PROBE 2023 guidelines for reporting observational studies in Endodontics: A consensus-based development study

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Running title: PROBE 2023 guidelines

Keywords: Consensus, Endodontics, root canal treatment, observational studies

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This is the author manuscript accepted for publication and has undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/iej.13873

Funding: This work was supported by the International Medical University, Kuala Lumpur, Malaysia under Grant no: IMU 450/2019.

Ethical statement: The approval to conduct the work was obtained from the Institutional Review Board on Research and Ethics of the International Medical University (IMU), Kuala Lumpur, Malaysia (No: IMU 450/2019), and University of Sharjah, Sharjah, UAE (REC 20-11-06-01).

Conflict of Interest: The authors have stated explicitly that there are no conflicts of interest in connection with this article.

Author contribution: All the authors made substantial contributions to the manuscript. All the authors have read and approved the final version of the manuscript.

Data availability statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

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ABSTRACT

Observational studies are non-interventional studies that establish the prevalence and incidence of conditions or diseases in populations or analyse the relationship between health status and other variables. They also facilitate the development of specific research questions for future randomized trials or to answer important scientific questions when trials are not possible to carry out. This article outlines the previously documented consensus-based approach by which the Preferred Reporting items for Observational studies in Endodontics (PROBE) 2023 guidelines were developed. A steering committee of nine members was formed, including the project leaders (PD, VN). The steering committee developed an initial checklist by combining and adapting items from the STrengthening the Reporting of Observational studies in Epidemiology (STROBE) checklist and the Clinical and Laboratory Images in Publications (CLIP) principles, as well as adding several new items specifically for the specialty of Endodontics. The steering committee then established a PROBE Delphi Group (PDG) and a PROBE Online Meeting Group (POMG) to obtain expert input and feedback on the preliminary draft checklist. The PDG members participated in an online Delphi process to reach consensus on the clarity and suitability of the items present in the PROBE checklist. The POMG then held detailed discussions on the PROBE checklist generated through the online Delphi process. This online meeting was held via the Zoom platform on 7th October 2022. Following this meeting, the steering committee revised the PROBE checklist, which was piloted by several authors when preparing a manuscript describing an observational study for publication. The PROBE 2023 checklist consists of 11 sections and 58 items. Authors are now encouraged to adopt the PROBE 2023 guidelines, which will improve the overall reporting quality of observational studies in Endodontics. The PROBE 2023 checklist is freely available and can be downloaded from the PRIDE website (https://pride-endodonticguidelines.org/probe/).

KEYWORDS: Consensus, endodontics, root canal treatment, observational studies.

INTRODUCTION

Observational studies include a range of study designs such as cohort, case-control, and cross-sectional (Gilmartin-Thomas et al., 2018). Observational studies differ from clinical interventional trials in which the participants are allocated to groups with the experiment being conducted under strictly controlled and generally randomized conditions. Observational studies are ranked lower than randomized clinical trials in the evidence-based hierarchy, e.g., Oxford (https://www.cebm.ox.ac.uk/resources/levels-of-evidence) (Forrest, 2009). Nevertheless, observational studies can contribute to the development of hypotheses or focussed research questions for future randomized clinical trials (Song & Chung, 2010). Observational studies, in comparison with randomized controlled trials, can be less expensive, more pragmatic, faster and simpler to conduct. They also tend to include a significantly greater sample size, and a broader scope of applicability, than randomized controlled trials which tend to have strict inclusion/exclusion criteria (Gilmartin-Thomas et al., 2018). In dentistry and medicine, observational studies have been utilized to address significant research problems in clinical situations where trials cannot be conducted (Gilmartin-Thomas et al., 2018). For example, in the field of plastic surgery, it can be difficult to undertake randomized controlled trials, with the consequence that observational studies are becoming more common. Such studies look at the relationship between exposures, such as risk factors or surgery, and outcomes, such as disease or complications (Song & Chung, 2010). Likewise, in the field of Endodontics observational studies allow the influence of certain factors on the outcome of an intervention to be studied when the exposure cannot be randomized in the population for ethical reasons; for example, the influence of smoking habits.

