Critical analysis of the reporting quality of animal studies within Endodontics using the Preferred Reporting Items for Animal Studies in Endodontics (PRIASE) 2021 quality standard checklist

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Keywords: Animal studies, Guidelines, PRIASE 2021, Reporting,

Running title: Appraisal of animal studies

Funding: The authors declare that there no funding was received.

Ethical statement: The study did not require ethical approval.

Data availability statement: All data are included in the manuscript

Patient consent statement: The study did not require patient consent

Conflict of Interest: The authors deny any conflicts of interest related to this study**.**

Author contribution

Study conception and design – GT, DK, AJ, JJ, HFD, VN, PMHD

Material preparation, data collection and analysis – GT, DK, AJ, JJ, HFD, VN, PMHD

First draft of the manuscript – GT, DK, AJ, JJ,

Final approval of the manuscript - GT, DK, AJ, JJ, HFD, VN, PMHD

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Abstract

Aim To critically evaluate the reporting quality of a random sample of animal studies within the field of endodontics against the Preferred Reporting Items for Animal Studies in Endodontics (PRIASE) 2021 checklist and to investigate the association between the quality of reporting and several characteristics of the selected studies.

Methodology Fifty animal studies related to endodontics were randomly selected from the PubMed database with publication dates from January 2017 to December 2021. For each study, a score of '1' was given when the item of the PRIASE 2021 checklist was fully reported, whereas a score of '0' was given when an item was not reported; when the item was inadequately or partially reported, a score of '0.5' was given. Based on the overall scores allocated to each manuscript, they were allocated into three categories of reporting quality: low, moderate, and high. Associations between study characteristics and reporting quality scores were also analysed. Descriptive statistics, and Fisher's exact tests were used to describe the data and determine associations. The probability value of 0.05 was selected as the level of statistical significance.

Results Based on the overall scores, four (8%) and 46 (92%) of the animal studies evaluated were categorised as 'High' and 'Moderate' reporting quality, respectively. A number of items were adequately reported in all studies related to background (Item 4a), relevance of methods/results (7a) and interpretation of images (11e), whereas only one item related to changes in protocol (6d) was not reported in any. No associations were confirmed between reporting quality scores and number of authors, origin of the corresponding author, journal of publication (endodontic specialty versus non- specialty), impact factor or year of publication.

Conclusions Animal studies published in the specialty of endodontics were mostly of 'moderate' quality in terms of the quality of reporting. Adherence to the PRIASE 2021 guidelines will enhance the reporting of animal studies in the expectation that all future publications will be high-quality.

Funding: none

Conflict of interest: none

Keywords: PRIASE 2021, reporting guidelines, animal studies, critical appraisal

Introduction

Animal experimentation is considered essential in biological research, particularly during the investigation of inflammatory, immunological, reparative or regenerative responses against a given disease or the safety assessment of new drugs and materials prior to their clinical use in humans (Barré-Sinoussi & Montagutelli 2015). Likewise, preclinical endodontic studies using animal models, have been carried out traditionally on rodents (mice, rats) to investigate the biological mechanisms of endodontic infections, the biocompatibility and cytotoxicity of new materials, the efficacy of novel treatment approaches, as well as the molecular mechanisms involved in a tissue that cannot be adequately replicated in two or three-dimensional culture systems or models (Cosme-Silva et al. 2020, Silva et al. 2021, Tawfik et al. 2013).

Animal experimentation is ethically challenging (Harper et al. 2018) and concerns have been raised regarding pain and injury inflicted on animals, which may be perceived as cruel and likely to compromise their quality of life (Clemence & Leaman 2016, Wadman 2017, Nagendrababu et al. 2019). For these reasons, to minimise animal suffering, proposals to improve animal welfare and limit animal use for scientific purposes have been developed. This development is framed under the 3Rs principles that are embedded within the legislation and guidelines governing the ethical use of animals in experiments, namely the Reduction, Refinement and Replacement of animals in research (https://www.nc3rs.org.uk/who-we-are/3rs) (Russel & Burch 1959, MacArthur Clark 2018, Nunn et al. 2019, Jarvis 2016, Shahbazi et al. 2017).

The ARRIVE guidelines (Animals in Research: Reporting In Vivo Experiments) were developed to advance the care and methodological rigour of animal research and to enhance the quality of reporting of animal studies (Kilkenny et al. 2010a, Percie du Sert et al. 2020a). The ARRIVE guidelines constitute a checklist of recommendations for inclusion when reporting animal research and have been considered as a means of enhancing transparency and diligence when using

animals in research. The checklist has a total of 21 items, and if they are reported adequately, they should lead to valid, clear, unbiased, and robust evidence from animal studies (Percie du Sert et al. 2020b). Several high-impact journals in dentistry (e.g. Journal of Dental Research) insist on the use of the ARRIVE checklist for any study that uses animals.

The introduction of the ARRIVE guidelines, however, has revealed wide variability in the quality of reporting in manuscripts related to preclinical animal research in Periodontology and Oral Surgery (Schwarz et al. 2012, Alemán-Laporte et al. 2019). Suboptimal reporting of key aspects of animal studies has been identified in multiple areas including: adequate presentation of sample size calculation (to avoid wastage or lack of significance), random sequence generation, animal care and husbandry as well as monitoring of the experimental procedures (Baker et al. 2014). An additional concern is the questionable external validity and ability to extrapolate animal study findings to human research and clinical trials. A report on animal studies published in high-impact journals in biomedicine reported that only a third of the concluded findings could be replicated in future randomized controlled trials in the field (Hackam & Redelmeier 2006).

The Preferred Reporting Items for Animal Studies in Endodontics (PRIASE) 2021 guidelines cover exclusively the field of endodontics and related animal research (Nagendrababu et al. 2021a). The guidelines were first introduced in 2021, following adaptation and integration of relevant existing primary documents in the field on animal and laboratory research, namely the ARRIVE guidelines (Kilkenny et al. 2010b, Percie du Sert et al. 2020a) and the Clinical and Laboratory Images and Publications (CLIP) (Lang et al. 2012). The PRIASE 2021 reporting guidelines were developed and validated by a steering committee of experts and Delphi Group of researchers in the field of endodontology, with the aim to promote completeness and transparency in reporting and reduce research waste. The PRIASE checklist consists of 43 individual items under 11 sections including Title, Keywords, Abstract, Introduction, Methods, Results, Discussion,

Conclusions, Funding details, Conflict of interest and the Quality of images (Nagendrababu et al. 2021a,b).

Evaluating how closely published animal studies adhere to the PRIASE 2021 checklist and analysing the association between their characteristics and these recently established reporting guidelines are both important components of improving the overall reporting quality of animal studies in endodontics. Assessing the reporting quality of animal studies published in endodontics is important as it will provide information on the items that are frequently not reported, inadequately described, or ignored by authors, which, if addressed, should result in authors producing higher-quality reports in future. Therefore, the aim of the present study was twofold: firstly, to critically appraise the reporting quality of a random sample of animal research studies published in endodontics, between 2017 and 2021, that is prior to the PRIASE guidelines being published, and secondly, to investigate the association between the quality of reporting of these studies and specific characteristics of each study such as authorship, continent, year and journal of publication along with the impact factor. Specific objectives were to record the level of reporting of each individual item included and according to the PRIASE 2021 guidelines.

Methods

Selection of animal studies

Animal studies related to endodontology, published from January 2017 to December 2021, were retrieved from the PubMed database using an agreed search strategy (Table S1). To find all studies related to animal experimentation, the search strategy used was complemented by previously developed PubMed methodological filters that identify studies on laboratory animals (Hooijmans et al. 2010). The publication information for each animal study identified in the PubMed database was exported to an Excel spreadsheet, and a random number with four decimal points ranging from 0 to 1 was assigned. Random numbers were generated and sorted in ascending order, thus reordering the retrieved articles. Based on the inclusion criteria, titles and abstracts of the first 50 eligible animal

studies were screened independently by two reviewers (AJ, JJ). If a selected animal study did not meet the selection criteria, the next study in the random sequence was used to replace it until a total of 50 animal studies were selected (n = 50). A third reviewer resolved disagreements between the two reviewers during the selection of animal studies.

Selection criteria

Animal studies related to the field of endodontology (including aspects related to pulp biology, pulpal and periapical disease, material science, biocompatibility) in which an animal was used as an experimental model and not just for tissue harvest, were included. Studies were considered with no restrictions on the journal or the language in which the study was published between 2017 and 2021. Studies using *ex vivo* animal cells or cell-lines as well as human clinical trials, observational studies, case series, case reports, as well as reviews were excluded.

Data extraction

Details of 50 animal studies were extracted and summarised using a data extraction sheet that included: the name of the first author, the country of the corresponding author(s), the year the study was published, the total number of authors, the name of the journal, the Impact Factor (IF) of the journal for the year in which the animal study was published, the IF of the journal based on the 2020 release of the Journal Citation Reports (JCRs), its current 5-year IF and data on the quartile ranking and JCR category for the 50 studies. Data extraction was performed independently by two reviewers (AJ, JJ), with disagreements being resolved by an independent third reviewer.

Quality assessment process using the PRIASE 2021 checklist

To establish a definitive scoring system, three of the 50 animal studies were randomly selected to pilot the efficacy of the initial scoring system. Pilot testing was performed by three reviewers (AJ, GNT, DK), with uncertainties and disagreements being resolved by team members (VN, HD, PD). Finally, all 50

articles were independently assessed by the three reviewers and a definitive score reached for each individual item among the reviewers.

To consider the reporting quality of animal studies, the adherence of manuscripts to each of the 43 items in the PRIASE 2021 checklist (Nagendrababu et al., 2021a, b) was assessed. Each item received a score of '1' if the manuscript met all relevant criteria, a score of '0' if it was not reported, and a score of '0.5' if it was reported inadequately. 'Not Applicable (NA)' was awarded for several other items that were irrelevant to the study, for instance, if the animal study was published without pictures or figures, it would receive a score of 'NA' for the items related to the 'Quality of images' domain.

The final PRIASE score for each animal study was estimated by adding up all the scores, with a maximum score of 43 (after subtracting any 'NA' scores). Based on the overall scores allocated to each manuscript, they were divided into three categories: low quality (up to the 25th percentile), moderate quality (the interquartile range), and high quality (the 75th percentile and above).

Descriptive analysis and data visualisation

Bibliometric analysis was conducted to describe the included animal studies (n=50) regarding authorship, geographic location or work, topics covered, journal, and its IF. The metadata of each chosen study was exported in plain text from the Web of Science (WoS) and imported into the R environment for statistical computing and graphics (R Core Team 2016). To clear transcription or indexing errors, the names of authors, institutions, and countries were manually checked and refined. Institutional affiliations were normalised and included at the university or research centre level, while individual departments or research units were discarded. Animal studies from England were recategorised as being from the United Kingdom.

R version 2022.07.1+554 (R Core Team 2016) and the R package bibliometrix version 4.0.0 (Aria & Cuccurullo 2017) were used for descriptive analysis and

network extraction of the 50 studies. The total number of authors and co-authors (the frequency of their appearances) were recorded in detail. To assess the contribution of each author, the full (e.g., four authors each receive one full credit) and fractionalized (e.g., four authors receive one-quarter of a credit) counting method (Abramo et al. 2013) was applied. The 'Authors per paper Index' was computed as the ratio between the total number of authors and the total number of animal studies, and the 'Co-Authors per paper Index' was defined as the ratio between the total number of co-authors and the total number of studies. The mean number of authors per mutual study (the 'Collaboration Index') was calculated as the total number of authors of multi-authored studies divided by the total number of multi-authored studies (Elango & Rajendran 2012, Koseoglu 2016). The collaboration analysis was applied to identify co-authorships and define networks of collaborating authors, institutions, and countries. In addition to the 'Impact Factor of the journal' in which the study was published, the significance of each evaluated animal study was estimated using the citation counts retrieved from the WoS Core Collection (Times Cited Count). Based on a frequency distribution of MeSH or EMTREE indexing terms and Keywords Plus, generated in the Clarivate Analytics databases, keyword analysis was performed to specify and illustrate the topical areas of the considered studies. Using the R packages bibliometrix version 4.0.0 (Aria & Cuccurullo 2017) and wordcloud2 version 0.2.1 (Dawei & Guan-tin 2018) bibliometric networks and geo locations were visualised.

Association between characteristics and quality of animal studies

The following characteristics were investigated:

1. Number of authors (1-2 vs. 3-4 vs. 5-6 vs. >6),
2. Geographical source of reports in terms of the continent of the corresponding author (North America and Canada vs. South America vs. Europe vs. Asia vs. Oceania vs. the Middle East),
3. Journal (Endodontic specialty vs. Non-Endodontic specialty journals),
4. Published in a journal with an IF (yes/no),
5. Year of publication (2017 vs. 2018 vs. 2019 vs. 2020 vs. 2021).

