ORIGINAL ARTICLE

PROBE 2023 guidelines for reporting observational studies in endodontics: explanation and elaboration

Abstract

Observational studies play a critical role in evaluating the prevalence and incidence of conditions or diseases in populations as well as in defining the benefits and potential hazards of health-related interventions. There are currently no reporting guidelines for observational studies in the field of Endodontics. The Preferred Reporting Items for study Designs in Endodontology (PRIDE) team have developed and published new reporting guidelines for observational-based studies called the "Preferred Reporting items for OBservational studies in Endodontics (PROBE) 2023" guidelines. The PROBE 2023 guidelines were developed exclusively for the specialty of Endodontics by integrating and adapting the "STrengthening the Reporting of OBservational studies in Epidemiology (STROBE)" checklist and the "Clinical and Laboratory Images in Publications (CLIP)" principles. The recommendations of the Guidance for Developers of Health Research Reporting Guidelines were adhered to throughout the process of developing the guidelines. The purpose of this document is to serve as a guide for authors by providing an explanation for each of the items in the PROBE 2023 checklist along with relevant examples from the literature. The document also offers advice to authors on how they can address each item in their manuscript before submission to a journal. The PROBE 2023 checklist is freely accessible and downloadable from the Preferred Reporting Items for study Designs in Endodontology (PRIDE) website (http://pride-endodonticguidelines.org/probe/).

Process involved in developing the Preferred Reporting items for OBservational studies in Endodontics (PROBE) 2023 guidelines

The PROBE 2023 guidelines were developed to help researchers address the challenges encountered when submitting manuscripts describing observational studies to peer-reviewed journals (Nagendrababu et al., 2023). The development of the PROBE 2023 guidelines followed the Guidance for Developers of Health Research Reporting Guidelines (Moher et al., 2010). The project leaders (VN, PD) formed a nine-member steering committee (PD, VN, HD, AF, LK, PP, MP, MV, JJ) to oversee the project. The steering group prepared the first draft of the checklist by modifying and adapting the STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) checklist (von Elm et al., 2008) and the Clinical and Laboratory Images in Publications (CLIP) principles (Lang et al., 2012). The steering committee formed a PROBE Delphi Group (PDG) of 30 experts from around the world in an attempt to improve the preliminary PROBE checklist using the Delphi approach. The revised PROBE checklist was discussed during an online meeting of experts on 7th October 2022 and the feedback received was used to refine and improve the checklist further. Several volunteer authors then piloted the amended PROBE checklist when writing manuscripts describing a hypothetical observational study related to Endodontics. The final PROBE 2023 checklist has 58 items in 11 sections (Nagendrababu et al., 2023).

PROBE 2023 explanation and elaboration document

The purpose of this document is to provide authors with a comprehensive explanation for each of the items in the PROBE 2023 checklist. In addition, it aims to guide authors through the process of preparing their manuscript for peer review prior to publication.

To help authors and stakeholders, the manuscript provides examples of effective reporting obtained from the published literature. For further clarity, the citations and website links within the text of the published research have been omitted, and abbreviations have been written in full.

Item 1a: Title - The specific area(s) of interest must be provided using words and phrases that identify the clinical problem(s) and focus of the study

Explanation

The title should include words that clearly identify the specific area(s) of interest and/or the clinical problem(s). It must be simple and clear, focused, concise, accurate, and not misleading. For indexing purposes and retrieval from search engines and scholarly databases, the most relevant words and phrases should be used (Tullu, 2019).

Example 1a.1

From Hoppe et al. (2017) – "Association between chronic oral inflammatory burden and physical fitness in males: a cross-sectional observational study".

Example 1a.2

From Serefoglu et al. (2021) – "A prospective cohort study evaluating the outcome of root canal retreatment in symptomatic mandibular first molars with periapical lesions".

Item 1b: Title - The study design must be included in the Title, e.g. cross-sectional, cohort, case-control, case series etc.

Explanation

The title should clearly identify the design of the study. The use of precise terms to describe the specific study design ensures it can be catalogued accurately in electronic databases (Vandenbroucke et al., 2007; Tullu, 2019); it will also enable readers to understand the focus of the manuscript.

Example 1b.1

From Hoppe et al. (2017) – "Association between chronic oral inflammatory burden and physical fitness in males: a cross-sectional observational study".

Example 1b.2

From Serefoglu et al. (2021) – "A prospective cohort study evaluating the outcome of root canal retreatment in symptomatic mandibular first molars with periapical lesions".

Item 2a: Keywords - Keywords indicating the specific area(s) of interest using MeSH terms or other more applicable terms must be included

Explanation

The important Medical Subject Headings (MeSH) terms related to the study should be used as keywords to facilitate accurate indexing in databases (Mondal et al., 2018). Alternatively, non-MeSH terms can be used if they add value and are meaningful.

Example 2a.1

From Timmerman et al. (2017) - For the observational study entitled "A cross sectional and longitudinal study of endodontic and periapical status in an Australian population", the key words used were "cross sectional studies, panoramic radiography, periapical index, retrospective studies, root canal therapy".

Item 3a: Abstract - The Introduction/Background must briefly explain the rationale or justification for the study

Explanation

When journals permit the background of a project to be included in the Abstract, the rationale and justification for the study should be defined briefly by providing pertinent information that is directly related to a recognizable problem. The gap(s) in knowledge and/or lack of understanding of the topic must be identified to justify the study (Forero et al., 2020).

Example 3a.1

From Scarano et al. (2012) – "Calcium sulfate (CaS) is a simple, biocompatible material with a long history of safe use in different fields of medicine. CaS is a rapidly resorbing material that leaves behind a calcium phosphate lattice, which promotes bone regeneration and hemostasis. The aim of this study was a clinical evaluation of the hemostatic effect of CaS hemi-hydrate (CaSO4), commonly known as plaster of Paris, in endodontic surgery".

Example 3a.2

From Khalighinejad et al. (2017) – "Preeclampsia (PE) is characterized by hypertension and proteinuria after the 20th week of gestation. There is an association between systemic inflammation and adverse pregnancy outcomes such as PE. Therefore, for the first time, the present study aimed to investigate the possible association between maternal apical periodontitis (AP) and PE".

Item 3b: Abstract – The aim(s)/objective(s) of the study must be provided

Explanation

The aim(s) or objective(s) of the study should be provided in the Abstract and describe the population(s) assessed, the exposure(s), comparison and outcome(s) (Mintzker et al., 2022). If relevant, the duration of the study should also be provided.

Example 3b.1

From Qudeimat et al. (2017) – "To prospectively investigate the clinical and radiographic success rates of pulpotomy in permanent molars with clinical signs and symptoms suggestive of irreversible pulpitis using mineral trioxide aggregate (MTA) as a pulp dressing agent."

Example 3b.2

From Ideo et al. (2022) – "The aim of this retrospective cohort study was to investigate the prevalence of apical periodontitis (AP) in patients affected by autoimmune diseases (Ads) taking biologic medications (BMs)."

Item 3c: Abstract – The Methodology must provide (where relevant) essential information on the nature of the study design (retrospective, cross-sectional, prospective etc.), setting, location(s), and relevant dates, including periods of recruitment, exposure, follow-up, outcome(s) assessed and statistical analysis

Explanation

The Abstract should provide the important details of the study and enable the reader to decide whether they wish to read the entire manuscript. Thus, the most key important aspects of the methodology must be summarised in the Abstract and include details on the study type, setting, location(s), duration of study (recruitment, follow-up, outcome assessment) and statistical analysis where appropriate (Haynes et al., 1990).

Example 3c.1

From Razdan et al. (2022) – "Two populations from Aarhus County, Denmark (age range: 20–64 years) were randomly selected using the Danish Civil Registration System. Full-mouth intraoral radiographs (14 periapical, 2 bitewing) of 616 individuals in 1997–1998 (C1: 16 018 teeth) and 398 individuals in 2007–2009 (C2: 10 668 teeth) were taken to ascertain the number of teeth, presence of root fillings (RFs) and apical periodontitis (AP) using the periapical index (PAI). T-tests with unequal variances were used to assess differences between C1 and C2 with respect to age and the number of teeth. Multivariable

and multinomial logistic regression analyses were used to assess the effect of cohort, age and tooth type on the prevalence and relative frequency of RFs and AP".

Example 3c.2

From Song et al. (2013) – "Data were collected from the Microscope Center of the Department of Conservative Dentistry at the Dental College of Yonsei University, Seoul, South Korea, between August 2004 and March 2011. In total, 199 teeth that required endodontic surgery were included in the study. During the surgical procedure, deficiencies of the periapical and marginal bone tissue were measured immediately before the flap was repositioned. The patients were recalled 6 months and 1 year after the surgical procedure to assess the clinical and radiographic signs of healing. The Student's t test or the Mann-Whitney U test and logistic regression were performed to evaluate the parameters. Significant associations between the outcome and all the evaluation parameters were analyzed using the Pearson chi-square test or the Fisher's exact test with a significance level of 0.05".

Item 3d: Abstract - The Results must describe the number of subjects that were included and analysed as well as the most significant results for all experimental and control groups. The results of statistical analysis must be reported in terms of unadjusted and confounder-adjusted outcomes (if relevant) with the results of the statistical analysis. Adverse events or side-effects must also be reported if present or confirmed as absent.

Explanation

If the study is comparative, the size of the exposure effect and its direction must be determined by a comparison of outcome measures in the respective exposure groups and must be reported explicitly. All measures should ideally have point estimates as well as 95% confidence intervals and p-values (Vandenbrouck et al., 2007). Adverse effects must be reported, or a clear statement included that confirms that none occurred.

Example 3d.1

From Pérez-Losada et al. (2020) – "The average glycated hemoglobin A1c (HbA1c) value was 7.0 ± 2.2%. Forty seven (21.8%) had HbA1c levels under 6.5% (mean ± standard deviation (SD) = 6.0 ± 2.2%), being considered well-controlled patients, and 169 (78.2%) had an HbA1c level ≥ 6.5% (mean ± SD = 7.8 ± 2.24%), being considered poor controlled patients. Forty four per cent of diabetics had apical periodontitis, 12.5% had root-filled teeth, and 52.3% had root filled teeth with radiolucent periapical lesions. No significant differences were observed in any of these three variables between patients with good or poor glycemic control. In the multivariate logistic regression analysis the presence of radiolucent periapical lesions in at least one tooth did not correlate significantly with HbA1c levels (Odds ratio (OR) = 1.4; 95% confidence interval (C.I.) = 0.70 - 3.09; p = 0.31)".

Example 3d.2

From Jakovljevic et al. (2020a) – "Tumour necrosis factor (TNF)-α (-308 G/A) single nucleotide polymorphisms (SNP) increased AP susceptibility for heterozygous (OR = 1.72, 95% CI = 1.06-2.80, P = 0.027) and homozygous (OR = 8.55, 95% CI = 1.77-41.36, P < 0.001) carriers of the variant A allele. On the other hand, interleukin (IL)-1β (-511 C/T)

polymorphism exerted a protective effect both in heterozygotes (OR = 0.540, 95% CI = 0.332-0.880, P = 0.013) and homozygotes (OR = 0.114, 95% CI = 0.026-0.501, P < 0.001). In addition, glutathione S-Transferase Mu 1 (GSTM1) and glutathione S-Transferase Theta 1 (GSTT1) null genotypes separately, as well as concomitantly, were associated with an increased risk for AP development (P < 0.001). The null GSTT1 genotype increased approximately twice the risk of Epstein-Barr infection (EBV) in AP (OR = 2.17, 95% CI = 1-4.71, P = 0.048), whilst TNF-α SNP decreased it, both in heterozygotes (OR = 0.20, 95% CI = 0.08-0.48, P < 0.001) and AA homozygotes (OR = 0.07, 95% CI = 0.01-0.37, P = 0.001)".

Item 3e: Abstract - The Conclusion must interpret and summarise the primary aim/ /objective and main findings as well as emphasise the clinical implications

Explanation

A summary of the main findings and the primary "take-home" message(s) should be stated clearly in the Conclusion of the Abstract.

Example 3e.1

From Razdan et al. (2022) – "Two similar general Danish populations examined, respectively, in 1997–1998 and 2007–2009, were associated with a decreasing trend in the prevalence and relative frequency of root fillings (RFs) over the decade. There was no difference in relative frequency of apical periodontitis (AP) in root filled teeth, but an increase in relative frequency of AP in non-root filled teeth. Further population-based

studies including analysis of non-root filled teeth using the full-scale periapical index (PAI) and quality assessment of restorations are recommended".

Example 3e.2

From Jakovljevic et al. (2018a) – "The observed low viral loads point to a relatively rare occurrence of active Epstein-Barr virus (EBV) and Human cytomegalovirus (HCMV) infection in our sample. Latent herpesviral infection does not enhance the production of investigated proinflammatory cytokines".

Item 3f: Abstract - The source(s) of funding must be provided

Explanation

The source(s) of funding for the study must be provided for readers to be aware of the financial support involved if any, and thus be able to evaluate potential conflicts of interest (Als-Nielsen et al., 2003; Nagendrababu et al., 2021a). This should include all sources of support and funding, including grants, donations, and the covering of costs provided by the university (or equivalent), e.g. dental chairs, equipment, materials, nurses and other relevant personnel. If no funding was received this should be stated (Nagendrababu et al., 2021a).

Example 3f.1

From Razdan et al. (2022) – "Funding information - This project was supported by Aarhus University, European Society of Endodontology, Danish Dental Association and Danish Endodontic Society".

Example 3f.2

From Hou et al. (2022) – "Funding information: This work was supported by the National Natural Science Foundation of China (No. 82001037 [X.L. T] and 81970936 [D.M. H])".

Item 4a: Introduction - The clinical problem/question, scientific background and rationale for the study must be provided, including the gap(s) or inconsistencies in the existing knowledge base

Explanation

The relevance of the research problem and the basis on which the proposed research will address the problems identified must be provided clearly in the Introduction and be supported by appropriate citations for readers to understand the scientific basis and rationale of the study (Vandenbroucke et al., 2007). The definition and significance of the problem which is directly addressed by the study should be emphasised. The Introduction should provide a brief outline of the existing knowledge base on the topic and also highlight the gaps in knowledge that will be addressed in the study (Vandenbroucke et al., 2007; Forero et al., 2020). The most current and relevant studies, including systematic reviews if available, should be used in the Introduction to support any statements made.

Example 4a.1

From Bronzato et al. (2021) – "Persistent infection following root canal treatment may result in nonhealing of periapical lesions, with root canal retreatment being indicated. However, if the retreatment fails, periapical surgery is often recommended. In the presence of a radiographically satisfactory root filling, new crown and persistent lesion, periapical surgery may be preferred over root canal retreatment. During periapical surgery, an excisional biopsy of the lesion for histopathological analysis is recommended. Since bacteria are the main cause of the formation and persistence of periapical lesions, a microbiological investigation can be also done in these samples to better understand the reason for failure of the root canal treatment".

Example 4a.2

From Sebring et al. (2022) – "In recent years, there has been increasing interest in possible connections between cardiovascular disease (CVD) and inflammatory conditions originating from the dental pulp. In a case–control population-based study of adolescents, the scores for decayed, missing and filled surfaces (DMFS) were significantly associated with CVD risk factors. Several investigations reported an association between periapical lesions and CVD, as well as root filled teeth per se. In contrast, a study on Swedish women reported an association between CVD and tooth loss, but found no association for either periapical lesions or root filled teeth. Some studies reported that root filled teeth were less common amongst patients with CVD than in controls. However, a higher prevalence of root filled teeth with periapical lesions amongst patients with CVD has also been reported, whilst Meurman et al. reported root filled teeth to be inversely associated with CVD: having at least one root filled tooth was associated with a 49%

reduction in the risk of CVD mortality. To date, the association between endodontic inflammatory disease (EID) and CVD is somewhat contradictory and not fully understood. The inconsistencies in the results are attributable to many factors such as variations in study design, population differences and ambiguities in assessments of independent and dependent variables. Moreover, established risk factors, if not appropriately accounted for in study design and statistical analyses, affect the results".

Item 4b: Introduction - The primary and, if applicable, any additional/secondary aim(s) and objective(s) of the study must be provided, including any pre-specified hypotheses

Explanation

The primary and any additional/secondary aims/objectives of the study and the research question must be provided. Objectives are specific statements on the various outcomes that will make the study achieve its aim(s). The populations, exposures, comparisons groups if relevant, outcomes and measurable parameters must be provided in the objectives. The hypothesis should lead to the development of specific aims/objectives and the research question(s) (Vandenbroucke et al., 2007). However, it is recognised that in exploratory or early discovery research, the objectives may be less specific (Vandenbroucke et al., 2007; Cals & Kotz, 2013).

Example 4b.1

From Jakovljevic et al. (2018b) – "Therefore, the aims of this study were (i) to investigate and compare the levels of oxidative stress biomarkers [8-hydroxydeoxyguanosine (8-

OHdG) and oxidized glutathione (GSSG)] and bone resorption regulators [receptor activator of nuclear factor kappa-B ligand (RANKL) and osteoprotegerin (OPG)] in apical periodontitis lesions and healthy pulp tissues and (ii) to compare these parameters between EBV-positive and EBV-negative apical periodontitis lesions. Additionally, the potential correlation between EBV copy numbers and levels of RANKL, OPG, 8-OHdG and GSSG in apical periodontitis samples was analysed".

Example 4b.2

From Ferrández et al. (2021) – "The primary aim of this study was to radiographically determine the 2-year periapical healing associated with non-surgical root canal treatment (NSRCT) completed through full coverage restorations in teeth with pre-operative periapical radiolucencies compared to those that had the existing restorations first removed (cuspal coverage and direct restorations) and subsequently restored with new full coverage restorations. The null hypothesis was that there was no significant difference in periapical healing between teeth that had NSRCT completed through a pre-existing full coverage restoration, compared to teeth that received root canal treatment after restoration removal, coupled with subsequent placement of a new crown. A secondary aim was to determine the complication rate (porcelain fracture and de-cementation) of accessing through existing extra-coronal restorations for up to 2 years later".

