Item 4a (scientific background and rationale) and 4b (specific aim/objective(s)) respectively. In other words, most reports did provide sufficient information within these items. The Introduction section should provide the scientific background to the clinical problem for the readers to understand the relevance and rationale for conducting the trial as well as the reason why conducting the study may add new or supplement existing knowledge. Importantly, authors should describe the research question(s), preferably using the PICO framework.

Methodology

The PRIRATE 2020 checklist has 18 items within the Methods domain. Overall, only 2 to 10% of trials adequately reported Items 5a, 5b and 5j. Of particular importance is the need for authors to provide all the elements within Item 5a, which demands they describe the type of trial (e.g. superiority, non-inferiority), its design (e.g. parallel, split mouth, single/double/triple blinded), allocation ratios and other important details about the trial design if applicable, e.g. pragmatic or preference trial, phase (drug trials) etc. When a clinical trial is undertaken to test an hypothesis in a 'real world' practice environment, the 'pragmatic' nature of the trial should be highlighted, while if patient preference was considered acceptable within the trial design this should also be mentioned. This information is important for practitioners to assess the relevance and transferability of the work to their own working environment.

Clinical trials should begin only after the protocol has been accepted by a research and ethics committee/board, which should be reported (Item 5b). Due to the unpredictable nature of trials, deviations from a protocol might be necessary; however, this must be mentioned explicitly along with an appropriate justification.

Authors are expected to provide details and a justification to explain omissions, additions or modification to the outcomes from the protocol that occurred during the actual conduct of a trial (Item 5j). If there were no deviations from the protocol, it is good practice to mention explicitly that "*no deviation from the protocol occurred*". These essential elements in the trials were poorly reported in the Methodology section and authors in future should focus on these critical elements when reporting trials.

None of the trials adequately reported Item 5r, which relates to the statistical management of cluster-effects (e.g. same patient or individual sites in a multi-centre trial) in the analysis. Although a common feature of randomized trials, the management of clusters are seldom reported in Endodontics. Two items (5k and 5m) were scored "NA" for all the included trials, which although reflective of current clinical trials in Endodontics is likely to change in the future. Item 5k relates to the

need to describe the relationship between surrogate outcomes and real clinical endpoints, which is becoming an area of increasing interest as levels of biomarkers or clinical symptoms are studied and related to actual outcomes in pulpitis or general health studies. Often within grant-funded research projects the trial will have an interim stopping point (Item 5m), at which point the early results of the study dictate whether it has enough merit to continue or should stop. Even if the study proceeds beyond the interim analysis, this should be described within the study.

Results

Overall, only 4-18% of trials, adequately reported Items 6g, 6h and 6i. The reporting of absolute (risk difference) and relative (risk ratio) (Item 6g) allows readers to evaluate the real clinical benefit that occurs as a result of a clinical trial (Moher *et al.* 2012). Additional analyses (if applicable) such as subgroup analyses should also be reported (Item 6h) as it divides participant's data into subsets and makes comparisons between them easier (e.g. gender (male, female), age (20-29 years, 30-39 years, 40 years and greater)). Subgroup analyses can help to explain heterogeneous results or answer more detailed research questions.

Authors also need to provide information about adverse events including serious events that occurred during the trial and the measures taken to reduce the effect of harm to the participants (Item 6i). If there are no untoward effects in a clinical trial, it is good practice to mention explicitly "*no adverse or side effect was observed in the clinical trial*".

Discussion

Less than 34% of clinical trials adequately reported Items 7e, 7f and 7g. Importantly, authors should report explicitly the strength of the trial (Item 7e). Compared to other study designs, clinical trials are robust in determining cause and effect and reducing bias. Weaknesses identified in a trial (bias, absence of blinding) should be admitted and reported (Item 7f). Imprecise measurements of the primary outcome and the elucidation of non-significant results should be reported clearly. Authors also need to

report directions for future research and clinical practice to address any deficiencies in their trial, which could help others to plan future clinical trials (item 7g).

Conclusion

Overall, only 4% of clinical trials adequately reported the rationale for the conclusion(s) and highlighted its clinical significance. Authors should provide conclusion(s) that reflect clinically significant findings (and their relative limitations) in order to help clinicians interpret and translate the findings into their daily clinical practice as well as provide direction for researchers to conduct future trials.

Source of funding

Only sixty-two percent of trials adequately reported the source of funding (Item 9a). Clearly, authors should report explicitly the funding source and grant number (if relevant). Manufacturing companies sponsoring clinical trials may evaluate their own product, which might result in a conflict of interest as the funder can influence the design, conduct, analysis and report of the sponsored trial. The funding information is important and if no funding in involved, this should be reported explicitly (Moher *et al.* 2012).

Conflict of interest

Ninety-two percent of clinical trials adequately reported potential conflicts of interest (Item 10a), which represents an area of high compliance. A conflict of interest is present when a researcher or clinician involved in the trial has a personal interest that could bias the conduct or reporting of trial (Probst *et al.* 2016). Hence, a conflict of interest statement must be reported or, if none exists, the authors should explicitly state this fact in the manuscript.

Quality of images

The items in the PRIRATE 2020 guidelines on quality of images ask authors to provide important information on the nature of images included in reports and the information they convey to readers. Overall, only 31% of the trials adequately reported Item 11d. Authors need to provide information on the resolution, original

magnification and any processing modifications made to the image in a manuscript. Original images are preferred but modifications/enhancements are acceptable if there is no elimination or misrepresentation of the original information. It could be deemed to be scientific misconduct when modifications/enhancements intentionally mask, misrepresent or falsify data (Rossner & Yamada 2004, Lang *et al*. 2012).

Relationship between characteristics of trials and their quality score

Clinical trials published with a European-based corresponding author had a significantly greater percentage of "High" quality scores, compared with those from Asia, the Middle East, North America and South America. A potential explanation is that all the clinical trials published from Europe appeared in journals with an impact factor, a feature previously commented on with regard to randomized clinical trials in pancreatic surgery (Hüttner *et al*. 2019). This link between the origin of the publication and quality has also been demonstrated in surgical randomized clinical trials, in which a lower risk of bias was associated with European studies (23%), whereas trials from Asia/Oceania (5%) had a significantly higher risk of bias (Ahmed Ali *et al.* 2013). Similarly, the quality of published protocols of randomized clinical trials within surgical specialties reported from Europe and Australasia was higher, compared to North America (van Rosmalen *et al.* 2017). In summary, the origin of a randomized trial seems to have an impact on the quality score of the resulting publication.