Statistical analysis

The compiled data were analysed with RStudio (version 2022.07.1) and Stata version 15.1 (Stata Corporation, College Station, Texas, USA). Descriptive statistics, frequency and percentage analyses, were used to represent the data. To determine associations between reporting quality categories and publication characteristics as indicated above, Fisher's exact test was used. The probability value 0.05 was considered as the level of significance.

Results

Characteristics of included studies

The literature search yielded 3766 articles that fitted the inclusion criteria, from which 50 animal studies were randomly selected. A total of 397 studies were screened until a random sample size of 50 was achieved, with 345 studies being discarded. Table 1 demonstrates the characteristics of the analysed studies, including first author, country of principle affiliation of the corresponding author, year published, number of authors, journal name, IF for the year in which the trial was published and the overall PRIASE score. A complete list of the 50 included studies is provided in Table S2. Table S3 reports the IF of the journal for the year in which the animal study was published, the IF of the journal based on the current release of JCR (2021), its current 5-year IF and data on the quartile ranking and JCR category for the 50 studies. Besides journals with an IF, journals that are not indexed in the JCR list also appear in the present study. Among them, two are indexed in the Clarivate Analytics' Emerging Sources Citation Index and two in MEDLINE.

The 50 animal study reports were authored or co-authored by 294 individuals and published between 2017 and 2021 (Table 2). The number of animal studies published in 2017, 2018, 2019, 2020, and 2021 was 7, 10, 8, 5, and 20, respectively. Of the 50 animal studies, one (Sabir & Sumidarti 2017) was published in a special issue of the Saudi Journal of Biological Sciences, in a call for papers and participation in the 13th Asian Apicultural Association conference, held in Jeddah, Kingdom of Saudi Arabia, over April 24–26, 2016 (Current

Research in Apiculture. Edited by Ahmad Al-Ghamdi and Mohammad Javed Ansari). The 50 studies were published in 38 journals (Table 3), with 45 being published in the most discipline-relevant journals referenced in the JCR (n=33). Most of the analysed studies (30%) were published in the *International Endodontic Journal,* followed by *Archives of Oral Biology*, *Journal of Applied Oral Science*, and *Journal of Endodontics*.

Among the included studies, the most productive individual authors are presented using full and fractional counting methods (Table 4). The ranking of authors was based on their total (TASs) and adjusted frequency (TANsF) that reflects animal studies with multiple authors (for instance, if an animal study is published by two authors, each receives half a credit). The most prolific author, appearing in five animal studies is Cintra LTA, affiliated with São Paulo State University (UNESP), Brazil, whose fractionalized frequency is equal to 0.67 when the number of co-authors is considered. The following authors with a total of four animal studies were Ervolino E (São Paulo State University (UNESP), Brazil) and Gomes JE (São Paulo State University (UNESP), Brazil), while Abbasnejad M (Shahid Bahonar University of Kerman, Iran) and Raoof M (Kerman University of Medical Sciences, Iran) were among the top three most productive authors, with a fractionalized frequency of 0.59.

The authors were associated with 100 institutions and the 20 most frequently stated affiliations are shown in Table 5. The 50 animal studies were published by authors from 24 countries, including nine Asian, seven Middle Eastern, six European, one North American, and one South American country (Table 6). Figure 1 offers a graphic of frequently used MeSH or EMTREE indexing terms and Keywords Plus, generated from analysed titles and associated with articles by Clarivate Analytics (as a word cloud), where the size of the displayed keyword is proportional to its frequency (interactive version Figure S1). Given the size of keywords presented in the figure, it is apparent that pulp tissue regeneration, effectiveness and biocompatibility of biomaterials used for pulp capping, as well

as pathogenesis of apical periodontitis, were highly prevalent topics covered within the studies.

Figure 2 shows the contribution and collaboration country map (each author's country based on the frequency of stated institutions). A complete collaboration network among countries is presented in Figure 3 (interactive version Figure S2). More than half of the analysed animal studies (64%) were conducted by authors from a single country, with Brazil (n = 12) and China (n = 6) being the countries with the highest number of studies. Eighteen studies were the result of international cooperation between two or more countries. The relationship among authors, their affiliations, and journals in which animal studies were published, are illustrated in a Sankey plot (Figure 4). The plot line connecting an institution and an author represents the frequency of all co-authors, while between an author and a journal reflects the number of animal studies published by that author in that journal. Figure 4 shows that the three most represented authors, Cintra LTA, Ervolino E, and Gomes JE, affiliated with São Paulo State University (UNESP), Brazil, published studies in the *International Endodontic Journal*, *Journal of Endodontics*, *Plos One*, and *Clinical Oral Investigations*.

Quality of included animal studies assessed using the PRIASE 2021 guidelines

The overall percentage scores for studies analysed against the requirements of the PRIASE 2021 guidelines are shown in Table 1. A graphical representation of the overall results related to the individual PRIASE items is provided in Figure 5. Amongst the 50 animal studies, one (de Gregorio et al. 2018) published in *Dental Traumatology* had the greatest (81.4 %) overall percentage score, followed by Kang et al. (2018) published in *Materials* (Basel) (76.7%). Based on the interquartile range (IQR) of the overall scores, four (8%) and 46 (92%) of the 50 animal studies were categorised as 'High' and 'Moderate' with respect to reporting quality.

The scores for individual PRIASE items are presented in Table 7. Several items were adequately reported in all animal studies, these included: Item 4a – The

relevant background information must be provided using terminologies consistent with professional standards and previous publications; Item 7a – A discussion on how the methods and results are relevant to the study aims, and how the results support or dispute prevailing theories advocated in prior publications must be provided; and Item 11e – An interpretation of the findings (meaning and implications) from the image (s) must be provided in the text. Only one item was not reported in all included studies: Item 6d – Any changes made to the experimental protocols to prevent the occurrence of animal adverse health events, analgesic or other medication overdoses, insufficient doses or unexpected deaths must be provided.

Relationship between study characteristics and reporting quality

1. The number of authors: No significant difference (P = 0.53) was observed between the number of authors associated with a manuscript and reporting quality (Table 8).
2. Continent of the corresponding author: No significant association (P = 0.70) was observed amongst the various continents and the reporting quality categories. The animal studies published from Asia, Europe, Middle East, and South America were associated with an equal percentage (25%) of studies with 'High' reporting quality, compared with North America (0%), albeit this finding corresponded to only 1 'High' reporting quality study for all four aforementioned continents. The vast majority achieved a 'Moderate' quality of reporting score. Countries that span two continents, namely Russia and Indonesia, were treated as countries of the Asian continent.
3. Journal (Endodontic specialty vs. Non-Endodontic specialty journals): No significant difference (P = 0.57) was observed between the Endodontic specialty and Non-Endodontic specialty journals, while 'High' reporting quality studies were confirmed only for non-Endodontic specialty journals and solely in 4 cases.
4. Impact Factor: There was no significant difference in the quality of reporting of studies published in journals with impact factor compared to those published in non-impact factor bearing journals (P=1.00). Only 5 studies were

published in non-impact factor journals and all of them were categorised as of 'Moderate' reporting quality.

5. Year of publication: Reporting quality was not associated with year of publication (P= 0.51). Reports of animal studies published in 2018 had the highest number of 'High' reporting quality studies, namely 2, while the rest of the years included either 1 or no study of 'High' reporting quality.

Discussion

The present critical appraisal is the first study to assess the quality of reporting of animal studies in endodontology using the PRIASE 2021 checklist (Nagendrababu et al. 2021b). A random selection of 50 studies published before the PRIASE 2021 guidelines were available were identified initially and included in the assessment. Only approximately one quarter of studies were categorised as of high quality of reporting overall. This finding confirms the results of previous reports which emphasised the suboptimal reporting associated with animal studies (Schwarz et al. 2012, Alemán-Laporte et al. 2019) and clearly highlights the need for improvement when conducting and reporting animal research studies.

Title

Two items were evaluated under the domain of Title. Item 1a was adequately reported in approximately two thirds of studies with the implication that in the remaining studies it would be very difficult for readers to understand under what conditions the experiments had been performed when looking at the title. Item 2b, however, was adequately reported in 88% of the articles and partially reported in the rest, which is somehow surprising, as one would expect that the specific test or treatment of interest would be provided clearly in all studies. Notwithstanding, one should bear in mind potential word limitations governing title presentation and structure, frequently endorsed by journals and editors, especially since this might constitute common practice across impactful biomedical journals. In essence, this might just reflect close adherence to journal publication policies and not just reflect inadequate or poor reporting quality.

Keywords

It is of particular note that only 1 out of 10 studies mentioned the terms "animal model" or "*in vivo* model" in the keywords provided. This means that only after reading the aim of the study in the Introduction or the Materials and Methods section, would readers be able to appreciate that the experiments were conducted using animals. This can be addressed easily in future animal studies, with simple adherence to reporting guidelines and having in mind a clear rationale of providing findings stemming from animal research. Given the restrictions in the number of keywords applied by journals, researchers should consider including keywords from the Key Medical Subject Headings (MeSH) that indicate additionally that the work is related to animal research; this might be implemented either directly with reporting of "animal model" terminology, or indirectly with reporting of the specific species/ strain of the animal (for example "transgenic knock-out" or "transgenic KO"). It is also noted that in most journals, the titles might serve as keywords for future searches, albeit authors are encouraged to report key and critical terms in both domains.

Abstract

Overall, six items were evaluated under the domain of Abstract. Noteworthy is the fact that only 1 out of 3 studies explained the significance and purpose of their research (Item 3a) in the abstract section. This finding may be due to a number of reasons. Word limitations in abstracts conditional on the requirements applied by several journals is one. The specific structure of the abstract in conjunction with word limitation may prevent authors from reporting the significance of their study. Thus, it may be necessary for journals to allow adequate word counts for authors in the abstract section to guarantee adequate reporting of significant elements of their work. Low scores were also recorded for items 3c and 3e. For clinicians, scientists and readers who do not usually go through the entire manuscript, it is very important that the key details of the animal and the experimental model are provided in the abstract section to further facilitate transparent and valid reporting, interpretation and extrapolation of research (Giannakoulas et al. 2022). Regarding item 3e, it was adequately and partially

reported in only 24% and 48% of the studies respectively. The inadequate description of all the essential elements of the results including reporting of the effect metrics and effect sizes along with a measure of precision (such as the confidence bounds), irrespective of the significance of the reported outcomes, is a constant shortcoming of research studies in endodontics. The present study highlights this crucial omission, not only for the statistically significant results but also for non-significant findings. It is however encouraging that a large number of the evaluated studies adequately described the purpose of their research (item 3b) as well as the key details of their methodology (item 3c), whereas clear and succinct conclusions (item 3f) were adequately provided by 3 out of 4 studies.

Introduction

The introduction section is the part which supports the entire hypothesis of the research presented in the manuscript. Various sections of the introduction should justify the research purpose and identify fully the gap(s) in knowledge. The present study revealed that a small number of the included studies justified the reasons why an experiment in animals was deemed essential and the appropriateness of the selected model. According to the PRIASE 2021 checklist, mentioning these two items (4b, 4c) is of utmost significance for the documentation of the experiments using an animal model. In this respect and before the initiation of any animal study project, authors should be cautious when designing their study and ensure they chose the appropriate model that would support their findings and thus constitute a gain for the scientific community.

Methodology

Overall, 10 items were assessed under the domain of Materials and Methods. The most significant finding was that only 6% of the studies adequately reported a power calculation to define the appropriate estimation of the sample size. This is in contrast with the results of a similar study (Nagendrababu et al. 2021c) regarding the PRIRATE appraisal of randomized clinical trials, where 80% of the studies evaluated adequately described the calculation of the sample size. The PRIASE guidelines and the present study aims to pinpoint this discrepancy and

promote a closer adherence to the reporting guidelines in this respect, since an appropriate and accurate assumption regarding the size of the sample to be included is of utmost significance for the credibility of the research findings overall. This should also be in line with the use of the minimum number of animals required to take part in a study according to a precise sample size estimation. However, in view of this inherently assumed contradiction, researchers who undertake animal experimentation might well decide to use a small number of animals of similar age and gender, and thus compromise the generalizability of their results. All the relevant items related to animal details (items 5c, 5d, 5e, 5h) were also inadequately described. Animal caretakers are expected to recognize signs or symptoms of animal discomfort or suffering and monitor health status and welfare of the animals throughout the experiment. Likewise, postoperative care should be clearly defined *a priori* irrespective whether animal pain or disability was detected during the experiment. In this way, the reporting of the relevant section within the Methodology will become more transparent and ethically acceptable by all relevant parties. For all the above reasons, the specific conditions under which the animals are kept throughout the experiment should be transparent. Regarding other items, it is worth noting that 1 out of 4 studies did not mention whether ethical approval had been granted (item 5a) for the animal research protocol. This finding is extremely important and sensitive as the practice of conducting animal research without official approval by an institutional ethics board, to assure clear and transparent research practices, should be no longer acceptable. On the other hand, almost 3 out of 4 studies described sufficiently the statistical analysis of the results, offering an acceptable reporting status in this respect and providing the basis for research reproducibility if and when needed. The above findings demonstrate overall, however, that the future submissions to journals related to animal research should incorporate major improvements in their methodology in order to be considered for publication.