Item 5a: Methods - The details (name, reference number, date) of the approval or exemption granted by an ethics committee, such as an Institutional Review Board, must be provided

Explanation

The research proposal or protocol must be approved *a priori* by the relevant institutional, local, regional, or national ethics and review board that monitors the safe and ethical conduct of the study, and on occasions its scientific rigour. All details including the name of the committee, reference number and approval date must be provided in the manuscript (Kotz & Cal, 2013). If ethical approval is not required, this must be explicitly stated, and the reasons should be provided.

Example 5a.1

From Jordal et al. (2022) – "The project was presented to the Regional Ethics Committee (REC South-East Norway) without objections (ref no. 2015/265 B) and was approved by the Norwegian Center for Research Data, NSD (Ref no 39991). Because the attending dentists adopted a standard, nonexperimental treatment protocol, and because knowledge about health or disease per se is not the purpose of this study, this project falls outside the provisions of the Health Research Act, cf. section 4 and does not require local review board approval according to the European Guidelines for Good Clinical Practice (CPMP/ICH/135/95). The confidentiality and anonymity of patients and course participants were maintained in accordance with national and regional (Office of the Møre and Romsdal Public Dental Health Service) requirements".

Example 5a.2

From Vehkalahti et al. (2020) – "Since register-based data gathered for this study are aggregated, no information exists on patient's identity. The observation unit is age group. Consequently, no ethics approval was required".

Example 5a.3

From Careddu & Duncan (2021) – "An application was submitted to the Research Ethics Committee at St James's Hospital (JREC), Dublin, and Ethical Approval (REC ref: 2017/04/01) was obtained on 25 April 2017".

Item 5b: Methods - The process used for obtaining and storing informed consent must be provided

Explanation

The consent/assent (in case of participants below the age of consent) of participants participating in the study (or of their legal guardian(s), if relevant) is important information that should be included in the application for ethical approval. The procedure of documenting the consent discussion with a potential study participant and method (and safeguards around) of storing should ideally be detailed. The details on waiver of consent (if given and approved) for retrospective record-based observational studies must also to be provided.

Example 5b.1

From Careddu & Duncan (2021) – “After a patient was considered potentially suitable for the study and expressed an interest in participating, an informed consent was obtained. Three copies of the consent were signed: one for the patient, one for the patient's dental chart and one for the researcher's own study record. Any data collected by Roberto Careddu (RCD) collected were stored on an encrypted computer”.

Example 5b.2

From Wikström et al. (2022) – “Before treatment, both spoken and written information about the study was given and written consent was signed by both the parents and their children*”*.

Example 5b.3

From Alyahya & Myers (2021) – “The requirement for obtaining informed consent was waived because of the retrospective nature of the study”.

Item 5c: Methods - The key elements of the study design must be described early in the Methods section

Explanation

Critical details of the study are important for readers to understand the fundamentals of the project and are best provided early in the Methodology section (Annesley, 2010, Kotz & Cal, 2013). A cohort study should have details on the nature of the various cohorts and their exposure details as well as the duration of follow-up. The details of the populations

from which the case and controls were sampled/selected should be described for a case-control study. A description of the population as well the time-point(s) of observation should be given for a cross-sectional study. Any deviation or variation from these three major study designs must be described fully, e.g., "a case-crossover study" or a "cross-sectional case-control study" (Vandenbrouck et al., 2007).

Example 5c.1

From Ruiz et al. (2017) – "This *in vivo* investigation was conducted as a passive retrospective cohort study on a consecutive referral Spanish population".

Example 5c.2

From Hoppe et al. (2017) – "The target population evaluated in this cross-sectional study comprised military police officers from Porto Alegre, Brazil. All of these officers regularly undergo comprehensive health and fitness evaluations twice per year through a standardized protocol called the physical fitness test (PFT)".

Item 5d: Methods - The details of setting(s), location(s), socioeconomic status of participants (if available) and relevant dates, including periods of recruitment, exposure, follow-up, and data collection must be provided

Explanation

Information on the study setting(s), period of study, duration of recruitment and follow-up, and study location(s) allows the readers to assess the context of the study, relevance

and determine the generalisability of the results to the intended population(s) (Vandenbroucke et al., 2007). If relevant, it is good practice to include the socioeconomic status of the participants.

Example 5d.1

From Sebring et al. (2022) – "Between May 2010 and February 2014, patients under 75 years of age, who had recently suffered a first myocardial infarction (MI), were recruited from 17 Swedish hospitals. Exclusion criteria were prior MI, heart valve replacement or any other condition limiting the ability to comply with the study protocol. The patients were recruited in connection with their hospitalization and scheduled for an outpatient visit at their local Departments of Cardiology and Dental Medicine 6–10 weeks later. Controls, matched for gender, age (±3 months) and geographical area (same postal code) and without a prior MI or heart valve replacement, were identified through the Swedish population registry. A total of 805 patients and 805 controls from 37 different regions were included. Information on medical and family history of cardiovascular disease (CVD), pharmacological treatment, level of education, occupation and marital status as well as risk and health-preserving factors, such as smoking and alcohol use, was collected by means of structured questionnaires (routine variables reported to the SWEDEHEART case record forms plus additional questions for the PAROKRANK study). Periodontal status of MI patients and controls was diagnosed from panoramic radiographs".

Example 5d.2

From Vernazza et al. (2015) – "Structured interviews were conducted by one researcher. Demographic, socio-economic and dental history questions were included based on best practice guidelines".

Item 5e: Methods - Information on how the sample size or sample population was determined *a priori* must be provided as well as the rationale for sample size calculation, preferably with reference to the published literature or a pilot study with additional detail as to why the defined sample size makes the study worthwhile.

Explanation

The importance of including an appropriate number of participants for the results to be valid cannot be over-emphasised. The number of participants should be determined (sample size calculation) prudently prior to the study in order to fulfil scientific and ethical standards (Annesley, 2010). The sample size should satisfy the clinical and statistical requirements and can be based on high quality studies, reported in the literature, population of interest or a pilot study, but importantly should account for any potential dropouts if relevant. The parameters and calculation used to define a sufficient sample size must be reported comprehensively. Underpowered studies run the risk of misinforming the reader by including non-significant findings due to lack of power. If a small sample size is used, such as when observing or treating rare conditions, a clear justification for using a small sample size or the need for early publication should be included. In matched case control and cohort studies, if a 1:1 or other ratio is selected this must be factored into the sample size calculation alongside any other stratification variables (e.g. age, gender).

Example 5e.1

From Rutsatz et al. (2012) – “Sample size was calculated considering a 95% confidence level, 80% power, and the ability of the study to detect at least a moderate correlation (r = 0.5) between the predictors (periodontal attachment loss and gingival recession) and the outcome (response to pulp sensibility test (PST)) as quantitative variables. These variables resulted in a minimum sample size of 29 subjects (9), which was increased by 50% for multivariate analysis purposes and to avoid a potential loss of information. The final sample comprised 45 subjects”.

Example 5e.2

From Silva et al. (2021) – "A pilot study was performed to calculate the sample size, using a convenience sample of 20 CBCT images of teeth with VRF and 20 matched control teeth (without VRF). Considering root dentin thickness as the main tested risk factor for VRF (exposure variable)—≤ 1.3 mm (exposed) and ≥ 1.4 mm (unexposed)—the proportion of exposed teeth was 54.2% (n = 11) for the cases and 35.0% (n = 7) for the controls. Other parameters included a 5% level of significance (type I error rate) and 80% power (20% type II error rate). Based on this information, the minimum odds ratio (OR) to detect was 2.2, and the estimated sample size was 81 cases and 81 controls for this matched case-control study (one-sided test)".

Item 5f: Methods - All studies should include inclusion/exclusion criteria as well as the sources and methods of participant selection. Methods of follow-up must also

be provided in cohort studies and the rationale for the choice of 'cases' and 'controls' in case-control studies

Explanation

The participants enrolled in a study should be described clearly for readers to be able to apply and compare the results to their own setting(s) and population(s) (Vandenbroucke et al., 2007; Annesley, 2010). Eligibility criteria, clinical, demographic, and other characteristics including age, gender, diagnosis and medical co-morbidities, used in the selection of study participants should be clearly described in the form of inclusion and exclusion criteria. The source population from which the study participants were derived (e.g. the general population of a region or country or a subpopulation) and the method of selection of the participants must also be described. All this data leads to an informed decision on the validity and generalisability of the results.

Example 5f.1

From Casey et al. (2022) – "Potential cases were screened for study eligibility using prespecified inclusion and exclusion criteria. These criteria were as follows: patients between 6 and 16 years at the time of treatment initiation of an immature (stage 1–4 according to Cvek's criteria), permanent tooth that received primary endodontic treatment with regenerative endodontic procedures (REPs), Calcium hydroxide $Ca(OH)_2$ apexification treatment (APEX), or mineral trioxide aggregate (MTA) APEX (apical barrier). Endodontic treatment was required to have been completed and an adequate restoration placed at the time of clinical record review. Because of the retrospective study design, we could not always confirm the restoration type from the patient clinical record,

so we depended on the radiographic appearance of an adequately sealed restoration. A documented clinical recall of 3 months or greater was also required. Eligible individuals without a minimum 3-month recall and all patients with a documented follow-up clinical visit were invited to attend a follow-up study visit; a modest compensation was offered. Prospective participation was voluntary, and assent/consent of the participant and/or guardian was obtained by study personnel. Cases with missing or incomplete clinical records were excluded from analyses".

Item 5g: Methods - For matched studies (e.g. cohort, case-control) the matching criteria and rationale must be provided

Explanation

The method and variables used to match in a cohort study (if applicable) should be elaborated. The matching of controls to cases needs to be performed in a sensible and rigorous manner. The ratio 1:1 or other should be stated. The variables that are to be matched and the method used for this needs to be described. Matching should be performed judiciously and the key potential confounders such as age, gender and tooth type should be mentioned (if relevant) and potentially stratified. If the potential confounders are not distributed uniformly, the appropriate analysis performed to address this lack of uniformity should be mentioned (Vandenbrouck et al., 2007; Costanza, 1995).

Example 5g.1

From Kim et al. (2018) – "Nearest neighbor 2:1 propensity score matching for the following 5 variables, without replacement, was performed for cases of primary microsurgery and those of micro-resurgery: age, sex, tooth type, lesion type, and postoperative restoration. A balance between the 2 groups with regard to each variable was evaluated by the determination of absolute standardized differences before and after matching. An absolute standardized difference of <0.1 was considered to represent good balance between the 2 groups".

Example 5g.2

From PradeepKumar et al. (2019) – "Cases were individually matched with controls in a ratio of 1:1 for age (±5 years), gender, tooth type, instrumentation system, master apical file (MAF) size and taper (Table 1), technique of canal filling and time period from canal filling (similar or more for controls). Cases and controls were selected from a pool of patients treated by three qualified endodontists with more than 10 years of experience. Vertical root fracture (VRF) cases were matched with controls treated by the same operator".

Item 5h: Methods - All outcomes, exposures, predictors, potential confounders, and effect modifiers must be defined clearly

Explanation

The definitions or criteria used to assess variables including outcomes, exposures, predictors, potential confounders, and effect modifiers should be provided and described clearly. The criteria used to determine the outcomes should also be described fully.

Example 5h.1

From Casey et al. (2022) – "The primary outcome in this study was the duration in months of patient-centered success of the original regenerative endodontic procedure (REP) or apexification treatment (APEX) treatment. Patient-centered success was defined as an asymptomatic, functional tooth that did not require further endodontic or surgical intervention after completion of the original REP or APEX treatment during the study observation period. Persistent or emergent symptoms, swelling, or sinus tracts and endodontic and surgical treatments subsequently performed after the primary REP or APEX on the treated tooth were assessed by reviewing the clinical treatment records and by direct evaluation of the participant and/or his or her guardian during the prospective clinical visit when possible. The date that clinical failure was determined or when an additional endodontic intervention or tooth extraction was performed was recorded as well as the documented reason for failure or additional clinical intervention. We did not include radiographic outcomes as part of the definition of patient-centered success because of the inherent difficulty in assessing radiographic periapical pathosis in immature teeth, inconsistent radiographic quality obtained in a pediatric population with traumatized anterior teeth, and not qualifying as a patient-centered outcome. Radiographic findings relating to longitudinal root thickening and lengthening from this cohort will be reported in a subsequent article reporting clinician-centered outcomes. In a multivariable analysis, several covariates that may influence patient-centered success including patients' age, preoperative swelling and/or a sinus tract, preoperative periapical radiolucency (PARL), stage of root development, trauma as the etiology of

endodontic pathology, and the type of procedure performed (REP vs APEX) were assessed.

The secondary outcome evaluated in this study was survival of the treated tooth, which was defined as the tooth being present in the dental arch throughout the study observation period. A submerged root was not considered survived. An exploratory aim of this study was to identify potential treatment factors that may be associated with the success of REPs. We also assessed the presence of tooth discoloration after treatment completion, and this was evaluated as a dichotomous outcome that was noted in the dental record and/or during the in-person prospective research visit".

Example 5h.2

From Kwak et al. (2019) – "The confounding variables that were extracted from the insurance cohort database included the treatment type, gender, age, institution type, diagnosis, arch type, tooth type, canal filling method, number of visits, and use of rubber dam. Age was divided into 4 groups (i.e., <20, 20–39, 40–64, ≥65). The institution type variable indicated where the patients underwent the treatment and was divided into 2 groups (i.e., dental hospital [code number 41] and local dental clinic [code number 51]). The top 10 diagnoses codes (i.e., asymptomatic irreversible pulpitis [National Health Insurance Cohort Database (NHICD) code: caries of dentin and caries of cementum], symptomatic irreversible pulpitis [NHICD code: pulpitis], pulp necrosis [NHICD code: pulp necrosis and pulp degeneration], symptomatic apical periodontitis [NHICD code: acute apical periodontitis], asymptomatic apical periodontitis [NHICD code: chronic apical periodontitis and chronic periodontitis], chronic apical abscess [NHICD code: periapical abscess with sinus], and acute apical abscess [NHICD code: periapical abscess

without sinus]) for endodontic treatment were selected within the scope of the NHICD. The arch-type variable indicated maxillary or mandibular teeth. The tooth-type variable indicated anterior, premolar, or molar teeth. The number of visits was categorized as single or multiple. Finally, use of a rubber dam by the medical professional was also investigated in the present study".

Item 5i: Methods - Sources of data and details of the methods of assessment (measurement) for each variable of interest must be provided

Explanation

The validity and reliability of a study are influenced by the exact method used to measure the exposure, confounding factors and outcome variables. The detection of a cause-effect relationship between the variables can be affected by measurement error on exposures and outcomes leading to spurious and misleading relationships. The risk of residual confounding increases when the identified confounders are measured inaccurately (Becher, 1992). If relevant, authors could report the validity and reliability estimates from the reference studies referenced in order to assist in the calculation of measurement error or sensitivity analyses (Vandenbroucke et al., 2007). Authors should also report if different methods were used for data collection among the groups compared.

Example 5i.1

From Bakhsh et al. (2022) – "Blood samples processing - The serum was analysed using the Magnetic Assay human premixed multi-analyte kit (R&D systems, Bio-techne) according to manufactures instructions for identification of inflammatory mediators

levels (Fibroblast growth factor (FGF)-23, Interleukin (IL)-1β, IL-6, IL-8, high-sensitivity C-reactive protein (hs-CRP), pentraxin 3, tumour necrosis factor (TNF)-α, matrix metalloproteinases (MMP)2, MMP8, MMP9), E-selectin, vascular cell adhesion molecule (VCAM)-1 and intercellular adhesion molecule (ICAM)-1) using the Bio-Rad Bio-Plex 200 analysers (Bio-rad). Levels of C3 and ADMA were detected using enzyme-linked immunosorbent assay (ELISA) and iMark microplate absorbance reader (Bio-Rad). Radiographic outcome analysis - Periapical radiographs and cone-beam computed tomography (CBCT) scans were assessed by two experienced endodontic specialists. The outcome scores were recorded after consensus agreement between both examiners using a six-point classification".

Example 5i.2

From Careddu & Duncan (2021) – "At every follow-up appointment (1 week, 3, 6 and 12 months), the teeth were assessed for the presence of signs and symptoms of pulpitis, whilst pulp vitality was verified and recorded. This involved carrying out a percussion test and a cold test at −50°C (Endofrost). The integrity of the coronal restoration was verified visually under the microscope. After 12 months, a periapical radiograph supplemented the history and clinical examination. For practical reasons, the pulp sensibility testing was carried out by the practitioner; however, the 12-month radiographs were assessed blindly by a second evaluator (HD) not involved in the provision of treatment. At all review points, the teeth were categorized as either "successful," "unresponsive but successful" or "failed." Treatment was considered "successful" when the tooth responded positively (including a consistently reduced response) to cold test, the response did not linger, was symptom-free and not tender to

percussion, and there was no evidence of an apical radiolucency. Unresponsive teeth that did not demonstrate any apical radiolucency and were symptom-free but did not respond to the cold tests were noted as "unresponsive but successful." A treatment failure was noted if either the patient reported pain, the tooth was tender to percussion and/or a periapical radiolucency was present".

Item 5j: Methods - Efforts taken to identify and address potential sources of bias must be provided

Explanation

Bias in any form causes systematic deviation from the truth and various measures must be incorporated into a study at the design stage to minimise the influence of bias (Sackett, 1979). All measures taken to reduce bias during the study design, data collection, data analysis and interpretation must be reported. As a further guide to researchers, information bias in case-control studies can be managed using an appropriate control group, while quality control programmes can identify any changes in data due to bias as a result of using multiple examiners (Vandenbroucke et al., 2007).