The STrengthening the Reporting of Observational studies in Epidemiology (STROBE) checklist was developed to improve the reporting quality of observational studies and encompasses three main study designs, namely cohort, case-control, and cross-sectional (Von Elm et al., 2008). To improve the reporting of observational studies, several extensions of the STROBE checklist have been developed and introduced for specific clinical areas. They include genetic association studies (STrengthening the REporting of Genetic Association Studies (STREGA): An Extension of the STROBE Statement) (Little et al., 2009); molecular

epidemiology (STrengthening the Reporting of OBservational studies in Epidemiology – Molecular Epidemiology (STROBE-ME): An extension of the STROBE statement) (Gallo et al., 2011); nutritional epidemiology (Strengthening the Reporting of Observational Studies in Epidemiology—Nutritional Epidemiology (STROBE-nut): An Extension of the STROBE Statement) (Lachat et al., 2016). Although several extensions of the original STROBE checklist are available in the field of medicine, no such extensions are available in any of the dental specialties. Despite the availability of the STROBE checklist and its extension(s), the overall reporting quality of observational studies has been demonstrated to be suboptimal, e.g., in otorhinolaryngology (Hendriksma et al., 2017), paediatric dentistry (Butani et al., 2006) and therapies for COVID-19 (Ziemann et al., 2022).

The observational study is one of the most commonly reported study designs included in the top 100 most-cited articles in Endodontology (Fardi et al., 2011). Although the STROBE checklist covers the majority of the items necessary for reporting observational studies, several key items specific to Endodontics are absent, for example, keywords, structured abstract, information on ethical approval, quality of images, implications for future research etc. Considering the impact of observational studies in Endodontics, and to improve the reporting quality of studies pertaining to this specialty, a study protocol on Preferred Reporting items for Observational studies in Endodontology (PROBE) guidelines has been published (Nagendrababu et al., 2020). The PROBE guidelines are based on the STROBE checklist, but with a focus on items specific to Endodontics. The items included within the PROBE guidelines will assist researchers in reporting their observational studies effectively as well as assist peer reviewers and editors of journals in determining the suitability of manuscripts for publication. The current initiative describes the development of the PROBE 2023 guidelines for reporting observational studies in Endodontics using a consensus-based approach.

METHODS

The approval to conduct the work was obtained from the Institutional Review Board on Research and Ethics of the International Medical University (IMU), Kuala Lumpur, Malaysia (No: IMU 450/2019), and University of Sharjah, Sharjah, UAE (REC 20-11-06-01). The

development of the PROBE 2023 guidelines was based on the recommendations provided in the Guidance for Developers of Health Research Reporting Guidelines (Moher et al., 2010) and the published protocol (Nagendrababu et al., 2020).

Initial steps

At its first face-to-face meeting, members of the Preferred Reporting Items for study Designs in Endodontology (PRIDE) steering committee highlighted the need to develop criteria for reporting observational studies in the specialty. Subsequently, the project leaders (VN and PD) initiated this specific project. The project leaders formed a steering committee of nine members (PD, VN, HD, AF, LK, PP, MP, MV and JJ). An initial draft checklist was created by modifying the original STROBE checklist for reporting observational studies (Von Elm et al., 2008). In addition, items from the Clinical and Laboratory Images in Publications principles (Lang et al., 2012) were analysed and included where relevant. An online Delphi approach was used to evaluate the initial draft checklist in order to make improvements and ultimately obtain consensus.

Online Delphi process

A PROBE Delphi Group (PDG) was formed by the steering committee to undertake the Delphi consensus process. The PDG consisted of 30 members, out of which 22 members were academics or researchers, four were specialist endodontists working in private clinics, two were general dentists, and two were representatives of the public. The academic members of the PDG were recruited based on their compliance with one of the following eligibility criteria: (1) had published at least two observational studies in Endodontics; (2) had published guidelines for research reporting; and (3) had a minimum of 15 years of academic or clinical experience in dentistry. All PDG members who were selected received an e-mail invitation to participate in the online Delphi process. The invitation package outlined the objectives and reasoning behind developing the PROBE guidelines, discussed the Delphi process, and defined the roles and responsibilities of the members of the PDG. A Delphi document that set out the process of anonymous consensus building and included the draft PROBE checklist was distributed to members who confirmed their involvement. The PDG members were informed of the criteria and scoring system used to determine whether to

include or exclude items from the draft checklist, which were evaluated for suitability and clarity. The clarity of an item was determined using a "Yes" or "No" response, whereas its suitability was determined using a nine-point Likert scale (1 = 'absolutely not include' to 9 = 'certainly include'). Additionally, the PDG members were asked to submit anonymous comments on each item to provide additional context for the checklist, as well as to assist the steering committee in understanding why they had awarded their specific scores.