Results

In the Results section, an alarming finding was that only 2 out of 3 studies

described properly their results along with any statistical inferences (item 6b). Suboptimal reporting and description of the findings of a study after conducting a clear, accurate and appropriate statistical analysis may lead to misleading conclusions with a subsequent negative impact on the interpretation of the results and the extrapolation of the findings to clinical practice. Nevertheless, one should acknowledge that there are certain types of research findings being presented solely qualitatively and descriptively, through histology and immunohistochemistry for example, and their value should be placed under a specific context of information provided to the readership. The next three items (6a, 6c and 6d) were inadequately described by most of the studies with percentages ranging between 0% and 8% for those which adequately reported them. Most important is the fact that only a few studies reported the average and baseline characteristics of the animals at the beginning of the experiment, which is related to the stage of animal recruitment. Similarly, few studies reported adverse events, whereas the method of euthanasia was not described in almost 1 out of 3 studies. Overall, authors of studies involving animal experimentation should appreciate that the Results section is a reflection of the Methodology and should follow the structure of set out in the methodology in terms of description of any baseline, follow-up and inferential statistical outcomes pre-specified. Adverse or any other negative events or effects should also be reported, and any change from the pre-planned activities should be mentioned clearly and transparently.

Discussion

The most important finding was that few studies (14%) incorporated adequately an objective presentation of the strengths and limitations of the aim of their research, their study design or methodology. Authors need to provide in distinct and separate paragraphs the strengths and weaknesses of their study. This may help other and future authors and researchers to maintain the strengths whilst reducing at the same time the shortcomings of their work. It is essential that the impact of the findings on future animal research studies and eventually on human oral health is considered. In addition, a clear direction should be given with regard

to future research plans identifying remaining gaps in the literature in the context of the research question under investigation.

Conclusion

Most of the studies (90%) reported explicitly their conclusions which were directly supported by the results. However, no proposals for future research were provided in almost half of the studies in this section, as recommended in item 8b. This is the reason why such a great difference is observed between reporting percentages of items 8a and 8b.

Funding and support

The vast majority of the studies provided adequate information regarding financial support (82%). This finding is encouraging as it shows that this type of research may attract funds to invest in new techniques or newly introduced materials for assessment of utilisation in clinical practice. It is obviously important if one considers the expenses incurred when using an animal model that all the above factors are followed by the researchers.

Conflict of interest

The majority of the studies (86%) reported potential conflicts of interest. This is of importance, since most of the animal studies investigate a number of newly introduced materials prior to their clinical use in humans. In many cases, dental commercial companies and related industry support such studies financially, reflecting their interest and investment in their commercial product. As such, researchers are obliged to incorporate a conflict-of-interest statement in their manuscript when there is a conflict and when there is none, irrespective of the journals' policy to incorporate such a statement.

Quality of images

Histological sections are very common in animal research studies. PRIASE 2021 guidelines adopt eight separate items under this domain, to emphasise the importance of presenting images of sufficient quality and relevance within the

manuscript. The findings of the present study may be considered satisfactory since the lowest achieved percentage was approximating 60% for the adequate reporting of item 11a. All the percentages of the remaining items surpassed this value, and for item 11e there was adequate reporting identified in all studies. It may be concluded that researchers who conduct animal studies have sufficiently understood and recognized the significance of capturing and reporting high quality images for the documentation of the study and the accurate evaluation of their results.

Relationship between characteristics of animal studies and their reporting quality

The results of the present study did not reveal any significant association between the type (Endodontic specialty vs. non-Endodontic specialty) or impact factor of the journal, the year of publication, the number of contributing authors, the continent of authorship and the reporting quality of the included studies. These findings seem reasonable if one considers that publication of animal studies requires an acceptable level of reporting for several important items; this was achieved at least for the assessed articles, since there was essentially a level of moderate reporting quality scores, verified overall. It is also of note that most of the authors have been prolific researchers in their field, with knowledge and appropriate experience in conducting such types of studies, as shown also by the fact that the twenty most productive authors were involved in conducting a total of 50 studies.

Impact factor of the journal did not appear as a significant predictor of reporting quality in the present sample; however, the effect of impact factor was estimated as a binary on-off criterion and most studies examined were indeed published in journals with an impact factor. Prior evidence from biomedical literature on methodological quality of systematic reviews published in core clinical journals has revealed an increase in quality score of such studies, supported by large differences in the reported impact factors of the journals of publication (Fleming et al. 2014). Nevertheless, there is an apparent difference in the design of studies

assessed compared to the present work, with systematic reviews possessing the highest level of evidence in the literature pyramid and thus following a profoundly far more established methodology and guidelines for reporting than animal studies. To add in this respect, the impact factor range of unit differences across journals is undoubtedly more evident in biomedical journals than in dentistry. In any case, researchers are certainly encouraged to follow a widely established procedure in the design, methodological conduct and reporting of their studies and adhere to respective recommendations to maximise reporting standards, irrespective of dissemination practices and related impact.

Continent of authorship nor the number of authors were associated with reporting quality of the included studies. The former reveals a universal standard of cognizance of the international scientific community regarding the importance of animal research conduct, and an adherence, at a specific level, to the ARRIVE reporting guidelines. The latter agrees with the respective evidence from reporting of randomized trials, according to the PRIRATE 2020 guidelines (Nagendrababu et al. 2021c). In fact, nearly three quarters of the present sample were co-authored by more than 6 researchers. This demonstrates a clear need for collaboration related to animal research implementation and reporting, which seems reasonable, given the nature and multi- level expertise required to achieve high standards in animal experimentation (Mendl et al. 2016).

The main topics covered in the 50 included animal studies are best illustrated through a word cloud, which emphasises the most frequently used keywords by the authors. Animal studies related to the use of calcium hydroxide were the most popular. This finding might be considered somehow strange, since nowadays the use of calcium hydroxide has been replaced in several applications within endodontics. One might consider, however, that calcium hydroxide could possibly constitute an intervention applied to a comparator group in animal research experimentation, to parallel and contrast with the potential of any newly designed material (Vatankhah et al. 2022, Khan et al. 2022). Stem cells differentiation and material cytotoxicity were the second most covered topics. This may be

considered reasonable, as biological applications, new technologies and safety of materials and interventions delivered to patients are most likely the main reason for conducting experiments on animals as the initial step as they provide a better understanding and simulation of clinical conditions for the benefit of patients. Evidence from an analogous study on critical analysis of the reporting quality of randomized trials in endodontics has revealed research on postoperative pain after root canal treatment or retreatment, as the most common topic (Nagendrababu et al. 2021c). This further illustrates the need and utilisation of very different types of study designs to provide knowledge on certain research and clinical fields and guide implementation of research endeavours for the benefit of the patient, either directly (i.e., clinical research), or in a stepwise process (animal and laboratory research followed by clinical applications).

Brazil, UK, Saudi Arabia, USA, China, Japan and Korea were the countries with the most numerous contributions performing animal studies. The most prolific researchers were also based in Brazil and largely within Sao Paulo State University. Traditionally, Brazil is considered a country with an increasing research output that has provided knowledge in previously undefined issues mostly in high impact factor journals (Tzanetakis et al. 2015).

Strengths and limitations

The present study included a random sample of 50 animal research studies appraised for 43 items by three experienced reviewers independently, following extensive piloting. The sample origin included both endodontic specialty and non-specialty journals, thus covering a range of potential readers and study designs. As such, the possibility of selection bias and sampling errors related to the included articles was eliminated. Indeed, most of the studies were published before the introduction of the PRIASE guidelines which is an element that increases the objectivity of the present study. In addition, it is considered that upon release of PRIASE 2021 and onwards, the level of awareness and adherence to reporting quality standards in this field of research shall increase, thus contributing to enhanced reporting. Furthermore, it is most likely that even for

studies published after the introduction of the guidelines, within 2021, these should have been submitted well before that time. As a consequence, it is unlikely that the guidelines had an impact on the quality scores. In this respect, the present study can be regarded as the basis for future research that would involve assessment of the quality of reporting of similar studies in the field after the introduction of the PRIASE 2021 guidelines, whilst also comparing journals that have adopted the guidelines in their author instructions with those that have not.

The current study is not free of limitations. Only one database was used (PubMed) for study retrieval, and the timeline of study publication was restricted to 2017-2021. However, since the aim of the study was to evaluate the reporting of the essential items of the PRIASE 2021 guidelines, these potential deficiencies are not relevant; this is also true if one considers the random nature of the sample. In future, similar studies might offer a direct evaluation of the impact of the PRIASE 2021 guidelines on the reporting of animal studies.

The introduction of the PRIASE 2021 guidelines offers the opportunity to assess in a quantitative way whether manuscripts published in the specialty of endodontics are written in accordance with current expectations of reporting standards in scientific research (Nagendrababu et al. 2020a,b). This assessment will assist towards an enhanced adherence to PRIASE 2021 guidelines, and an improvement on the level of reporting and dissemination of research. Increased awareness is anticipated by authors, reviewers, editors, readers, funding agencies, institutions and other stakeholders to evaluate submissions to journals and published research for their transparency and quality of reporting.

Conclusions

Overall, the reporting quality of animal studies during the period 2017-2021 in the specialty of endodontics was moderate, with only 8% of manuscripts being of high reporting quality. Several domains could benefit from better reporting and presentation of the results of animal research. Endorsement and close adherence

to the PRIASE 2021 guidelines by editors, reviewers and authors of future articles will provide more consistent and higher quality reporting.

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Legends

Table S1: List of animal studies included in the current study

Table 1. Characteristics of included animal studies

Table S2: Additional features of included animal studies

Table S3: Characteristics of the included animal studies

Table 2. Key information from 50 animal studies

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Figure 1. Word cloud representation of frequently used indexing terms

Figure S1. Word cloud based on indexing terms frequency (interactive version)

Figure 2. The contribution of each country (country of each author based on the frequency of stated institutions)

Figure 3. Country's co-authorship network

Figure S2. Country's co-authorship network (interactive version)

Figure 4. Sankey plot showing the relationship among authors, their affiliations, and journals in which studies were published

Figure 5. Overall results related to the individual PRIASE items

Table 1. Characteristics of included animal studies

Study number	First author	Country (Corresponding author(s))	Year published	Number of authors	Journal name	JCR® IF for the year in which the study is published	Overall score (%)
1	PRABHAKAR AR	INDIA	2019	3	INDIAN J DENT RES	-[a]	68.60%
2	BAKIR EP	TURKEY	2021	4	DENT MATER J	2.418	56.98%
3	EDANAMI N	JAPAN	2021	7	AUST ENDOD J	1.719	68.60%
4	GAO L	PEOPLES R CHINA	2021	8	J ORAL REHABIL	3.558	63.95%
5	AL-MAULA BH	IRAQ	2021	8	INT J DENT	-[b]	67.44%
6	ISLAM R	JAPAN	2021	10	INT ENDOD J	5.165	68.60%
7	KIM SG	USA	2021	2	J ENDODONT	4.422	69.77%
8	PARAS S	SERBIA	2021	7	INT J MOL SCI	6.208	74.42%
9	SARRA G	BRAZIL	2021	6	TISSUE CELL	2.586	60.47%
10	HE J	PEOPLES R CHINA	2021	6	INFLAMMATION	4.657	59.30%
11	ALGHUTAIMEL H	ENGLAND	2021	6	INT ENDOD J	5.165	61.63%
12	DENG SJ	PEOPLES R CHINA	2021	4	J MOL HISTOL	3.156	69.77%
13	BAGHERI A	IRAN	2021	5	ARCH ORAL BIOL	2.64	75.58%
14	LEE DJ	JAPAN, SOUTH KOREA	2021	6	BIOCHEM BIOPHYS REP	-[b]	47.67%
15	WANG L	PEOPLES R CHINA, NETHERLANDS	2021	9	ACTA BIOMATER	10.633	69.77%
16	MOREIRA MS	BRAZIL	2021	9	BIOMED RES INT	3.246	55.81%
17	EL-MAL EOA	EGYPT	2021	3	INT J EXP PATHOL	2.793	66.28%
18	REIS MD	BRAZIL	2021	6	BRAZ ORAL RES	2.674	63.95%
19	SANTOS JM	PORTUGAL	2021	8	BIOMEDICINES	4.757	72.09%