Example 5j.1

From Vehkalahti et al. (2020) – "The 5-year interval was selected to find and verify changes, if any, in the volume and content of endodontic treatments. No sampling was done since this study included all cases and treatments in the years observed. Instead of individual-based micro-level data, aggregated macro-level data were used. Such data

provide information constructed by combining information on the lower-level units (here: patients), forming the basis for the higher-level units (here: age groups)".

Example 5j.2

From Gomes et al. (2016) – "As described in a previous study, prior to conducting the radiographic analysis, the examiner underwent a training period using 34 images independent of the Baltimore Longitudinal Study of Ageing (BLSA) radiographs. Calibration training was performed by two examiners, both were experienced specialists in endodontics, who independently evaluated the panoramic radiographs twice, with a period of 45 days between the first and the second evaluation Inter examiner agreement levels after the second examination yielded a kappa of 0.912 for root canal treatment (RCT) and a kappa of 0.801 for apical periodontitis (AP). The intra-examiner agreement (MSG) demonstrated a kappa of 0.983 for RCT and a kappa of 0.959 for AP".

Item 5k: Methods - The handling of quantitative variables in the analyses must be explained. Decisions on how groupings were made and/or how category boundaries were defined for continuous variables must be described

Explanation

The method of data collection and any analyses on exposures, effect modifiers and confounders should be determined before the commencement of a study. In some cases, continuous variables are categorised or dichotomized (Altman, 2005). If so, the rationale for the categorization and how it might affect the interpretation and generalisability of the results must be explained. The number and frequency of cases and controls in each

category should be given along with mean values, percentages, or results of model analysis. The relationship between an outcome and the exposure may not necessarily be linear and other types of relationships should be investigated and analysed (Vandenbroucke et al., 2007).

Example 5k.1

From Bakhsh et al. (2022) – "Due to the lack of normality in biomarker levels, the values were transformed to a logarithmic scale and the difference between Median of the Control and the Disease groups was calculated using two-sample t-test. Linear associations with other continuous variables were tested using Pearson's correlations and for other non-linear associations Spearman's correlation was used. Furthermore, regression models were conducted to estimate beta coefficients involved in those significant correlations. Multiple regression models were also conducted to control the potential confounding effect of some variables at T0 [glycated hemoglobin A1c (HbA1c), Triglycerides, high-density lipoproteins (HDL), Body Mass Index (BMI), waist circumference, age and gender)] on the primary relationships".

Example 5k.2

From Hoppe et al. (2017) – "For analytical purposes, both apical periodontitis (AP) and root canal treatment (RCT) variables were dichotomized as absent or ≥1 teeth with AP or RCT. Endodontic Burden (EB) was calculated as the sum of the total number of teeth with AP and/or RCT for each individual. EB was categorized as zero, 1–2 or ≥3 teeth, based on the stratification used on previous studies. The oral inflammatory burden (OIB) was

calculated combining EB and clinical attachment loss (AL) and was defined according to four categories: EB < 3 and no AL ≥ 4 mm; EB ≥ 3 and no AL ≥ 4 mm; EB < 3 and AL ≥ 4 mm; and EB ≥ 3 and AL ≥ 4 mm".

Item 5l: Methods - All statistical methods, including those used to control of confounding factors in the study and in the analysis of the data must be described

Explanation

The data acquired to answer a research question can be analysed using various statistical models. The authors should clearly state the statistical models used to analyse the primary study objectives. The collected data may provide opportunities for additional statistical analyses than those stated *a priori*. Any additional analyses performed due to the nature of the data collected should be reported along with the revised rationale and an interpretation of the additional results. The various groups may not be similar to the baseline data, due to the effects of confounding. This should be managed by stratification or multiple regression analyses depending on the study design (Slama & Werwatz, 2005). The rationale for the selection of variables in the statistical tests/models should be explained. The method of and rationale for selecting specific variables as potential confounders for inclusion in the final statistical model should be described. The variables responsible for the major confounding among the identified potential confounders should be identified. The imputation procedures, data transformation, and calculations of attributable risks, other novel statistical methods and software should be described and referenced as necessary. The description should enable any reader with access to the original data to replicate the analyses and results (Vandenbroucke et al., 2007).

Example 5l.1

From Moreno et al. (2013) – "Statistical analyses were performed by using the SPSS software (Statistical Package for the Social Sciences, version 17.0; IBM, Chicago, IL). Initially, a descriptive analysis was performed including the variable healthy treated tooth (dependent variable) and the covariates (independent variables) gender, quality of coronal restoration, quality of endodontic treatment, apical limit of obturation, and presence of post. Descriptive data were obtained as frequencies of the categories within each variable. The $\chi 2$ test was applied to each covariate in relation to the periradicular status of treated teeth to look for significant associations ($P < .05$). A bivariate analysis was also performed to evaluate the combined effects of quality of coronal restoration and endodontic treatment. Next, unadjusted univariate logistic regression was applied between the dependent variable and the covariates to evaluate the association of each one with healthy periradicular conditions through calculation of odds ratio and 95% confidence interval. Finally, adjusted multivariate logistic regression was used to deduce the influence of each covariate on the periradicular conditions. This multiple analysis included only the variables that presented $P < .05$ in the previous analysis. The method used to insert the variables in the logistic model was the backward stepwise, which involved all variables chosen. Furthermore, these variables were gradually excluded until the final model was formed. A probability level of .05 was used as the criterion for statistical significance".

Example 5l.2

From Prati et al. (2018) – "Descriptive analysis using subject and tooth as unit of analysis was performed; mean (standard deviation) or proportion and bivariate tables according to the type of parameters (quantitative or qualitative) were computed. The $\chi 2$ test was used aiming to evaluate the association between anatomical, clinical and radiographic parameters with the final status (survival and lesion). Cox proportional hazards analysis was used to compare the distributions of time-to-event among teeth having the event for extracted teeth and for teeth that developed an endodontic lesion [(evidenced by periapical index (PAI) ≥ 3)]. These two distributions were compared without the inclusion of censored values. Bootstrapping technique was used to obtain confidence intervals and a P-value aiming to obtain a more accurate estimate, given the skewed distribution of time-to-event data. Creating a large number of datasets and computing the statistics on each of these datasets fits better to the definition of confidence interval. Bias-corrected and accelerated (BCa) 95% confidence intervals were computed. A survival curve was constructed by means of Kaplan–Meier evaluation using extraction as the end-point. Multilevel analysis was carried out at patient and tooth level. A logistic binary regression was applied as the outcome was dichotomous (survival and lesion), using as a reference category, respectively, extraction and not healthy. Age and gender were set as person specific fixed effects whereas clinical parameters (tooth location, tooth type, initial diagnosis, initial PAI, root filling length and coronal restoration) as tooth specific fixed effects. α- level was a priori set at 0.05".

Item 5m: Methods - The methods used to examine subgroups and interactions must be described, if applicable

Explanation

The need for subgroup analyses should be anticipated during the design of the study based on the variables under investigation. If subgroup analyses were subsequently indicated based on the data collected, the rationale for such analyses and the analytic methods used must be described. Presence of interactions (i.e., when the effect of one variable depends on the value of another variable), effect modification (i.e., when a variable differentially modifies in a positive or negative manner of the observed effect) and their nature should be described along with the analytic methods used to identify them.

Example 5m.1

From Hoppe et al. (2017) – "Binary logistic regression models with robust variance estimator were used to assess the association between endodontic/periodontal variables and physical fitness. In these models, the dichotomous physical fitness test (PFT) was coded as 1 when an individual reached the highest PFT score, and 0 otherwise. Four models were fitted, always including age, body mass index (BMI) and regular exercise. Model 1 included only endodontic burden (EB) as the main independent variable, whereas models 2 and 3 included also clinical attachment loss (AL) and probing depth (PD), respectively. Model 4 included the oral inflammatory burden (OIB). Odds ratio (OR) and 95% confidence interval (CI) were reported. P-values were calculated using Wald tests with parametrization using ratios. No interactions were found during model fitting".

Example 5m.2

From Prati et al. (2018) – "Bootstrapping technique was used to obtain confidence intervals and a P-value aiming to obtain a more accurate estimate, given the skewed distribution of time-to-event data. Creating a large number of datasets and computing the statistics on each of these datasets fits better to the definition of confidence interval. Bias-corrected and accelerated (BCa) 95% confidence intervals were computed".

Item 5n: Methods - Missing data (e.g. drop-outs, data not reported) must be addressed and described

Explanation

Missing data (e.g. unanswered questionnaire items, gaps in secondary data sources etc.) may influence the validity and reliability of the study (Morshed et al., 2009). The quantity of missing information in each variable should be described. Statistical methods applied to interpret the effect of missing data should be described (Vandenbroucke et al., 2007). It is recognised that it is not always possible to attain missing information in retrospective study designs. If no dropouts occurred, this must be reported explicitly.

Example 5n.1

From Fransson et al. (2021) "As some individuals had missing data and were excluded, the data were based on 216,764 individuals and the logistic regression on 215,940 individuals".

Example 5n.2

From Signor et al. (2021) “A total of 239 variables related to endodontic diagnosis, retreatment procedures, and follow-up visits were collected. Unnecessary features (patient identity code, date of appointments) and variables with all missing values were eliminated. Some attributes were integrated, recoded, or calculated to construct new variables.”

Item 5o: Methods - The analytical methods that take account of the sampling strategy (if applicable) in Cross-sectional studies must be described

Explanation

In cross-sectional studies, the method used for sampling from the source population must be described and elaborated upon. The type of stratification used for sampling must be detailed.

Example 5o.1

From Irinakis et al. (2020) - “After the external cervical resorption (ECR) group was finalized, a second group of patients with an equal number of participants (n = 76), and similar age and sex distribution was created from the same pool of endodontic patients to form a control group. There was no statistically significant age difference between the control (53.56 ± 20.2 years) and the ECR group (50.96 ± 18.8 years) (independent sample t test, P= 0.409). The inclusion criteria for this group were the same as for the ECR group, except for the presence of ECR”.

Example 5o.2

From Segura-Sampedro et al. (2022) – "An additional 28 subjects, eight men and 20 women (58.6 ± 11.9 years), who agreed and met the same inclusion/exclusion criteria, healthy and who reported no history of inflammatory bowel disease (IBD), were matched for age and sex, constituting the "control group". Controls were recruited from patients in the same city and health district, seeking for the first time routine dental care (not emergency care) in the same hospital between 2018 and 2021".

Item 5p: Methods - Sensitivity analyses must be described when used

Explanation

The robustness of the primary results should be evaluated by varying the assumptions or restricting data of certain variables (e.g., inclusion criteria of variables, various case definitions for exposures or outcomes, confounding adjustment, missing data analyses) when entered into the statistical method/models. These actions will not affect the direction and magnitude of the primary results if the data are robust. If the sensitivity analyses lead to results that are different from the primary analyses, the changes should be reported and explained. Wherever possible, the influence of bias and assumptions should also be evaluated statistically (Vandenbroucke et al., 2007).

Example 5p.1

From Kim et al. (2018) – "For the matched cases, survival analysis was performed to estimate the prognosis of primary endodontic microsurgery and endodontic micro-resurgery over time. Estimated success rates were calculated by using the Kaplan-Meier

method. Log-rank tests were applied to evaluate differences in success rates between the primary microsurgery and micro-resurgery groups. The second step of the analysis was the investigation of potential prognostic factors influencing the outcome of endodontic micro-resurgery. All variables were subjected to multivariate Cox proportional hazard regression analysis, followed by stepwise regression with the backward elimination method".

Example 5p.2

From Gomes et al. (2016) – "Bivariate and multivariate models using Poisson regression with robust variance estimated the relationship (relative risk) between apical periodontitis (AP), root canal treatment (RCT), endodontic burden (EB), pocket depth (PD), oral inflammatory burden (OIB) and long-term risk of incident cardiovascular event (CVE). All variables associated with CVE in the bivariate analysis with a P-value <0.25 were considered potential confounders [(known risk factors for cardiovascular disease (CVD)] and were included in the multivariate models predicting CVE, where the value for rejection of the null hypothesis was set at $P \leq 0.05$. Wald chi-square test estimated the strength of the association".

Item 6a: Results - The number of participants in each stage of the study (i.e., eligibility, recruitment, available at follow-up and included in analyses for relevant outcome(s)) must be described

Explanation

Relevant descriptive data must be reported prior to assessing the association between exposure(s) and outcome(s). Detailed reporting on the relevant patient exposure and the number of outcome events or summary measures over time (in case of cohort studies / cross sectional studies) and number of exposures or summary measures of exposures (in case of case control studies) must be performed. In matched studies, the participant numbers in each group including stratifications should also be detailed.

Example 6a.1

From Careddu & Duncan (2021) – "Eighty-seven patients were assessed for eligibility having presented with a symptomatic carious lesion in a premolar or molar tooth. Of those patients, 25 were excluded due to preferring root canal treatment (RCT)/extraction (12 patients), refusing to participate (6 patients) and not meeting inclusion criteria for deep/extremely caries (7 patients). Sixty-two teeth were enrolled for this study and 11 were subsequently excluded intraoperatively. Of those 11 cases, seven (one with severe, two with moderate and four with mild pulpitis) did not have carious pulp exposure after non-selective removal of caries and they were treated either with resin-based composite (RBC) restorations or with an indirect pulp capping and a calcium hydroxide lining. Subsequently, one of the teeth without pulp exposure but with a diagnosis of moderate pulpitis required RCT after 5 months as it displayed signs of pulpal necrosis and apical radiolucency. Of the remaining 4 cases, one case provisionally diagnosed with mild pulpitis and three cases with severe pulpitis were treated immediately with RCT as after access to the pulp chamber partial pulpal necrosis was diagnosed. Fifty-one teeth were finally included and treated within this study, with 41 teeth reviewed after 1 year".

Example 6a.2

From Rechenberg et al. (2021) – "Over a period of 15 months, 368 patients suspected of having a painful endodontic condition presented at the emergency unit of the Clinic of Conservative and Preventive Dentistry and were further evaluated to participate in the study. Of the 368 patients, two hundred fifty-six (n = 256) had painful endodontic conditions confirmed by a dentist specialized in endodontics and could be recruited for participation. Subsequently, ninety-four patients (n = 94) had to be excluded from the analysis with reasons".

Item 6b: Results - Reasons for non-participation (e.g., not eligible, losses/drop-outs) must be described

Explanation

If a systematic reason for non-participation or non-completion of the study is present, it may bias the study results. When a participant withdraws or is lost from the study prior to the end of the observation period, it is collectively called 'loss to follow-up'. The validity of a study may be adversely affected by lack of detail regarding loss to follow-up and it is therefore essential to describe participants lost to follow-up in the results section and the reason for their loss (Ferreira et al., 2019). For example, if a participant in a pulp capping trial does not wish to attend follow-up because they already had a pulpectomy during an emergency visit due to pain, not accounting for this patient would lead to a possible overestimation of the success rate of the treatment. Thus, the number of participants who were lost to follow-up must be documented and included in the flowchart along with a reason for their unavailability.

Example 6b.1

From Careddu & Duncan (2021) – "Of those patients, 25 were excluded due to preferring root canal treatment (RCT)/extraction (12 patients), refusing to participate (6 patients) and not meeting inclusion criteria for deep/extremely caries (7 patients). Ten patients did not re-attend for 1-year review and were excluded from the study (5 reversible, 5 irreversible pulpitis; 5 moderate, 5 mild pulpitis. Specifically, four of the ten patients did not attend the second appointment for permanent filling placement; however, they subsequently attended the clinic as an emergency presenting with pain and sensitivity due to dislodgement of the Biodentine™ restoration. All four teeth had subsequent RCT. The remaining 6 patients returned to get the permanent restoration placed, but not the subsequent 1-year review".

Example 6b.2

From Kirkevang et al. (2015) – "Of these, 46 recordings were not included in the analyses due to insufficient quality of the radiographs".

Item 6c: Results - Changes in baseline dates of recruitment, follow-up, and study duration reported in the Methodology must be described, if applicable

Explanation

Comprehensive details about the recruitment of participants, which will be considered as the baseline, and the intervals at which the recruitment and follow-ups were

performed must be provided in the Results section. The total duration of the observation period of the study should also be defined. If no changes to baseline dates of recruitment, follow-up, and study duration occurred, this must be reported explicitly.

Example 6c.1

From Jonasson et al. (2017) – "From 1 January 2008 until 31 December 2012, 57 patients were consecutively recruited. Four patients were examined but excluded according to the exclusion criteria. At the 1-year follow-up, the recall rate was 98% and at the 2-year follow, the recall rate was 93%".

Example 6c.2

From Azim et al. (2016) – "Follow-up time periods ranged from 6 months to 8 years with a mean follow-up period of 2 years/tooth".

Item 6d: Results - The baseline demographic and clinical characteristics of study participants as well as information on exposures and potential confounders must be provided

Explanation

To provide clarity on the generalisability of the results to readers, the relevant details of the study participants and their exposure must be provided. Complete data on recruited study participants at each stage must be provided. Potential confounders and how they were measured and handled should be mentioned. Categorical variables, such as types of

root canal patterns or types of tooth fracture should be preferentially presented as proportions as well as absolute numbers. For continuous data, results should be presented as mean values and standard deviations (for symmetrical distributions) or as medians and percentile ranges (for asymmetric distributions). For rank order or ordinal data (e.g., Likert-type scale), medians and percentile ranges can be used. The same information should not be duplicated in both the text and the tables. If tables are used, only the most important results should be mentioned in the text.

