Reporting quality of systematic reviews with network meta-analyses in Endodontics

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ABSTRACT

Objectives: To evaluate the reporting quality of systematic reviews with network meta-analyses (NMAs) in Endodontics using the the Preferred Reporting Items for Systematic reviews and Meta-analyses (PRISMA) for NMA checklist.

Methods: The current investigation extends a recently published study in the *International Endodontic Journal* (Nagendrababu V, Faggion Jr CM, Pulikkotil SJ, Alatta A, Dummer PM Methodological assessment and overall confidence in the results of systematic reviews with network meta-analyses in Endodontics. *International Endodontic Journal* 2022;55:393-404) that assessed the methodological quality of systematic reviews with NMAs in Endodontics using the A MeaSurement Tool to Assess systematic Reviews (AMSTAR 2) tool. In the present study, the PRISMA for NMA checklist with 32 items was used to assess the reporting quality of the systematic reviews with NMAs (n= 12). Two independent assessors assigned '1' when an item was completely addressed, '0.5' when it was partially addressed, and '0' when it was not addressed. Disagreements were resolved through reviewer discussion until consensus was reached. If conflicts persisted, a third reviewer made the final decision. The PRISMA for NMA scores were shared with the relevant authors of the individual reviews to reduce the likelihood of misinterpretation and verify the scores assigned. The results for each individual item of the PRISMA-NMA items were calculated by summing the individual scores awarded; the maximum score for each item was 12.

Results: All the systematic reviews with NMAs adequately reported the following items: Title, Introduction section (Objectives), Methods section (Eligibility criteria and Information sources), Results section (Study selection, Study characteristics and Risk of bias within studies), and Discussion section (Summary of evidence). The items that were reported least often were the "geometry of the network" and "the summary of network geometry" with only 2 manuscripts (17 %) including these items.

Conclusion: A number of the items in the PRISMA-NMA checklist were adequately addressed in the NMAs; however, none adequately reported all the PRISMA-NMA items. The inadequacies of published NMAs that have been identified should be taken into

consideration by authors of NMAs in Endodontics and by editors when managing the peer review process. In future, researchers who are writing systematic reviews with NMAs should comply with the PRISMA-NMA checklist.

Clinical Relevance: ~~Several the items in the PRISMA-NMA checklist were adequately addressed in the NMAs; however,~~ None of the included systematic reviews with NMA adequately reported all the PRISMA-NMA items. Inadequate reporting of a systematic review with NMA increases the possibility that it will provide invalid results. Therefore, authors should follow the PRISMA-NMA guidelines when reporting systematic reviews with NMA in endodontics.

KEY WORDS: Endodontics, network meta-analyses, reporting quality, systematic review,

INTRODUCTION

Systematic reviews and meta-analyses are a potential source of evidence when developing clinical practice guidelines and are also useful for identifying objectives for future research through knowledge gap analysis [1,2]. A meta-analysis makes a pairwise comparison between two interventions to identify which is superior in terms of effectiveness or safety [3-5]. This type of comparison has limited utility when there are no head-to-head trials comparing two interventions [4]. A network meta-analysis (NMA) is a versatile methodology to compare studies where there are direct (head-to-head intervention comparison) as well as indirect studies that have a common intervention against other interventions [6-8]. The NMA creates a network of all the interventions that have been evaluated, indicating their relative magnitude and ranking [6,7,9].

Poor reporting of systematic reviews will result in flawed or biased conclusions, as well as create concerns over their reproducibility, transparency, reliability, and readability that will ultimately reduce their utility in the relevant healthcare setting [10]. In 2009, the Preferred Reporting Items for Systematic reviews and Meta-analyses (PRISMA) statement was published to guide authors when reporting traditional pairwise (comparing two interventions) systematic reviews and meta-analyses [1,8]. PRISMA 2009 consists of a checklist with 27 items and a flowchart. PRISMA 2009 has been superseded by PRISMA 2020 [11]. In 2015, the original PRISMA 2009 statement was extended to include the reporting of systematic reviews comparing multiple treatments using direct and indirect evidence in NMAs of health care interventions [8]. The PRISMA for NMA statement consists of a checklist and flowchart with 32 items (27 general items and 5 NMA items) [8].