20	TIBURCIO-MACHADO CD	BRAZIL	2021	9	LIFE SCI	6.78	65.12%
21	SILVA ECA	BRAZIL	2021	6	INT ENDOD J	5.165	63.95%
22	ZHAI Y	PEOPLES R CHINA	2020	5	FRONT PHYSIOL	4.566	67.44%
23	SHAHSAVARI F	IRAN	2020	4	ARCH ORAL BIOL	2.635	65.71%
24	COSME-SILVA L	BRAZIL	2020	9	INT ENDOD J	5.264	70.93%
25	KHAN SZ	SAUDI ARABIA	2020	11	BOSNIAN J BASIC MED	3.363	53.49%
26	SILVA LA ASSED BEZERRA DA	BRAZIL	2020	8	BRAZ DENT J	-[a]	63.95%
27	MANDAKHBAYAR N	SOUTH KOREA, EGYPT	2019	4	ACS BIOMATER SCI ENG	4.152	58.14%
28	KOLESNIKOVA LR	RUSSIA	2019	9	B EXP BIOL MED+	0.775	42.86%
29	QI SC	PEOPLES R CHINA	2019	11	MOL MED REP	2.1	70.93%
30	GALLINARI MD	BRAZIL	2019	6	PLOS ONE	2.74	66.28%
31	BUENO CRE	BRAZIL	2019	8	CLIN ORAL INVEST	2.812	62.79%
32	HIRAI K	USA	2019	9	J DENT RES	4.914	66.28%
33	LOPES CS	BRAZIL	2019	9	J APPL ORAL SCI	1.797	75.58%
34	DE GREGORIO C	SPAIN	2018	9	DENT TRAUMATOL	1.494	81.40%
35	KANG CM	SOUTH KOREA	2018	6	MATERIALS	2.972	76.74%
36	KIM S	SOUTH KOREA	2018	7	J ENDODONT	2.833	73.26%
37	DIANAT O	IRAN	2018	5	J ORAL SCI	1.104	66.28%
38	FERREIRA LL	BRAZIL	2018	7	INT ENDOD J	3.331	72.09%
39	SHAH A	USA	2018	6	ORAL DIS	2.625	63.95%
40	ZHU XF	USA	2018	7	TISSUE ENG PART C-ME	2.638	68.60%
41	DA SILVA-COSTA RSG	BRAZIL	2018	7	J APPL ORAL SCI	1.506	66.28%

42	NABESHIMA CK	BRAZIL	2018	5	J APPL ORAL SCI	1.506	67.44%
43	RAOOF M	IRAN	2018	7	ARCH ORAL BIOL	1.663	70.00%
44	RAOOF M	IRAN	2017	5	KOREAN J PAIN	-[c]	57.14%
45	SABIR A	INDONESIA	2017	2	SAUDI J BIOL SCI	3.138	55.81%
46	LEE CS	USA	2017	7	MOL PAIN	3.205	70.93%
47	AZUMA MM	BRAZIL	2017	8	J ENDODONT	2.886	70.93%
48	LIU Q	PEOPLES R CHINA	2017	6	PLOS ONE	2.766	73.26%
49	NEGM AM	EGYPT	2017	4	EXP TOXICOL PATHOL	2.023	59.30%
50	BRASIL SC	BRAZIL	2017	7	INT ENDOD J	3.015	67.86%

[a] The journal indexed in MEDLINE.
[b] The journal indexed in the Clarivate Analytics' Emerging Sources Citation Index.
[c] The journal received an IF the following year (IF2018=1.563).

Table 2. Key information from 50 animal studies

Timespan	**2017-2021**
Sources (journals, books, etc.)	38
Average number of years from publication	2.58
Average citations per paper[a]	5.36
Average citations per year per paper[a]	1.309
References	1809
Document types	
Article	49
Article; proceedings paper	1
Document contents	
Keywords Plus/Indexed Keywords[b]	249
Author's Keywords	173
Authors	
Authors	294
Author Appearances	330
Authors of single-authored papers	0
Authors of multi-authored papers	294
Authors collaboration	
Single-authored papers	0
Papers per author	0.17
Authors per paper	5.88
Co-Authors per paper	6.6
Collaboration Index	5.88

[a] The source of citations was Web of Science Core Collection Times Cited Count (TC).
[b] Keywords Plus are words or phrases generated from cited titles and associated with articles by Clarivate Analytics databases. Indexed keywords are MeSH or EMTREE indexing terms.

Table 3. Animal studies (n = 50) published in various journals

Journal	Number of studies
INTERNATIONAL ENDODONTIC JOURNAL	6
ARCHIVES OF ORAL BIOLOGY	3
JOURNAL OF APPLIED ORAL SCIENCE	3
JOURNAL OF ENDODONTICS	3
PLOS ONE	2
ACS BIOMATERIALS SCIENCE & ENGINEERING	1
ACTA BIOMATERIALIA	1
AUSTRALIAN ENDODONTIC JOURNAL	1
BIOCHEMISTRY AND BIOPHYSICS REPORTS	1
BIOMED RESEARCH INTERNATIONAL	1
BIOMEDICINES	1
BOSNIAN JOURNAL OF BASIC MEDICAL SCIENCES	1
BRAZILIAN DENTAL JOURNAL	1
BRAZILIAN ORAL RESEARCH	1
BULLETIN OF EXPERIMENTAL BIOLOGY AND MEDICINE	1
CLINICAL ORAL INVESTIGATIONS	1
DENTAL MATERIALS JOURNAL	1
DENTAL TRAUMATOLOGY	1
EXPERIMENTAL AND TOXICOLOGIC PATHOLOGY	1
FRONTIERS IN PHYSIOLOGY	1
INDIAN JOURNAL OF DENTAL RESEARCH	1
INFLAMMATION	1
INTERNATIONAL JOURNAL OF DENTISTRY	1
INTERNATIONAL JOURNAL OF EXPERIMENTAL PATHOLOGY	1
INTERNATIONAL JOURNAL OF MOLECULAR SCIENCES	1
JOURNAL OF DENTAL RESEARCH	1
JOURNAL OF MOLECULAR HISTOLOGY	1
JOURNAL OF ORAL REHABILITATION	1
JOURNAL OF ORAL SCIENCE	1
KOREAN JOURNAL OF PAIN	1
LIFE SCIENCES	1
MATERIALS	1
MOLECULAR MEDICINE REPORTS	1
MOLECULAR PAIN	1

ORAL DISEASES	1
SAUDI JOURNAL OF BIOLOGICAL SCIENCES	1
TISSUE & CELL	1
TISSUE ENGINEERING PART C-METHODS	1

Table 4. The 20 most productive authors from 50 animal studies

Rank	Authors	Total number of animal studies (TASs)	Authors-Frac	Total number of animal studies fractionalized (TASsF)
1	CINTRA LTA	5	CINTRA LTA	0.67
2	ERVOLINO E	4	ABBASNEJAD M	0.59
3	GOMES JE	4	RAOOF M	0.59
4	ABBASNEJAD M	3	ABU-SEIDA AM	0.58
5	CABALLERO-FLORES HV	3	ERVOLINO E	0.55
6	RAOOF M	3	GOMES JE	0.5
7	ABU-SEIDA AM	2	KIM SG	0.5
8	AMANPOUR S	2	SABIR A	0.5
9	BENETTI F	2	SOLOMON CS	0.5
10	BRISO ALF	2	SUMIDARTI A	0.5
11	COHENCA NESTOR	2	CABALLERO-FLORES HV	0.48
12	COSME-SILVA L	2	LEE JH	0.42
13	JUNG HS	2	MACHADO MED	0.37
14	KANG MK	2	AMANPOUR S	0.34
15	KIM S	2	KOOSHKI R	0.34
16	KOOSHKI R	2	BHAT K	0.33
17	LEE JH	2	EL-MAL EOA	0.33
18	LOPES CS	2	EL ASHRY SH	0.33
19	LUCISANO MARLIA PACFICO	2	MANDROLI PS	0.33
20	MACHADO MED	2	PRABHAKAR AR	0.33

Table 5. Twenty most productive institutions from 50 animal studies

Affiliations	Number of animal studies
University of São Paulo, Brazil	24
Yonsei University, South Korea	10
Kerman University of Medical Sciences, Iran	8
Dankook University, South Korea	6
University of Coimbra, Portugal	6
Hokkaido University, Japan	4
Nanjing Medical University, China	4
Shahid Beheshti University of Medical Science, Iran	4
University of Belgrade, Serbia	4
Federal University of Rio Grande do Norte, Brazil	4
Vrije Universiteit Amsterdam, Netherlands	4
Dalian Medical University, China	3
Forsyth Institute, USA	3
Harvard University, USA	3
Niigata University, Japan	3
Peking University, China	3
University of California, Los Angeles, USA	3
Federal University of Alfenas, Brazil	3
University of Kufa, Iraq	3
University of Washington, USA	3

Table 6. Animal studies (n = 50) published from various countries

Country	Frequency
BRAZIL	51
CHINA	27
USA	24
IRAN	18
SOUTH KOREA	18
JAPAN	10
EGYPT	7
NETHERLANDS	6
PORTUGAL	6
IRAQ	5
RUSSIA	5
SERBIA	5
TURKEY	4
UK	4
INDIA	3
SAUDI ARABIA	3
PAKISTAN	2
QATAR	2
BANGLADESH	1
INDONESIA	1
JORDAN	1
MALAYSIA	1
SLOVENIA	1
SPAIN	1

Table 7. Percentage of adequately reported for each PRIASE items

PRIASE Checklist Items	Overall score (%)	Overall score (%) – partially adequately reported items
1a. Title – The specific animal species and its health or disease status (sometimes called 'animal model') must be provided	66.00%	0.00%
1b. Title – The specific test, field, subject, treatment of interest within the animal model must be provided	88.00%	12.00%
2a. Keywords – Keywords such as 'animal model or 'in vivo model' and the specific area(s) of interest must be provided	10.00%	80.00%
3a. Abstract – The Introduction of the Abstract must explain the significance of the study	34.00%	12.00%
3b. Abstract – The unambiguous aim(s) and objective(s) of the study must be provided	90.00%	10.00%
3c. Abstract – The most important details of the animal and the experimental model must be provided	42.00%	48.00%
3d. Abstract – Key details of the methodology must be provided	86.00%	10.00%
3e. Abstract – The most relevant and important results must be presented succinctly including differences amongst the means, medians or modes of the dependent variables (treatment outcome and test results) and any significant P-values	24.00%	48.00%
3f. Abstract – Succinct conclusions supported by the results must be provided	76.00%	20.00%
4a. Introduction – The relevant background information must be provided using terminologies consistent with professional standards and previous publications	100.00%	0.00%
4b. Introduction – The appropriateness of the selected animal model to address the aims and objectives of the study must be explained	14.00%	10.00%
4c. Introduction – A justification of the reasons why the investigation was necessary using an animal model must be provided	28.00%	12.00%
4d. Introduction – The unambiguous aim(s) and objectives(s) of the animal study must be provided	90.00%	8.00%

5a. Materials and Methods – The reference number of the approval granted by the ethics board, such as an Institutional Review Board or Institutional Animal Care committee, must be provided along with a reference to the applicable institutional and/or national regulations that were enforced. Any identifying details about the authors institution should not be disclosed during the blind peer review	72.00%	26.00%
5b. Materials and Methods – The sample size must be justified by citing prior similar studies and/or be estimated by using statistical power calculations to ensure an adequate sample size is used to detect any significant differences and answer the research questions. This is to avoid making any type I and type II errors	6.00%	16.00%
5c. Materials and Methods – Details of how animal pain and disability was monitored and how animal suffering was prevented during all aspects of experimentation must be provided	10.00%	40.00%
5d. Materials and methods – The job titles and qualifications of the animal caretakers must be provided	6.00%	2.00%
5e. Materials and methods – Specific details of the animals must be provided, including their species, strain, immune system, breeding programme, age, weight, health status and any special characteristics	18.00%	82.00%
5f. Materials and methods – The experimental design must include details of the numbers of animals, numbers of experimental units (e.g. teeth) and timelines (e.g. 5, 30 and 60 days) used	94.00%	6.00%
5g. Materials and methods – The primary outcome data measures or categories as well as any other secondary outcome data measures or categories that will be assessed must be provided	64.00%	36.00%
5h. Materials and Methods – Details must be provided on (1) steps in the interventions and treatments, (2) instruments, medicaments or device allocation, and (3) concealment and randomization prior to data collection	18.00%	82.00%
5i. Materials and methods – Details regarding postdisease and postoperative care of the animals must be provided	20.00%	8.00%
5j. Materials and methods – Details on the statistical analysis, statistical tests, the type of software used, and the steps taken to control, interpret success or failure, and to validate the accuracy of the data must be provided	72.00%	22.00%
6a. Results – Average baseline characteristics of the animals (e.g. age, weight, gender, microbiological status) at the beginning of the experiment must be provided	8.00%	90.00%