The steering committee evaluated the ratings for each item using an established set of inclusion and exclusion criteria. Items awarded a score of 7–9 by at least 70% of PDG members were included, as were items with a score of 1–3 by less than 30% of members. Items with a score of 1 to 3 from more than 70% of members or a score of 7 to 9 from less than 30% of members were omitted from the checklist. The Delphi rounds were repeated until a predetermined level of consensus was reached and a final list of items was approved (Agha et al., 2017). Following this, an online meeting was arranged to discuss the PROBE checklist.

Online meeting

A PROBE Online Meeting Group (POMG) was formed by the steering committee. The eligibility criteria were similar for both POMG and the PDG members and several individuals served as members of both groups. In addition, two postgraduate students were invited to attend the meeting. The agenda of the meeting was shared with the POMG and included details of the meeting (date, time, Zoom link) in addition to the results of the online Delphi rounds, and the revised PROBE checklist. The online meeting was conducted through the Zoom platform (Zoom Video Communications Inc. San Jose, CA, USA) on 7th October 2022.

Post-meeting activities

Based on the feedback obtained at the online meeting, the steering committee revised the PROBE checklist. Once the content was finalized, several experts were then asked to pilot the guidelines when drafting a manuscript using the PROBE 2023 checklist. Their feedback was considered by the steering committee and any essential changes to the checklist were made.

RESULTS

Online Delphi process

The online Delphi process was completed in two rounds. Thirty individuals were involved in total, with the response rates for rounds 1 and 2 being 100% and 94%, respectively.

Online meeting

The online Zoom meeting was chaired by two steering committee members (PD, VN) and consisted of 27 individuals including two postgraduate students and four steering committee members (PD, VN, HD, MV). The attendees discussed the suitability of the items for inclusion in the PROBE checklist and provided feedback on several specific items.

Post-meeting activities

The steering committee reviewed the feedback from the POMG and made several changes to the checklist. Two authors then piloted the PROBE checklist when drafting manuscripts describing observational studies. Table 1 sets out the final PROBE 2023 checklist that consists of 11 sections and 58 items.

DISCUSSION

The consequences of suboptimal reporting of biomedical research are significant in both medical and dental research (Montengro et al., 2002; Cairo et al., 2012). Complete, clear and transparent reporting of studies is of critical importance to ensure the availability and valid interpretation of all aspects of a study as well as for subsequent evidence synthesis.

The current report describes the process of developing reporting guidelines exclusively for observational studies in Endodontics. The PROBE 2023 guidelines consist of 11 sections with 58 individual items that provide guidance to authors when reporting case control, cohort and cross-sectional studies in Endodontics, and directs them to use a reproducible, standardized and comprehensive approach. All components of the relevant study designs were considered when drafting the checklist, resulting in a standardized template that was produced using an accepted process. Following the PROBE 2023

guidelines will enable researchers to design, conduct and report case control, cohort and cross-sectional studies in Endodontics in an effective manner.