The fact that randomized clinical trials with "High' scores only appeared in journals with an impact factor is likely in part to reflect the stricter and more rigorous review processes that such journals demand and also that high-quality researchers target journals with an impact factor. Ahmed Ali *et al*. (2017) studied the relationship between the impact factor of the journal and the methodological quality of surgical randomized controlled trials, before concluding that clinical trials published in higher impact factor journals were associated with improved methodological quality compared to trials published in lower impact factor journals. As a consequence, the impact factor of journals can potentially be considered a surrogate marker for methodological quality of randomized clinical trials (Ahmed Ali *et al.* 2017).

Additionally, high-impact journals included in the study such as *Journal of Dental Research, International Endodontic Journal, Journal of Endodontics, Clinical Oral Investigations,* have all endorsed the CONSORT guidelines. Journals that adhered to the CONSORT guidelines were associated in general with reports of a higher quality compared with those that did not, reflecting their utility. Journals that endorse the CONSORT guidelines facilitate transparent and unbiased reporting of trials (Hays *et al*. 2016). In addition, Hopewell *et al.* (2012) reported that endorsement and active implementation of the CONSORT for Abstracts guidelines by editors led to improvements in the reporting of abstracts for randomized trials. This clearly confirms that endorsement and enforcement of reporting guidelines by journals improves the quality of manuscripts.

Clinical trials where the protocol had been registered *a priori* in a public repository were more likely to be of a "High" quality compared to the trials without registration. The protocol of a clinical trial is important in terms of transparency in order to maintain validity and reliability (Viergever & Ghersi 2011). Trial registries are important tools to reduce the risk of selective reporting of outcomes or indeed altering results after publication (Chen *et al.* 2019). Hence, it is important for authors to provide the name of the registry and registration number. If authors have not registered their trial, they should explicitly state this in the manuscript and provide the reason why they failed to do so (Moher *et al.* 2012).

No significant difference was observed between the journal (Endodontic specialty vs Non-Endodontic specialty journals), year of publication and number of authors and the resulting quality of the clinical trials. The potential reasons for the lack of an association between endodontic and non-endodontic specialty journals are that most of the non-endodontic specialty journals included in the current study also have an impact factor, e.g. *Clinical Oral Investigations, International Journal of Paediatric Dentistry, Journal of Dental Research*, *Quintessence International,* which, as mentioned above, were associated with trials having a higher score. Saltaji *et al.* (2017) categorized the clinical trials published in dentistry into four time periods (before 1990, 1990–1999, 2000–2006, 2007–2013) and reported that their reporting

quality had increased over time. In the current study, there was no difference between the time periods, perhaps because the time period was limited to a short time span (one year). Pandis *et al.* (2010) assessed the quality of randomized trials published in dental journals and concluded that a positive association existed between quality and number of authors; however, in the current study no difference was observed for this parameter. This may be explained by the fact that Pandis *et al*. (2010) categorized the number of authors into three groups (≤ 4, 5-8, >8), whereas in the current study they were categorized into four (1-2 *vs* 3-4 *vs* 5-6 *vs* >6).

The main topics covered in the 50 included trials are shown through the word cloud, which accentuates the most frequently used keywords used by authors. Randomized clinical trials related to postoperative pain was the most common topic. These manuscripts dealt principally with the effect of using different canal shaping instrumentation systems and various irrigation or instrumentation techniques (manual, reciprocating or continuous rotary instruments, single or multi-file system) on postoperative pain after root canal treatment or retreatment. The influence of low-level laser or photobiomodulation therapy on post-endodontic pain, followed by the efficacy of pre-medication with nonsteroidal anti-inflammatory drugs were also frequent topics. Pain is a common problem faced by clinician and patients during or after root canal treatment (Parirokh & Abbott 2014), which may explain why trials in Endodontics, focused mostly on this area. Another reason why pain is commonly investigated, is that these studies do not require patient compliance over a sustained time-period, as pain is generally investigated only up to seven days. In fact, in the current study, the four most prolific authors (Beck M, Drum M, Nusstein J, and Reader A) all conducted clinical trials related to pain (e.g. irreversible pulpitis, incision and drainage). As with the present study, Ahmad *et al*. (2019) reported that these four authors contributed most to the top 100 most-cited articles in Endodontic journals.

Strength and limitations

In the current study, 50 clinical trials were randomly selected and appraised by two independent reviewers, with good agreement between them. Clinical trials published in the field of Endodontics were included from both endodontic specialty and non-

specialty journals. This reduced the likelihood of bias due to selected sampling, or reviewer bias. A limitation of the current study is reflected in the fact that only one database was used to search for clinical trials; in addition, reports published only in English and only those published in the last 5 years (2015-2019) were included that inevitably resulted in a somewhat restricted pool of articles. However, since the aim of the study was to study the applicability of the new PRIRATE 2020 guidelines, these potential deficiencies are not particularly relevant.

The clinical trials included were published before the release of the PRIRATE 2020 guidelines and the results provide a baseline for future studies on the impact of these guidelines within Endodontics. Clearly, if authors follow the PRIRATE 2020 guidelines, they should produce better quality reports of clinical trials in the field of Endodontics. The *BMJ open* journal started using an automated online software tool, Penelope (https://blogs.bmj.com/bmjopen/2017/02/06/bmj-open-trials-penelope/), from February 2017. This checks manuscripts for completeness and provides feedback to authors, which should improve the reporting quality of manuscripts. Similarly, in future, software can be developed to check adherence to the PRIRATE 2020 guidelines prior to authors submitting manuscripts to journals; this would ease the burden on journal administrators, reviewers and editors.

Conclusion

Reports of randomized clinical trials published in the specialty of Endodontics have numerous deficiencies. As a consequence, authors need to carefully consider the domains and items in the PRIRATE 2020 guidelines when preparing manuscripts for the benefit of clinicians and patients. Endorsement of the PRIRATE 2020 guidelines by editors will lead to a wider adoption and allow improvements in the reporting quality of randomized clinical trials to be achieved more rapidly and consistently across the globe.