6b. Results – The results for each group of primary and secondary outcomes should describe the means, median or mode, as well as differences and their statistical significance	64.00%	30.00%
6c. Results – All adverse events during the animal experimentation and the method of euthanasia must be reported	6.00%	64.00%
6d. Results – Any changes made to the experimental protocols to prevent the occurrence of animal adverse health events, analgesic or other medication overdoses or underdoses, or unexpected deaths must be provided	0.00%	2.00%
7a. Discussion – A discussion on how the methods and results are relevant to the study aims, and how the results support or dispute prevailing theories advocated in prior publications must be provided	100.00%	0.00%
7b. Discussion – An objective presentation of the strengths and limitations of the animal model, study design, methods, materials, instruments, drugs and devices, and outcomes must be provided, including any biology/functional variability between the animal model and humans	14.00%	32.00%
7c. Discussion – The potential influence of the results on future research plans must be discussed	40.00%	16.00%
7d. Discussion – If appropriate, the impact the findings have on human health, treatments or healthcare must be explained	32.00%	20.00%
8a. Conclusion – A rational basis for the conclusion(s) must be provided, that is, they must be directly supported by the results of the study	90.00%	10.00%
8b. Conclusion – Explicit conclusion(s) from the study, including appropriate follow-up research ideas, must be provided	54.00%	36.00%
9a. Funding and support – All funding, donations, assistance and support provided for the study must be reported	82.00%	4.00%
10a. Conflicts of interest – An explicit statement on conflicts of interest must be provided	86.00%	0.00%
11a. Quality of images – Details of the equipment (model, supplier, city, country), software (version, supplier city, country) and settings used to acquire image(s) must be described in the Methods and/or figure legend	60.87%	28.26%
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 text	93.48%	6.52%

11c. Quality of images – The circumstances (conditions) under which the image(s) was viewed and evaluated must be provided in the text	63.04%	36.96%
11d. Quality of images – The resolution, magnification and any important manipulation(s) on any image (e.g. brightness, image smoothing, staining etc.) must be described in the text or legend	66.67%	33.33%
11e. Quality of images – An interpretation of the findings (meaning and implications) from the image (s) must be provided in the text	100.00%	0.00%
11f. Quality of images – The legend associated with each image must clearly describe the subject matter specific feature(s) illustrated. Images of animals must describe their age and test duration, and other relevant features such as important anatomical landmarks and relevant features	84.78%	15.22%
11g. Quality of images – Arrow markers and relevant labels must be provided in image(s), if relevant, in order to identify key information	69.57%	21.74%
11h. Quality of images – The legend of each image must include an explanation whether it refers to pretreatment, intratreatment, post-treatment or postsacrifice, and if relevant, how images were standardized over time	84.78%	15.22%

Table 8. Relationship between the reporting quality and characteristics of the included studies

Characteristics	Groups	Quality of Reporting*				*P* values [fisher's exact test]
		Moderate		High		
		N	Percentage (%)	N	Percentage (%)	
Authors	1-2	2	4.35	0	0.00	0.53
	3-4	7	15.22	0	0.00	
	5-6	4	8.70	1	25.0	
	>6	33	71.74	3	75.00	
Continents	Asia	15	32.61	1	25.00	0.70
	Europe	3	6.52	1	25.00	
	Middle East	9	19.57	1	25.00	
	North America	5	10.87	0	0.00	
	South America	14	30.43	1	25.00	
Journal	Non-Endodontic Specialty	36	78.26	4	100.00	0.57
	Endodontic Specialty	10	21.74	0	0.00	
Impact Factor	No	5	10.87	0	0.00	1.00
	Yes	41	89.13	4	100.00	
Year	2017	7	15.22	0	0.00	0.51

	2018	8	17.39	2	50.00	
	2019	7	15.22	1	25.00	
	2020	5	10.87	0	0.00	
	2021	19	41.30	1	25.00	

* 'Low' reporting quality is not presented as there were no studies identified falling into this category

Supplemental Table 1: PubMed database search strategy

Search No.	Search expression	No. of hits
#1	pulp[Title/Abstract] OR 'root canal'[Title/Abstract] OR endod*[Title/Abstract] OR 'periapical surgery'[Title/Abstract] OR 'periradicular surgery'[Title/Abstract] OR apicoectomy[Title/Abstract] OR apicectomy[Title/Abstract] OR pulpotomy[Title/Abstract] OR pulpectomy[Title/Abstract]	77,917
#2[a]	("animal experimentation"[MeSH Terms] OR "models, animal"[MeSH Terms] OR "invertebrates"[MeSH Terms] OR "Animals"[Mesh:noexp] OR "animal population groups"[MeSH Terms] OR "chordata"[MeSH Terms:noexp] OR "chordata, nonvertebrate"[MeSH Terms] OR "vertebrates"[MeSH Terms:noexp] OR "amphibians"[MeSH Terms] OR "birds"[MeSH Terms] OR "fishes"[MeSH Terms] OR "reptiles"[MeSH Terms] OR "mammals"[MeSH Terms:noexp] OR "primates"[MeSH Terms:noexp] OR "artiodactyla"[MeSH Terms] OR "carnivora"[MeSH Terms] OR "cetacea"[MeSH Terms] OR "chiroptera"[MeSH Terms] OR "elephants"[MeSH Terms] OR "hyraxes"[MeSH Terms] OR "insectivora"[MeSH Terms] OR "lagomorpha"[MeSH Terms] OR "marsupialia"[MeSH Terms] OR "monotremata"[MeSH Terms] OR "perissodactyla"[MeSH Terms] OR "rodentia"[MeSH Terms] OR "scandentia"[MeSH Terms] OR "sirenia"[MeSH Terms] OR "xenarthra"[MeSH Terms] OR "haplorhini"[MeSH Terms:noexp] OR "strepsirhini"[MeSH Terms] OR "platyrrhini"[MeSH Terms] OR "tarsii"[MeSH Terms] OR "catarrhini"[MeSH Terms:noexp] OR "cercopithecidae"[MeSH Terms] OR "hylobatidae"[MeSH Terms] OR "hominidae"[MeSH Terms:noexp] OR "gorilla gorilla"[MeSH Terms] OR "pan paniscus"[MeSH Terms] OR "pan troglodytes"[MeSH Terms] OR "pongo pygmaeus"[MeSH Terms]) OR ((animals[tiab] OR animal[tiab] OR mice[Tiab] OR mus[Tiab] OR mouse[Tiab] OR murine[Tiab] OR woodmouse[tiab] OR rats[Tiab] OR rat[Tiab] OR murinae[Tiab] OR muridae[Tiab] OR cottonrat[tiab] OR cottonrats[tiab] OR hamster[tiab] OR hamsters[tiab] OR	7,460,147

	cricetinae[tiab] OR rodentia[Tiab] OR rodent[Tiab] OR rodents[Tiab] OR pigs[Tiab] OR pig[Tiab] OR swine[tiab] OR swines[tiab] OR piglets[tiab] OR piglet[tiab] OR boar[tiab] OR boars[tiab] OR "sus scrofa"[tiab] OR ferrets[tiab] OR ferret[tiab] OR polecat[tiab] OR polecats[tiab] OR "mustela putorius"[tiab] OR "guinea pigs"[Tiab] OR "guinea pig"[Tiab] OR cavia[Tiab] OR callithrix[Tiab] OR marmoset[Tiab] OR marmosets[Tiab] OR cebuella[Tiab] OR hapale[Tiab] OR octodon[Tiab] OR chinchilla[Tiab] OR chinchillas[Tiab] OR gerbillinae[Tiab] OR gerbil[Tiab] OR gerbils[Tiab] OR jird[Tiab] OR jirds[Tiab] OR merione[Tiab] OR meriones[Tiab] OR rabbits[Tiab] OR rabbit[Tiab] OR hares[Tiab] OR hare[Tiab] OR diptera[Tiab] OR flies[Tiab] OR fly[Tiab] OR dipteral[Tiab] OR drosophila[Tiab] OR drosophilidae[Tiab] OR cats[Tiab] OR cat[Tiab] OR carus[Tiab] OR felis[Tiab] OR nematoda[Tiab] OR nematode[Tiab] OR nematodes[Tiab] OR sipunculida[Tiab] OR dogs[Tiab] OR dog[Tiab] OR canine[Tiab] OR canines[Tiab] OR canis[Tiab] OR sheep[Tiab] OR sheeps[Tiab] OR mouflon[Tiab] OR mouflons[Tiab] OR ovis[Tiab] OR goats[Tiab] OR goat[Tiab] OR capra[Tiab] OR capras[Tiab] OR rupicapra[Tiab] OR rupicapras[Tiab] OR chamois[Tiab] OR haplorhini[Tiab] OR monkey[Tiab] OR monkeys[Tiab] OR anthropoidea[Tiab] OR anthropoids[Tiab] OR saguinus[Tiab] OR tamarin[Tiab] OR tamarins[Tiab] OR leontopithecus[Tiab] OR hominidae[Tiab] OR ape[Tiab] OR apes[Tiab] OR "pan paniscus"[Tiab] OR bonobo[Tiab] OR bonobos[Tiab] OR "pan troglodytes"[Tiab] OR gibbon[Tiab] OR gibbons[Tiab] OR siamang[Tiab] OR siamangs[Tiab] OR nomascus[Tiab] OR symphalangus[Tiab] OR chimpanzee[Tiab] OR chimpanzees[Tiab] OR prosimian[Tiab] OR prosimians[Tiab] OR "bush baby"[Tiab] OR bush babies[Tiab] OR galagos[Tiab] OR galago[Tiab] OR pongidae[Tiab] OR gorilla[Tiab] OR gorillas[Tiab] OR "pongo pygmaeus"[Tiab] OR orangutan[Tiab] OR orangutans[Tiab] OR lemur[Tiab] OR lemurs[Tiab] OR lemuridae[Tiab] OR horse[Tiab] OR horses[Tiab] OR equus[Tiab] OR cow[Tiab] OR calf[Tiab] OR bull[Tiab] OR chicken[Tiab] OR chickens[Tiab] OR gallus[Tiab] OR	

	quail[Tiab] OR bird[Tiab] OR birds[Tiab] OR quails[Tiab] OR poultry[Tiab] OR poultries[Tiab] OR fowl[Tiab] OR fowls[Tiab] OR reptile[Tiab] OR reptilia[Tiab] OR reptiles[Tiab] OR snakes[Tiab] OR snake[Tiab] OR lizard[Tiab] OR lizards[Tiab] OR alligator[Tiab] OR alligators[Tiab] OR crocodile[Tiab] OR crocodiles[Tiab] OR turtle[Tiab] OR turtles[Tiab] OR amphibian[Tiab] OR amphibians[Tiab] OR amphibia[Tiab] OR frog[Tiab] OR frogs[Tiab] OR bombina[Tiab] OR salientia[Tiab] OR toad[Tiab] OR toads[Tiab] OR "epidalea calamita"[Tiab] OR salamander[Tiab] OR salamanders[Tiab] OR eel[Tiab] OR eels[Tiab] OR fish[Tiab] OR fishes[Tiab] OR pisces[Tiab] OR catfish[Tiab] OR catfishes[Tiab] OR siluriformes[Tiab] OR arius[Tiab] OR heteropneustes[Tiab] OR sheatfish[Tiab] OR perch[Tiab] OR perches[Tiab] OR percidae[Tiab] OR perca[Tiab] OR trout[Tiab] OR trouts[Tiab] OR char[Tiab] OR chars[Tiab] OR salvelinus[Tiab] OR minnow[Tiab] OR cyprinidae[Tiab] OR carps[Tiab] OR carp[Tiab] OR zebrafish[Tiab] OR zebrafishes[Tiab] OR goldfish[Tiab] OR goldfishes[Tiab] OR guppy[Tiab] OR guppies[Tiab] OR chub[Tiab] OR chubs[Tiab] OR tinca[Tiab] OR barbels[Tiab] OR barbus[Tiab] OR pimephales[Tiab] OR promelas[Tiab] OR "poecilia reticulata"[Tiab] OR mullet[Tiab] OR mullets[Tiab] OR eel[Tiab] OR eels[Tiab] OR seahorse[Tiab] OR seahorses[Tiab] OR mugil curema[Tiab] OR atlantic cod[Tiab] OR shark[Tiab] OR sharks[Tiab] OR catshark[Tiab] OR anguilla[Tiab] OR salmonid[Tiab] OR salmonids[Tiab] OR whitefish[Tiab] OR whitefishes[Tiab] OR salmon[Tiab] OR salmons[Tiab] OR sole[Tiab] OR solea[Tiab] OR lamprey[Tiab] OR lampreys[Tiab] OR pumpkinseed[Tiab] OR sunfish[Tiab] OR sunfishes[Tiab] OR tilapia[Tiab] OR tilapias[Tiab] OR turbot[Tiab] OR turbots[Tiab] OR flatfish[Tiab] OR flatfishes[Tiab] OR sciuridae[Tiab] OR squirrel[Tiab] OR squirrels[Tiab] OR chipmunk[Tiab] OR chipmunks[Tiab] OR suslik[Tiab] OR susliks[Tiab] OR vole[Tiab] OR voles[Tiab] OR lemming[Tiab] OR lemmings[Tiab] OR muskrat[Tiab] OR muskrats[Tiab] OR lemmus[Tiab] OR otter[Tiab] OR otters[Tiab] OR marten[Tiab] OR martens[Tiab] OR martes[Tiab] OR weasel[Tiab] OR	