The two major areas of concern in an observational study design that necessitate adequate reporting are *precision* and *validity*, both of which enable the results of a study to be validated. The effect of an "exposure" or intervention on subjects is usually inferred from observational studies. Patients are observed in their natural setting without a randomization process for group assignment. As a consequence, confounders can play a major role in observational studies (Carlson et al., 2009), for example, the aetiology of external root resorption is considered multifactorial, with a combination of injury to the cementum, periodontal tissues as well as multiple local and systemic factors playing a role. Thus, analysing the aetiology of root resorption must consider all the potential factors and also include appropriate multivariable statistical analyses to identify confounding factors and associations (Irinakis et al., 2020). A precise estimate of outcomes can be obtained only when using an appropriate sample size and sampling methods that can reduce the random error of the study. The lack of systematic errors is referred to as the validity of the study, which can have internal and external components. It is essential to determine whether the observed changes or outcomes can be attributed to the exposure and not to other possible causes (Rothman, 1998). It is also essential to determine whether the study results can be generalized to other populations and 'real-world' settings. In case control studies, the main areas of concern are a) recruiting appropriately matched controls (that is, from the same hypothetical population as the cases), b) potential for reviewer bias (e.g., data reviewer in record-based studies) c) recall bias of participants (e.g., the trauma history provided by a participant with root resorption where their recall of symptoms may be more complete in comparison to a participant without symptoms who has been recruited as a control). The recruitment of matched controls in case control studies is of pivotal importance. Items 5e-g deal exclusively with the reporting of sample size calculation, source and selection of participants, matching the criteria for the participants in exposed / unexposed groups as well as in cases / controls in addition to reporting potential confounders. The choice of unit of analysis (patient, tooth or root) should reflect the research question and be considered in the design phase. If multiple teeth (or roots) from the same patient are used, this may

introduce bias. Hence, patients with multiple teeth included in the study should be analysed using the appropriate statistical methods that adjust for the effect of this clustering.

A major problem in analysing the data derived from observational studies is the bias introduced due to unmeasured / uncontrolled confounding factors. Thus, the mere presence of an association does not imply a true causal effect. The strength, consistency, specificity, temporality, coherence, biological gradient and plausibility of the association to the disease outcome all need to be addressed to confirm causation (Hill, 1965). Performing sensitivity analysis provides evidence on the strength and impact of any confounders on the outcome (Vanderweele & Ding, 2017). In order to improve the robustness of a study, several items in the guidelines specifically address the issue of bias and the reporting of the statistical models used for the analysis.

Unaccounted-for loss to follow-up in a cohort study introduces bias in the observed results, particularly differential loss to follow-up when the attrition rate differs in the exposed and non-exposed groups (Carlson et al., 2009). Item 6e provides details on reporting loss to follow-up. In Endodontics, the patient might have teeth extracted for several reasons and not only due to endodontic disease; the guidelines reflect the importance of reporting these special clinical situations as failure of treatment instead of loss to follow-up.

Estimation and hypothesis testing, though appearing similar, each convey distinct information and a thorough understanding of these parameters is mandatory for accurate interpretation of results (Morshed et al., 2009). Calculating the point estimate/ effect / prevalence along with variability (confidence interval) is more appropriate than hypothesis testing and enables better interpretation of the results (Altman, 1991; Rothman, 1998). The statistical test chosen depends on the type of study design used for observational studies. For therapeutic and prognostic studies, confounders play an important role. Stratification and matching negate the confounders to an extent, as does multivariable analysis, depending on the type of outcomes selected. However, causation cannot be established unless strict predictors and outcomes are accounted for. Reporting the choice of confounders, and the statistical procedures used are essential. Model fit or model assumption enable the

reviewers and editors to assess the quality of the manuscript (Morshed et al., 2009). Section 6 in the guidelines covers the statistical tests and reporting of results for observational studies in Endodontics.

Due to the significance of images (e.g., radiographs, CBCT/CT/MRI scans, clinical photographs) in observational studies, the PROBE 2023 guidelines include several items relating to the quality of images included in manuscripts. The "quality of images" domain in the PROBE 2023 checklist is a feature that enables authors to provide essential information that may be used to explain the nature of the images as well other important information that will assist the understanding of readers.

An instructive and well-structured flowchart can quickly and easily communicate information that would otherwise require a lengthy explanation (Vandenbroucke et al., 2014). The flowchart may contain useful information, such as the number of individuals recruited, assessed for eligibility, attrition and final number included for analysis. The STROBE guidelines do not provide specific flowcharts for each study design. The PROBE 2023 guidelines do not propose a particular flowchart type, but authors should be aware that well-designed flowcharts are helpful ways of illustrating the design and other key features of an observational study.