Legends

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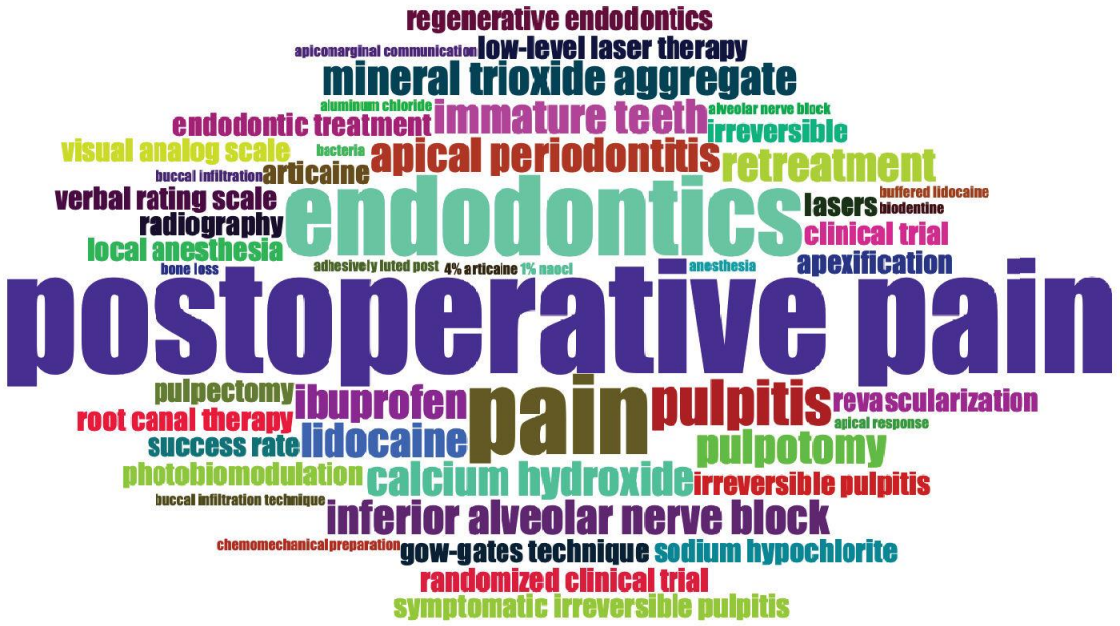

Figure 1: WordCloud based on authors' keywords frequency

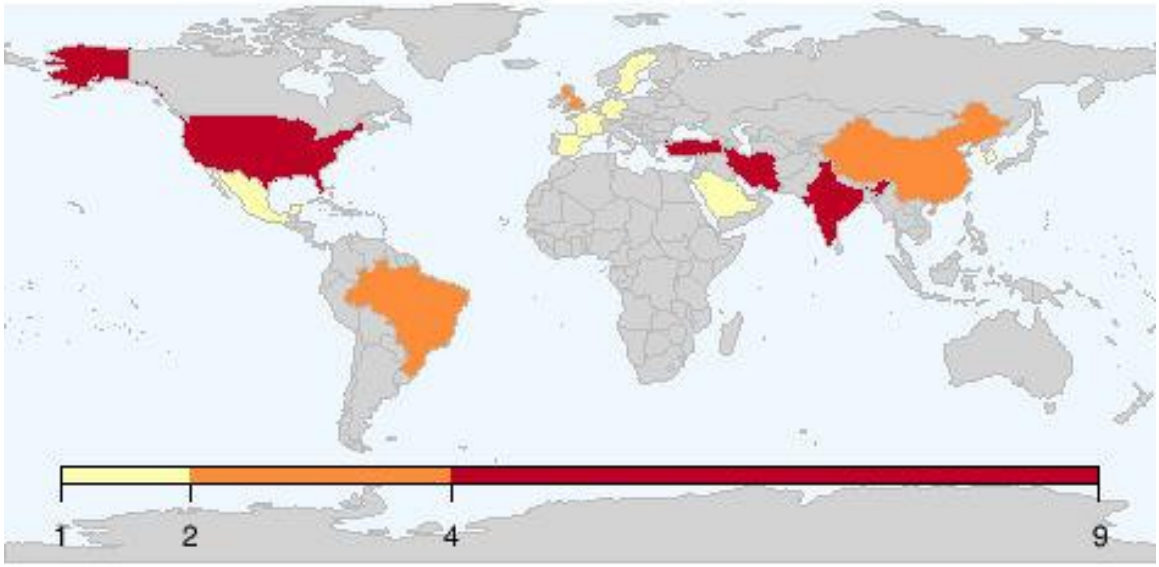

Figure 2a: Country (of corresponding author) production based on its frequency

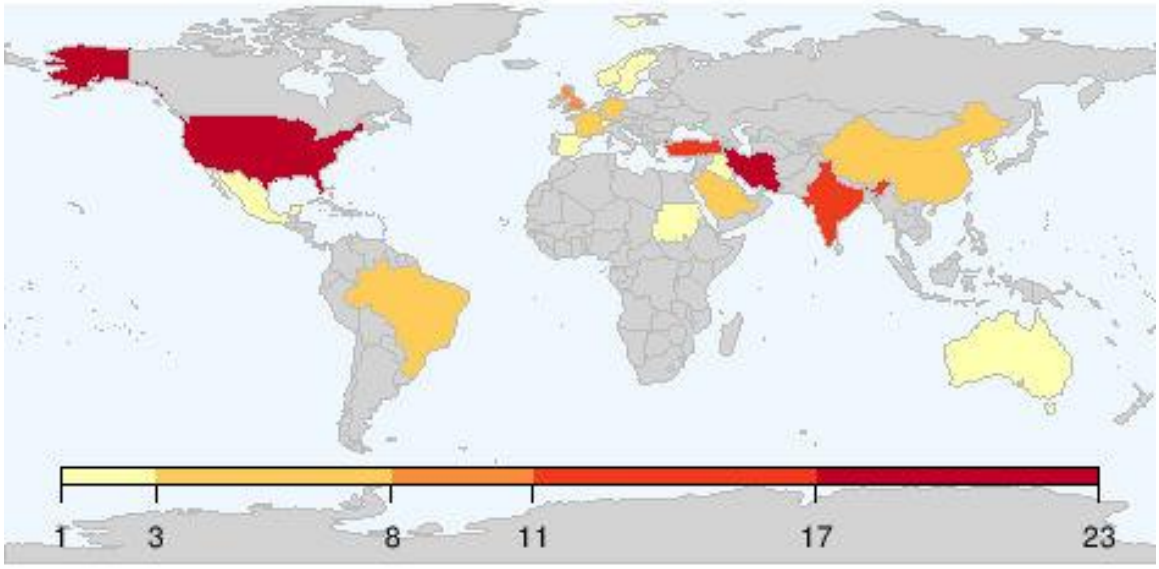

Figure 2b: Country (showed each country of each author) production based on its frequency

