Preferred Reporting Items for RAndomized Trials in Endodontics (PRIRATE) guidelines: a development protocol

Abstract

Randomized clinical trials are acknowledged as the most appropriate methodology for demonstrating the efficacy or effectiveness of one intervention as opposed to another and thus play a major role in clinical decision making. However, it is recognized that despite the existence of various guidelines, for example, the Consolidated Standards for Reporting Trials (CONSORT) statement, the quality of manuscripts describing randomised trials is often suboptimal. The current project aims to develop and disseminate new guidelines, Preferred Reporting Items for RAndomized Trials in Endodontics (PRIRATE), to improve the planning and reporting quality of randomized trials in the field of Endodontics. The project leads (VN, PD) designed a robust process to develop the PRIRATE guidelines. At first, a steering committee of eight members, including the project leads, was formed. Thereafter, a five-stage consensus process will be followed: Initial steps, Pre-meeting activities, Face-to-face consensus meeting, Post-meeting activities and Post-publication activities. The steering committee will develop the first draft of the PRIRATE guidelines by identifying relevant and important items from various sources including the CONSORT guidelines and the Clinical and Laboratory Images in Publications (CLIP) principles. This will be followed by the establishment of a PRIRATE Delphi Group (PDG) consisting of 30 members. The individual items of the first draft of the PRIRATE guidelines developed by the steering committee will be evaluated and scored on a 9-point Likert scale by the PDG members. Items with a score of seven and above by more than 70% of PDG members will be included in the second draft of the guidelines and the Delphi process will be repeated until each item fulfils the set conditions. After obtaining consensus from the PDG, the PRIRATE guidelines will be discussed by 20 selected individuals within a PRIRATE Face-to-face Consensus Meeting Group (PFCMG) to arrive at a final consensus. The final PRIRATE guidelines will be accompanied with an explanation and elaboration document developed by the steering committee and approved by six members, three from the PDG and three from the PFCMG. The PRIRATE guidelines will be published in journals and actively disseminated to educational institutions, national and international academic societies and presented at scientific meetings.

Keywords: Endodontics, Health research reporting guidelines, Protocol, Randomized clinical trial

Introduction

Evidence-based dentistry that includes research-informed healthcare requires both clinicians and patients to make clinical decisions based on the best available evidence (Antoniou *et al.* 2013). In the traditional model of evidence-based dentistry, the process of generating evidence largely begins with randomized clinical trials (RCTs), due to their ability to avoid bias (systematic error) when comparing the respective value of the two or more treatment modalities (Brocklehurst *et al.* 2017). RCTs have been considered as the hallmark for demonstrating the efficacy or effectiveness of an intervention in health sciences (Juni *et al.* 2001). The findings of homogeneous RCTs are then pooled statistically by conducting meta-analyses that lay at the pinnacle of the hierarchy of evidence (Ismail *et al.* 2004, Dhar 2016). This distilled and synthesised evidence then forms the foundation to create evidence-based guidelines and policies providing accessible data to support informed decision-making (Dhar 2016, Lucena *et al.* 2017). However, RCTs are often subject to bias if they have weak study designs, retrospective power calculations and/or poorly reported methodological standards, such as unclear description of the sampling or randomization procedures, blinded interventions or evaluation of outcome measures. A transparent, comprehensive and detailed requirement on reporting of RCTs helps researchers plan their trials more effectively and allows readers to understand the findings and their relevance. Additionally, this clarity is also crucial to allow extraction of relevant data during subsequent systematic reviews and meta-analyses. Moher *et al*. (1998) explored the effects of the reporting quality of RCTs on quantitative results and discovered that studies of low quality were associated with an increased estimate of benefit of 34% when compared to high quality trials. Such an overestimation of the effectiveness of a RCT may impair the quality of subsequent systematic reviews and meta-analyses, as well as create difficulties when making decisions regarding dental treatments (Schulz *et al.* 1995).