Due to the specific nature, complexity and scope of observational studies, a potential limitation of the PROBE 2023 guidelines is that they do not focus on specific topics. For example, genome-wide association studies (GWAS), molecular epidemiology, or epidemiology for respondent-driven sampling studies. Authors of observational studies that address such studies are still advised to use the PROBE 2023 checklist but, in addition, make use of topic-specific recommendations such as STREGA (Little et al., 2009), STROBE-ME (Gallo et al. 2012), and STROBE-ID (Field et al., 2014). If the need arises in future, the PROBE steering group will consider expanding the primary PROBE guidelines to add recommendations associated with particular observational study designs. In health research, observational studies include various designs such as cohort, case control, cross-sectional and case series (Gilmartin-Thomas et al., 2018). At the protocol stage of the PROBE

project, the steering group considered incorporating case series into the PROBE guidelines. However, due to the differences in study designs between case series and cohort, case control, and cross-sectional studies, the PROBE steering group chose not to include case series. It is worth emphasising therefore that authors are advised to only use the STROBE guidelines when publishing cohort studies, case control studies, and cross-sectional studies, but not case series (Vandenbroucke et al., 2014).

The observational study is an essential study design in Endodontics, particularly to study clinical situations or conditions such as trauma or root resorption, where randomized trials are not possible. Confounding plays a pivotal role in observational studies and needs to be managed and reported with rigour using adequate analytical techniques (Mamdani et al., 2005). Thorough knowledge of the strength and weakness of these techniques and judicious application will make them a powerful tool in endodontic research.

Future plans

1. *Explanation and elaboration document*: This document will describe and define the items in the PROBE 2023 checklist in greater detail with an explanation provided on why they were included in the checklist and their importance. Appropriate examples from the literature or hypothetical examples will be included to support the explanations.
2. *Translation*: The PROBE 2023 guidelines will be published in various languages to improve reach and dissemination.
3. *Preferred Reporting Items for study Designs in Endodontology (PRIDE) website*: The PROBE 2023 guidelines will be made available for download and be free to access on the PRIDE website (https://www.pride-endodonticguidelines.org). Authors, academics, clinicians, students, researchers, and journal editors can provide feedback on the guidelines to inform the steering committee as it considers updates and modifications over time.

4. *Endorsement*: The editors of relevant journals will be contacted to ask them to adopt the PROBE 2023 guidelines and include them in their Author Instructions so that authors are aware of the guidelines and use them while preparing their articles.

CONCLUSION

The PROBE 2023 guidelines have been developed using a validated consensus method. The PROBE 2023 guidelines will allow authors to undertake and report high-quality observational studies in the field of Endodontics, improving transparency and eventually enhancing patient care.

Acknowledgements

We would like to thank those who participated in the online Delphi process and online meeting: Paul Abbott, Australia; Francesc Abella Sans, Spain; Anita Aminoshariae, USA; Hari krishnan Babhu, India; David Barnard, Australia; Bhavinder Bhuva, UK; Mohan Bhuvaneswar, India; Sebastian Bürklein, Germany; Antonis Chaniotis, Greece; Stefano Corbella, Italy; Elisabetta Cotti, Italy; David Edwards, UK; Manal Matoug Elwerfelli, Qatar; Mark Evans, Australia; Helena Fransson, Sweden; Johnah Galicia, UK; Alexis Gaudin, France; Aleksandar Jakovljevic, Serbia; Jayaraman Nagaiah, India; Angambakkam Rajasekaran Pradeep Kumar, India; Gabriel Krastl, Germany; Shaul Lin, Israel; Jorge NR Martins, Portugal; Neeraj Menon, India; Kajal Modi, India; Arun Prasad, UAE; Chiara Priani, Italy; Dan-Krister Rechenberg, Switzerland; Giampiero Rossi-Fedele, Australia; Juan Jose Segura-Egea, Spain; Frank Setzer, USA; Ya Shen, Canada; Emmanuel Silva, Brazil; Jose F Siqueira Jr, Brazil; Pia Titterud Sunde, Norway; Tugba Turk, Turkey; Matthias Widbiller, Germany; Victoria Yu, Singapore; Phillippe Zimet, Australia.