	badger[Tiab] OR badgers[Tiab] OR ermine[Tiab] OR mink[Tiab] OR minks[Tiab] OR sable[Tiab] OR sables[Tiab] OR gulo[Tiab] OR gulos[Tiab] OR wolverine[Tiab] OR wolverines[Tiab] OR mustela[Tiab] OR llama[Tiab] OR llamas[Tiab] OR alpaca[Tiab] OR alpacas[Tiab] OR camelid[Tiab] OR camelids[Tiab] OR guanaco[Tiab] OR guanacos[Tiab] OR chiroptera[Tiab] OR chiropteras[Tiab] OR bat[Tiab] OR bats[Tiab] OR fox[Tiab] OR foxes[Tiab] OR iguana[Tiab] OR iguanas[Tiab] OR xenopus laevis[Tiab] OR parakeet[Tiab] OR parakeets[Tiab] OR parrot[Tiab] OR parrots[Tiab] OR donkey[Tiab] OR donkeys[Tiab] OR mule[Tiab] OR mules[Tiab] OR zebra[Tiab] OR zebras[Tiab] OR shrew[Tiab] OR shrews[Tiab] OR bison[Tiab] OR bisons[Tiab] OR buffalo[Tiab] OR buffaloes[Tiab] OR deer[Tiab] OR deers[Tiab] OR bear[Tiab] OR bears[Tiab] OR panda[Tiab] OR pandas[Tiab] OR “wild hog”[Tiab] OR “wild boar”[Tiab] OR fitchew[Tiab] OR fitch[Tiab] OR beaver[Tiab] OR beavers[Tiab] OR jerboa[Tiab] OR jerboas[Tiab] OR capybara[Tiab] OR capybaras[Tiab] OR canine [tiab] OR bovine [tiab] OR porcine [tiab] OR hog [tiab] OR hogs [tiab]) NOT medline[sb])	
#3	("2017/01/01"[Date - Publication] : "2021/12/31"[Date - Publication])	6,592,918
#4	#1 AND #2 AND #3	3,766

[a] - PubMed methodological filter identifying studies on laboratory animals (Hooijmans et al., 2010)

Supplemental Table 2: List of animal studies included in the current study

Alghutaimel, H., Yang, X., Drummond, B., Nazzal, H., Duggal, M. & Raif, E. (2021) Investigating the vascularization capacity of a decellularized dental pulp matrix seeded with human dental pulp stem cells: in vitro and preliminary in vivo evaluations, International Endodontic Journal, 54, 1300–1316.

Al-Maula, B.H., Wally, Z.J., Al-Magsoosi, M.J.N., Dosh, R.H., Mustafa, R.M., Al-Nasrawi, S.J.H., Alfutimie, A. & Haider, J. (2021) Studying Effects of Calcium Oxide Nanoparticles on Dentinogenesis in Male Wistar Rats, International Journal of Dentistry, 2021, 9983538.

Azuma, M.M., Gomes-Filho, J.E., Ervolino, E., Pipa, C.B., Morais Cardoso, C. de B., Andrada, A.C., Kawai, T. & Angelo Cintra, L.T. (2017) Omega 3 Fatty Acids Reduce Bone Resorption While Promoting Bone Generation in Rat Apical Periodontitis, Journal of Endodontics, 43, 970–976.

Bagheri, A., Ebrahimpour, S., Nourbakhsh, N., Talebi, S. & Esmaeili, A. (2021) Protective effect of quercetin on alteration of antioxidant genes expression and histological changes in the dental pulp of the streptozotocin-diabetic rats, Archives of Oral Biology, 125, 105088.

Bakir, E.P., Yildirim, Z.S., Bakir, S. & Ketani, A. (2022) Are resin-containing pulp capping materials as reliable as traditional ones in terms of local and systemic biological effects?, Dental Materials Journal, 41, 78–86.*

Brasil, S.C., Santos, R.M.M., Fernandes, A., Alves, F.R.F., Pires, F.R., Siqueira, J.F. & Armada, L. (2017) Influence of oestrogen deficiency on the development of apical periodontitis, International Endodontic Journal, 50, 161–166.

Cosme-Silva, L., Dal-Fabbro, R., Cintra, L.T.A., Ervolino, E., Plazza, F., Mogami Bomfim, S., Duarte, P.C.T., Junior, V.E.D.S. & Gomes-Filho, J.E. (2020) Reduced bone resorption and inflammation in apical periodontitis evoked by dietary supplementation with probiotics in rats, International Endodontic Journal, 53, 1084–1092.

Deng, S., Fan, L., Wang, Y. & Zhang, Q. (2021) Constitutive activation of beta-catenin in odontoblasts induces aberrant pulp calcification in mouse incisors, Journal of Molecular Histology, 52, 567–576.

Dianat, O., Mashhadiabbas, F., Ahangari, Z., Saedi, S. & Motamedian, S.R. (2018) Histologic comparison of direct pulp capping of rat molars with MTA and different concentrations of simvastatin gel, Journal of Oral Science, 60, 57–63.

Edanami, N., Ibn Belal, R.S., Yoshiba, K., Yoshiba, N., Ohkura, N., Takenaka, S. & Noiri, Y. (2021) Effect of a resin-modified calcium silicate cement on inflammatory cell infiltration and reparative dentin formation after pulpotomy in rat molars, Australian Endodontic Journal.

El-Mal, E.O.A., Abu-Seida, A.M. & El Ashry, S.H. (2021) Biological evaluation of hesperidin for direct pulp capping in dogs, teeth, International Journal of Experimental Pathology, 102, 32–44.

Emerenciano Bueno, C.R., Veiga Vasques, A.M., Sandoval Cury, M.T., Sivieri-Araujo, G., Jacinto, R.C., Gomes-Filho, J.E., Angelo Cintra, L.T. & Dezan-Junior, E. (2019) Biocompatibility and biomineralization assessment of mineral trioxide aggregate flow, Clinical Oral Investigations, 23, 169–177.

Ferreira, L.L., Gomes-Filho, J.E., Benetti, F., Carminatti, M., Ervolino, E., Briso, A.L.F. & Cintra, L.T.A. (2018) The effect of dental bleaching on pulpal tissue response in a diabetic animal model: a study of immunoregulatory cytokines, International Endodontic Journal, 51, 347–356.

Gallinari, M. de O., Angelo Cintra, L.T., Benetti, F., Rahal, V., Ervolino, E. & Fraga Briso, A.L. (2019) Pulp response of rats submitted to bleaching and the use of different anti-inflammatory drugs, Plos One, 14, e0210338.

Galvao da Silva-Costa, R.S., de Lima Ribeiro, A.E., de Assuncao, I.V., de Araujo Junior, R.F., de Araujo, A.A., Bernardo Guerra, G.C. & Dutra Borges, B.C. (2018) In-office tooth bleaching with 38% hydrogen peroxide promotes moderate/severe pulp inflammation and production of ll-1 beta, TNF-beta, GPX, FGF-2 and osteocalcin in rats, Journal of Applied Oral Science, 26, e20170367.

Gao, L., Fan, F., Wang, L., Tang, B., Wen, Z., Tang, J., Dai, T. & Jin, H. (2022) Polarization of macrophages in the trigeminal ganglion of rats with pulpitis, Journal of Oral Rehabilitation, 49, 228–236.*

de Gregorio, C., Cohenca, Nestor, Romano, F., Pucinelli, C.M., Cohenca, Nathalie, Romero, M., Lucisano, M.P., Bezerra da Silva, R.A. & Bezerra da Silva, L.A. (2018) The effect of immediate controlled forces on periodontal healing of teeth replanted after short dry time in dogs, Dental Traumatology, 34, 336–346.

He, J., Qin, M., Chen, Y., Hu, Z., Ye, L. & Hui, T. (2021) EZH2 Promotes Extracellular Matrix Degradation via Nuclear Factor-kappa B (NF-kappa B) and p38 Signaling Pathways in Pulpitis, Inflammation, 44, 1927–1936.

Hirai, K., Furusho, H., Kawashima, N., Xu, S., de Beer, M.C., Battaglino, R., Van Dyke, T., Stashenko, P. & Sasaki, H. (2019) Serum Amyloid A Contributes to Chronic Apical Periodontitis via TLR2 and TLR4, Journal of Dental Research, 98, 117–125.

Islam, R., Toida, Y., Chen, F., Tanaka, T., Inoue, S., Kitamura, T., Yoshida, Y., Chowdhury, A.F.M.A., Ahmed, H.M.A. & Sano, H. (2021) Histological evaluation of a novel phosphorylated pullulan-based pulp capping material: An in vivo study on rat molars, International Endodontic Journal, 54, 1902–1914.

Kang, C.-M., Hwang, J., Song, J.S., Lee, J.-H., Choi, H.-J. & Shin, Y. (2018) Effects of Three Calcium Silicate Cements on Inflammatory Response and Mineralization-Inducing Potentials in a Dog Pulpotomy Model, Materials, 11, 899.

Khan, S.Z., Mirza, S., Karim, S., Inoue, T., Bin-Shuwaish, M.S., Al Deeb, L., Al Ahdal, K., Al-Hamdan, R.S., Maawadh, A.M., Vohra, F. & Abduljabbar, T. (2020) Immunohistochemical study of dental pulp cells with 3D collagen type I gel in demineralized dentin tubules in vivo, Bosnian Journal of Basic Medical Sciences, 20, 438–444.

Kim, S., Lee, S., Jung, H.-S., Kim, S.-Y., Shin, S.-J., Kang, M.K. & Kim, E. (2018) Evaluation of the Biodistribution of Human Dental Pulp Stem Cells Transplanted into Mice, Journal of Endodontics, 44, 592–598.

Kim, S.G. & Solomon, C.S. (2021) Regenerative Endodontic Therapy in Mature Teeth Using Human-Derived Composite Amnion-Chorion Membrane as a Bioactive Scaffold: A Pilot Animal Investigation, Journal of Endodontics, 47, 1101–1109.

Kolesnikova, L.R., Darenskaya, M.A., Kolesnikova, L.I., Grebenkina, L.A., Korytov, L.I., Batoroev, Y.K., Belinskaya, E.I., Mikhalevich, I.M. & Kolesnikov, S.I. (2019) Changes in the Periodontium and Pulp in ISIAH Rats Caused by Stress Exposures in Different Modes, Bulletin of Experimental Biology and Medicine, 166, 722–725.

Lee, C.S., Ramsey, A.A., De Brito-Gariepy, H., Michot, B., Podborits, E., Melnyk, J. & Gibbs, J.L. (2017) Molecular, cellular and behavioral changes associated with pathological pain signaling occur after dental pulp injury, Molecular Pain, 13, 1744806917715173.

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Liu, Q., Ma, Y., Wang, J., Zhu, X., Yang, Y. & Mei, Y. (2017) Demineralized bone matrix used for direct pulp capping in rats, Plos One, 12, e0172693.

Lopes, C.S., Junqueira, M.A., Cosme-Silva, L., Rodini Pegoraro, C. de O., Dezan Garbelini, C.C., Oliveira, T.M., Martins, N.S., Neves, J. dos S. & Sakai, V.T. (2019) Initial inflammatory response after the pulpotomy of rat molars with MTA or ferric sulfate, Journal of Applied Oral Science, 27, e20180550.

Mandakhbayar, N., El-Fiqi, A., Lee, J.-H. & Kim, H.-W. (2019) Evaluation of Strontium-Doped Nanobioactive Glass Cement for Dentin-Pulp Complex Regeneration Therapy, Acs Biomaterials Science & Engineering, 5, 6117–6126.

Moreira, M.S., Sarra, G., Carvalho, G.L., Goncalves, F., Caballero-Flores, H.V., Fagundes Pedroni, A.C., Lascala, C.A., Catalani, L.H. & Marques, M.M. (2021) Physical and Biological Properties of a Chitosan Hydrogel Scaffold Associated to Photobiomodulation Therapy for Dental Pulp Regeneration: An In Vitro and In Vivo Study, Biomed Research International, 2021, 6684667.