The quality of the reporting of systematic reviews with NMAs has been evaluated in several studies with deficiencies being reported in the specialties of Chinese medicine, acupuncture, and moxibustion [12-14]. More importantly for Dentistry, Lee and Shin [15] concluded that the reporting quality of systematic reviews with NMAs was low and noted deficiencies in areas such as exploring the geometry of the network (S1), assessment of insistency (S2) in the method section, presentation of the network structure (S3),

summary of the network geometry (S4), exploration for inconsistency (S5) in the result section, risk of bias across studies, protocol registrations, and additional analysis.

The recent increase in the number of systematic reviews with NMAs in Endodontics is to be welcomed, but there are concerns over their methodological and reporting quality. Hence, the authors of the current study aimed to assess both the methodological and reporting quality of NMAs to identify flaws that need to be remedied in future studies. As a first phase, the methodological quality of NMAs in Endodontics was assessed using the AMSTAR 2 guidelines [16] with the conclusion that the overall confidence in the results for most of the studies was 'Critically low' in relation to methodological quality. The aim of the present study, as the second phase of the overall project, was to assess the *reporting* quality of systematic reviews with NMAs in Endodontics using the PRISMA for NMA checklist [8].

METHODS

Data searching and selection

The current investigation complements a previous study [16] that appraised the methodological quality of systematic reviews with NMAs in Endodontics using the AMSTAR 2 tool. In that study, systematic reviews with NMAs were identified using the following search strategy: "(((((((((((pulp) OR ("root canal")) OR (Endodontic)) OR (Endodontology)) OR ("periapical surgery")) OR ("periradicular surgery")) OR (apicoectomy)) OR (apicectomy)) OR (pulpotomy)) OR (pulpectomy)) AND ("network meta-analysis")) OR ("indirect meta-analysis")". The literature search was performed in PubMed, EbBSCOhost and SCOPUS databases from inception to July 2021. The Grey Literature was identified using the OpenGrey database and further searches were also conducted by screening the reference lists of the included reviews. Systematic reviews with NMAs in the specialty of endodontics published in English were included. Twelve systematic reviews (Supplementary Table 1) involving NMAs were identified by Nagendrababu et al. [16], and the same reviews have been included in the current study. As a result, no specific independent literature search was performed.

Data extraction

The items related to the NMAs were extracted by two independent reviewers (VN and SJ). Disagreements among the reviewers were resolved through conversation until a consensus was established. If the disagreements persisted, a third reviewer made the ultimate decision (CF). The following items were extracted: Name of the first author, year of publication, country of the first and corresponding author, name of the journal, type of reporting guidelines, number of citations according to Google scholar (https://scholar.google.com), source of funding and number of primary studies included in the NMA.

Training sessions for assessors

In an attempt to increase the accuracy of the definitive data extraction and when assessing the quality of NMAs, a pilot exercise was undertaken by the two primary reviewers on a quarter of the retrieved systematic reviews with NMAs. Of the 12 reviews included, three were selected at random for this purpose by the lead investigator (VN). Differences between the two reviewers during the pilot were resolved through discussion and areas of concern that could have occurred in the main study were resolved. Disagreement that could not be overcome by the two reviewers was resolved by a third reviewer.

Reporting quality

The PRISMA for NMA checklist with 32 items were used to assess the reporting quality of the included systematic reviews with NMAs. The checklist has 27 general items and 5 items with a focus on the elements relating to the NMA: the general items include 11 modifications to the 27 within the PRISMA 2009 items. The five specific items for the NMA component include: S1: geometry of the network, S2: assessment of inconsistency, S3: presentation of network structure, S4: summary of network geometry and, S5: exploration for inconsistency [1,8]. Two reviewers (VN and SN) scored each item independently, allocating '1' when it was fully addressed, ''0.5'when it was partially addressed, and '0' when it was not addressed. Disagreements were resolved through discussion among the reviewers until consensus was achieved. If conflicts continued, a final judgment was made by a third reviewer (CF). The corresponding authors of the individual NMAs were contacted with a request to provide information that was unclear or missing in the included reviews. To minimize any possible misinterpretation and to

corroborate the scores awarded, the PRISMA for NMA scores were communicated with the corresponding authors of the individual reviews. The overall scores for each item were calculated by adding up the individual scores, with a maximum potential score of 12; the total scores were also converted into percentages.