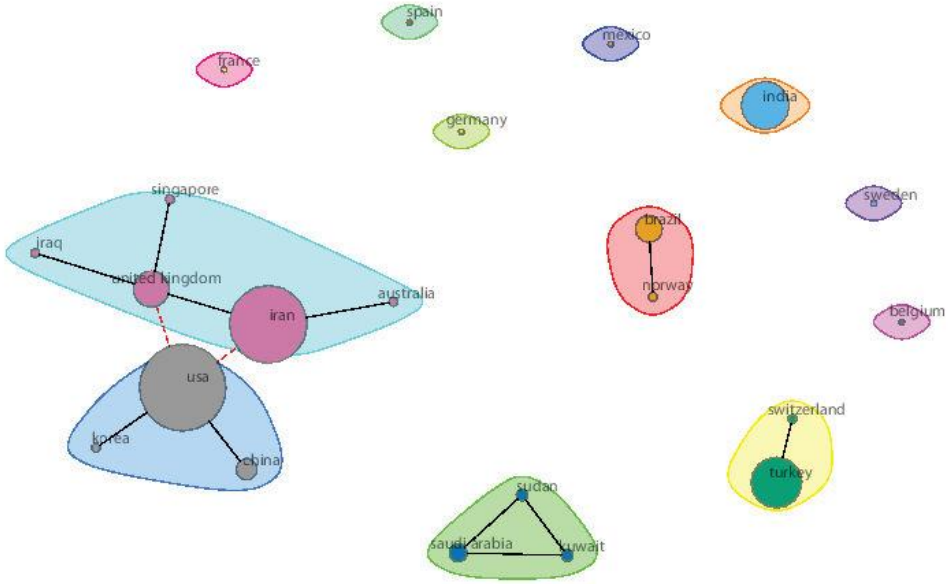

Figure 3: Country's co-authorship network. Each network node represents a country whose size is proportional to the frequency, that is, the number of randomized clinical trials. A line is established when two nodes have a relationship of co-authorship. Different colors represent distinct clusters.

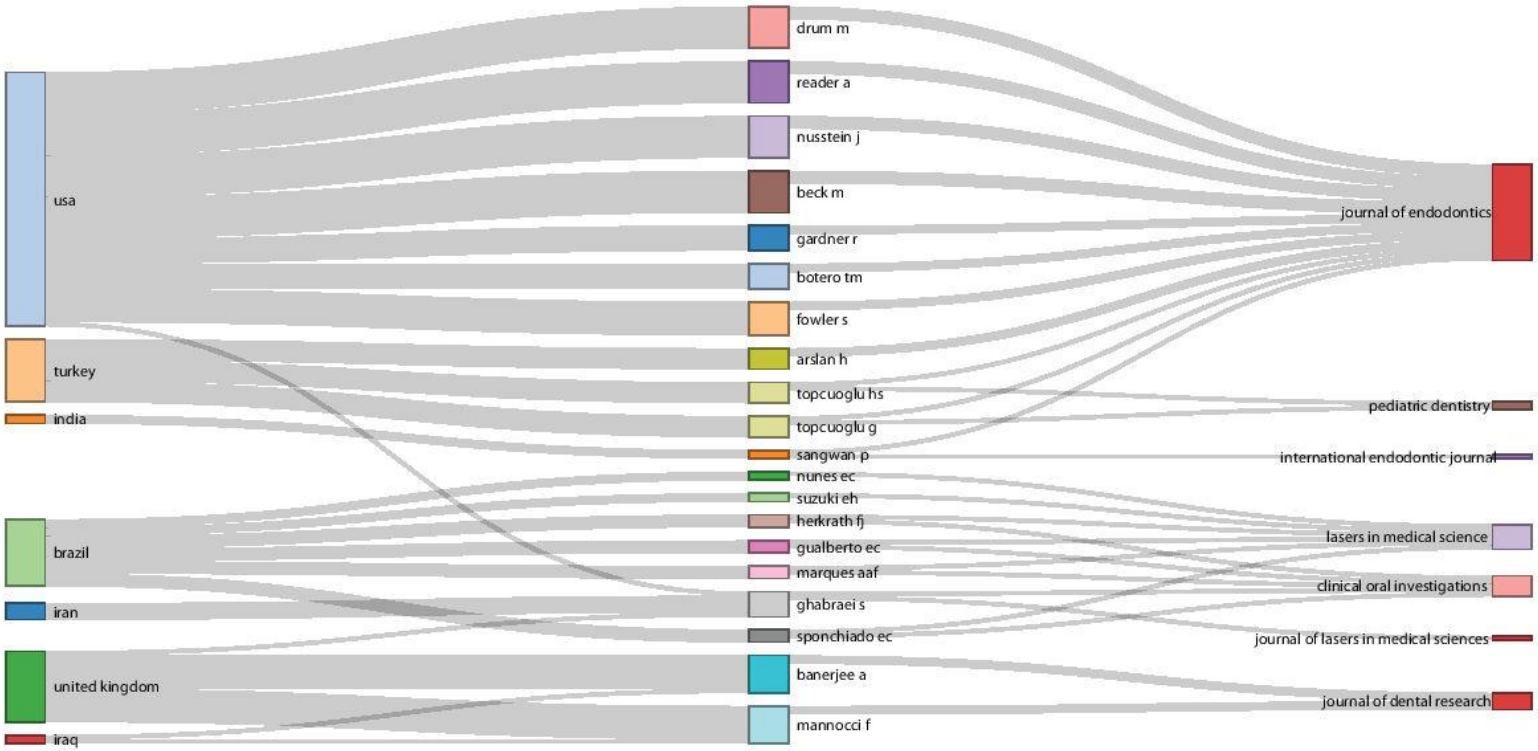

Figure 4: Sankey plot showing the relationship among top countries, authors and journals in which trials were published.