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*During literature search study was published in the year 2021

Supplemental Table 3: Characteristics of the included animal studies

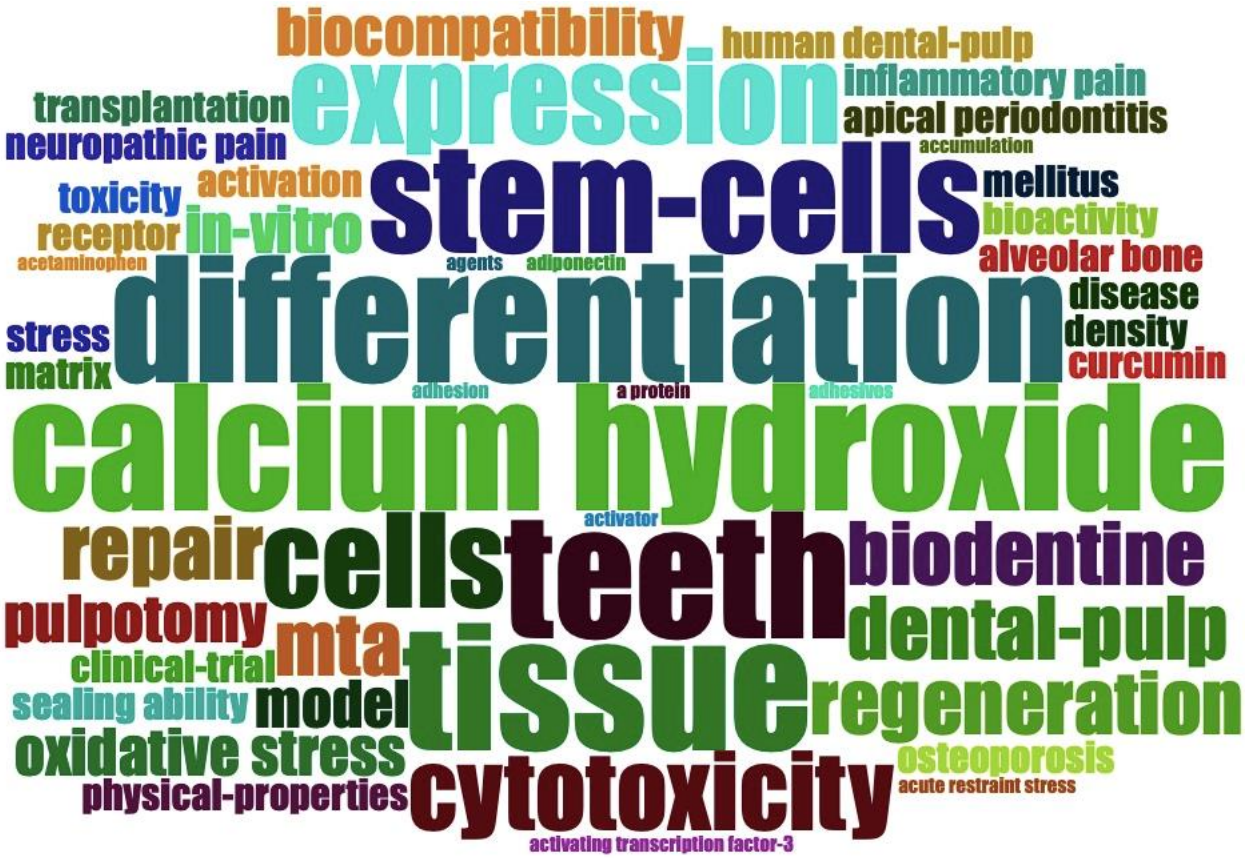
Study number	First author	Year published	Journal name	JCR® IF for the year in which the study is published	JCR® IF2021	5-year JCR® IF2021	JCR® Category	JCR® Category Quartile	Citations No[d]	Average citations per year
1	PRABHAKAR AR	2019	INDIAN J DENT RES	-[a]	-	-	-	-	0	0
2	BAKIR EP	2021	DENT MATER J	2.418	2.418	2.7	DENTISTRY, ORAL SURGERY & MEDICINE; MATERIALS SCIENCE, BIOMATERIALS	Q3; Q4	0	0
3	EDANAMI N	2021	AUST ENDOD J	1.719	1.719	1.805	DENTISTRY, ORAL SURGERY & MEDICINE	Q4	0	0
4	GAO L	2021	J ORAL REHABIL	3.558	3.558	4.096	DENTISTRY, ORAL SURGERY & MEDICINE	Q2	0	0
5	AL-MAULA BH	2021	INT J DENT	-[b]	-	-	DENTISTRY, ORAL SURGERY & MEDICINE	-	0	0
6	ISLAM R	2021	INT ENDOD J	5.165	5.165	5.093	DENTISTRY, ORAL SURGERY & MEDICINE	Q1	2	2
7	KIM SG	2021	J ENDODONT	4.422	4.422	4.986	DENTISTRY, ORAL SURGERY & MEDICINE	Q1	4	4
8	PARAS S	2021	INT J MOL SCI	6.208	6.208	6.628	BIOCHEMISTRY & MOLECULAR BIOLOGY; CHEMISTRY, MULTIDISCIPLINARY	Q1; Q2	0	0
9	SARRA G	2021	TISSUE CELL	2.586	2.586	2.331	ANATOMY & MORPHOLOGY; CELL BIOLOGY	Q2; Q4	1	1
10	HE J	2021	INFLAMMATION	4.657	4.657	4.361	CELL BIOLOGY; IMMUNOLOGY	Q3	1	1
11	ALGHUTAIMEL H	2021	INT ENDOD J	5.165	5.165	5.093	DENTISTRY, ORAL SURGERY & MEDICINE	Q1	2	2
12	DENG SJ	2021	J MOL HISTOL	3.156	3.156	2.825	CELL BIOLOGY	Q4	0	0

13	BAGHERI A	2021	ARCH ORAL BIOL	2.64	2.64	2.687	DENTISTRY, ORAL SURGERY & MEDICINE	Q3	1	1
14	LEE DJ	2021	BIOCHEM BIOPHYS REP	-[b]	-	-	BIOCHEMISTRY & MOLECULAR BIOLOGY	-	0	0
15	WANG L	2021	ACTA BIOMATER	10.633	10.633	10.227	MATERIALS SCIENCE, BIOMATERIALS; ENGINEERING, BIOMEDICAL	Q1	3	3
16	MOREIRA MS	2021	BIOMED RES INT	3.246	3.246	3.767	BIOTECHNOLOGY & APPLIED MICROBIOLOGY; MEDICINE, RESEARCH & EXPERIMENTAL	Q3; Q3	3	3
17	EL-MAL EOA	2021	INT J EXP PATHOL	2.793	2.793	2.74	PATHOLOGY	Q3	1	1
18	REIS MD	2021	BRAZ ORAL RES	2.674	2.674	3.115	DENTISTRY, ORAL SURGERY & MEDICINE	Q3	0	0
19	SANTOS JM	2021	BIOMEDICINES	4.757	4.757	5.225	BIOCHEMISTRY & MOLECULAR BIOLOGY; MEDICINE, RESEARCH & EXPERIMENTAL; PHARMACOLOGY & PHARMACY	Q2	10	10
20	TIBURCIO-MACHADO CD	2021	LIFE SCI	6.78	6.78	6.044	PHARMACOLOGY & PHARMACY; MEDICINE, RESEARCH & EXPERIMENTAL	Q1	2	2
21	SILVA ECA	2021	INT ENDOD J	5.165	5.165	5.093	DENTISTRY, ORAL SURGERY & MEDICINE	Q1	2	2
22	ZHAI Y	2020	FRONT PHYSIOL	4.566	4.755	5.316	PHYSIOLOGY	Q1	4	2
23	SHAHSAVARI F	2020	ARCH ORAL BIOL	2.635	2.64	2.687	DENTISTRY, ORAL SURGERY & MEDICINE	Q3	0	0
24	COSME-SILVA L	2020	INT ENDOD J	5.264	5.165	5.093	DENTISTRY, ORAL SURGERY & MEDICINE	Q1	8	4

25	KHAN SZ	2020	BOSNIAN J BASIC MED	3.363	3.759	3.681	MEDICINE, RESEARCH & EXPERIMENTAL	Q3	1	0.5
26	SILVA LA ASSED BEZERRA DA	2020	BRAZ DENT J	-[a]	-	-	-	-	0	0
27	MANDAKHBAYAR N	2019	ACS BIOMATER SCI ENG	4.152	5.395	5.77	MATERIALS SCIENCE, BIOMATERIALS	Q2	13	4.33
28	KOLESNIKOVA LR	2019	B EXP BIOL MED+	0.775	0.737	0.741	MEDICINE, RESEARCH & EXPERIMENTAL	Q4	2	0.67
29	QI SC	2019	MOL MED REP	2.1	3.423	3.112	MEDICINE, RESEARCH & EXPERIMENTAL; ONCOLOGY	Q3	9	3
30	GALLINARI MD	2019	PLOS ONE	2.74	3.752	4.069	MULTIDISCIPLINARY SCIENCES	Q2	5	1.67
31	BUENO CRE	2019	CLIN ORAL INVEST	2.812	3.606	3.734	DENTISTRY, ORAL SURGERY & MEDICINE	Q2	14	4.67
32	HIRAI K	2019	J DENT RES	4.914	8.924	8.463	DENTISTRY, ORAL SURGERY & MEDICINE	Q1	14	4.67
33	LOPES CS	2019	J APPL ORAL SCI	1.797	3.144	3.329	DENTISTRY, ORAL SURGERY & MEDICINE	Q2	5	1.67
34	DE GREGORIO C	2018	DENT TRAUMATOL	1.494	3.328	2.949	DENTISTRY, ORAL SURGERY & MEDICINE	Q2	2	0.5
35	KANG CM	2018	MATERIALS	2.972	3.748	4.042	METALLURGY & METALLURGICAL ENGINEERING; CHEMISTRY, PHYSICAL; MATERIALS SCIENCE, MULTIDISCIPLINARY; PHYSICS, APPLIED; PHYSICS, CONDENSED MATTER	Q1; Q3; Q3; Q2; Q2	5	1.25
36	KIM S	2018	J ENDODONT	2.833	4.422	4.986	DENTISTRY, ORAL SURGERY & MEDICINE	Q1	4	1

37	DIANAT O	2018	J ORAL SCI	1.104	1.63	1.818	DENTISTRY, ORAL SURGERY & MEDICINE; MATERIALS SCIENCE, BIOMATERIALS	Q4	1	0.25
38	FERREIRA LL	2018	INT ENDOD J	3.331	5.165	5.093	DENTISTRY, ORAL SURGERY & MEDICINE	Q1	13	3.25
39	SHAH A	2018	ORAL DIS	2.625	4.068	3.974	DENTISTRY, ORAL SURGERY & MEDICINE	Q1	6	1.5
40	ZHU XF	2018	TISSUE ENG PART C-ME	2.638	3.273	3.646	CELL BIOLOGY; ENGINEERING, BIOMEDICAL; MATERIALS SCIENCE, BIOMATERIALS; CELL & TISSUE ENGINEERING	Q3; Q3; Q3; Q4	36	9
41	DA SILVA-COSTA RSG	2018	J APPL ORAL SCI	1.506	3.144	3.329	DENTISTRY, ORAL SURGERY & MEDICINE	Q2	3	0.75
42	NABESHIMA CK	2018	J APPL ORAL SCI	1.506	3.144	3.329	DENTISTRY, ORAL SURGERY & MEDICINE	Q2	5	1.25
43	RAOOF M	2018	ARCH ORAL BIOL	1.663	2.64	2.687	DENTISTRY, ORAL SURGERY & MEDICINE	Q3	8	2
44	RAOOF M	2017	KOREAN J PAIN	-[c]	2.6	2.579	CLINICAL NEUROLOGY	Q3	4	0.8
45	SABIR A	2017	SAUDI J BIOL SCI	3.138	4.052	4.247	BIOLOGY	Q2	11	2.2
46	LEE CS	2017	MOL PAIN	3.205	3.37	3.685	NEUROSCIENCES	Q3	12	2.4
47	AZUMA MM	2017	J ENDODONT	2.886	4.422	4.986	DENTISTRY, ORAL SURGERY & MEDICINE	Q1	25	5
48	LIU Q	2017	PLOS ONE	2.766	3.752	4.069	MULTIDISCIPLINARY SCIENCES	Q2	7	1.4
49	NEGM AM	2017	EXP TOXICOL PATHOL	2.023	-	2.148	PATHOLOGY; TOXICOLOGY	Q2; Q3	11	2.2
50	BRASIL SC	2017	INT ENDOD J	3.015	5.165	5.093	DENTISTRY, ORAL SURGERY & MEDICINE	Q1	8	1.6