RESULTS

Characteristics of the included reviews

The characteristics of the included studies are presented in Table 1. The studies were published between 2014 and 2021. The first and corresponding authors of the systematic reviews were from Bahrain, Brazil, Canada, Egypt, Italy, Malaysia, and Taiwan. Eight reviews were reported according to PRISMA for NMA, three according to PRISMA, and one review provided no information. Among the 12 reviews, 50% were published in Endodontic specialty journals, with the other 50% being published in non-specialty journals. Among the 12 reviews, ten were clinical trials, and two were laboratory-based studies. Two reviews mentioned the source of funding, while five explicitly stated that no funding was received; five reviews did not disclose any details on funding.

Reporting of items in the PRISMA-NMA checklist

The adequate reporting rate (%) for each item present in the PRISMA-NMA checklist is presented in Table 2. Number of NMAs adequately reported for each items presented in Figure 1. After assessing the compliance of the NMAs using the 32-item PRISMA-NMA checklist, none of the systematic reviews with NMAs in Endodontology complied with all 32 items. All the NMAs adequately reported the following items: Title, Introduction section (Objectives), Methods section (Eligibility criteria and Information sources), Results section (Study selection, Study characteristics and Risk of bias within studies), and Discussion section (Summary of evidence). The least reported items among the included NMAs were Methods section (Geometry of the network (17 %)) and Results section (Summary of network geometry (17 %)).

DISCUSSION

In the current study, the reporting quality of 12 systematic reviews with NMAs in Endodontics was appraised using the PRISMA for NMA checklist. Lee and Shin [15] appraised the quality of systematic reviews with NMAs in Dentistry using the PRISMA for

NMA checklist. However, among the 12 NMAs included in the present investigation, only one [17] was included in the study by Lee and Shin [15]. This is most likely related to the search period used by Lee and Shin [15] which ended in May 2017. In the present investigation, only one NMA was published before 2017 [17].

Systematic reviews that are poorly conducted and/or reported are likely to be biased and have only limited usefulness in healthcare settings [18,19], indeed they may be misleading. Over the years, methodologists working on systematic reviews have proposed and created a number of methodological and reporting principles in an attempt to improve both the methodological rigor and reporting quality of systematic reviews [20].

In the present study, all of the NMAs reported the "*Title*" item adequately, that is they correctly included the term NMA. Obviously, this will improve the probability of readers and search engines identifying the scope of the study as a NMA [8]. Readers will benefit from a title that represents the Population, Intervention, Comparison, Outcome, Study design (PICOS) approach because it provides essential information about the scope of the review [1].

All the included NMAs received a score of "0.5" for the "Abstract" item. Even though the main source of funding for a systematic review should be included in the abstract [21], none of the studies included "*Funding*" in this section of the manuscript. According to research evaluating the relationship between pharmaceutical company funding and clinical trial or review findings [22-24], commercially funded studies are more likely to produce outcomes that favour the sponsor. Thus, journals should insist that authors of systematic reviews with NMAs include details on funding in the abstracts and include such advice in their author guidelines. For example, the authors of the *International Endodontic Journal* are expected to include the following information in the abstract: "*Background, Objective, Methods, Results, Discussion, Conclusion, Funding, Registration*," as mentioned in the author guidelines (https://onlinelibrary.wiley.com/page/journal/13652591/homepage/forauthors.html) The PRISMA for Abstracts checklist has 12 items and was introduced to assist authors when reporting systematic reviews in manuscripts submitted to journals and in abstracts

submitted to conferences [21]. For the benefit of authors writing systematic reviews in Endodontology, the importance of the items in the PRISMA for Abstract checklist has been emphasised using examples specifically related to the specialty [25].