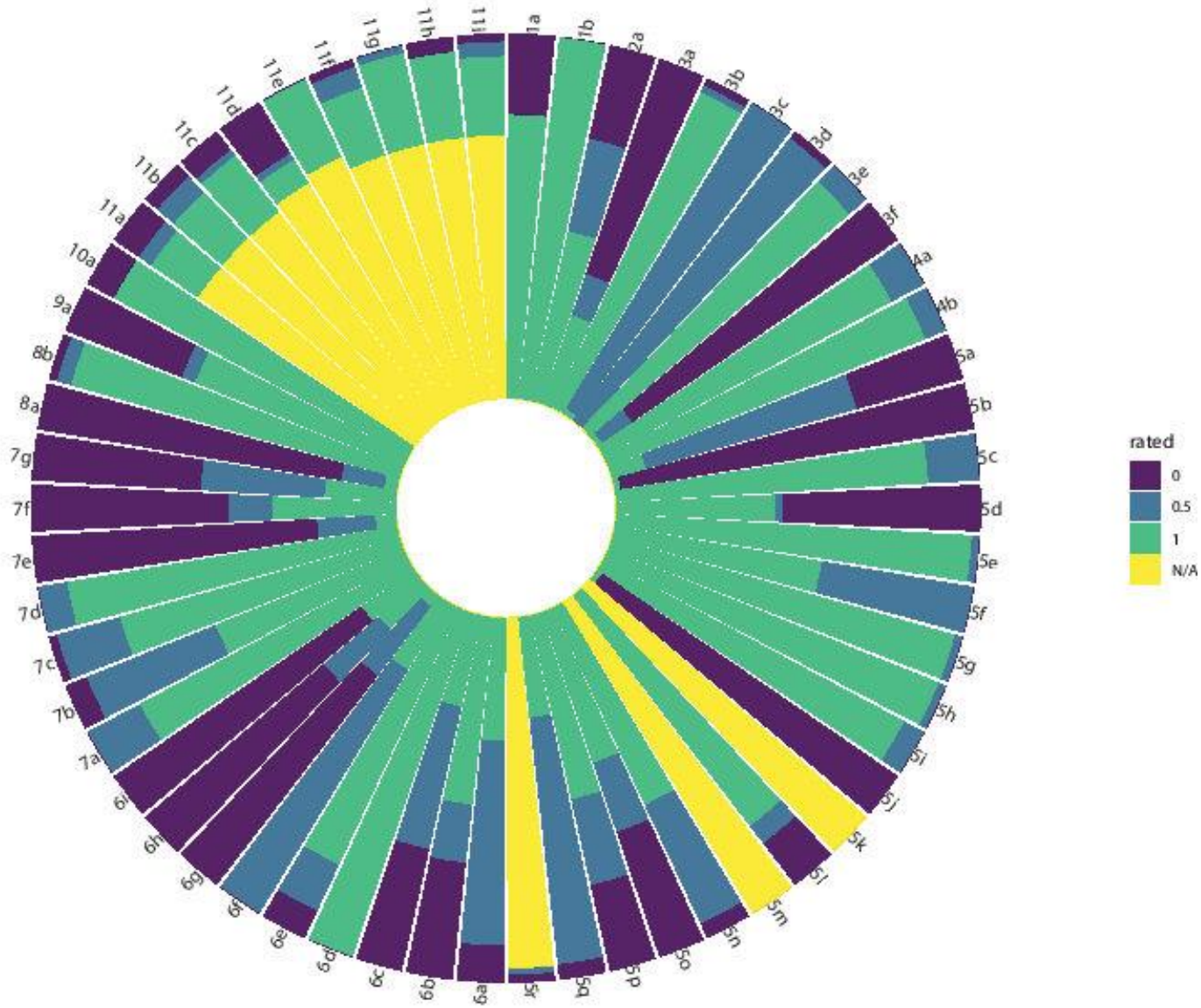

Figure 5

Table 1: Characteristics of the included clinical trials

S No	First author	Country (Corresponding author)	Year published	Number of authors	Journal name	JCR® IF for the year in which the trial is published	Journal adhered to CONSORT guidelines	Protocol registered in a clinical trial registry	Overall score (%)
1	Lin J	USA, CHINA	2017	9	JOE	2.886	No	Yes	67.59%
2	Talebzadeh B	IRAN	2016	6	IrEJ	-	Yes (CONSORT flowchart only)	Yes	65.22%
3	Rodrigues RCV	BRAZIL	2017	8	JOE	2.886	No	No	47.87%
4	Granevik Lindström M	SWEDEN	2017	3	JOE	2.886	Yes (CONSORT RCT, no CONSORT flowchart)	No	72.83%
5	Shapiro MR	USA	2018	5	JOE	2.833	Yes (CONSORT RCT, CONSORT flowchart)	Yes	68.48%
6	Alomaym MAA	SAUDI ARABIA	2019	4	JISPCD	-$$	No	No	58.70%
7	Schellenberg J	USA	2015	6	JOE	2.904	Yes (CONSORT RCT, no flowchart)	No	65.22%
8	Metri M	INDIA	2016	3	JCD	-	No	No	63.04%
9	Yilmaz K	TURKEY	2018	3	NJCP	0.43	No	No	46.74%
10	Mollashahi NF	IRAN	2017	4	IrEJ	-	No	Yes	63.04%
11	Beus H	USA	2018	7	JOE	2.833	Yes (CONSORT RCT, no flowchart)	No	57.27%
12	Ghabraei S	IRAN	2018	5	JLMS	-$$	No	Yes	51.09%
13	Doğanay Yıldız E	TURKEY	2018	2	JOE	2.833	YES	No	58.70%
14	Ghoddusi J	IRAN	2018	4	IrEJ	-	No (no CONSORT flowchart)	Yes	60.87%
15	Tajonar RGSY	MEXICO	2017	4	EEJ	-	Yes (CONSORT flowchart only)	No	62.73%
16	Bonte E	FRANCE	2015	4	COI	2.207	No (no CONSORT flowchart)	Yes	76.36%
17	Farhin K	INDIA	2015	4	JCPD	0.562	No	No	43.48%
18	Click V	USA	2015	5	JOE	2.904	Yes (CONSORT	No	54.35%

							RCT, no flowchart)		
19	Eyuboglu TF	TURKEY	2019	2	QI	1.46	Yes (CONSORT flowchart only)	Yes	62.96%
20	Dhiman M	INDIA	2015	5	JOE	2.904	Yes (CONSORT RCT, CONSORT flowchart)	No	73.15%
21	Nabi S	INDIA	2018	6	IJDR	-#	No	No	45.65%
22	Çiçek E	TURKEY	2017	5	JAOS	1.709	Yes (CONSORT flowchart only)	Yes	66.30%
23	Hashem D	ENGLAND	2015	7	JDR	4.602	Yes	Yes	79.09%
24	Ghorbanzadeh S	USA	2019	4	RDE	-	No	No	57.61%
25	Rajasekharan S	BELGIUM	2017	6	IEJ	3.015	Yes	Yes	81.82%
26	Lopes LPB	BRAZIL	2019	6	COI	2.812	Yes (CONSORT flowchart only)	Yes	72.83%
27	Genc Sen O	TURKEY	2019	2	PPLS	0 (1.918)**	Yes (CONSORT flowchart only)	No	69.57%
28	von Stein-Lausnitz M	GERMANY	2019	7	COI	2.812	No (no CONSORT flowchart)	Yes	77.27%
29	Peñarrocha-Oltra D	SPAIN	2019	6	JOE	3.118	Yes	No	64.55%
30	Kaladi SR	INDIA	2019	6	Cureus	-	No	No	48.91%
31	Shivashankar VY	INDIA	2017	7	JCDR	-$$	Yes (CONSORT flowchart only)	No	68.18%
32	Nunes EC	BRAZIL	2019	6	LMS	2.342	Yes	Yes	73.91%
33	Alzahrani F	SINGAPORE	2018	4	IJPD	2.057	No (no CONSORT flowchart)	Yes	81.52%
34	Maljaei E	IRAN	2017	4	IrEJ	-	Neo (no CONSORT flowchart)	Yes	68.48%
35	Topçuoğlu HS	TURKEY	2018	3	JOE	2.833	Yes (checklist)	Yes	60.87%
36	Botero TM	USA	2017	6	JOE	2.886	No (no CONSORT flowchart)	No	60.00%
37	Saini HR	INDIA	2016	3	IEJ	3.015	Yes (CONSORT flowchart only)	No	68.48%