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Table 1: PROBE 2023 checklist of items to be included when reporting observational studies in Endodontics

Section/ Topic	Item Number	Checklist items	Reported on page number
Title	1a	The specific area(s) of interest must be provided using words and phrases that identify the clinical problem(s) and focus of the study	
	1b	The study design must be included in the Title, e.g. cross-sectional, cohort, case-control, case-series etc.	
Keywords	2a	Keywords indicating the specific area(s) of interest using MeSH terms or other more applicable terms must be included	
Abstract	3a	The Introduction/Background must briefly explain the rationale or justification for the study	
	3b	The aim(s)/objective(s) of the study must be provided	
	3c	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	
	3d	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). Adverse events or side-effects must also be reported if present or confirmed as absent	
	3e	The Conclusion must interpret and summarise the primary aim/objective and main findings as well as emphasise the clinical implications	
	3f	The source(s) of funding must be provided	
Introduction	4a	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	
	4b	The primary and, if applicable, any additional/secondary aim(s) and objective(s) of the study must be provided, including any pre-specified hypotheses	
Methods *Ethics*	5a	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	
	5b	The process used for obtaining and storing informed consent must be provided	
Study design	5c	The key elements of the study design must be described early in the Methods section	
Setting	5d	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	
Sample size	5e	Information on how the sample size 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	
Participants – unmatched studies	5f	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	
Participants – matched studies	5g	For matched studies (e.g. cohort, case-control) the matching criteria and the numbers of participants in each group must be provided	
Variables	5h	All outcomes, exposures, predictors, potential confounders, and effect modifiers must be defined clearly	
Data sources/ measurement	5i	Sources of data and details of the methods of assessment (measurement) for each variable of interest must be provided.	
Bias	5j	Efforts taken to identify and address potential sources of bias must be provided	

Quantitative variables	5k	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	
Statistical methods	5l	All statistical methods, including those used to control of confounding factors in the study and in the analysis of the data, must be described	
	5m	The methods used to examine subgroups and interactions must be described, if applicable	
	5n	Missing data (e.g. drop-outs, data not reported) must be addressed and described	
	5o	The analytical methods that take account of the sampling strategy (if applicable) in *Cross-sectional studies* must be described	
	5p	Sensitivity analyses, must be described when used	
Results *Participants*	6a	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	
	6b	Reasons for non-participation (e.g., not eligible, losses/drop-outs) must be described	
Dates	6c	Changes in baseline dates of recruitment, follow-up, and study duration reported in the Methodology must be described, if applicable	
Descriptive data	6d	The baseline demographic and clinical characteristics of study participants as well as information on exposures and potential confounders must be provided	
	6e	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)	
Outcome data	6f	Information on number of outcomes or summary measures over time must be described	
	6g	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)	
Main results	6h	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	
	6i	Results in terms of relative risk should also be translated to absolute risk for a meaningful time period, if relevant	
Additional analyses	6j	The results from any other analyses (e.g., sensitivity, subgroup analyses) must be described, if applicable, as well as adjusted analyses, distinguishing pre-specified from exploratory	

Discussion *Key results*	7a	The main findings must be summarized with reference to the study aim(s)/objective(s)	
Rationale	7b	The rationale for inclusion/exclusion criteria, exposure, and duration must be provided	
Clinical relevance	7c	An explanation of the clinical relevance of the primary and any additional/secondary outcome(s) must be provided	
Strength	7d	The strength(s) of the study must be provided	
Limitations	7e	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	
Summary and validity	7f	The discussion of the strength and limitations should be summarized in an overall assessment of the internal validity of the study	
Interpretation	7g	A detailed interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence must be provided	
Generalisability	7h	The generalizability (external validity, applicability, real-world relevance etc.) of the study findings must be discussed	
Future directions	7i	Implication for future research and clinical practice must be described	
Conclusion(s)	8a	Explicit conclusion(s) from the study must be provided and address all the aims/objectives	
Funding details	9a	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	
Conflict of interest	10a	An explicit statement on conflicts of interest must be provided, together with full affiliations of every author(s)	
Quality of images (if applicable)	11a	Details of the equipment, software and settings used to acquire the image(s) must be described in the text or legend (if applicable)	
	11b	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	
	11c	The circumstances (conditions) under which the image(s) were viewed and evaluated by the author(s) must be provided in the text	
	11d	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	

	11e	Patient(s) identifiers (names, patient numbers) must be removed for General Data Protection Regulation (GDPR) and to ensure they are anonymized or de-identified in all images	
	11f	An interpretation of the findings (meaning and implications) from the image(s) must be provided in the text	
	11g	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	
	11h	Markers/labels must be used to identify the key information in the image(s) and defined in the figure legend	
	11i	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	