RCTs generally provide information on the superiority (and less commonly equivalence or non-inferiority) of one clinical intervention compared with another. To ensure the accuracy of such trials, it is imperative that reporting guidelines and standards are employed that can reduce or eliminate bias. Several guidelines have been developed to assure the quality of RCTs, for example, the Consolidated Standards for Reporting Trials (CONSORT) statement (Moher *et al*. 2010) and the SPIRIT statement (Chan *et al.* 2013). The CONSORT statements are the most widely used,

frequently endorsed and well reported in the literature. It has been reported that the CONSORT statements have improved the quality of RCTs in the medical and dental fields (Kane 2007, Vere & Joshi 2011, Lucena *et al.* 2017). Furthermore, a number of complementary guidelines have been developed by modifying the CONSORT statements to specific medical specialties, such as infertility treatments (Improving the Reporting of Clinical Trials of Infertility Treatments (IMPRINT)) (Harbin Consensus Conference Workshop Group 2014), herbal interventions (Gagnier *et al.* 2016), and acupuncture (STandards for Reporting Interventions in Clinical Trials of Acupuncture (STRICTA)) (MacPherson *et al.* 2010). Indeed, the STRICTA guidelines have been officially endorsed by the CONSORT group.

The CONSORT statement covers the majority of the essential components for the reporting of RCTs in Endodontics and is officially recommended by leading dental journals; however, several items, including a list of keywords, a rationale for the selected period of review, details of preoperative diagnostic tests, the strength of the RCT and implications of the work on future research and clinical practice are missing. Furthermore, endodontic studies can be particularly challenging when attempting to 'blind' participants, operators and evaluators, and more detail on blinding is required than is currently contained within the CONSORT checklist. In addition, Endodontics is a subject within which radiographs and/or alternative images are often central to the primary and secondary outcome measure and as a result, the absence of guidelines for image presentation and reporting is a limitation of the CONSORT statement for reporting RCTs in Endodontics. At the same time, Endodontics, as well as other disciplines in Dentistry, should focus on patient-related outcomes in a clinical trial and there is a need to identify the data to be collected. (Fleming *et al*. 2016).

There are no recommendations that guide the reporting of RCTs contextualized to Endodontics or indeed include guidance on image quality reporting (Lang *et al*. 2012). Hence, the objective of this protocol is to develop a set of quality guidelines, the Preferred Reporting Items for RAndomized Trials in Endodontics (PRIRATE). In a similar manner to the CONSORT statement, the PRIRATE guidelines will comprise a checklist and a flow chart that aims to improve the quality of planning and reporting RCTs in Endodontics. By creating guidelines bespoke to Endodontics, the PRIRATE guidelines will help authors not only improve the quality,

completeness, accuracy and transparency of randomized trials reported in the literature, but also provide a blueprint for trials to be better designed and implemented more effectively. Consequently, this will reduce bias in interpreting and implementing the results of RCTs. Critically, the hope is that this will benefit dentists and patients to facilitate accurate clinical decision-making, and to researchers when conducting unbiased systematic reviews and meta-analyses. In addition, it is expected that the PRIRATE guidelines will be adopted by all journals that publish RCTs in endodontics by being endorsed by journal editors and reviewers to objectively evaluate and appraise RCTs during the editorial review process.

Methods

The PRIRATE guidelines will be developed based on the Guidance for Developers of Health Research Reporting Guidelines (Moher *et al*. 2010).

Phase I: Initials steps

Following a literature search and extensive discussion, the project leaders (VN, PD) came to the conclusion that comprehensive guidelines for the reporting of RCTs in Endodontics were required. A steering committee (SC) (PD, VN, HD, LB, TK, EP, SP, JJ), including the project leads, was formed to develop a set of draft PRIRATE guidelines through an iterative approach. The draft PRIRATE guidelines will be developed by adapting and elaborating the CONSORT statements (Moher *et al*. 2010) and Clinical and Laboratory Images in Publications (CLIP) principles (Lang *et al*. 2012) to the speciality of Endodontics.

Phase II: Pre-meeting activities.