In the "*Introduction"* section, authors should briefly explain why a systematic review with a NMA approach was selected to answer the research question. A lack of head-to-head randomized trials comparing interventions of interest, or the necessity to analyse numerous treatments to acquire a clinically useful understanding of the relative effectiveness or harms of different treatment options, are possible rationales [8]. Authors should describe the objective of the study in the PICOS format (Population, Intervention, Comparison, Outcome and study design) [8]. It is worth noting that the more recent PRISMA 2020 guidelines, recommend that a research question should be developed based on the PICO format [26].

In the present study, 83% of reviews adequately addressed the "*Methods of analysis*" item in the Methods section. The adoption of Bayesian methods in many NMAs is recommended for two reasons: (1) initial development of techniques and software based on the Bayesian method, (2) in complex and sparse data situations Bayesian methods are robust. However, recent inclusion of non-Bayesian techniques in STATA and R statistical software packages requires the need to provide justifications on the assumptions made for the inferential method used [8].

Only 17% of NMAs adequately addressed the item "Geometry of the network" and "Summary of network geometry. The "network geometry" is used to refer to the architecture of the treatment comparisons that have been established for the condition under investigation [8]. The review of network geometry is greatly assisted by the development of a network graph. The structure of the evidence, both direct and indirect, can be visualised by the connections of various interventions from the trials included in a review. The treatment comparisons are presented in the form of a network geometry graph for readers to understand the structure of evidence. The network geometry summary provides information on the completeness and incompleteness of the treatment comparisons. This is necessary for readers to understand the direct and indirect evidence that formed the basis for the NMA [8]. The geometry also provides

information on potential bias towards inclusion of a certain treatment over others in the included studies due to sponsorship or other reasons. These biases can affect the strength of evidence [27,8]. The evaluation of network geometry is recommended for authors reporting NMAs.

The assumptions of heterogeneity, transitivity, and consistency are crucial in an NMA [15]. In a systematic review, heterogeneity is the measure of the variation between the included studies. It could be due to clinical (e.g., variability among the interventions and outcomes studies) or methodological diversity (e.g., study design, outcome measurement tools), or both [28]. The assumption that direct and indirect evidence is comparable is known as the consistency of treatment effects. For example, comparing the success rate of three pulpotomy materials (MTA, calcium hydroxide, and Biodentine). The success rates between MTA and Biodentine are such that an odds ratio determined from studies of MTA versus Biodentine should be similar to the odds ratio comparing MTA versus Biodentine estimated indirectly based on studies of MTA versus calcium hydroxide and Biodentine versus calcium hydroxide [8]. By comparing the distribution of effect modifiers across different comparisons, transitivity can be assessed. Unbalanced distributions would jeopardize the plausibility of the transitivity assumption and, thus, the validity of indirect comparison [29]. To improve evidence-based dental care, authors and readers should investigate these assumptions in greater detail and present results that are valid and appropriate [15]. When available, authors conducting NMAs should present systematic data on patient and study characteristics. By evaluating the distribution of potential effect modifiers across trials, this information enables readers to empirically evaluate the validity of the assumption of transitivity [8].

In the present study, 75% of reviews adequately addressed the item "*Assessment of inconsistency*". The assumption of consistency of treatment effects (treatment effects from direct and indirect evidence are equivalent) is an essential requirement for the conduct of an NMA. The consistency assumption should be assessed by global and local methods. The details of the assessment and its outcome on the suitability of the consistency assumption should be reported for readers to ascertain the confidence in the overall results [8]. The reasons for the observed inconsistencies in the NMAs should be described based on the geometry and evidence analysed.

Overall, 67% of the reviews adequately addressed the item "*Additional analysis*" in the Methods section. Additional analyses including sensitivity analysis, subgroup analysis, and meta-regression [1] assess the robustness of the results and should be reported if performed. This allows the readers to assess the validity and reliability of the reported results and its interpretation.