Example 6d.1

From Rechenberg et al. (2021) – "The mean age of these included patients was 40 ± 15 years. The gender ratio was 61 females to 101 males. Most of these individuals had a tooth that was negative to cold but did not have a periapical swelling (Table 1). The pain history of the teeth that still tested positive to cold was significantly ($P < 0.05$) longer than that of cold-negative counterparts (Table 1). Additionally, in this group of teeth that were still sensible to cold there were significantly more molars ($P < 0.05$) and fewer restored teeth than in the groups that tested negative to the cold test (Table 1)".

Example 6d.2

From Kirkevang et al. (2015) – "Three hundred and thirty persons (mean age 42.9 years, 8744 teeth) participated in all three examinations (group 1); an additional 143 persons (mean age 42.3 years, 3696 teeth) participated only in the two first examinations (group 2). In all, 21133 periapical index (PAI) score transitions between two successive examinations were possible".

Item 6e: Results - The number of participants with missing data must be provided for each variable. If relevant, follow-up times should be summarised clearly and accurately (e.g., average, or total time).

Explanation

Information on missing data must be described clearly since it may affect the generalisability of the results (Morrow, 2013). The authors should provide an explanation why data are missing, in an attempt to avoid bias. In longitudinal studies, authors may present the follow-up time as mean or median follow-up time. A maximum and minimum time of follow-up should also be provided. If the distribution of the participants is not representative of the target population, it could lead to participation bias. In case-control studies, to conclude valid estimates of the exposure to the disease, it is of pivotal importance that the sample of patients recruited in the case and control groups are comparable in other respects. Low participation does not automatically reduce the validity of the results, but transparent information needs to be provided. The same information should not be duplicated in the text and tables.

Example 6e.1

From Serefoglu et al. (2021) – Of the final included 103 patients (50 males and 53 females), the age of the patients ranged between 18 and 68 years and with a mean of 32.64 (± 12.92) years. The follow-up period was 24–48 months after root canal retreatment; 46% teeth were followed up for 24 months, and 54% teeth were followed

up for 25–48 months. The mean follow-up periods were 29, 28 and 32 months for healed, healing and nonhealing cases respectively [with a mean of 29 (± 6)].

Item 6f: Results - Information on number of outcomes or summary measures over time must be described

Explanation

Reporting relevant data prior to concluding associations between exposure and outcome is mandatory in all study designs. Well-constructed tables might be useful to summarise data (with caution not to repeat information provided in the text). In case-control studies, the exposure must be reported separately for cases and controls. In cohort studies, the number of events (outcomes) must be presented in the results. The change in the event rate at every follow-up needs to be presented. Similarly, in the cross sectional studies the number of events / prevalent outcomes should be mentioned.

Example 6f.1

From Kirkevang et al. (2012) – "Figure 1 shows the distribution of number of teeth with AP, number of teeth with root fillings and number of lost teeth for the 327 individuals who participated in all three examinations. The proportion of individuals who had no apical periodontitis (AP) and the proportion of individuals who had no root fillings decreased during the 10-year observation period".

Example 6f.2

From Weissman et al. (2022) – "Age, gender, the presence of an isthmus and length of the retro-preparation had no significant effect on the outcome. The size of the lesion had a significant influence on the outcome after 6 months, where large lesions were associated with a lower success rate (p = .007), but the significance was lost after 12, 24 and 48 months. Regarding tooth type, mandibular anterior and premolar teeth had a lower success rate after 12 months (p = .036), but there were no significant differences at the 6-, 24- and 48-month follow-up visits".

Item 6g: Results - For multivariable analyses developing risk profiles or reducing the effect of confounders, the effect of all included independent variables may be reported, as well as their effects on the prediction model (if applicable)

Explanation

To reduce the effect of confounders, multivariable analysis may be used. If sufficient data is available, data should be stratified on relevant variables that could potentially affect the outcome, e.g., age, gender, socio-economic status, or type of teeth, and estimates of association should be provided within each stratum. Independent variables with missing data should be addressed in the Discussion section (see item 7).

Example 6g.1

From Prati et al. (2018) – "Multilevel analysis concerning the outcome healthy versus endodontic lesion group (Table 6), confirmed the clinical relevance of tooth type (P = 0.007) and location (P = 0.045), with anterior type being associated with more healing in comparison with posterior teeth [Odds ratio (OR) = 2.983)]. Maxillary location improved

healing (OR = 1.994) in comparison with the mandible. Furthermore, an initial diagnosis of pulpal disease increased healing status in comparison with re-exacerbated diagnosis (OR = 3.536) ".

Example 6g.2

From Murillo-Benítez et al. (2020) – "Multivariate logistic regression analyses were run with pre-operative pain (numerical visual analogue scale (VAS) scale), anxiety (short-form Dental Anxiety Inventory (S-DAI), 0 = 9–23; 1 = 24–45), endodontic diagnosis (0 = irreversible pulpitis; 1 = apical periodontitis) and anti-inflammatories intake (0 = no; 1 = yes) as independent explicative variables and intraoperative pain (0 = absent or mild; and 1 = moderate or intense) as dependent explained variable. Only high level of anxiety [Odds ratio (OR) = 4.0; 95% confidence interval (C.I.)] = 1.7–9.3; P = 0.001) and diagnosis of apical periodontitis (OR = 4.4; 95% C.I. = 1.9–10.0; P < 0.001) correlated significantly with greater intraoperative pain. Pre-operative pain and intake of anti-inflammatories did not correlate with intraoperative pain".

Item 6h: Results - Unadjusted (or uncorrected or crude) estimates and, if applicable, confounder-adjusted estimates and their precision (e.g. 95% confidence intervals) must be described. Which confounders were adjusted for and why they were included must also be described

Explanation

The unadjusted exposure estimate reports the result of a crude comparison of the exposed and the unexposed group. In an observational study, this comparison may be

biased, since other factors (so-called confounders) associated with the outcome may differ between the groups. These potential confounders must be identified, and a rationale described. The confounder-adjusted exposure estimate represents the best attempt to minimise/eliminate this bias. In some situations, it may be relevant to consider more than one set of confounders and present several adjusted estimates. This is true when some of the confounders are known to interact with one another, and their individual effects are important to discern.

Example 6h.1

From Segura-Sampedro et al. (2022) – "Twenty-three patients with inflammatory bowel disease (IBD) (82%) had at least one tooth with radiolucent periapical lesion (RPLs), whilst in the control group (CG) 17 subjects (61%) showed radiographic signs of apical periodontitis (AP) [Odds ratio (OR)= 2.98; 95% confidence interval (CI) = 0.87–10.17; p = .076)]. The number of subjects with one or more root filled teeth (RFT) in the CG was 14 (50.0%) whilst in the study group (SG) they were 22 (78.6%; OR = 3.67; 95% CI = 1.14–11.79; p = .026). At least one RFT with AP was found in three subjects (10.7%) in the CG, whilst in the SG 15 patients (53.6%) showed RFT with AP (OR = 9.60; 95% CI = 2.35–39.35; p = .001). To further analyse the possible association between endodontic variables and IBD, multivariate logistic regressions were run. In the multivariate analysis, including the number of teeth, number of carious teeth, periodontal status, periapical status, and endodontic status as independent variables, and taking as dependent variable the status of IBD (Table 3), only endodontic status was shown to be associated with IBD (OR = 1.86; 95% CI = 1.24–2.80; p = .003)".

Example 6h.2

From Razdan et al. (2022) – "The prevalence of root filled teeth was significantly lower in C2 than in C1; [Odds ratio (OR) = 0.76; 95% confidence interval (CI): 0.59, 0.98; p = .03)]. A correction for age further increased the difference between the two cohorts (OR = 0.55; 95% CI: 0.41, 0.74; p < .001)".

Example 6h.3

From Krall et al. (2006) "The age-adjusted risk of incident root canal treatment was significantly greater in current cigarette smokers, relative to never-smokers, but not in cigar or pipe smokers. The hazards ratio attributable to cigarette smoking was similar, but remained statistically significant, in models that also controlled for number of teeth present, any teeth with periradicular radiolucency, and percentages of teeth with crowns, coronal caries, and alveolar bone loss > 20%. The results were not changed when education, brushing, or flossing was included in the models. Multivariate analyses of root canal treatment risk at the tooth level yielded similar hazards ratios when controlled for age, presence of a crown, any coronal caries, radiolucency, and alveolar bone loss level (HR and 95%CI for current cigarette use = 1.9, 1.4 to 2.5; for current cigar/pipe use = 1.3, 0.9 to 1.7)".

Item 6i: Results - Results in terms of relative risk should also be translated to absolute risk for a meaningful time period, if relevant

Explanation

From a public health perspective, estimates of relative risks and other exposure estimates from multiplicative models are less useful since the overall impact of the exposure is not available. A translation of the relative risk estimate to an appropriate absolute risk estimate may clarify the consequences of the exposure (Vandenbroucke et al., 2007).

Example 6i.1

From Patel et al. (2022) – "In models stratified by cancers with or without established screening, relative risk associations were generally similar. Two notable exceptions were current smoking and BMI, in which associations were stronger for cancers without established screening.

The absolute risk of developing any cancer within 5 years was ≥2% regardless of risk factor profile for nearly all men and women aged 50 years or older and was as high as 29% in men and 25% in women for some risk factor profiles at the oldest ages. In addition, within any given 5-year age range, absolute rates differed by about 2.5-fold in men and 4-fold in women based on risk factor profiles. In men younger than 50 years, absolute risks were only higher than 2% among current or former smokers (<30 years since quitting) at age 45 to <50 years with the highest risk (2.7%) for male current smokers who were also exposed to all other risk factors included (i.e., heavy drinkers with a family history of cancer who did not limit red meat intake and were physically inactive)."

Item 6j: Results - The results from any other analyses (e.g. sensitivity, subgroup analysis) must be described if applicable, as well as adjusted analyses, distinguishing pre-specified from exploratory.

Explanation

In observational studies, various subgroup analyses in addition to the main analyses may be performed and, if so, they must be reported. The consideration of the additional analyses is a matter of some debate and must be interpreted carefully. Despite the absence or limited association on the overall results, authors might have a tendency to search for sub-group specific associations that perhaps were not in the original protocol (i.e., unplanned). Exploration of such analyses adds value only when the study is large enough and comprises a substantial volume of data in each group (Cuzick, 1999). It is otherwise conceivable that the study is not sufficiently powered to identify subgroup differences (for example, identify age or gender differences in a study aiming to compare groups with different exposures). Another aspect of debate in subgroup analysis is the data that arose interestingly by chance during the assessment, which might be important (unplanned subgroups analysis). The authors must specify clearly, which analyses were planned initially and appear in the Aims/Objectives (and protocol), and which were not, in order to allow readers to interpret the study results.

Example 6j.1

From Careddu & Duncan (2021) – "The results were subdivided by preoperative caries depth (judged radiographically) into "deep" and "extremely" deep caries where it can be seen the majority of cases included in the study were "extremely deep" (n = 50), rather

than “deep” (n = 12) caries. Of the 12 “deep” cases, 7 were later excluded as the pulp was not exposed after non-selective caries removal, whilst all the “extremely” deep cases were exposed; 4 were excluded as the pulp was necrotic on entry to the pulp chamber. The 4 deep “caries” cases were all successful, albeit one case with irreversible/moderate pulpitis was unresponsive to sensibility testing, whilst all 5 failures presented within the “extremely” deep caries group (Table 5). The two “blinded” evaluators demonstrated a moderate level of agreement in assessing caries depth from an intraoral periapical radiograph (κ = 0.57)”.

Example 6j.2

From Baruwa et al. (2022) – “For predictor 1 (adjacent to implant-supported crown), the chances of a tooth present an endodontic treatment when adjacent to an implant-supported crown is 2.57 times [confidence interval (CI) 1.95–3.39, p = .0001)] higher than when nonadjacent; and the odds of a coronal restoration are 1.63 (CI 1.29–2.06, p = .0001) times higher when adjacent to an implant-supported crown compared to when not. Similarly, for predictor 2 (adjacent to tooth-supported crown), the chances of a tooth present a previous endodontic treatment when adjacent to a tooth-supported crown is 4.39 times (CI 3.49–5.53, p = .0001) higher than when nonadjacent; and the odds of a coronal restoration are 2.30 (CI 1.92–2.76, p = .0001) times higher when adjacent to a tooth-supported crown compared to when not”.

Example 6j.3

From Steele et al. (2004) “The influences on the relationship between tooth loss and OHIP scores were explored further through additional analysis of the Australian data, which were stratified into the three categories of place of birth described. Justification for the additional stratification was provided first by adding an interaction term between country of birth and number of teeth to the ANOVA model revealing a statistically significant (P=0.003) interaction. Adjusted means from this model revealed subtle differences in gradients between number of teeth and adjusted OHIP scores.”

Item 7a: Discussion - The main findings must be summarised with reference to the study aim(s)/objective(s)

Explanation

The Discussion should begin with a summary of the principal findings and be correlated with the main objective of the study. If the authors have hypothesized/provided a null or alternate hypothesis, it must be rejected or not, based on the statistical analysis.

Example 7a.1

From Bakhsh et al. (2022) – “In this longitudinal cohort study patients with apical periodontitis (AP) showed an increased systemic inflammatory burden compared with controls. In particular, interleukin (IL)-1β, high-sensitivity C-reactive protein (hs-CRP) and fibroblast growth factor (FGF)-23 were significantly higher in AP patients than controls. Furthermore, higher levels of IL-1β and FGF-23 were found in patients with larger apical radiolucencies. It is therefore evident that AP increases the systemic inflammatory burden”.

Example 7a.2

From Hoppe et al. (2017) – "The results of this study indicate that endodontic variables alone were not associated with poor physical fitness. However, probing depth (PD) and clinical attachment loss (AL) were significantly associated with physical fitness, corroborating previous findings with a similar sample. Interestingly, when endodontic and periodontal characteristics were merged in an oral inflammatory burden (OIB) variable, the negative effect of the endodontic burden (EB) on physical fitness became apparent. In this regard, the combination of endodontic and periodontal variables strengthened the association between clinical AL and physical fitness alone, indicating a synergistic effect".

Item 7b: Discussion - The rationale for inclusion/exclusion criteria, exposure and duration must be provided

Explanation

The Discussion should justify the inclusion and exclusion of subjects based on criteria relevant to the study. The follow-up period or interval between exposure and assessment of effect must be justified so that the readers can assess whether the results can be applicable and can be extrapolated to other clinical situations / populations.

Example 7b.1

From Bakhsh et al. (2022) – "This is also the first study in which the variation of inflammatory marker levels between baseline and 1 year (yr) in the treated patients has been compared with that of a control group of healthy subjects. The comparison with the control group allowed us to demonstrate that the variations of the levels of biomarkers detected in patients treated for apical periodontitis were different from the normal variations detected in healthy subjects which may depend on other sources of inflammation. Even though Coronavirus disease (COVID)-19 lockdown restrictions caused a reduction in the recall rate at 6 months (M) (n = 37); at 1-year post-treatment, the recall rate reached above 76% (n = 50)".

Example 7b.2

From Gomes et al. (2016) – "This study is novel in providing up to 44 years of longitudinal data on the relationship between incident cardiovascular event (CVE) including cardiovascular-related mortality and baseline radiographic findings of both root canal treatment (RCT) and apical periodontitis (AP)".

Item 7c: Discussion - An explanation of the clinical relevance of the primary and any additional/secondary outcome(s) must be provided

Explanation

The Discussion must explain the clinical utility of the results to the related general or intended population based on the primary and additional/secondary outcomes. The significance of the results and, if relevant, their translation to direct or indirect benefits for patients should be elaborated. Any observation that could revolutionise or

significantly change Endodontics / alter treatment aspects in Dentistry must be emphasised and placed in context. It would be a good practice to justify the sample size in the Discussion section.

Example 7c.1

From de Castro et al. (2023) – “Thus, considering that the genes evaluated in this study are part of the inflammatory cascade involved in the formation and repair of apical periodontitis (AP), and that the study of genetic polymorphisms is one of the latest research topic in the endodontics scenario, the association between the rs1800629 variation in tumour necrosis factor (TNF)-α with the development of persistent periapical lesions suggests possible therapeutic targets of interest for clinical practice in cases of root canal treatment failures, where in the near future, subjects with a higher risk for persistent apical periodontitis (PAP) would be screened and enrolled in specific clinical follow-ups”.

Example 7c.2

From Jonsson Sjögren et al. (2019) – "Whilst some of the findings seem to point towards AP as the most likely origin of pain, other findings contradicted this. For example, only 26 of the 62 painful root filled teeth displayed periapical radiolucency. This strongly suggests that AP is not the only reason for persistent pain or discomfort associated with a root filled tooth. Other possible pain origins should be considered, such as acute marginal periodontitis, sinusitis, neuropathic pain, referred pain from TMD, and persistent dentoalveolar pain disorder secondary to nerve injury or of idiopathic origin".

Item 7d: Discussion - The strength(s) of the study must be provided

Explanation

The uniqueness / novelty of the research, or any ground-breaking discoveries, or how the findings address a gap in knowledge, along with the clinical relevance of the research question should be addressed adequately in the Discussion. Study strengths can also be methodologically related, such as generalisability of the data, size of the material or robustness of the general approach.

Example 7d.1

From Hoppe et al. (2017) – "Some methodological limitations and strengths must be considered regarding the present study. This cross-sectional study did not include smokers and females to avoid any confounding effect in the association between periodontal disease and physical fitness. Females were not included to create a homogeneous study sample and to avoid the potential differences in physical activity between genders. Stratified analysis by gender would have been a possibility, but the small number of female military police officers made such an analysis impracticable. Moreover, general health issues were not confounders, as participants presenting any general health problem were not allowed to perform the physical fitness test (PFT), according to the standard medical clinical and laboratory examinations of the Military Police Health Department".