38	Jiang X	PEOPLES R CHINA	2017	3	JOE	2.886	Yes	No	78.18%
39	Topçuoğlu G	TURKEY	2017	5	PD	-$	No	No	48.91%
40	Kim S	SOUTH KOREA	2016	4	JOE	2.807	Yes (CONSORT RCT, no CONSORT flowchart)	No	57.61%
41	Wong AW	PEOPLES R CHINA	2015	6	BMC Oral Health	1.21	No (no CONSORT flowchart)	Yes	65.22%
42	Elzaki WM	SAUDI ARABIA	2016	4	JOE	2.807	Yes (CONSORT RCT, no CONSORT flowchart)	Yes	78.26%
43	Asnaashari M	IRAN	2017	4	PPT	2.895	Yes (CONSORT flowchart only)	No	59.78%
44	Marques NC	BRAZIL	2015	7	LMS	2.461	No	No	50.91%
45	Keskin C	TURKEY	2019	4	IEJ	3.801	Yes (CONSORT flowchart only)	No	61.96%
46	Panchal V	INDIA	2019	3	JISPPD	-#	No	No	60.87%
47	Ghabraei S	IRAN, WALES, USA	2019	4	COI	2.812	Yes (CONSORT flowchart only)	Yes	77.17%
48	Ali AH	ENGLAND	2018	7	JDR	5.125	YES	Yes	84.78%
49	Asgary S	IRAN	2017	3	AJD	0.76	No	Yes	59.57%
50	Shafie L	IRAN	2018	7	IrEJ	_	Yes	Yes	69.57%

*-AJD - American Journal of dentistry, COI - Clinical Oral Investigations, EEJ - European Endodontic Journal, IEJ – International Endodontic Journal, IJDR - Indian Journal of Dental Research, IJPD - International Journal of Paediatric Dentistry, IrEJ – Iranian Endodontic Journal, JAOS - Journal of Applied Oral Science, JCD – Journal of Conservative Dentistry, JCDR - Journal of Clinical and Diagnostic Research, JCPD - Journal of Clinical Pediatric Dentistry, JDR - Journal of Dental Research, JISPCD – Journal of International Society of Preventive and Community Dentistry, JISPPD - Journal of Indian Society of Pedodontics and Preventive Dentistry, JLMS - Journal of Lasers in Medical Sciences, JOE- Journal of Endodontics, LMS - Lasers in Medical Science, NJCP - Nigerian Journal of Clinical Practice, PD - Pediatric Dentistry, PPT - Photodiagnosis and Photodynamic Therapy, PPLS - Photobiomodulation, Photomedicine, and Laser Surgery, RDE - Restorative Dentistry and Endodontics, QI - Quintessence International

**Photobiomodulation, Photomedicine, and Laser Surgery has IF2019 equal to zero and belongs to the Quartile 4 in Journal Citation Reports (JCR) category Surgery due to title change. From 2019 this journal continues Photomedicine and laser surgery. The Impact Factor (IF) value in parentheses (IF2019=1.918) is the IF of the superseded title, which belongs to the Quartile 2 in JCR category Surgery.

$Journal Pediatric Dentistry was suppressed from 2017 JCR Data due to anomalous citation patterns found in the 2017 citation data.

$$Journal indexed in the Clarivate Analytics' Emerging Sources Citation Index.

#Journal indexed in MEDLINE.

Table 2. Key information from 50 Randomized clinical trials

Timespan	2015-2019
Sources (Journals, Books, etc)	25
Average number of years from publication	2.7
Average citations per paper*	7.36
Average citations per year per paper*	1.71
DOCUMENT TYPES	
Article	49
Article; proceedings paper	1
DOCUMENT CONTENTS	
Keywords Plus/Indexed Keywords**	267
Author's Keywords	168
AUTHORS	
Authors	220
Author Appearances	242
Authors of single-authored documents	0
Authors of multi-authored documents	220
AUTHORS COLLABORATION	
Single-authored paper	0
Papers per Author	0.227
Authors per paper	4.4
Co-Authors per paper	4.84
Collaboration Index	4.4

*The source of citations was Web of Science Core Collection *Times Cited Count* (TC). **Keywords Plus are words or phrases generated from cited titles and associated with articles by Clarivate Analytics databases. Indexed keywords are MeSH or EMTREE indexing terms.

Table 3: Randomized clinical trials (RCTs) (n=50) published in various journals

Journal	Number of RCTs
JOURNAL OF ENDODONTICS	15
IRANIAN ENDODONTIC JOURNAL	5
CLINICAL ORAL INVESTIGATIONS	4
INTERNATIONAL ENDODONTIC JOURNAL	3
JOURNAL OF DENTAL RESEARCH	2
LASERS IN MEDICAL SCIENCE	2
AMERICAN JOURNAL OF DENTISTRY	1
BMC ORAL HEALTH	1
CUREUS	1
EUROPEAN ENDODONTIC JOURNAL	1
INDIAN JOURNAL OF DENTAL RESEARCH	1
INTERNATIONAL JOURNAL OF PAEDIATRIC DENTISTRY	1
JOURNAL OF APPLIED ORAL SCIENCE	1
JOURNAL OF CLINICAL AND DIAGNOSTIC RESEARCH	1
JOURNAL OF CLINICAL PEDIATRIC DENTISTRY	1
JOURNAL OF CONSERVATIVE DENTISTRY	1
JOURNAL OF INDIAN SOCIETY OF PEDODONTICS AND PREVENTIVE DENTISTRY	1
JOURNAL OF INTERNATIONAL SOCIETY OF PREVENTIVE AND COMMUNITY DENTISTRY	1
JOURNAL OF LASERS IN MEDICAL SCIENCES	1
NIGERIAN JOURNAL OF CLINICAL PRACTICE	1
PEDIATRIC DENTISTRY	1
PHOTOBIOMODULATION PHOTOMEDICINE AND LASER SURGERY	1
PHOTODIAGNOSIS AND PHOTODYNAMIC THERAPY	1
QUINTESSENCE INTERNATIONAL	1
RESTORATIVE DENTISTRY AND ENDODONTICS	1

Table 4. The 20 most productive authors from 50 Randomized clinical trials (RCTs).

Authors	Total number of RCTs (TRCTs)	Authors-Frac	Total number of RCTs Fractionalized (TRCTsF)
BECK M	3	ARSLAN H	0.833
DRUM M	3	SANGWAN P	0.533
NUSSTEIN J	3	TOPCUOGLU G	0.533
READER A	3	TOPCUOGLU HS	0.533
ARSLAN H	2	BECK M	0.51
BANERJEE A	2	DRUM M	0.51
BOTERO TM	2	NUSSTEIN J	0.51
FOWLER S	2	READER A	0.51
GARDNER R	2	DOGANAY YILDIZ E	0.5
GHABRAEI S	2	EYUBOGLU TF	0.5
GUALBERTO EC	2	GENC SEN O	0.5
HERKRATH FJ	2	KAYA M	0.5
MANNOCCI F	2	OZCAN M	0.5
MARQUES AAF	2	GHABRAEI S	0.45
SANGWAN P	2	BOTERO TM	0.367
SPONCHIADO EC	2	GARDNER R	0.367
TOPCUOGLU G	2	ASGARY S	0.333
TOPCUOGLU HS	2	BAGHEBAN AA	0.333
ABBOTT PV	1	BHANDI S	0.333
ABUBAKR NH	1	EGHBAL MJ	0.333

Table 5: Twenty most productive institutions from 50 Randomized clinical trials (RCTs).