The quality of primary studies included in a systematic review is a crucial factor; if they are of poor quality, they may introduce bias, which will influence the results and conclusions of the systematic review [30]. The authors of a systematic review must specify which risk of bias tool(s) they used as well as the domains or items used to assess the risk of bias in the studies the included [26]. In addition, the rationale used to support ratings of risk of bias should be reported in order to facilitate the reader's understanding and the reproducibility of the assessments. Clearly, researchers should only conduct and report high quality primary studies, which will ultimately improve the overall quality of systematic reviews.

Using the PRISMA–NMA checklist, the quality of NMAs has previously been evaluated in several medical specialties, including Chinese medicine, acupuncture, and moxibustion [12-14]. Using the PRISMA-NMA checklist, Lee and Shin [15] evaluated the quality of NMAs in dental care. For items S1–5, 71% of NMAs in dental care did not define the network in detail. In the present study, 83 % of NMAs did not describe the Geometry of the network (item S1), while 91% of NMAs did not describe this item in the specialty of acupuncture [14], and 45% did not describe it in the field of acupuncture and moxibustion [13]. Research done in the past [12-15] reported that substantial improvement in a number of areas was required, especially those related to NMAs, which is in accordance with the findings of the current study.

Strength and limitations
The current study included a relatively small number of systematic reviews with NMAs and included NMAs involving clinical trials as well as laboratory investigations. It also included publications in both Endodontic specialty and non-Endodontic specialty journals to provide a comprehensive overview. To reduce bias, each NMA was appraised

by two reviewers. Individual review scores were shared with the corresponding authors of each review in order to obtain their feedback on the results. As a consequence, the corresponding authors were able to evaluate the results and provide input on whether or not they believed the assessment was accurate and fair. This additional step was done in the hope of improving the accuracy of the grading and to minimize the negative consequences of inaccurate reporting. However, despite contacting all the authors, only two responded; one indicated that they accepted the scores awarded in the current study, and the other questioned the scores awarded in relation to several items; after discussion, these differences were resolved. The limitations of the study include: assessing the quality of reporting only and not the relevance and credibility of the NMAs. To ensure the statistical validity of NMAs, an advanced assessment of their quality is required [31]. The present analysis was based on what the authors reported in their studies, and was carried from the standpoint of a reader. It is always possible that the authors used the correct methodology but omitted to report it in the manuscript. Although the PRISMA score has been verified in prior studies, this checklist was not created as a scored instrument [32]. Another limitation of the present study is that only English-language systematic reviews were included. It is generally accepted that systematic reviews with MNAs involve sophisticated statistical approaches and are inevitably published in high quality journals in English. It is unlikely that the results of the study would vary if non-English manuscripts had been included.

CONCLUSION

None of the included NMAs in the current study adequately addressed all the items in the PRISMA-NMA checklist with the consequence that the reporting of systematic reviews with NMAs in Endodontology needs to be improved, particularly the following items: structured summary, protocol and registration; geometry of the network; risk of bias across studies; additional analysis; summary of network geometry and limitations. When an NMA is reported with insufficient information, the likelihood of invalid results increases. The PRISMA for NMA guidelines can guide authors when writing a NMA. To improve the reporting quality of NMAs, journals should endorse the PRISMA for NMAs guidelines in their author instructions.

Author Contributions

Conceptualization: VN, CF, PD

Methodology: VN, SN, LD, CF, SP, VG, PD

Writing original draft: VN, SN, LD, CF, SP, VG, PD

Writing- Review and Editing: VN, SN, LD, CF, SP, VG, PD

All authors have read and approved the manuscript.

Compliance with Ethical Standards

Conflict of interest Not applicable.

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Ethical approval Not applicable.

Informed consent Not applicable.

Legends

Table 1: Characteristics of the included systematic reviews with network meta-analyses

Table 2: Summary of reporting quality assessment

Figure 1: Number of NMAs adequately reported for each items (n)

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