Example 7d.2

From Sanner et al. (2022) – “The strengths of this study include the fact that an attempt was made to systematically exclude nociceptive odontogenic pain, referred pain, facial headaches and post-traumatic neuropathic pain to the maximum extent possible. The inclusion and exclusion criteria were chosen to avoid creating a mixture of different characteristics within the group with otherwise unexplained non-odontogenic pain (headache variants, referred pain, odontogenic pain) and to identify characteristics of specific groups that may be due to changes in the pain processing system typical of persistent idiopathic dentoalveolar pain (PIDAP)”.

Item 7e: Discussion - The limitations of the study must be provided, addressing the sources of potential bias, imprecision, study design, study size and potentially important but missing confounding variables. Both direction and magnitude of any potential bias must be discussed

Explanation

Acknowledging the flaws and weaknesses of a study makes the reporting and manuscript stronger and helps the reader to identify the potential bias involved in the research (Ioannidis, 2007). Limitations pertaining to sample size, methodological flaws in relation to the data collection, inclusion/exclusion criteria, dropout rate or outcome assessment methods should be mentioned. Bias inherent within the study design used should be mentioned. For example, a) recall bias is common in retrospective clinical studies, b) obtaining inappropriate controls or an adequate number of cases in a case-control study can incorporate bias.

Example 7e.1

From Sanner et al. (2022) – "Nevertheless, this observational study was limited by the fact that it was not a cross-sectional study, and the pain and treatment history depended on the patient's memory. As a result, no conclusions can be drawn regarding the prevalence of the conditions under investigation. Furthermore, there was a selection bias because patients were mostly seen in endodontic clinics, which represents a specific cohort and may not be representative. However, because persistent idiopathic dentoalveolar pain (PIDAP) is experienced in teeth, patients frequently seek help from endodontists, or cases are referred because general practitioners have already initiated root canal treatment. Another limitation of this study is that no comparisons were made pertaining to the signs and symptoms that were identified in the current cohort in comparison to patients experiencing infection-related tooth pain. Nevertheless, the current results can be compared with reported data in the literature on both atypical odontalgia and in contrast to 'typical' infection-related tooth pain. Since there is a regional and cultural element to pain, it has to be taken into consideration, that the study was performed on a German patient population".

Example 7e.2

From Irinakis et al. (2022) – "In the present study, follow-up rates for patients (88.2%) and teeth (90.8%) were relatively high. Although comprehensive search strategies were used in our study, there might have been some undetected teeth with external cervical resorption (ECR) as we did not have full mouth radiographic examinations. The relatively small sample size is also a limitation of the present study. Teledentistry is an approved means for data collection recommended by the American Dental Association; however, it

might be considered to be a limitation when used for research purposes. More specifically, in the present study, it should be considered a limitation as whilst most of the data were evaluated by the two specialist examiners, some data were also obtained from general dentists (n = 10) and over telephone interviews with patients (n = 8). In an effort to eliminate any potential reporting bias, only simple information such as "is the tooth present or not" were collected when an in-person follow-up was not feasible. Also, comparison of findings between two independent analyses of both a complete dataset (A, all cases) and a reduced dataset (B, only cases followed up at the university setting) showed the same trends for the assessed determinants, which were identically either significant or nonsignificant in both analyses. The rationale behind this statistical methodology was that dataset A included both followed up cases at university and non-university settings, whilst dataset B included only cases followed up by calibrated examiners at the university setting. The reason we tested and compared findings from both datasets was that in real-life scenarios, some of the follow-up information can only be acquired from non-university settings (nonstandardized patient data acquired from general dentists might potentially lack reliability and/or validity)".

Item 7f: Discussion - The discussion of the strength and limitations should be summarised in an overall assessment of the internal validity of the study

Explanation

An overall (summary) assessment of the study should be detailed in order to establish internal validity based on the reported strengths and limitations that will help the reader to interpret the findings.

Example 7f.1

From Hoppe et al. (2017) – “These criteria strengthen the methodology and increased the internal validity of the study, whereas they decreased extrapolation of the findings”.

Example 7f.1

From Fransson et al. (2021) – "In conclusion, despite the limitations related to this study where the actual reasons for extractions cannot be ascertained, the findings implicate that dentists planning for RCT should consider age, tooth group, and the type of restoration. These variables had the strongest associations for extraction 5 y after root filling, whereas socioeconomic indicators were not associated with extraction. In particular, when root fillings are performed in molar teeth in older individuals, clinicians should pay attention to their choice of restoration to promote tooth retention over time."

Item 7g: Discussion – A detailed interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence must be provided

Explanation

The overall interpretation of the results from the study should be discussed cautiously avoiding over-interpretation. The potential bias involved, loss to follow-up and any non-participation should be explored during the interpretation. The potential confounders, results of the sensitivity analyses, and subgroup analyses should be discussed. The strength of the relative risks must be interpreted cautiously depending on the clinical scenario. Other potentially relevant confounding factors must be considered while

interpreting the results of the study (Vandenbroucke et al., 2007). The discussion should also focus on the relevant literature and its unbiased role in interpreting the current study. Publications that confirm or are contrary to the findings of the current study should be cited and discussed. Extensive repetition of content from the Introduction or duplication of the results should be avoided.

Example 7g.1

From Saini et al. (2022)– "Independent predictive factors were assessed for their association with treatment outcome. Age and gender had no impact, which was consistent with previous literature. The preoperative lesion volume did not influence the success or failure of treatment. At 24 months, although the osseous healing was reduced in lesions with volume greater than 3000 mm3, the difference was not statistically significant. This finding suggests that once a cyst-like periapical lesions (LCPL) is established, the size of the lesion does not affect the outcome but the time required for complete resolution may be prolonged in larger lesions. The other preoperative factors investigated (Tables 2 and 3) did not affect the treatment outcome. This is in agreement with other investigators who observed no significant effect of intraoral draining (IOD) sinus on treatment outcome in asymptomatic teeth with LCPL. In contrast, the presence of IOD sinus has been associated with treatment failure in primary endodontics, but the sample observed was not LCPL. Pulp canal obliteration (PCO) and root resorption have also been associated with treatment failure in cases of pulp necrosis. However, only three cases with lesion size greater than 10 mm were observed. The majority of the LCPLs (62%) in the present study had bicortical defects. The presence of a preoperative cortical bone defect (buccal, palatal, bicortical) had no impact on success or failure. However, the

presence of a palatal cortical bone defect affected osseous healing. These LCPLs presented with a large palatal bone erosion with defect dimensions greater than 11 × 11 mm. The periosteum plays a key role in endogenous bone repair and remodelling as it serves as a reservoir of osteo-competent periosteum-derived progenitor cells. Damage to the periosteum and concomitant erosion of the cortical bone by the infective process could have resulted in prolonged healing. Further, it can be speculated that owing to the effect of gravity, lesion decompression was difficult to achieve, thus impacting osseous healing. However, this observation has been made on a limited number of cases (9%), and hence, more data would be required to better understand the influence of this preoperative factor on treatment outcome".

Example 7g.2

From Sanner et al. (2022) – "In this observational study, strict persistent idiopathic dentoalveolar pain (PIDAP) criteria were applied to illuminate the condition from the dentist's perspective. This allowed the identification of PIDAP features that have not been described previously, including the absence of nocturnal pain and the presence of allodynia in otherwise healthy periodontal sites. Similar pain descriptors as in this study have been reported previously in the literature. A striking typical pain characteristic in the population studied here is the burning pain quality, which affected 42% of the patients. Burning pain is also generally described as a characteristic of neuropathic pain. Undisturbed sleep and a pain-free interval after waking are typical characteristics of neuropathic pain".

Item 7h: Discussion - The generalisability (external validity, applicability, real-world relevance) of the study findings must be discussed

Explanation

The extent to which the findings of the study are applicable and can be extrapolated to another population or situations is called external validity. External validity should address various issues such as: a) whether the findings can be applicable to population / individuals who differ from those who were recruited for the study with regards to basic demographic such as age, gender, co-morbidities etc.; b) whether the results can be applicable to populations under the care of different healthcare systems or different geographical regions. External validity depends on various parameters such as study settings, population characteristics and the outcomes assessed. Thus, providing the information about various parameters plays a pivotal role for readers to interpret the generalisability of the study (Vandenbroucke et al., 2007).

Example 7h.1

From Segura-Sampedro et al. (2022) – "A striking result of this study is the high proportion of inflammatory bowel disease (IBD) patients (54%) who have endodontically treated teeth with radiolucent periapical lesions (RPLs), compared to only 11% in the control group (CG) [Odds ratio (OR) = 9.6; p = .001)]. The periapical lesion in root filled teeth (RFT) should be interpreted with caution, as it may be a healing lesion or an apical scar. In the orthograde endodontic treatment, as in periapical surgery, the lesion heals through tissue regeneration processes, but always involving some formation of periapical fibrotic tissue. The regeneration of the periapical tissues would never be

complete, since it involves the repair of a postnatal injury, and in these cases, there is always scar formation. Therefore, this finding could be explained, at least in part, by the high prevalence of low bone mass in IBD patients, together with changes in the OPG/RANKL/RANK system, and the effect of the medication they take to treat IBD. The increased activation of the NLRP3 inflammasome could also be an explanation. The NLRP3 inflammasome participates in the pathogenesis of IBD, and in turn is involved in the loss of alveolar bone that occurs in AP. Patients with IBD may have delayed healing of the periapical osteolytic lesion".

Example 7h.2

From Cruz et al. (2022) – "This is the first study that associates the −871 C > T polymorphism of the TNFSF13B gene with primary apical periodontitis (pAP) susceptibility. However, this result should be interpreted with caution, because due to the small number of acute apical abscess (AAA) and secondary apical periodontitis (sAP) cases, the power of the study was low (63%) after the evaluation performed with the Genetic Association Study (GAS) Power Calculator (http://csg.sph.umich.edu/abecasis/cats/gas_power_calculator/index.html) (Johnson & Abecasis, 2017). The sample size should be increased in further studies in order to lower the risk of missing an actual true effect. The allele frequencies in healthy subjects (HS) were similar with those reported previously in a Mexican population [cytosine (C) = 74/ thymine (T) = 26)], American population (C = 75/T = 25) and Colombian subpopulation (C = 74/T = 26) in the 1000 Genomes database. However, we observed that the allele frequency differs with those reported for European and South Asian populations (C = 49/T = 51). This could reflect a lower T allele penetrance in our population. This is

predominantly explained by the genetic heterogeneity of the Mexican Mestizo subpopulation and suggest that this diversity is mainly related to a differential distribution of Amerindian and European ancestral components. Since single nucleotide polymorphisms (SNPs) make modest predisposing contributions to complex diseases such as AP, a large-scale association study in other populations will be necessary to validate this finding. Additionally, a study design that includes case-parent cases or a cohort study could be helpful to understand the biological contribution of genetic markers in AP pathogenesis".

Item 7i: Discussion - Implication for future research and clinical practice must be described

Explanation

The execution of the study and how the outcomes were selected and recorded must be thoroughly analysed to discover areas for improvement. To address any shortcomings, clear directions for future research as well as the implications for clinical practice must be offered.

Example 7i.1

From Gorni et al. (2022) – "The dissolution of mineral trioxide aggregate (MTA) over time when exposed to an acidic pH, which may reflect an environment caused by microbial colonization, and these changes may facilitate the penetration of microorganisms or their metabolic products into the periapical tissues through gaps and voids along the marginal

sealing. Future research needs to address such mechanisms and to study the interactions of the material with a colonizing biofilm to improve its performances on the long term".

Example 7i.2

From Kumar et al. (2022) – "Future research should also focus on the assessment of the levels of different inflammatory markers in patients with varied systemic conditions and apical periodontitis (AP). Well-planned intervention studies are also required to establish a temporal relation between systemic disease and AP. Furthermore, these findings suggest the inclusion of endodontic diagnosis and a treatment protocol for the management of AP in cardiac patients to minimize the systemic inflammatory burden".

Item 8a: Conclusion - Explicit conclusion(s) from the study must be provided, and address all the aims/objectives

Explanation

The conclusion(s) must be stated explicitly and should be based on an overall interpretation of the results which considers the factors that might contribute to bias in the design and execution of the study.

Example 8a.1

From Bakhsh et al. (2022) – "Apical periodontitis contributes to the increased levels of systemic inflammatory markers and potentially increases the risk of chronic systemic inflammatory conditions such as atherosclerosis and cardiovascular diseases (CVDs). The

transient increase of inflammatory markers' levels after both root canal retreatment and apical surgery potentially might increase the risk of vascular events especially in vulnerable patients. However, successful endodontic treatment does have a long-term benefit on vascular and systemic health which is likely to outweigh the short-lived adverse effect".

Example 8a.2

From Martinho et al. (2021) – "This retrospective clinical study revealed that type 2 diabetes mellitus (DM) is linked to a lower success rate of root canal treatment, when compared to controlling nondiabetic subjects in a Portuguese population sample. Moreover, type 2 diabetic rats with increased apical periodontitis (AP) supported such observations, showing angiogenic deficits and impaired tissue repair".

Item 9a: Funding details - All sources of funding and other support (such as supply of drugs, equipment etc.) as well as the role of funders must be acknowledged and described

Explanation

Details of the funding source(s), including grant number(s) (if available), and scholarships, for observational studies must be provided. Research sponsored by pharmaceutical or dental manufacturing or supply companies may involve the evaluation of their own product(s). This may cause a conflict of interest if the funding organisation or company has influenced the outcomes of the research by being involved in the design, conduct, analysis and/or reporting of the sponsored prospective studies (Lexchin et al.,

2003; Moher et al., 2012; Nagendrababu et al., 2020a). Sources of funding, such as provision of equipment, drugs or involvement in data analysis must therefore be reported. The names of individuals (if any) who assisted in the study (e.g., translation/planning/data collection) or preparation of the manuscript (illustrations/statistical analysis/editing) must be provided in detail. If the funder was not involved in the study, the authors should explicitly deny such participation and clarify their role in the manuscript (Moher et al., 2012).

Example 9a.1

From Bakhsh et al. (2022) – "The study is funded by British Endodontic Society (Grant for Research Work) and European Society of Endodontology (Annual Research Grant). Sadia Ambreen Niazi is the principal grant holder of these grants. Abdulaziz Bakhsh is a PhD student Funded by a scholarship from Umm Al-Qura University, Makkah, Saudi Arabia. Grant number: 4360144104".

Example 9a.2

From Careddu & Duncan (2021) – "The work was self-funded. Funding Statement: Open access funding provided by IReL. WOA Institution: The University of Dublin Trinity College. Blended DEAL: IreL".

Item 10a: Conflict of interest – An explicit statement on conflicts of interest must be provided, together with full affiliations of every author(s)

Explanation

A conflict of interest (COI) could arise if a researcher or clinician has commercial, legal, professional or personal relationships with organisations or companies that could influence the results of the research. A potential COI may arise if a person is, or appears to be, at risk of being biased due to professional or personal interests (Bekelman et al., 2003; Romain, 2015). Hence, a COI statement must be provided in the manuscript, or otherwise, the authors should explicitly indicate that there is no COI (Nagendrababu et al., 2021a). Any potential conflict of interest must be transparent for the readers to appreciate the risk of bias but does not bar the study from publication.

Example 10a.1

From Jakovljevic et al. (2020b) – "No potential conflict of interest was reported by the authors".

Example 10a.2

From Nikolic et al. (2019) – "The authors deny any conflicts of interest related to this study".

Item 11a: Quality of images – Details of the equipment, software and settings used to acquire the image(s) must be described in the text or legend (if applicable)

Explanation

Details of the equipment or software used to capture and process image(s) must be provided. In addition, details of the manufacturer and the model/version number of device(s) used for capturing, recording and reproduction should also be provided. If the study involves statistical analysis of the images, the name of the statistical package software along with the details of the developer and version must be provided. If the image was modified in any way this must be clearly stated.

Example 11a.1

From Kirkevang et al. (2014) – "At each examination, all participants underwent a full-mouth radiographic survey consisting of 14 periapicals and two bitewings, one in each side. Radiographs were taken by a 'GX 1000' x-ray unit (Gendex Corporation, Milwaukee, WI, USA), using the paralleling technique, 70 Kv, 10 Ma, a film-focus distance of 28 cm. Film processing was automated (Dürr 1330; AC 245L, Bietigheim-Bissingen, Germany). The radiographic procedure used in 1997, 2003 and 2008 did not differ, except for the radiographic film used. In 1997, Kodak Ektaspeed Plus film (Eastman Kodak, Rochester, NY, USA), and in 2003 and 2008, Kodak Insight film (Eastman Kodak, Rochester, NY, USA) were used. In all three studies, the fastest well-documented film on the market was chosen in order to minimize the radiation dose to the participants".

Example 11a.2

From Mota de Almeida et al. (2015) – "All CBCT examinations were performed with a 3D-Accuitomo 170 (J. Morita Mfg. Corporation, Kyoto, Japan). The radiologists selected one protocol of four pre-defined protocols tailored for the different diagnostic tasks. The

protocols used were the same at both hospitals. All protocols consisted of the following exposure parameters: 85 Kv and 5 Ma. They differed in rotation (180° and 360°) and exposure time (9 s, 17.5 s and 30.8 s). Isotropic voxels with a size of 0.08 mm for 40 × 40 mm volumes and 0.125 mm for volumes of 60 × 60 mm volumes were used. Image reconstruction was performed in the axial, coronal and sagittal planes. Slice thickness varied between 0.24-, 0.48-, and 1.0-mm, with 0.16-, 0.24-, 0.75-mm intervals, respectively".

Item 11b: Quality of images – The reason why the image(s) was acquired and the rationale for its inclusion in the manuscript must be provided in the manuscript. A justification for all images that involve ionising radiation must be included

Explanation

The images included in the manuscript should be provided with the highest possible resolution and accompanied by descriptive information in appropriate places within the text (Nagendrababu et al., 2020a). The justification to include an image may be attributed to illustrate the severity of a condition, diagnosis, illustrate specific treatment procedures, or demonstrate effectiveness/outcomes or failures of the treatment.