Affiliations	**Number of RCTs**
KING'S COLLEGE LONDON, UK	8
OHIO STATE UNIVERSITY, USA	8
SHAHID BEHESHTI UNIVERSITY OF MEDICAL SCIENCES, IRAN	6
SUN YAT-SEN UNIVERSITY, CHINA	5
KERMAN UNIVERSITY OF MEDICAL SCIENCES, IRAN	4
TABRIZ UNIVERSITY OF MEDICAL SCIENCES, IRAN	4
UNIVERSITY OF MICHIGAN, USA	4
ERCIYES UNIVERSITY, TURKEY	3
UNIVERSITY OF OSLO, NORWAY	3
TEHRAN UNIVERSITY OF MEDICAL SCIENCES, IRAN	3
YONSEI UNIVERSITY, SOUTH KOREA	3
ATATURK UNIVERSITY, TURKEY	2
HORMOZGAN UNIVERSITY OF MEDICAL SCIENCES, IRAN	2
ONDOKUZ MAYIS UNIVERSITY, TURKEY	2
PARIS DESCARTES UNIVERSITY, FRANCE	2
PEKING UNIVERSITY, CHINA	2
TERNA DENTAL COLLEGE, INDIA	2
AUTONOMOUS UNIVERSITY OF QUERETARO, MEXICO	2
FEDERAL UNIVERSITY OF AMAZONAS, BRAZIL	2
UNIVERSITY OF LEEDS, UK	2

Table 6: Randomized clinical trials (n=50) published from various countries

Country	Frequency
IRAN	23
USA	22
INDIA	17
TURKEY	14
UK	11
BRAZIL	8
CHINA	8
FRANCE	6
GERMANY	6
SAUDI ARABIA	6
BELGIUM	3
MEXICO	3
NORWAY	3
SOUTH KOREA	3
SWEDEN	2
AUSTRALIA	1
IRAQ	1
KUWAIT	1
SINGAPORE	1
SPAIN	1
SUDAN	1
SWITZERLAND	1

Table 7: Percentage of adequately reported for each PRIRATE items

PRIRATE Checklist Items	Overall score (%)	Overall score (%) - partially adequately reported items
1a. The phrase 'Randomized clinical trial' or 'Randomized controlled trial' must be included in the title	78.00%	0.00%
1b. Details of the specific area(s) of interest using words and phrases that identify the clinical problem and the intervention(s) must be provided	100.00%	0.00%
2a. Keywords indicating the specific area(s) of interest using MeSH terms must be included	48.00%	26.00%
3a. The Introduction of the Abstract must explain briefly the rationale for the trial	26.00%	12.00%
3b. Abstract – The aim/objective(s) of the trial must be provided at the end of the introduction section within the Abstract	96.00%	2.00%
3c. The Methodology section within the Abstract must provide essential information on the nature of the trial (e.g. superiority, noninferiority, equivalence), its design (e.g. parallel, split mouth, crossover), the inclusion/ exclusion criteria, randomization process, blinding process and statistical analysis	2.00%	98.00%
3d. The Results section within the Abstract must describe the number of participants that were randomized and analysed, the size and direction (group favoured) of the difference(s) between the intervention(s) and control groups with statistical analysis (P values and 95% CI). Adverse events or side effects (if any) must also be reported or if none occurred, that must be mentioned explicitly	0.00%	98.00%
3e. The Conclusion section within the Abstract must summarize the findings and emphasize the clinical implication(s) of the results	94.00%	6.00%
3f. The prospective registration (number and name of the registry) and source(s) of funding must be provided	2.00%	10.00%
4a. The scientific background and rationale for the trial must be provided, including the gap(s) or inconsistencies in knowledge	90.00%	10.00%
4b. The specific aim/objective (s) of the trial must be provided and the main clinical research question formulated clearly, preferably use the PICO framework (Problem/ Population, Intervention, Control and Outcome)	94.00%	6.00%
5a. Details of the nature of the trial (superiority, noninferiority, equivalence of experimental intervention(s)), its design (parallel, split mouth, crossover, single/double-blinded) and test:control allocation ratio must be provided. If applicable, important information about the study design must also be provided, for example pragmatic or preference trial, phase (drug trials), patient or public involvement in planning, etc.	10.00%	60.00%
5b. Changes to the methodology after the trial commenced (such as eligibility criteria) must be provided along with detailed explanations	2.00%	0.00%
5c. Details of the ethical approval of the protocol and the process for obtaining informed consent must be provided	86.00%	14.00%
5d. Details of the trial protocol including registration number and name of registry/clinical database and where it can be accessed (open access webpage, if applicable) must be provided	44.00%	2.00%
5e. A list of inclusion and exclusion criteria at the individual/tooth/root level must be provided	98.00%	2.00%
5f. Details of the setting/ environment of the trial must be provided. Details on how many operators were involved in performing the intervention and control and their relevant experience/qualifications are essential. The setting where the data were collected must be described. If several operators are included and/or if it is a multi-centre set-up, details of how standardization/calibration between individuals or centres were achieved must be provided	58.00%	42.00%
5g. The treatments in the intervention (experimental) group(s) must be described with sufficient detail to allow replication, including how and when they were actually administered	98.00%	2.00%
5h. The interventions or absence of interventions in the control group must be described with sufficient details to allow replication, including how and when the interventions(s) was actually administered	98.00%	2.00%
5i. The primary and secondary (if any) outcome measures must be described, including how and when they were assessed and by whom	94.00%	6.00%

