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REVIEW ARTICLE

The importance of establishing a core outcome set for endodontic clinical trials and outcomes studies

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Abstract

Endodontic therapy aims to preserve teeth by preventing and treating apical disease, therefore, evaluation of treatment outcome in clinical trials and outcomes studies should effectively assess if it achieves these aims. Traditionally, treatment outcomes have been reported by clinicians after history and clinical examination in what is known as clinician-reported outcomes (CROs). Much less commonly employed however, are patient-reported outcomes (PROs) in which patients directly report on their condition. Endodontic treatment outcome reporting is evolving from a focus on CROs to increasing consideration for patient and disease-focused outcomes, with different criteria being proposed for assessment of treatment outcomes. Unfortunately, this has led to considerable variability and a lack of consensus on the definition, appropriate measurement and reporting of these outcomes. Heterogeneity in outcome reporting in clinical research provides a significant major barrier to conduct meta-analysis, guidelines development, clinical decision making, and ultimately affecting patient care. These effects could, however, be reduced by the establishment of a core outcome set (COS) in endodontics, which is defined as an agreed, standardized set of outcomes that should be included, measured and reported as a minimum in all trials and outcome studies. COS development is a regulated and validated process requiring involvement of appropriate stakeholders as well as a rigorous methodology. To date, COS has been developed for the management of traumatic dental injuries, orthodontic and periodontal treatment and is currently being developed for endodontic treatment. The aim of this review is to discuss the importance of COS in endodontics with focus on the evidence for and impact of heterogeneity in reporting endodontic treatment outcomes. An overview of an ongoing process for development of COS for different endodontic treatment modalities will also be provided.

KEYWORDS

clinical outcomes, endodontics, outcome measures, patient-reported outcomes

INTRODUCTION

The goal of endodontic therapy is to prevent or treat apical periodontitis (Ørstavik & Pitt Ford, 1998). Achieving this requires various endodontic treatment modalities including, procedures that aim to maintain pulp vitality, such as vital pulp treatments (VPTs) and revitalization procedures, and therapies focused on prevention and treatment of apical periodontitis, including nonsurgical root canal treatment and surgical endodontics. The successes and failures of these procedures in fulfilling the aim of the treatment are often referred to as treatment outcomes and reported either by patients during history or phone call or by clinicians during clinical examination and special investigations. The reporting of endodontic treatment outcomes are evolving from purely clinician-focused to a greater consideration of patient and disease-focused outcomes (Chugal et al., 2017). However, outcome reporting in endodontics is blighted by constantly changing definitions and a lack of standardized criteria for measuring outcome in clinical studies. This has long been recognized as a major cause for heterogeneity in reports on treatment outcomes (Friedman, 2002) and has been confirmed in recent reports demonstrating the lack of consensus in the definitions employed, and how and when endodontic treatment outcomes are measured (Azarpazhooh et al., 2022; Duncan, Nagendrababu, et al., 2021; El Karim et al., 2021, 2022). This lack of consensus in outcome reporting has damaging implications in evidence synthesis, clinical guideline development and ultimately for patient care.

REVIEW

Outcomes and outcome measures

Interventions or treatments are generally designed to eliminate or prevent disease and promote health, therefore, the outcomes and outcome measures chosen to assess their effects should reflect these objectives as fully as possible. An outcome is defined as a change in patient status over time, whereas an outcome measure is a tool or test used to assess a patient's status over time (Fetters & Tilson, 2019). These may include methods and tools used for data acquisition or collection during history taking, clinical examination and special investigations. Outcome measurement tools should have high-quality evidence for good content validity, internal consistency and feasibility (Prinsen et al., 2016). Outcomes and outcome measures can be broadly considered as clinician or patient-reported. Patient-reported outcomes (PROs) are reports of a patient's health status that originate directly from the patient and are not interpreted in any way by a clinician (Lamont & Clarkson, 2022). Conversely, clinician-reported outcomes (CROs) are reports about a patient's health assessed by a healthcare professional (Powers et al., 2017).