Example 11b.1

From Keerthana et al. (2021) – "Since the advent of cone-beam computed tomography (CBCT) in Dentistry, its incorporation into endodontic practice has been increasing. Although, CBCT offers more detailed and reliable diagnostic information of the examined structure in three dimensions and at sub-millimetric image slicing, it has drawbacks such

as a high level of scattering and noise, decreased spatial resolution (1–2 lp/mm) and higher radiation doses ranging between 19–368 μSv compared to intraoral radiography (15–20 lp/mm, 2–9 μSv). In addition, late-onset effects of exposure to ionizing radiation remains a major concern. There appears to be no study available that has assessed the diagnostic efficacy of CBCT and PR with a reliable gold standard in cases of various resorptive defects, root perforations, apico-marginal bone defects, through and through periapical bone defects and proximity of periapical lesions to critical anatomical structures of clinical relevance that might influence treatment planning".

Example 11b.2

From Pigg et al. (2011) – "No studies have investigated the use of cone-beam computed tomography (CBCT) as an adjunct in pain investigations. If neuropathic pain could be differentiated from nociceptive pain with greater accuracy, patient benefit would be considerable. Additional, inappropriate dental treatment could be avoided in favour of targeted neuropathic pain treatment. As symptomatic apical periodontitis (SAP) resembles atypical odontalgia (AO) in several aspects, unidentified cases of apical periodontitis may occur amongst patients diagnosed with AO. It was hypothesized that the additional information on anatomical structures in the pain area provided by CBCT examination – compared with conventional intraoral periapical and panoramic radiographs – improves the possibilities to identify AO".

Item 11c: Quality of images - The circumstances (conditions) under which the image(s) were viewed and evaluated by the authors must be provided in the text

Explanation

The process involved in the assessment and interpretation of the image(s) should be mentioned. The examiner(s) involved in the assessment and interpretation of the images should be provided with their credentials along with information on how they were calibrated to perform the interpretation. If applicable, the equipment used to view the conditions or additional tools involved in the examination by the examiners should be presented. If more than one evaluator, the degree of agreement among the examiners during image evaluation or interpretation should be provided in the text. In this case the level of agreement must be provided as inter- or intra-rater agreement by Kappa statistics or proportion of concordant interpretations or other relevant statistical analysis (Nagendrababu et al., 2020a).

Example 11c.1

From Khabbaz et al. (2010) – "Evaluation of the final root filling was performed through magnifying lenses on a diaphanascope by three independent investigators. All investigators examined all cases. In cases of interexaminer disagreement (52 root canals), examiners came to a consensus. Measurements were recorded using a transparent ruler of 0.5 mm accuracy. In cases of maxillary premolars and mandibular molars, exposed with alteration in horizontal angulation by the students, it was considered that they had been exposed with a mesial angulation. Consequently, this fact rendered it possible to differentiate the palatal from the buccal root canal in maxillary premolars and the mesiobuccal from the mesiolingual root canal in mandibular molars according to Clark's rule".

Example 11c.2

From Kirkevang et al. (2014) – "One observer (L-LK) examined all radiographs. All teeth were recorded according to the World Dental Federation (FDI) nomenclature using the full-mouth radiographic surveys. Third molars were excluded. In all teeth, the variables and thresholds listed in Table 1 were assessed. Apical periodontitis was assessed by the five-category periapical index. The observer in the present study participated in a calibration course for the periapical index (PAI) system. The course involves scoring of 100 radiographic images of teeth; the teeth consist of various tooth types, with and without root fillings. For each tooth, a 'true periapical status' has been established by consensus between five endodontists, one dental radiologist, four general practitioners and one dental assistant. The defined 'truth' of the 100 teeth forms a 'gold standard atlas'. The observer demonstrated high reproducibility ($\kappa = 0.813$). A tooth was recorded extracted if it was present in 1997, but not in 2003 and/or 2008".

Example 11c.3

From Kazzi et al. (2007) – "Each radiograph was examined simultaneously by two assessors (DK and VER) using standardized viewing conditions. These comprised a standard X-ray viewer with masking, 2× magnification with all films viewed in a darkened room. The scoring of faults and the assessment was by consensus of the observers. The radiographs were assessed for total technical faults using a classification (Table 1) previously developed by Rushton & Horner. The assessors then made a decision whether the radiograph was 'excellent', 'diagnostically acceptable' or 'unacceptable' for diagnostic

purposes (National Radiological Protection Board 2001) according to national guidelines (Table 2). In those films deemed 'unacceptable', the faults specifically causing failure (significant faults) were noted".

Item 11d: Quality of images - The resolution, any magnification of the image(s) or modifications/enhancements (e.g. adjustments for brightness, colour balance, magnification, image smoothing, staining etc.) that were carried out must be described in the text or figure legend

Explanation

The type of X-ray technology (analogue or digital), imaging (e.g. periapical X-ray using sensor or imaging storage plate, CBCT) and settings (e.g. voxel size, FOV (field of view), mAs, KV), and modifications made to the image(s) from its original resolution and magnification must be provided either in the text or in the legend. A scale bar with measurements should be included with magnified images to provide the degree of magnification of the image from its original size. Modifications or enhancements made are acceptable only if they are applied to the entire image. Such modification should not mask, crop, remove or misrepresent any details from the original image. Any changes that appear to intentionally mask, misrepresent or falsify data are unacceptable and could be treated as scientific misconduct (Rossner & Yamada, 2004; Lang et al., 2012). When automatic proprietary algorithms are used to enhance images, this must be stated along with any variation between sections of an image or between images described. Original magnification should be stated in the figure legend.

Example 11d.1

From Bornstein et al. (2015) – “Figure 1. (A–D) Nonepithelialized granuloma. A radiographic and histologic example of a periapical lesion associated with the maxillary left lateral incisor. Image A shows the periapical radiograph and B the coronal section of the cone-beam computed tomography scan. Within the periapical lesion, the CBCT image shows a hyperdense structure that was suspected to be overfilled root canal filling material. (C) The longitudinal section of the biopsy of the periapical lesion. A distinct collagenous tissue (CT) capsule surrounds the lesion. A central lumen (LU) and a former border (BO) between the tooth and the periapical lesion can be suspected. (D) The higher image magnification shows the massive presence of inflammatory cells (IC), lymphocytes, plasma cells, and neutrophilic granulocytes), but no epithelium is present (magnification: C, ×31.3; D, ×200)”.

Example 11d.2

From Ricucci et al. (2014) – "With the microtome set at 4–5 μm/L, meticulous longitudinal serial sections were taken until the pulp was exhausted. This implied that 500–600 sections were cut for molar teeth. Every fifth section was stained with hematoxylin-eosin for screening purposes and the assessment of inflammation. These sections were used to locate the areas with the most severe inflammatory reaction. Based on this initial evaluation, all slides adjacent to the location with the most severe reaction were stained. In addition, a modified Brown and Brenn technique for staining bacteria was used for selected slides. Figure 2. Clinical reversibility matching histologic reversibility (case #29). (*A*) A maxillary third molar in a 33-year old woman with a deep mesial caries cavity and only slight sensitivity to cold stimuli. (*B*) Preparation of a

mesiodistal sectioning plan. (*C*) An overview of the pulp chamber. No necrosis can be seen. Tertiary dentin is present under the carious cavity (hematoxylin-eosin, original magnification ×25). (*D*) A detailed view of the mesial pulp horn; a reduction of the odontoblast layer and the absence of inflammatory cells can be seen (original magnification ×100). (*E*) A high-power view of the area indicated by the *arrow* in *D*. An atubular tertiary dentin is layered by flattened cells resembling fibroblasts (original magnification × 400). (*F*) Magnification of the area demarcated by the rectangle in *C*. Vessels and nerve bundles in an uninflamed connective tissue (original magnification ×100, inset ×400)".

Item 11e: Quality of images - Patient(s) identifiers (names, patient numbers) must be removed for General Data Protection Regulation (GDPR) and to ensure they are anonymised or de-identified in all images

Explanation

All personal identifying information such as name, date of birth, patient identification number, eyes, face, etc. must be deleted or masked in all images, taking care to mask all visual or verbal information that would allow identification of the individual.

Example 11e.1

From Alaugaily & Azim (2022) – "Radiographic presentation of teeth with clinical evidence of longitudinal fractures. (A–D) An angular defect associated with a cracked tooth. (A) A PA radiograph of a mandibular left first molar showing a shallow fill and no

apparent periradicular pathology. (B) A cone-beam computed tomography sagittal view of the same tooth showing an angular defect on the distal aspect of the tooth. (C) A clinical photograph showing a horizontal fracture line running on the roof of the pulp chamber. (D) After completion of the root canal treatment, the crack line is running on the distal wall extending to the distal canal orifice. (E–H) A J-shaped lesion associated with vertical root fracture (VRF). (E) A periapical (PA) radiograph of a maxillary left first molar showing a short fill on the mesiobuccal root and a PA radiolucency associated with the root. (F) A CBCT sagittal view of the same tooth showing a J-shaped lesion associated with the mesiobuccal root. (G) A clinical photograph showing a fracture line running on the lingual aspect of the root. (H) A clinical photograph after root amputation of the mesiobuccal root. (I–L) A combined lesion associated with a cracked tooth. (I) A PA radiograph of a mandibular right first and second molar showing a shallow fill and no apparent periradicular pathology. (J) A CBCT sagittal view of the mandibular right second molar showing an angular defect on the mesial aspect of the root and a J-shaped lesion extending to the furcation area. (K) A clinical photograph showing a crack line running on the mesial marginal ridge and extending to the mesiolingual canal. (L) The mandibular right second molar extracted and showing a crack line on the mesial aspect of the tooth extending to the radicular part of the tooth".

Item 11f: Quality of images - An interpretation of the findings (meaning and implications) from the image(s) must be provided in the text

Explanation

All relevant details and information derived from the evaluation and interpretation of the images must be presented. The meaning and implications of the findings from the image(s) must be included.

Example 11f.1

From Khabbaz et al. (2010) – "From 438 root canal treatments (RCTs) performed in the 4th year of study, acceptable fillings were detected in 226 (51.6%). From 671 RCTs performed in the 5th year of study, acceptable fillings were detected in 382 (57%) and in both academic years the percentage of acceptable fillings was (54.8%) (Table 3). From the 1109 root canals treated by the students in both academic years, 595 were in the maxilla, from which 345 (58%) were acceptable. Of the 514 in the mandible, 263 (51.2%) were acceptable. Significantly more acceptable root fillings were detected in the maxilla than in the mandible ($P<0.05$)".

Example 11f.2

From Kirkevang et al. (2014) – "When extractions and revisions were combined, the associations were similar, but the presence of voids had a statistically significant association ($P=0.03$), whilst the association of a coronal restoration with radiographic signs of overhangs or open margins was less pronounced ($P = 0.04$). On the other hand, the risk of having apical periodontitis (AP) in 2008 was significantly higher if the root filling was either short or long ($P = 0.001$) or there was voids; ($P < 0.001$), or if there was overhang or open margin of the restoration ($P = 0.01$). Apical periodontitis present at the initial examination was also associated with an increased risk of having AP in 2008 ($P <$

0.001), and the associations between having AP in 2008 and the quality of a root filling and coronal restoration were less pronounced when adjusted for presence of AP in 1997".

Item 11g: Quality of images - The figure legend associated with each image must describe clearly what the subject is and what specific feature(s) is illustrated. If cases are offered to illustrate descriptions of a cohort, then the age, gender, ethnicity and other specific attributes that are relevant to the cohort should be provided

Explanation

Figure legends for images should be self-explanatory, and comprehensive. This should include the type of image views (e.g., type of radiographic view), and sections (e.g., sagittal view of cone-beam computed tomography [CBCT]) if relevant. The text supplied by the image in the context of the observational study should be fully complete, stand alone and comprehensible to readers.

Example 11g.1

From Keerthana et al. (2021) – "Figure 3. Vertical root fracture (a) and (b) periapical radiograph showing a root-filled tooth. No evidence of fracture line in suspected teeth (c and d) sagittal and coronal cone-beam computed tomography (CBCT) image shows dehiscence of buccal cortex and periapical pathosis. No evident fracture line due to beam hardening artefact (e and f) surgical visualization of vertical root fracture of tooth 11".

Example 11g.2

From Restrepo-Restrepo et al. (2019) – "Figure 3 - Maxillary right first premolar showing a radiolucent area in both the distal and apical region of the root. (a) Preoperative radiograph showing two isolated periapical radiolucencies <10 mm in diameter confined to the retro-alveolar spongiosa. (b) Fifty-six months after root canal treatment the patient was symptom-free and digital periapical radiography (DPR) showed that the lesion was completely healed even though to have underfilled root canals (>2 mm from apex). (c) Coronal, (d), axial and (e) sagittal cone-beam computed tomography (CBCT) slices disclose the persistence of the two periapical hypodensities. The outcome was classified as asymptomatic function".

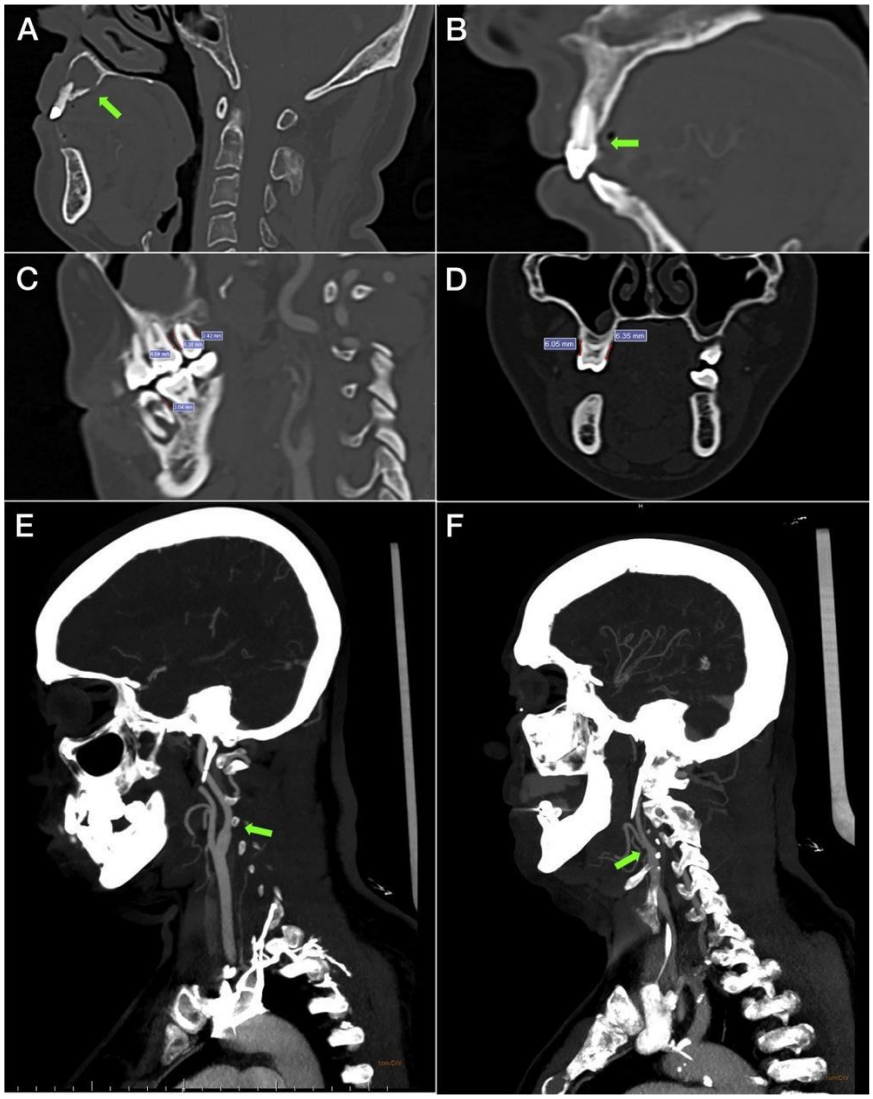
Item 11h: Quality of images - Markers/labels must be used to identify the key information in the image(s) and defined in the figure legend

Explanation

The areas of importance within an image should be identified using markers such as label(s), arrow(s) or key(s) with an explanation provided in the legend. Each image and the associated legend should be meaningful on its own (Lang et al., 2012). Markers must not obscure or mask important information within the image and should be of sufficient size to be readily discernible (Lang et al., 2012).

Example 11h.1

From Keerthana et al. (2021) – Figure 1: Arrows have been used to identify the key information and mentioned in Legend.



Item 11i: Quality of images - The figure legend of each image must include an explanation on whether it is pre-, intra- or post-treatment and follow-up and, if relevant, how images were standardised over time

Explanation

The time point when the image was obtained (i.e. pre, intra or immediate post-treatment or follow-up) must be provided. If multiple images are provided, they should be presented and labelled in a chronological sequence based on the timing of obtaining the images or otherwise the rationale for deviation should be explained (Nagendrababu et al., 2020a). Any efforts to standardise the images for the purpose of comparison must be described (e.g. exposure angle or technical settings of the imaging device).

Example 11i.1

From Yazdi et al. (2007) – "Example of complete healing. Radiographs taken preoperatively (a), postoperatively (b), at 1-year follow-up (c) and at final examination after 9 years (d)".

Example 11i.2

From von Arx et al. (2016) – "Radiographs taken 1 year after periapical surgery of the mesial root of a mandibular left first molar (58-year-old male) and corresponding ratings by three observers: periapical radiograph (a), mesio-distal cone-beam computed tomography (CBCT) (b) and bucco-lingual CBCT (c)".