5j. Details of any changes made to the study outcomes after the commencement of the trial must be described	2.00%	0.00%
5k. If primary or secondary outcomes are to be regarded as surrogate outcomes, the rationale and empirical support for the connection between surrogate(s) and the outcome(s) of clinical relevance must be provided	NA	NA
5l. How the sample size was determined must be described with reference to the published literature, or a pilot study. The sample size may be modified after an internal feasibility study. Sample size calculations should generally refer to the primary outcome measure. If secondary outcome measures constitute the base for sample size calculation, an explanation must be provided	80.00%	6.00%
5m. Any interim analyses and stopping guidelines must be described, when applicable	NA	NA
5n. The method used to generate the random allocation sequence along with any details of the type of restriction (e.g. blocking) if applicable must be described. The persons responsible for randomization and recruitment must be provided. For multi-centre trials, a central randomization procedure is preferred and must be described. The unit of randomization should be specified and justified. Any stratification variables must be detailed	60.00%	36.00%
5o. Methods for allocation concealment up to the assignment of the participants into the intervention groups must be described	44.00%	20.00%
5p. Information on who was/were blinded after assignment to the interventions (e.g. participants, caregivers, evaluators) must be described in detail. Blinding through masking of interventions (e.g. similar looking drugs/instruments) should be described. Detailed reasons for lack of blinding (if applicable) must be described	52.00%	24.00%
5q. The statistical methods used for analysis of the primary and secondary (if any) outcomes, additional subgroup analyses and adjusted analyses (if applicable) must be described in detail. Consideration of dropouts should be included in the calculations	28.00%	68.00%
5r. How any cluster effects were managed during the analysis must be described	0.00%	50.00%
6a. The number of participants who were randomly assigned, received the intended treatment and were analysed for the primary and secondary (if any) outcome(s) for each group must be described. A flowchart must be provided	34.00%	56.00%
6b. Reasons for losses/dropouts and exclusions after randomization must be described for each group and included in the flowchart. If intention-to-treat analyses are used, details of the process must be provided	52.00%	16.00%
6c. The dates of recruitment, follow-up and study duration must be described	26.00%	40.00%
6d. Reason(s) for any early termination of the trial must be described	100.00%	0.00%
6e. The baseline demographic and clinical characteristics of each group must be provided	78.00%	14.00%
6f. The results for each group for each primary and secondary (if any) outcome(s), along with the estimated effect size and its precision, must be provided	22.00%	78.00%
6g. Both absolute and relative effect sizes for binary outcomes must be provided	4.00%	24.00%
6h. The results from any other analyses performed must be described, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	16.00%	20.00%
6i. The incidence and management of any adverse effects or unintended effects in each group must be described	18.00%	0.00%
7a. An estimate of the overall internal validity must be provided as well as the generalizability (external validity, applicability, real-world relevance) of the trial findings	84.00%	16.00%
7b. The rationale for inclusion, exclusion criteria and study duration must be provided	56.00%	38.00%
7c. An explanation of the clinical relevance of the primary and secondary outcomes must be provided	80.00%	18.00%
7d. A detailed interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence must be provided	92.00%	8.00%
7e. The strength(s) of the trial must be provided	6.00%	16.00%
7f. The limitations of the study must be provided, addressing the sources of potential bias, imprecision and, if applicable, multiplicity of analyses	34.00%	12.00%
7g. Implication for future research and clinical practice must be described	20.00%	34.00%
8a. A rationale for the conclusion(s) must be provided, and the clinical significance highlighted	4.00%	12.00%
8b. Explicit conclusion(s) from the trial must be provided	94.00%	4.00%

9a. Sources of funding and other support (such as supply of drugs, equipment) as well as the role of funders must be acknowledged and described	62.00%	4.00%
10a. An explicit statement on conflicts of interest must be provided	92.00%	0.00%
11a. Details of the equipment, software and settings used to acquire the image(s) must be described in the text or legend	57.14%	14.29%
11b. The reason why the image(s) was acquired and the rationale for its inclusion in the manuscript must be provided in the text. A justification for all images which involve radiation must be included	64.29%	21.43%
11c. The circumstances (conditions) under which the image(s) were viewed and evaluated by the authors must be provided in the text	71.43%	7.14%
11d. The resolution and any magnification of the image(s) or any modifications/enhancements (e.g. adjustments for brightness, colour balance, or magnification, image smoothing, staining) that were carried out must be described in the text or legend	30.77%	7.69%
11e. Patient(s) identifiers (names, patient numbers) must be removed to ensure they are anonymized	100.00%	0.00%
11f. An interpretation of the findings (meaning and implications) from the image (s) must be provided in the text	71.43%	21.43%
11g. The legend associated with each image must describe clearly what the subject is and what specific feature(s) it illustrates. Images of patients must describe the age, gender and ethnicity of the person, if relevant	92.86%	7.14%
11h. Markers/labels must be used to identify the key information in the image(s) and defined in the legend	85.71%	0.00%
11i. The legend of each image must include an explanation whether it is pre-treatment, intra-treatment or post-treatment and, if relevant, how images were standardized over time	78.57%	14.29%

Table 8: Relationship between quality of the included trials and characteristics of the trials

Characteristics	Groups	Number and percentage	Quality Categories			P values
			Low	Moderate	High	
Authors	1 - 2	Number	0	3	0	p=.555
		Percentage	0.0%	12.0%	0.0%	
	3 - 4	Number	4	12	6	
		Percentage	33.3%	48.0%	46.2%	
	5 - 6	Number	5	7	4	
		Percentage	41.7%	28.0%	30.8%	
	> 6	Number	3	3	3	
		Percentage	25.0%	12.0%	23.1%	
Continents*	Asia	Number	4	5	2	p=.0002
		Percentage	33.3%	20.8%	16.7%	
	Europe	Number	0	1	7	
		Percentage	0.0%	4.0%	58.3%	
	Middle East	Number	3	14	1	
		Percentage	25.0%	58.3%	8.3%	
	North America	Number	3	4	0	
		Percentage	25.0%	16.0%	0.0%	
	South America	Number	2	0	2	
		Percentage	16.7%	0.0%	16.7%	
Journal	Non-Endodontic specialty	Number	7	9	8	p=.233
		Percentage	58.3%	36.0%	61.5%	
	Endodontic Speciality	Number	5	16	5	
		Percentage	41.7%	64.0%	38.5%	
Impact factor*	No	Number	5	10	0	p=.023
		Percentage	41.7%	40%	0.0%	
	Yes	Number	7	15	13	
		Percentage	58.3%	60%	100%	
Year	2015	Number	3	2	3	p=.760
		Percentage	25.0%	8.0%	23.1%	
	2016	Number	1	3	1	
		Percentage	8.3%	12.0%	7.7%	
	2017	Number	2	9	3	
		Percentage	16.7%	36.0%	23.1%	
	2018	Number	4	5	2	
		Percentage	33.3%	20.0%	15.4%	
	2019	Number	2	6	4	
		Percentage	16.7%	24.0%	30.8%	
Adhered to CONSORT guidelines*	No	Number	9	9	2	p=.008
		Percentage	75.0%	36.0%	15.4%	
	Yes	Number	3	16	11	
		Percentage	25.0%	64.0%	84.6%	
	No	Number	11	13	3	p=.003

Protocol registered*		Percentage	91.7%	52.0%	23.1%
	Yes	Number	1	12	10
		Percentage	8.3%	48.0%	76.9%

*-statistically significant difference was present.