To improve the PRIRATE guidelines, an online consensus process will be performed with the help of a Delphi group. A PRIRATE Delphi Group (PDG) will be formed of individuals who fulfil at least one of the following eligibility criteria: published at least one RCT in Endodontics; published any reporting guidelines for *in vitro* / *in vivo* research; a minimum 15 years of clinical experience as an endodontist or general dental practitioner. The SC will identify potential PDG members in order to ensure global representation and invite them to participate in the consensus process for developing the guidelines. The PDG will consist of 30 members (22 academicians or researchers, four clinical Endodontists, two general dental practitioners and two public representatives).. A

document explaining the Delphi process will be shared with members who will then participate in sequential online surveys to gain consensus on the inclusion of the proposed items within the draft PRIRATE guidelines. Comments on each item will be independently and confidentially requested from the PDG to avoid bias. Each item will be evaluated by the PDG members on its clarity (yes or no) and suitability for inclusion using a 9-point Likert scale (1 = 'definitely not include' to 9 = 'definitely include'). There will be provision for open comments to better understand the scoring of each item included in the guidelines (Maher *et al.* 2015). Items achieving a score of 7 and above by at least 70% of PDG members will become eligible for inclusion. Likewise, items will be excluded from the checklist if 70% or more participants score any item between 1 and 3. Items scored between 4 and 6 will be closely examined and revised based the comments provided by the PDG. The sequential surveys will be repeated with any modifications to the text of each item that become necessary as a result of the previous round of surveys, until this standard is achieved (Agha *et al*. 2017). In all subsequent rounds of the Delphi process, the PDG members will be informed of progress through summarized results, including the descriptive group statistics for each item including percentage distribution, median (with interquartile range) and combined anonymized comments. Being more robust to the effect of outliers, reporting the median and inter-quartile range will ensure that members will have some indication of the extent of consensus achieved (Murphy *et al.* 1998).

Once the initial consensus on the items within the guidelines is achieved by the PDG, a face-to-face consensus meeting will be organized. The SC will decide the venue, date and the time of the meeting. The SC will select two chairpersons and 18 members to form the PRIRATE face-to-face consensus meeting group (PFCMG). The eligibility criteria for the PFCMG will be similar to the PDG but with a conscious decision to appoint new individuals, PDG members will be eligible to join the PFCMG. In addition, two postgraduate students on Endodontic programmes will be identified to provide their views. Following confirmation of the PFCMG members, details of the venue, date and time of the meeting will be provided. The PRIRATE checklist, flow chart, results of Delphi process, members' details and agenda of the meeting will be shared with the group at least 10 days prior to the meeting.

Phase III: Face-to-face consensus meeting

Initially, the project leads (PD, VN) will review the objectives of the meeting followed by the presentation of the results of the Delphi process and explain the reasons for the inclusion of the items in the PRIRATE checklist and the flow chart. Any outstanding issues will also be clarified during the meeting. Thereafter, elaboration and explanation of the individual items in the PRIRATE checklist and the flow chart will be discussed with the members to finalize the reporting guidelines. Finally, a publication strategy, plans for disseminating the guidelines in scientific meetings, journal endorsement and adherence to the reporting guideline will be discussed. Notes of the discussions will be kept.

Phase IV: Post-meeting activities

Following the face-to-face meeting, SC members will finalize the PRIRATE guidelines using concise, unambiguous and comprehensive wording, taking into account the comments obtained from the PFCMG. The guidelines will be supported with an Explanation and Elaboration document supplemented with examples of good reporting for each item prepared by the SC and sent to six members for final approval, three from the PDG and three from the PFCMG. The PRIRATE guidelines and supporting documents will be published in journals and presented at scientific meetings.

Phase V: Post-publication activities

Endorsement of the guidelines by journals will improve the quality of reporting for randomized trials. The PRIRATE guidelines also will be freely available on a dedicated website, the Preferred Reporting Items for study Designs in Endodontics (PRIDE). The PRIRATE checklist will be translated into several languages. Academicians, researchers, journal editors, peer reviewers and others will be able to provide feedback on the PRIRATE guidelines either individually to SC members or via the dedicated website. Based on the feedback, the project leaders will periodically update the PRIRATE guidelines.

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