Discussion

Evidence-based data on the aetiology and progression of a disease or condition, its treatment, and prognosis is essential for good healthcare practice and is obtained mainly from interventional trials and observational studies. Observational studies involve

various study designs such as a) ecological, b) case-control, c) retrospective/prospective cohort, and d) cross-sectional studies, and have been reported to contribute approximately 20% of all endodontic research (Yilmaz et al., 2019). Each observational study design has strengths and weaknesses that need to be addressed adequately during the reporting stage. Failure to report a study properly will often lead to the rejection of manuscripts during the peer review process, which ultimately results in a waste of resources and time.

The PROBE 2023 checklist was developed by adapting and integrating the principles of the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement (von Elm et al., 2008) and the Clinical and Laboratory Images in Publications (CLIP) principles (Lang et al., 2012). The purpose of the PROBE reporting guidelines is to help researchers to improve the overall quality of biomedical research and report the findings in a systematic and comprehensive manner. Authors are advised to make use of the PROBE 2023 guidelines while reporting observational research in Endodontics.

This explanation and elaboration document supports the PROBE 2023 guidelines by helping authors understand the rationale of each item in the checklist as well as provide a template that will assist authors to develop high-quality manuscripts describing their observational research in Endodontics. An attempt has been made under each item to provide examples from the endodontic, dental or medical literature to aid understanding of each item within the guidelines. Observational studies that follow the PROBE 2023 guidelines should include the following sentence at the beginning of the Methodology: "This observational study is reported according to the PROBE 2023 guidelines (Nagendrababu et al., 2022)" where the reference should relate to the PROBE

2023 consensus publication. This will confirm to readers as well as to editors and referees that the guidelines were followed during the development of the manuscript.

Observational studies are considered as level II evidence in the evidence pyramid and each study design has its own inherent strengths and limitations. Case-control studies are an appropriate epidemiological study design to assess rare / infrequent diseases such as root resorption as a consequence of dentoalveolar trauma. Since the outcome of the condition has already occurred, data collection can be rapid and allow multiple risk factors to be studied simultaneously (Martinez et al., 2019). However, challenges such as selection of controls, recall bias, and confirming the relationship of the cause to the outcome are inherent in this study design. Similarly, cohort studies provide complete data on a subject's exposure (multiple outcomes for single exposure can also be assessed) and are the best study design to assess the incidence of a disease/pathosis as well as limit the recall bias from patients. However, the inherent disadvantages in cohort studies are selection bias, confounders, as well as loss to follow-up of patients, which might affect the outcome or generalisability of the study (Morrow, 2013). A cross-sectional study not only offers the advantage of rapid data collection but is also favoured to assess prevalence, establish associations as well as to avoid the problem of loss to follow up. A major challenge in cross-sectional study design is the risk of selection bias. Patients with the pathologic condition might recall the exposure more than patients who were recruited as controls. Thus, while designing case-control studies, matching the controls based on age and gender as well as exposure to a similar environment / exposure must be considered. Tooth et al. (2005) has shown that in reporting of observational studies, the criteria determining selection bias were the least reported. Thus, an elaborate description of the study participants based on the eligibility criteria and

selection of controls as well as sampling strategy (cross-sectional studies) needs to be reported too in order to help the readers in assessing the applicability of the results.

Precision and validity are two major challenges in observational studies. Thus, a reader should evaluate the results of a study by assessing the sample size, appropriate representation of the sample from the population under investigation, whether uncontrolled confounders were introduced, and differential loss to follow-up, which might lead to varying attrition rates. Proper reporting of all these parameters makes it possible to draw appropriate inferences from the study (Carlson et al., 2009).

The results section of an observational study should be strengthened by tables which detail the basic demographic distribution of the cases, controls, and exposure to risks and confounders. Providing unadjusted estimates and adjusted estimates with precision (confidence interval), if applicable, allows the reader to comprehend the data behind the measures of association (Vandenbroucke et al., 2007). This enables the reader to interpret the adjusted estimates and aids in predicting the direction of an association which increases the validity of the study. All potential confounders should be explained, and the criteria for including them in the statistical models need to be detailed. Results must convey information on missing data with a clear justification to assess the generalisability of the results. In addition to the main results, a descriptive and illustrative representation (in form of tables) of additional analysis (subgroup/regression analysis) needs to be provided.

Providing a flowchart enhances the quality of reporting and interpretation of e.g. randomised trials and systematic reviews. It helps to convey the information in a clear and transparent manner and can often replace lengthy descriptions in the Methods and

Results sections. Though the use of flow diagrams is highly recommended, it is included only as an option in the PROBE 2023 guidelines. This is because of the complexity and variability of the study designs that are possible in observational research, which means a generic flow-chart template would not be possible to create. Notably, the earlier Endodontic-specific guidelines for case reports, randomised clinical trials, laboratory studies, and animal studies all stipulated completion of a mandatory flowchart (Nagendrababu et al. 2020a, b, 2021b,c).

Conclusion

Observational study designs play a major role in endodontic research for unusual clinical conditions, to analyse associations to exposures/causes as well as situations where interventional trials cannot be performed. Selection of an appropriate study design is only one of the key parameters for successful research. Proper, complete and transparent reporting of research enables the dissemination of results in a systematic manner and forms the basis for the generation of high-level evidence in healthcare. Furthermore, it increases the chances that the research will be included in systematic literature reviews and can contribute to meta-analyses of data. The PROBE 2023 guidelines will enable authors, reviewers, and readers to design, report, and analyse observational studies effectively. This Explanation and Elaboration document provides an explanation of each item in the checklist, supplemented with examples from published observational studies to demonstrate how authors can improve the quality of their manuscript and its chances of being published. It should be noted and acknowledged that reporting guidelines are dynamic and will evolve over time, hence the need for their periodic reassessment and modification over time.

Acknowledgement

We would like to express our sincere thanks to everyone who provided feedback on the PROBE 2023 Explanation and Elaboration document: Sebastian Bürklein, Germany; Giampiero Rossi-Fedele, Australia; Ya Shen, Canada; Emmanuel Silva, Brazil; Matthias Widbiller, Germany; Victoria Yu, Singapore. The authors gratefully acknowledge the contributors whose work has been reproduced in this publication. The authors deny any responsibility for any potential errors, omissions, or artefacts that may be discovered outside of their control.

Legends

Figure 1: Arrows have been used to identify the key information and mentioned in Legend. “Multidetector computed tomography angiography images showing the presence of apical periodontitis (arrow in A), root canal treatment (arrow in B), the methods for the measurement of crestal alveolar bone loss: the distance between the cementoenamel junction and the alveolar ridge in all sides of each tooth (C: mesial and distal measurements; and D: buccal and lingual measurements) and the absence/presence of atheroma plaque into the carotid artery (arrow in E and F, respectively)”. Reprinted from *Journal of Endodontics*, Vol 48, Leão TSS, Tomasi GH, Conzatti LP, Marrone LCP, Reynolds MA, Gomes MS. Oral Inflammatory Burden and Carotid Atherosclerosis Among Stroke Patients, pages No. 597–605, Copyright (2022) with permission from Elsevier.

References

Alaugaily, I. & Azim, A.A. (2022) CBCT Patterns of Bone Loss and Clinical Predictors for the Diagnosis of Cracked Teeth and Teeth with Vertical Root Fracture. *Journal of Endodontics*, 48, 1100–1106.

Als-Nielsen, B., Chen, W., Gluud, C. & Kjaergard, L.L. (2003) Association of funding and conclusions in randomized drug trials: a reflection of treatment effect or adverse events? *JAMA*, 290, 921–928.

Altman D.G., (2005) Categorizing continuous variables, in: P. Armitage, T. Colton (Eds.), Encyclopedia of Biostatistics, second ed., John Wiley, Chichester, pp. 708-711.

Alyahya, L. & Myers, G.L. (2021) Denosumab Use as a Predictor Variable for External Cervical Resorption: A Case-Control Study. *Journal of Endodontics*, 47, 366–373.

Annesley T.M. (2010) Who, what, when, where, how, and why: the ingredients in the recipe for a successful Methods section. *Clinical Chemistry,* 56, 897-901.

Antunes, L.S., Carvalho, L., Petean, I.B.F., Antunes, L.A., Freitas, J.V., Salles, A.G., Olej, B., Oliveira, D.S.B., Küchler, E.C. & Sousa-Neto, M.D. (2021) Association between genetic polymorphisms in the promoter region of the defensin beta 1 gene and persistent apical periodontitis. *International Endodontic Journal*, 54, 38–45.

von Arx, T., Janner, S.F.M., Hänni, S. & Bornstein, M.M. (2016) Agreement between 2D and 3D radiographic outcome assessment one year after periapical surgery. *International Endodontic Journal*, 49, 915–925.

Azim, A.A., Griggs, J.A. & Huang, G.T.J. (2016) The Tennessee study: factors affecting treatment outcome and healing time following nonsurgical root canal treatment. *International Endodontic Journal*, 49, 6–16.

Bakhsh, A., Moyes, D., Proctor, G., Mannocci, F. & Niazi, S.A. (2022) The impact of apical periodontitis, non-surgical root canal retreatment and periapical surgery on serum inflammatory biomarkers. *International Endodontic Journal*, 55, 923–937.

Baruwa, A.O., Martins, J.N.R., Pereira, B., Meirinhos, J., Ordinola-Zapata, R., Souza, E.M. & Ginjeira, A. (2022) Prevalence of periapical lesions, root canal treatments and restorations in teeth adjacent to implant- or tooth-supported crowns: A multi-centre cross-sectional study. *International Endodontic Journal*, 55, 30–37.

Becher, H. (1992) The concept of residual confounding in regression models and some applications. *Statistics in Medicine*, 11 1747-1758

Bekelman, J.E., Li, Y. & Gross, C.P. (2003) Scope and impact of financial conflicts of interest in biomedical research: a systematic review. *JAMA*, 289, 454–465.

Bornstein, M.M., Bingisser, A.C., Reichart, P.A., Sendi, P., Bosshardt, D.D. & von Arx, T. (2015) Comparison between Radiographic (2-dimensional and 3-dimensional) and Histologic Findings of Periapical Lesions Treated with Apical Surgery. *Journal of Endodontics*, 41, 804–811.

Bronzato, J.D., Davidian, M.E.S., de Castro, M., de-Jesus-Soares, A., Ferraz, C.C.R., Almeida, J.F.A., Marciano, M.A. & Gomes, B.P.F.A. (2021) Bacteria and virulence factors in periapical lesions associated with teeth following primary and secondary root canal treatment. *International Endodontic Journal*, 54, 660–671.

Cals, J.W., & Kotz, D. (2013) Effective writing and publishing scientific papers, part III: introduction. *Journal of Clinical Epidemiology*, 66, 702.

Careddu, R. & Duncan, H.F. (2021) A prospective clinical study investigating the effectiveness of partial pulpotomy after relating preoperative symptoms to a new and established classification of pulpitis. *International Endodontic Journal*, 54, 2156–2172.

Carlson, M.D., & Morrison, R.S. (2009) Study design, precision, and validity in observational studies. *Journal of Palliative Medicine* 12, 77-82.

Casey, S.M., Fox, D., Duong, W., Bui, N., Latifi, N., Ramesh, V., Podborits, E., Flake, N.M., Khan, A.A. & Gibbs, J.L. (2022) Patient Centered Outcomes among a Cohort Receiving Regenerative Endodontic Procedures or Apexification Treatments. *Journal of Endodontics*, 48, 345–354.

de Castro, G.A.P., Petean, I.B.F., de Paula-Silva, F.W.G., Kuchler, E.C., Antunes, L.D.S., Segato, R.A.B., da Silva, L.A.B., Silva-Sousa, A.C. & Sousa-Neto, M.D. (2023) Genetic polymorphism in the tumour necrosis factor alpha gene (G-308A) is associated with persistent apical periodontitis in Brazilians. *International Endodontic Journal*, 56, 17–26.

Costanza, M.C. (1995) Matching. *Preventive Medicine* 24, 425e433.

Cuzick, J. (1999) Interaction, subgroup analysis and sample size. *IARC Scientific Publications* 148, 109-121.

Cruz, A., Gascón, L.G., Palafox-Sánchez, C.A., Flores-García, C., Espinoza-García, N., Sagrero-Fabela, N., Cintra, L.T.A., Mejía-Flores, R. & Salazar-Camarena, D.C. (2022) TNFSF13B rs9514828 gene polymorphism and soluble B cell activating factor levels: Association with apical periodontitis. *International Endodontic Journal*. doi: 10.1111/iej.13879.

von Elm, E., Altman, D.G., Egger, M., Pocock, S.J., Gøtzsche, P.C., Vandenbroucke, J.P., & STROBE Initiative (2008) The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *Journal of Clinical Epidemiology*, 61, 344–349.

Ferrández, L.M., Ng, Y.-L., Rhodes, J.S., Mistry, S.S. & Gulabivala, K. (2021) Radiographic periapical healing associated with root-treated teeth accessed through existing crowns: a historical controlled cohort study. *Clinical Oral Investigations*, 25, 5807–5814.

Fransson, H., Bjørndal, L., Frisk, F., Dawson, V.S., Landt, K., Isberg, P.-E., EndoReCo, null & Kvist, T. (2021) Factors Associated with Extraction following Root Canal Filling in Adults. *Journal of Dental Research*, 100, 608–614.

Gomes, M.S., Hugo, F.N., Hilgert, J.B., Sant'Ana Filho, M., Padilha, D.M.P., Simonsick, E.M., Ferrucci, L. & Reynolds, M.A. (2016) Apical periodontitis and incident cardiovascular events in the Baltimore Longitudinal Study of Ageing. *International Endodontic Journal*, 49, 334–342.

Gorni, F.G., Ionescu, A.C., Ambrogi, F., Brambilla, E. & Gagliani, M.M. (2022) Prognostic Factors and Primary Healing on Root Perforation Repaired with MTA: A 14-year Longitudinal Study. *Journal of Endodontics*, 48, 1092–1099.

Ferreira, J.C., & Patino, C.M. (2019) Loss to follow-up and missing data: important issues that can affect your study results. *Jornal Brasileiro de Pneumologia* , 45, e20190091.

Forero, D.A., Lopez-Leon, S., & Perry, G. (2022) A brief guide to the science and art of writing manuscripts in biomedicine. *Journal of Translational Medicine*, 18, 425.

Haynes, R.B., Mulrow, C.D., Huth, E.J., Altman, D.G., & Gardner, M.J. (1990) More informative abstracts revisited. *Annals of Internal Medicine,* 113, 69-76.

Hoppe, C.B., Oliveira, J. a. P., Grecca, F.S., Haas, A.N. & Gomes, M.S. (2017) Association between chronic oral inflammatory burden and physical fitness in males: a cross-sectional observational study. *International Endodontic Journal*, 50, 740–749.

Hou, Y., Wang, L., Zhang, L., Tan, X., Huang, D. & Song, D. (2022) Potential relationship between clinical symptoms and the root canal microbiomes of root filled teeth based on the next-generation sequencing. *International Endodontic Journal*, 55, 18–29.

Ideo, F., Niazi, S., Mezzena, S., Mannocci, F. & Cotti, E. (2022) Prevalence of Apical Periodontitis in Patients with Autoimmune Diseases under Immunomodulators: A Retrospective Cohort Study. *Journal of Endodontics*, 48, 722–729.

Ioannidis, J.P. (2007) Limitations are not properly acknowledged in the scientific literature. *Journal of Clinical Epidemiology*, 60, 324–329

Irinakis, E., Aleksejuniene, J., Shen, Y. & Haapasalo, M. (2020) External Cervical Resorption: A Retrospective Case-Control Study. *Journal of Endodontics*, 46, 1420–1427.

Irinakis, E., Haapasalo, M., Shen, Y. & Aleksejuniene, J. (2022) External cervical resorption - Treatment outcomes and determinants: A retrospective cohort study with up to 10 years of follow-up. *International Endodontic Journal*, 55, 441–452.

Jakovljevic, A., Andric, M., Nikolic, N., Coric, V., Krezovic, S., Carkic, J., Knezevic, A., Beljic-Ivanovic, K., Pljesa-Ercegovac, M., Miletic, M., Soldatovic, I., Radosavljevic, T., Jovanovic, T., Simic, T., Ivanovic, V. & Milasin, J. (2018b) Levels of oxidative stress biomarkers and bone resorption regulators in apical periodontitis lesions infected by Epstein-Barr virus. *International Endodontic Journal*, 51, 593–604.

Jakovljevic, A., Knezevic, A., Nikolic, N., Soldatovic, I., Jovanovic, T., Milasin, J. & Andric, M. (2018a) Herpesviruses viral loads and levels of proinflammatory cytokines in apical periodontitis. *Oral Diseases*, Blackwell Publishing Ltd, 24, 840–846.

Jakovljevic, A., Nikolic, N., Carkic, J., Andric, M., Miletic, M., Beljic-Ivanovic, K., Jovanovic, T. & Milasin, J. (2020b) Notch–a possible mediator between Epstein-Barr virus infection and bone resorption in apical periodontitis. *Acta Odontologica Scandinavica*, Taylor and Francis Ltd, 78, 126–131.

Jakovljevic, A., Nikolic, N., Carkic, J., Beljic-Ivanovic, K., Soldatovic, I., Miletic, M., Andric, M. & Milasin, J. (2020a) Association of polymorphisms in TNF-α, IL-1β, GSTM and GSTT

genes with apical periodontitis: is there a link with herpesviral infection?. *International Endodontic Journal*, Blackwell Publishing Ltd, 53, 895–904.

Jonasson, P., Lennholm, C. & Kvist, T. (2017) Retrograde root canal treatment: a prospective case series. *International Endodontic Journal*, 50, 515–521.

Jonsson Sjögren, J., Kvist, T., Eliasson, A., EndoReCo, & Pigg, M (2019) The frequency and characteristics of pain and discomfort associated with root filled teeth: a practice-based study. *International Endodontic Journal* 52, 1264-1273.