Historical background to endodontic treatment outcomes

Traditionally, endodontic treatment outcomes are defined as success or failure, but differing definitions of success and failure has resulted in wide variability in reporting endodontic treatment outcomes. In his landmark study on endodontic outcome assessment, Strindberg (1956) established criteria for the evaluation of endodontic outcome, commonly referred to as Strindberg criteria. Using these criteria success is defined as absence of symptoms and normal radiographic appearance of the periapical tissues, which implies clinical, radiologic and histologic resolution of inflammation whereas presence of symptoms or radiographic changes is considered treatment failure. An uncertain outcome was also included in this classification when there are minor radiographic rarefaction or the radiograph is insufficient to define with certainty the periapical status of the tooth. The Strindberg criteria, however, were regarded as inflexible and an alternative classification taking into account patient comfort and function was suggested (Bender et al., 1966). This included, in addition to radiographic evidence of resolution or reduction of periapical radiolucency the absence of symptoms, disappearance of sinus tract and no associated loss of function (Bender et al., 1966). However, these early classification systems were considered not to reflect the dynamics of endodontic disease and calls were made for a departure from this treatment-specific outcome and moving on to disease and patient-specific outcomes approach in which the focus was placed on the disease and healing process (Friedman & Mor, 2004). Using such an approach, different definitions for outcome were suggested including; "completely healed, incompletely healed or healing, and not healed" (Byström et al., 1987). In reality, the patient-focused approach suggested by (Bender et al., 1966) was actually later reintroduced by Friedman and Mor (2004), in their classification which defined outcomes as "healed, healing, disease and functional retention." Functional retention referred to a normal clinical presentation with or without radiographic evidence of periapical radiolucency. The concept of functional retention or survival as an outcome was reintroduced in the light of the high success rate of implants and changes in treatment planning dynamics involving extraction and replacement with a dental implant. If a positive outcome for teeth was defined as retention without symptoms, regardless of the periapical

status, the survival of endodontically treated teeth could be as high as that of implants (Setzer & Kim, 2014). Subsequently, the American Association of Endodontists (AAE) defined new terms for endodontic treatment outcomes to replace the Strindberg criteria. The terminology of healed, not healed, healing and functional was introduced (AAE, 2005). To add to the complexity and ambiguity in endodontic treatment outcome definitions, further modification of outcome criteria were introduced such as stringent and lenient (Friedman, 2002) and strict and loose (Ng et al., 2007, 2011), all based on planar 2D radiographic assessment.

The debate and controversies in defining endodontic treatment outcomes are ongoing. Other more recent suggestions propose that the terms success and failure be replaced with 'effective' and 'ineffective' treatment. 'Effective' treatment represent the categories 'healed' and 'healing' and will not result in further treatment, whilst the latter indicate the emergence or enlargement of the periapical radiolucency and/or symptoms and signs that will require intervention (Wu et al., 2011).

Alongside this debate, there are emerging endodontic treatments, such as VPTs and revitalization procedures, which have led to many studies reporting on the outcomes of these treatments using different definitions for success (Cushley et al., 2022). Although, VPT shares common outcomes with other endodontic treatment modalities, there are some procedure-specific outcomes that are particular for VPT that will require further validation (Duncan, Nagendrababu, et al., 2021).

Types of endodontic treatment outcomes

Clinician-reported outcomes

Clinician-reported outcomes are reports of a patient's health status by a trained healthcare professional (Powers et al., 2017). The professional uses clinical judgement and reports on observed patient behaviours or clinical signs of disease. In endodontics, CROs are interpretation of data obtained from detailed history taking together with clinical and/or radiographic examination. CROs such as a history of pain and heightened, painful response to percussion/palpation are crucial outcomes that have been used in recent endodontic treatment outcomes studies (Cushley et al., 2022; Shah et al., 2022). However, the measures used for CROs are often not standardized or validated. For instance, pain history data (which could also be PRO) is often obtained based on questions asked by clinicians and these questions and how they are asked can differ amongst clinicians. Similarly, clinical tests such as tenderness to tooth percussion and palpation of the adjacent soft tissues can be carried out differently amongst clinicians and reported to, subjectively, by patients. Assessment of pulp vitality could also be considered a CRO that would determine the type of endodontic treatment required and the long-term prognosis for the tooth. Different tools can be used to measure this outcome, including pulp sensibility tests (e.g., thermal, electric pulp tester), laser Doppler flowmetry and pulse oximeter. Sensibility tests are the most widely reported tools in outcomes studies for VPT and revitalization procedures (Cushley et al., 2022); however, they are associated with varying sensitivity and specificity (Mainkar & Kim, 2018). Unfortunately, there is currently no test that can objectively determine the status of the dental pulp and degree of inflammation (Mejàre et al., 2012).