[a] The journal indexed in MEDLINE.
[b] The journal indexed in the Clarivate Analytics' Emerging Sources Citation Index.
[c] The journal received an IF the following year (IF2018=1.563).
[d] The source of citations was Web of Science Core Collection.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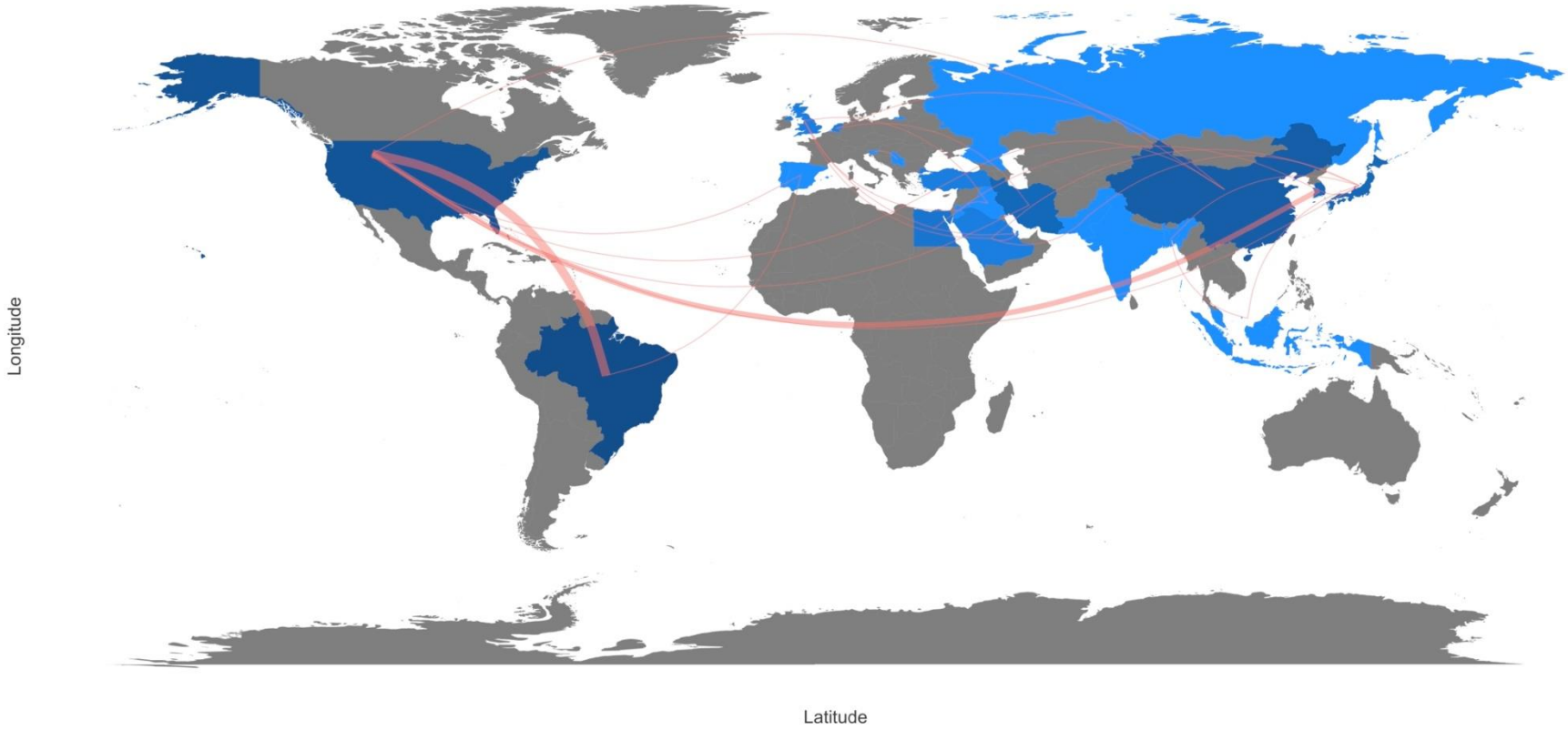
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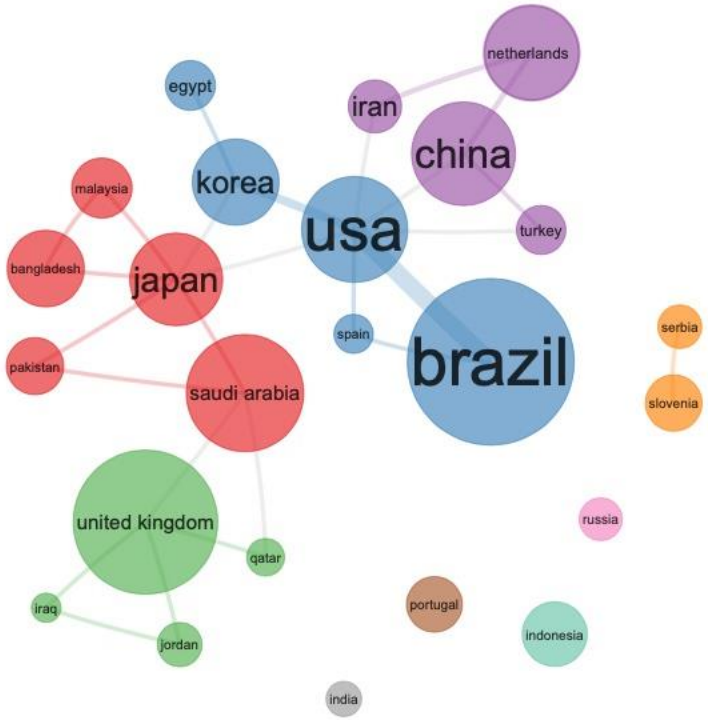
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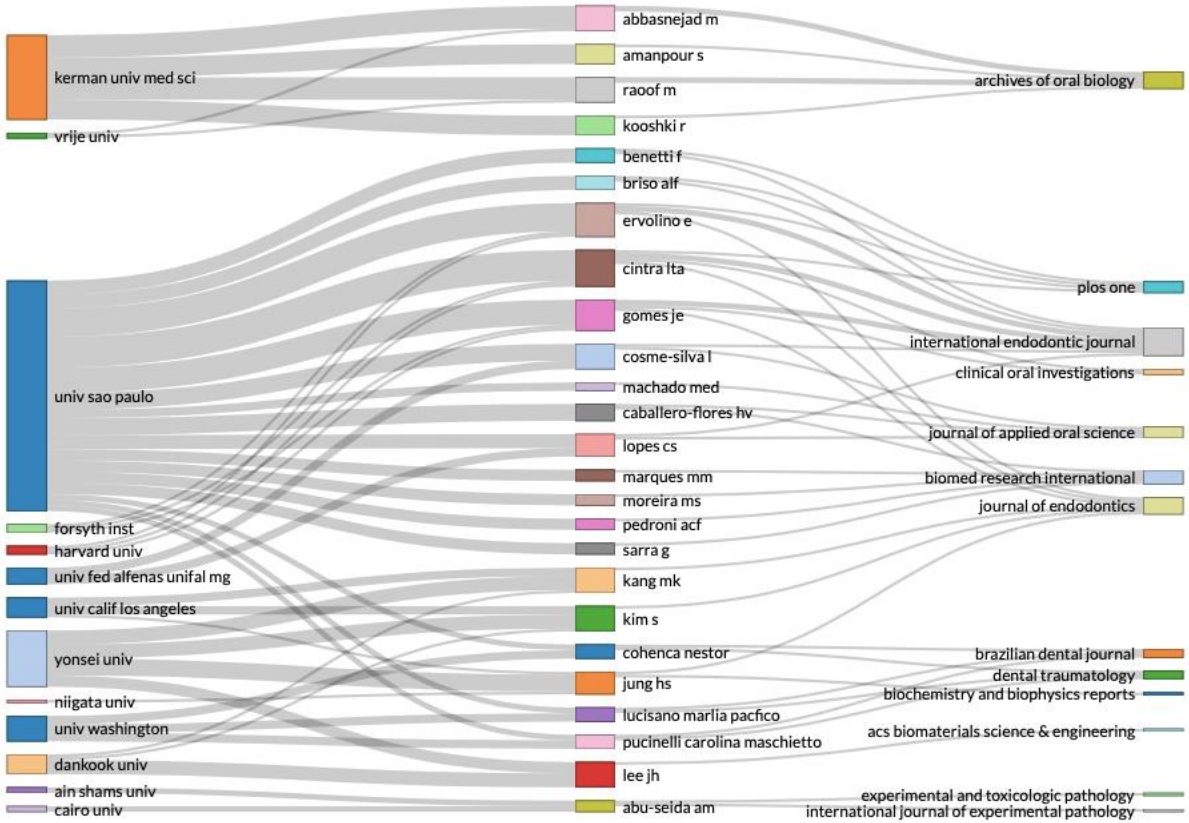
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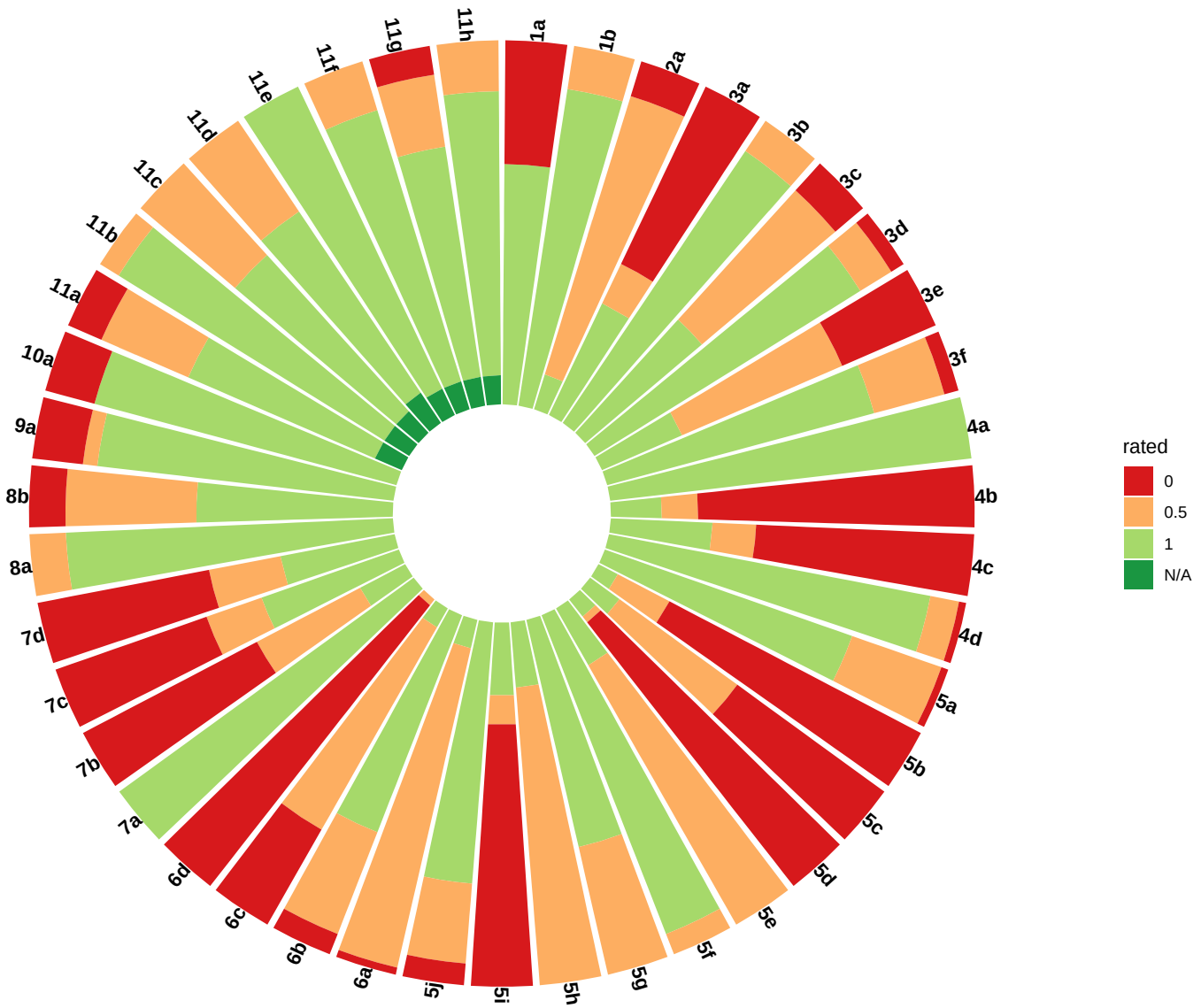
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