Jordal, K., Skudutyte-Rysstad, R., Sen, A., Torgersen, G., Ørstavik, D. & Sunde, P.T. (2022) Effects of an individualized training course on technical quality and periapical status of teeth treated endodontically by dentists in the Public Dental Service in Norway: An observational intervention study. *International Endodontic Journal*, 55, 240–251.

Kazzi, D., Horner, K., Qualtrough, A.C., Martinez-Beneyto, Y. & Rushton, V.E. (2007) A comparative study of three periapical radiographic techniques for endodontic working length estimation. *International Endodontic Journal*, 40, 526–531.

Keerthana, G., Singh, N., Yadav, R., Duhan, J., Tewari, S., Gupta, A., Sangwan, P. & Mittal, S. (2021) Comparative analysis of the accuracy of periapical radiography and cone-beam computed tomography for diagnosing complex endodontic pathoses using a gold standard reference - A prospective clinical study. *International Endodontic Journal*, 54, 1448–1461.

Khabbaz, M.G., Protogerou, E. & Douka, E. (2010) Radiographic quality of root fillings performed by undergraduate students. *International Endodontic Journal*, 43, 499–508.

Khalighinejad, N., Aminoshariae, A., Kulild, J.C. & Mickel, A. (2017) Apical Periodontitis, a Predictor Variable for Preeclampsia: A Case-control Study. *Journal of Endodontics*, 43, 1611–1614.

Kim, D., Kim, S., Song, M., Kang, D.R., Kohli, M.R. & Kim, E. (2018) Outcome of Endodontic Micro-resurgery: A Retrospective Study Based on Propensity Score-matched Survival Analysis. *Journal of Endodontics*, 44, 1632–1640.

Kirkevang, L.-L., Ørstavik, D., Wenzel, A. & Vaeth, M. (2015) Prognostic value of the full-scale Periapical Index. *International Endodontic Journal*, 48, 1051–1058.

Kirkevang, L.-L., Vaeth, M. & Wenzel, A. (2012) Ten-year follow-up observations of periapical and endodontic status in a Danish population. *International Endodontic Journal*, 45, 829–839.

Kirkevang, L.-L., Vaeth, M. & Wenzel, A. (2014) Ten-year follow-up of root filled teeth: a radiographic study of a Danish population. *International Endodontic Journal*, 47, 980–988.

Krall, E.A., Abreu Sosa, C., Garcia, C., Nunn, M.E., Caplan, D.J., & Garcia, R.I. (2006) Cigarette smoking increases the risk of root canal treatment. *Journal of Dental Research* 85, 313-317.

Kotz, D., & Cals, J.W. (2013) Effective writing and publishing scientific papers, part IV: methods. *Journal of Clinical Epidemiology,* 66, 817.

Kumar, G., Tewari, S., Kamboj, M., Yadav, A., Gill, P.S. & Kharb, S. (2022) Comparative Evaluation of Serum High-sensitivity C-Reactive Protein and Complete Hemogram Indices in Subjects with and without Apical Periodontitis: A Prospective Interventional Study. *Journal of Endodontics*, 48, 1020–1028.

Kwak, Y., Choi, J., Kim, K., Shin, S.-J., Kim, S. & Kim, E. (2019) The 5-Year Survival Rate of Nonsurgical Endodontic Treatment: A Population-based Cohort Study in Korea. *Journal of Endodontics*, 45, 1192–1199.

Lang, T.A., Talerico, C. & Siontis, G.C.M. (2012) Documenting clinical and laboratory images in publications: the CLIP principles. *Chest*, 141, 1626–1632.

Lexchin, J., Bero, L.A., Djulbegovic, B. & Clark, O. (2003) Pharmaceutical industry sponsorship and research outcome and quality: systematic review. *BMJ*, 326, 1167–1170.

Martinho, J.P., Coelho, A., Oliveiros, B., Pires, S., Abrantes, A.M., Paulo, S., Carvalho, A.C., Carrilho, E., Paula, A., Carvalho, L., Seiça, R., Botelho, M.F., Marto, C.M., Spagnuolo, G., Matafome, P. & Ferreira, M.M. (2021) Impairment of the angiogenic process may contribute to lower success rate of root canal treatments in diabetes mellitus. *International Endodontic Journal*, 54, 1687–1698.

Martínez, D., Papuzinski, C., Stojanova, J., & Arancibia, M. (2019). General concepts in biostatistics and clinical epidemiology: observational studies with case-control design. *Medwave* ,19, e7716.

Mintzker, Y., Blum, D. & Adler, L. (2022) Replacing PICO in non-interventional studies. *BMJ evidence-based medicine*. doi: 10.1136/bmjebm-2021-111889.

Moher, D., Hopewell, S., Schulz, K.F., Montori, V., Gøtzsche, P.C., Devereaux, P.J., Elbourne, D., Egger, M., Altman, D.G., & CONSORT (2012) CONSORT 2010 explanation and elaboration: updated guidelines for reporting parallel group randomised trials. *International Journal of Surgery*, 10, 28–55.

Moher, D., Schulz, K.F., Simera, I. & Altman, D.G. (2010) Guidance for Developers of Health Research Reporting Guidelines. *PLOS Medicine*, 7, e1000217.

Mondal, H., Mondal, S., & Mondal, S. (2018) How to choose title and keywords for manuscript according to medical subject headings. *Indian Journal of Vascular and Endovascular Surgery* 5, 141.

Moreno, J.O., Alves, F.R.F., Gonçalves, L.S., Martinez, A.M., Rôças, I.N. & Siqueira, J.F. (2013) Periradicular status and quality of root canal fillings and coronal restorations in an urban Colombian population. *Journal of Endodontics*, 39, 600–604.

Morrow, B. (2013) An overview of cohort study designs and their advantages and disadvantages. *International Journal of Therapy and Rehabilitation*, Mark Allen Group, 17, 518–523.

Morshed, S., Tornetta, P. 3rd, & Bhandari, M. (2009) Analysis of observational studies: a guide to understanding statistical methods. *The Journal of Bone & Joint Surgery* 91, 50-60.

Mota de Almeida, F,J., Knutsson, K., & Flygare, L. (2015) The impact of cone beam computed tomography on the choice of endodontic diagnosis. *International Endodontic Journal* 48, 564-72.

Murillo-Benítez, M., Martín-González, J., Jiménez-Sánchez, M.C., Cabanillas-Balsera, D., Velasco-Ortega, E. & Segura-Egea, J.J. (2020) Association between dental anxiety and intraoperative pain during root canal treatment: a cross-sectional study. *International Endodontic Journal*, 53, 447–454.

Nagendrababu, V., Duncan, H.F., Fouad, A.F., Kirkevang, L.-L., Parashos, P., Pigg, M., Væth, M., Jayaraman, J., Suresh, N., Arias, A., Wigsten, E. & Dummer, P.M.H. (2023) PROBE 2023 guidelines for reporting observational studies in Endodontics: A consensus-based development study. *International Endodontic Journal*. ,56:308-317..

Nagendrababu V, Duncan HF, Bjørndal L, et al. (2020a) PRIRATE 2020 guidelines for reporting randomized trials in Endodontics: a consensus-based development. Int Endod J. 53:764-773.

Nagendrababu V, Chong BS, McCabe P, et al. (2020b) PRICE 2020 guidelines for reporting case reports in Endodontics: a consensus-based development. Int Endod J. 2020;53:619-626.

Nagendrababu V, Kishen A, Murray PE, et al. (2021c)PRIASE 2021 guidelines for reporting animal studies in Endodontology: a consensus-based development. Int Endod J. 2021;54:848-857.

Nagendrababu V, Murray PE, Ordinola-Zapata R et al. (2021b) PRILE 2021 guidelines for reporting laboratory studies in Endodontics: a consensus-based development. Int Endod J. 2021;54:1482-1490

Nagendrababu, V., Murray, P.E., Faggion Jr., C.M. & Dummer, P.M.H. (2021a) Promoting integrity in scholarly research and its publication: International Endodontic Journal policy on reporting conflicts of interest, funding and acknowledgements within manuscripts submitted for publication. *International Endodontic Journal*, 54, 1969–1973.

Nikolic, N., Jakovljevic, A., Carkic, J., Beljic-Ivanovic, K., Miletic, M., Soldatovic, I., Andric, M., Ivanovic, V. & Milasin, J. (2019) Notch Signaling Pathway in Apical Periodontitis: Correlation with Bone Resorption Regulators and Proinflammatory Cytokines. *Journal of Endodontics*, 45, 123–128.

Patel, AV., Deubler, E., Teras, L.R., Colditz, G.A., Lichtman, C.J., Cance, W.G., & Clarke, C.A. (2022) Key risk factors for the relative and absolute 5-year risk of cancer to enhance cancer screening and prevention. *Cancer*, 128, 3502-15.

Pérez-Losada, F. de L., López-López, J., Martín-González, J., Jané-Salas, E., Segura-Egea, J.J. & Estrugo-Devesa, A. (2020) Apical periodontitis and glycemic control in type 2 diabetic patients: Cross-sectional study. *Journal of Clinical and Experimental Dentistry*, 12, e964–e971.

Pigg, M., List, T., Petersson, K., Lindh, C. & Petersson, A. (2011) Diagnostic yield of conventional radiographic and cone-beam computed tomographic images in patients with atypical odontalgia. *International Endodontic Journal*, 44, 1092–1101.

PradeepKumar, A.R., Shemesh, H., van Loveren, C., JothiLatha, S., Shireen, F., VijayaBharathi, R. & Kishen, A. (2019) Impact of apical extent of root canal filling on vertical root fracture: a case-control study. *International Endodontic Journal*, 52, 1283–1289.

Prati, C., Pirani, C., Zamparini, F., Gatto, M.R. & Gandolfi, M.G. (2018) A 20-year historical prospective cohort study of root canal treatments. A Multilevel analysis. *International Endodontic Journal*, 51, 955–968.

Ricucci, D., Loghin, S., & Siqueira, JF Jr. (2014) Correlation between clinical and histologic pulp diagnoses. *Journal of Endodontics* 40, 1932-9.

Qudeimat, M.A., Alyahya, A. & Hasan, A.A. (2017) Mineral trioxide aggregate pulpotomy for permanent molars with clinical signs indicative of irreversible pulpitis: a preliminary study. *International Endodontic Journal*, 50, 126–134.

Razdan, A., Jungnickel, L., Schropp, L., Vaeth, M. & Kirkevang, L.-L. (2022) Trends of endodontic and periapical status in adult Danish populations from 1997 to 2009: A repeated cross-sectional study. *International Endodontic Journal*, 55, 164–176.

Rechenberg, D.K., Munir, A. & Zehnder, M. (2021) Correlation between the clinically diagnosed inflammatory process and periapical index scores in severely painful endodontically involved teeth. *International Endodontic Journal*, 54, 172–180.

Restrepo-Restrepo, F.A., Cañas-Jiménez, S.J., Romero-Albarracín, R.D., Villa-Machado, P.A., Pérez-Cano, M.I. & Tobón-Arroyave, S.I. (2019) Prognosis of root canal treatment in teeth with preoperative apical periodontitis: a study with cone-beam computed

tomography and digital periapical radiography. *International Endodontic Journal*, 52, 1533–1546.

Romain, P.L. (2015) Conflicts of interest in research: looking out for number one means keeping the primary interest front and center. *Current Reviews in Musculoskeletal Medicine*, 8, 122–127.

Rossner, M. & Yamada, K.M. (2004) What's in a picture? The temptation of image manipulation. *The Journal of Cell Biology*, 166, 11–15.

Ruiz, X.-F., Duran-Sindreu, F., Shemesh, H., García Font, M., Vallés, M., Roig Cayón, M. & Olivieri, J.G. (2017) Development of Periapical Lesions in Endodontically Treated Teeth with and without Periodontal Involvement: A Retrospective Cohort Study. *Journal of Endodontics*, 43, 1246–1249.

Rutsatz, C., Baumhardt, S.G., Feldens, C.A., Rösing, C.K., Grazziotin-Soares, R. & Barletta, F.B. (2012) Response of pulp sensibility test is strongly influenced by periodontal attachment loss and gingival recession. *Journal of Endodontics*, 38, 580–583.

Sackett, D.L. (1979) Bias in analytic research. *Journal of Chronic Diseases* 32, 51- 63.

Saini, A., Nangia, D., Sharma, S., Kumar, V., Chawla, A., Logani, A. & Upadhyay, A. (2022) Outcome and associated predictors for nonsurgical management of large cyst-like periapical lesions: A CBCT-based prospective cohort study. *International Endodontic Journal*. doi: 10.1111/iej.13860.

Sanner, F., Sonntag, D., Hambrock, N. & Zehnder, M. (2022) Patients with persistent idiopathic dentoalveolar pain in dental practice. *International Endodontic Journal*, 55, 231–239.

Scarano, A., Artese, L., Piattelli, A., Carinci, F., Mancino, C. & Iezzi, G. (2012) Hemostasis control in endodontic surgery: a comparative study of calcium sulfate versus gauzes and versus ferric sulfate. *Journal of Endodontics*, 38, 20–23.

Sebring, D., Buhlin, K., Norhammar, A., Rydén, L., Jonasson, P., EndoReCo, Lund, H. & Kvist, T. (2022) Endodontic inflammatory disease: A risk indicator for a first myocardial infarction. *International Endodontic Journal*, 55, 6–17.

Segura-Sampedro, J.J., Jiménez-Giménez, C., Jane-Salas, E., Cabanillas-Balsera, D., Martín-González, J., Segura-Egea, J.J. & López-López, J. (2022) Periapical and endodontic status of patients with inflammatory bowel disease: Age- and sex-matched case-control study. *International Endodontic Journal*, 55, 748–757.

Serefoglu, B., Miçooğulları Kurt, S., Kandemir Demirci, G., Kaval, M.E. & Çalışkan, M.K. (2021) A prospective cohort study evaluating the outcome of root canal retreatment in symptomatic mandibular first molars with periapical lesions. *International Endodontic Journal*, 54, 2173–2183.

Steele, J.G., Sanders, A.E., Slade, G.D., Allen, P.F., Lahti, S., Nuttall, N., & Spencer, A.J. (2004) How do age and tooth loss affect oral health impacts and quality of life? A study comparing two national samples. *Community Dentistry and Oral Epidemiology* 32, 107-14.

Signor, B., Blomberg, L.C., Kopper, P.M.P., Augustin, P.A.N., Rauber, M.V., Rodrigues, G.S. & Scarparo, R.K. (2021) Root canal retreatment: a retrospective investigation using regression and data mining methods for the prediction of technical quality and periapical healing. *Journal of applied oral science: revista FOB*, 29, e20200799.

Silva LR, de Lima KL, Santos AA, Leles CR, Estrela C, de Freitas Silva BS, Yamamoto-Silva FP (2021) Dentin thickness as a risk factor for vertical root fracture in endodontically treated teeth: a case-control study. *Clinical Oral Investigation* 25, 1099-1105

Slama, R., Werwatz, A. (2005) Controlling for continuous confounding factors: non - and semi-parametric approaches. *La Revue d'épidémiologie et de santé publique*, 53, 2S65-80.

Song, M., Kim, S.G., Shin, S.-J., Kim, H.-C. & Kim, E. (2013) The influence of bone tissue deficiency on the outcome of endodontic microsurgery: a prospective study. *Journal of Endodontics*, 39, 1341–1345.

Timmerman, A., Calache, H. & Parashos, P. (2017) A cross sectional and longitudinal study of endodontic and periapical status in an Australian population. *Australian Dental Journal*, 62, 345–354.

Tooth, L., Ware, R., Bain, C., Purdie, D.M. & Dobson, A. (2005) Quality of reporting of observational longitudinal research. *American Journal of Epidemiology*, 161, 280–288.

Tullu, M.S. (2019) Writing the title and abstract for a research paper: Being concise, precise, and meticulous is the key. *Saudi Journal of Anaesthesia*, 13, S12–S17.

Vandenbroucke, J.P., von Elm, E., Altman, D.G., Gøtzsche, P.C., Mulrow, C.D., Pocock, S.J., Poole, C., Schlesselman, J.J., Egger, M., & STROBE initiative (2007) Strengthening the Reporting of Observational Studies in Epidemiology (STROBE): explanation and elaboration. *Annals of Internal Medicine*, 147, W163-194.

Vehkalahti, M.M., Palotie, U. & Valaste, M. (2020) Age-specific findings on endodontic treatments performed by private dentists in Finland in 2012 and 2017: a nationwide register-based observation. *International Endodontic Journal*, 53, 754–763.

Vernazza, C.R., Steele, J.G., Whitworth, J.M., Wildman, J.R. & Donaldson, C. (2015) Factors affecting direction and strength of patient preferences for treatment of molar teeth with nonvital pulps. *International Endodontic Journal*, 48, 1137–1146.

Weissman, A., Wigler, R., Blau-Venezia, N., Goldberger, T. & Kfir, A. (2022) Healing after surgical retreatment at four time points: A retrospective study. *International Endodontic Journal*, 55, 145–151.

Wikström, A., Brundin, M., Romani Vestman, N., Rakhimova, O. & Tsilingaridis, G. (2022) Endodontic pulp revitalization in traumatized necrotic immature permanent incisors: Early failures and long-term outcomes-A longitudinal cohort study. *International Endodontic Journal*, 55, 630–645.

Yazdi, P.M., Schou, S., Jensen, S.S., Stoltze, K., Kenrad, B. & Sewerin, I. (2007) Dentine-bonded resin composite (Retroplast) for root-end filling: a prospective clinical and radiographic study with a mean follow-up period of 8 years. *International Endodontic Journal*, 40, 493–503.

Yılmaz, B., Dinçol, M.E. & Yalçın, T.Y. (2019) A bibliometric analysis of the 103 top-cited articles in endodontics. *Acta Odontologica Scandinavica*, 77, 574–583.