The principal CRO that is used when deciding if the endodontic treatment was a success or failure is radiographic evidence of healing and/or progression of the disease. Conventional radiographic examination is the most commonly used measure to assess the periapical status of the tooth, but, for some time, reports have suggested lack of robust correlation between histological and radiographic findings after root canal treatment (Bender et al., 1966; Kruse et al., 2017). The introduction of more sensitive imaging techniques, such as cone-beam computed tomography (CBCT) may provide details that are not available from conventional radiographs, however, recent reports showed that the diagnostic accuracy of CBCT was reduced with root filled compared with nonroot filled teeth with small periapical radiolucencies, in which CBCT was shown to overestimate the prevalence of inflammation in root filled teeth (Kruse et al., 2019). For these reasons, and the risk of increased radiation doses means that use of CBCT may be unjustifiable, at least for routine assessment of the effect of treatment (ESE, 2019).

Patient-reported outcomes

Patient-reported outcomes are obtained by the patient self-reporting on their health status. They are directly reported by the patient (via self-reported questionnaires), without interpretation of the patient's response to treatment by a clinician or anyone else, and pertain to the patient's health, quality of life, or functional status associated with health care or treatment (Higgins et al., 2022). In the European Society of Endodontology S3-level guidelines, "tooth survival" was considered as the "*most critical*" outcome, whereas "pain, tenderness, swelling" were "*critical*" outcomes, and "*important*" outcomes were "Oral Health Related Quality of Life (OHRQoL), need for further intervention, adverse effects, and tooth function" (Duncan, Chong, et al., 2021). It is worth noting that, OHRQoL is

generally considered the most important dental PRO due to its direct relationship with the impacts of oral disease and dental treatment on patients (John, 2020).

Patient-reported outcomes are used to evaluate treatment outcomes and care quality, both of which are critical to patient health. In endodontics, PROs have traditionally been attributed less importance than CROs, which have been the primary focus of evaluations of the effects of endodontic therapy treatment for many years. For instance, a scoping review discovered 300 CROs but only 114 PROs in studies of root canal treatment, retreatment and apexification published throughout the past four decades (1980–2020) (Azarpazhooh et al., 2022). Over that period, there has been a decline in the reporting of CROs and a small but steady increase in the reporting of PROs such as pain and quality of life (Azarpazhooh et al., 2022).

Outcomes reporting: The need for core outcome sets

It is evident from the recent scoping reviews that there is significant heterogeneity and a lack of standardization in reporting the outcomes of endodontic treatment, as well as an absence of consensus as to when and how these outcomes should be measured (Cushley et al., 2022; Shah et al., 2022). This variability and lack of consensus on reporting treatment outcomes is a major barrier to evidence synthesis, guideline development and clinical decision making, and it contributes to research waste (Glasziou et al., 2014). Recognition of these problems across many areas of health led to initiatives for the development of what are known as core outcome sets (COS) (Devane et al., 2007; Sinha et al., 2012; Tugwell et al., 2007). A COS is defined as an agreed, standardized set of outcomes that should be included, measured and reported as a minimum in all trials or outcome studies in a particular field (Williamson et al., 2012). COS should support outcome choices in clinical trials, routine clinical care (Davis et al., 2018) and systematic reviews (Clarke & Williamson, 2016). The benefits of COS are not just limited to evidence synthesis but, most importantly, they can enhance the validity of studies by reducing heterogeneity and reporting bias in clinical trials (Clarke, 2008).

The development of COS involves a rigorous methodology (Williamson et al., 2012). It should start with identification of the scope and existing knowledge by carrying out a robust review of the literature. An important aspect of COS development is the involvement of various stakeholders, including patients, clinicians, researchers and policy makers whose input will be important for the validity of the COS and its later dissemination and uptake. The involvement of appropriate stakeholders is crucial to the consensus process used to develop a COS, which is usually completed via a Delphi process or focus group meetings (Biggane et al., 2019).

Core outcome set—Dentistry

In dentistry, COS have been developed for the management of traumatic dental injuries (Kenny et al., 2018), orthodontic treatment (Tsichlaki et al., 2020) and periodontal treatment (Lamont et al., 2021). The later employed standard COS development protocols and included patients as important stakeholders and produced a five-item COS to include probing depths, quality of life, quantified levels of gingivitis, quantified levels of plaque and tooth loss. Using similar methodology Tsichlaki et al. (2020) developed a 7 item COS for orthodontic treatment that included both CROs and PROs. In a consensus involving experts 13 generic items and 10 injury specific items were identified as outcomes to be reported for traumatic dental injuries (Kenny et al., 2018).

Need for a core outcome set for endodontic treatment

In endodontics, a focused but abbreviated COS was developed to guide the European Society of Endodontology S3-level clinical practice guidelines development process (Duncan, Nagendrababu, et al., 2021). In addition, a literature-based synthesis of outcomes of nonsurgical root canal treatment, nonsurgical retreatment, and apexification procedures has been reported (Azarpazhooh et al., 2022). However, the latter process did not include emerging endodontic treatment modalities, such as VPTs and revitalization, and most importantly did not involve consensus development as suggested in standard COS development protocols (Williamson et al., 2012). Therefore, there is a need for the development of COS for endodontic treatment using a standard and approved methodology in line with the recommendation from the COMET initiative: Core Outcome Set-STAndards for Development (COS-STAD) and Core Outcome Set–STAndards for Reporting (COS-STAR) (Kirkham et al., 2016, 2017).

Core outcome set for endodontic treatment project

Core outcome set for endodontic treatment (COSET) has been established as an international collaborative project to develop COS and COMS (core outcome measurement sets) for different endodontic treatment modalities. This

involves determining which important outcomes need to be included in the COS and when and how these outcomes should be measured. An *a priori* protocol for the COSET project was published and registered in COMET (El Karim et al., 2021, 2022). The project will divide endodontic treatment broadly into VPT, nonsurgical root canal treatment including retreatment, surgical endodontics and revitalization.

The COSET project will be carried out in two phases:

(i) In the first phase, structured scoping reviews have identified all outcomes reported for different endodontic treatment modalities including VPT (Cushley et al., 2022), surgical root canal treatment (Shah et al., 2022), nonsurgical root canal treatment and revitalization procedures. This phase generated lists of outcomes that have been grouped into five domains of the healthcare taxonomy (Dodd et al., 2018); 'tooth and /or dental pulp survival', 'clinical/physiological changes', 'life impact', 'resource use' and 'adverse events'. The list of outcomes will be the basis for the first round of consensus development in the next phase of the COSET project.
(ii) The second phase involves a consensus process using the Delphi method, semi-structured interviews and consensus meeting to agree on the most important outcomes and how best to measure them. Stakeholders from different geographical locations will be involved in the development of the consensus and will include patients, clinicians, researchers and journal editors. It is expected that consensus will be achieved on a list of core outcomes to be reported for each endodontic treatment modality, how these outcomes should be measured as well as the optimal time for their measurement.

Relevance of COS to endodontic clinical practice

Clinicians often rely on the results of randomized clinical trials and systematic reviews for evidence-based decision making in their day-to-day practice. However, the applicability of research to clinical practice depends not only on the quality or the validity of the primary study, but on the consistency, relevance and importance of the chosen outcomes. Due to the fact that the clinical trials attempted to answer similar research questions but evaluated different outcomes, or the same outcome at different times or with different tools, it is difficult to combine the results of these clinical trials in systematic reviews and meta-analyses to assist with clinical practice. Similarly, when the researchers intend to measure outcomes that are of no, or less relevance, patients even in well-designed trial, the translation of the findings to clinical practice becomes meaningless. The relevance of a clinical trial is directly related to its outcomes, but most trials in Dentistry are focused on outcomes that are important to clinicians, but not to the patients (Fleming et al., 2016). An evaluation of Endodontic trials, highlights that treatment outcome is based on clinician perception of success in the form of clinical and radiographic evidence of absence of apical periodontitis (Kirkevang et al., 2022), but whether this is the most important outcome for patients is not clear. There is currently a paucity of studies in endodontics investigating patient outcomes that are a priority for patients, therefore, development and uptake of COS including outcomes that are important for patients may change our traditional approach in assessing outcomes and success of endodontic treatment in research and ultimately clinical practice.

CONCLUSION

Similar to other clinical medical and dental disciplines, there is a lack of consensus in the reporting of the outcomes of endodontic treatment. The negative impact of this on evidence synthesis, guideline development and clinical care has led to initiatives to establish an endodontic COS using validated, rigorous methodology. The development of COS in endodontics improves the relevance and consistency of reported outcomes, promotes efficient research synthesis and reduces research waste. The COS helps the researchers to select the most important outcomes to be included in clinical trials and how and when these outcomes should be measured.

AUTHOR CONTRIBUTIONS

Planning of manuscript—IEK, HD, VN, MC. First draft—IEK. Editing and final approval of the manuscript—IEK, HD, VN, MC.

CONFLICT OF INTEREST

The authors deny any conflicts of interest related to this study.

DATA AVAILABILITY STATEMENT

Data sharing not applicable to this article as no datasets were generated or analysed during the current study.

ETHICAL STATEMENT

The study does not need ethical approval.

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