



Challenges in conducting clinical research in primary care dentistry

BAC Loomans^{a,*}, FM Mendes^{a,b}, S Vinayahalingam^a, T Xi^a, NJM Opdam^a, CM Kreulen^a, T Pereira-Cenci^a, MS Cenci^a

^a Department of Oral and Maxillofacial Surgery, Radboud Institute for Medical Innovation, Radboud University Medical Center, Philips van Leydenlaan 25, EX 6525 Nijmegen, The Netherlands

^b Department of Pediatric Dentistry, School of Dentistry, University of São Paulo, São Paulo, Brazil

ARTICLE INFO

Keywords:

Clinical trials
Primary care
Dentistry
Artificial intelligence

ABSTRACT

The integration of dentistry into primary health care is crucial for promoting patient well-being. However, clinical studies in dentistry face challenges, including issues with study design, transparency, and relevance to primary care. Clinical trials in dentistry often focus on specific issues with strict eligibility criteria, limiting the generalizability of findings. Randomized clinical trials (RCTs) face challenges in reflecting real-world conditions and using clinically relevant outcomes. The need for more pragmatic approaches and the inclusion of clinically relevant outcomes (CROs) is discussed, such as tooth loss or implant success. Solutions proposed include well-controlled observational studies, optimized data collection tools, and the integration of artificial intelligence (AI) for predictive modelling, computer-aided diagnostics and automated diagnosis. In this position paper advocates for more efficient trials with a focus on patient-centred outcomes, as well as the adoption of pragmatic study designs reflecting real-world conditions. Collaborative research networks, increased funding, enhanced data retrieval, and open science practices are also recommended. Technology, including intraoral scanners and AI, is highlighted for improving efficiency in dental research. AI is seen as a key tool for participant recruitment, predictive modelling, and outcome evaluation. However, ethical considerations and ongoing validation are emphasized to ensure the reliability and trustworthiness of AI-driven solutions in dental research. In conclusion, the efficient conduct of clinical research in primary care dentistry requires a comprehensive approach, including changes in study design, data collection, and analytical methods. The integration of AI is seen as pivotal in achieving these objectives in a meaningful and efficient way.

1. Introduction

Dentistry is embedded into primary health care as dental professionals promote patient well-being. The traditional definition of primary care focuses on delivering health care with a patient-centred approach, including health promotion, disease prevention, and coordination of health care services. The dental profession inherently acts at those levels, evolving in addressing general health issues, especially as the population ages and chronic illnesses become more prevalent [1]. Another aspect of integrating dentistry into primary care is the outstanding possibility of conducting research in a context that matters, addressing clinical questions that are important for the oral and general health of individuals. Designing studies and collecting data in the primary care environment is fundamental for improving oral health, yet it faces considerable challenges [1,2].

Literature has shown evidence of the problems and limitations faced

by current clinical trials in dentistry. Despite a substantial increase in the number of trials and significant advancements over the past decades, clinical research in dentistry faces challenges in study design, external and internal validity, trial duration, and selection of outcomes and associated costs. Studies have addressed the lack of transparency [3], limitations of the report [4,5], and the risk of bias in the dental literature [6]. The problems regarding reproducibility in medical research, which are also present in dentistry, require further investigation.

However, challenges and limitations should be addressed when conducting research in the primary care setting [7]. The first point is that most clinical studies in dentistry **focus on specific issues, adopting strict eligibility criteria** [7], which jeopardises the extrapolation of the findings to a broader population. Moreover, randomized clinical trials (RCTs) are conducted under “highly ideal” situations that do not reflect “real” world conditions. Also, they **use surrogate outcomes or report on secondary outcomes** since limitations in the duration of

* Corresponding author at: Department of Dentistry, Radboud University Medical center, PO Box 9101, NL 6500 HB Nijmegen, The Netherlands.

E-mail address: Bas.loomans@radboudumc.nl (B. Loomans).

<https://doi.org/10.1016/j.jdent.2024.104958>

Received 18 March 2024; Accepted 19 March 2024

Available online 23 March 2024

0300-5712/© 2024 The Author(s). Published by Elsevier Ltd. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>).

clinical trials block the use of practical relevant outcome measures [8]. In contrast, the use of clinically relevant outcomes (CROs), such as tooth loss, implant success, or retention of restorations, is not consistently emphasized. Even considering that most CROs in dentistry require many years to manifest, in the context of primary care, it is important to promote the collection of CROs [8,9].

These primary challenges should be addressed using proper trial designs, adopting more pragmatic approaches, and especially performing studies closer to the context of primary care. Based on our experience in conducting this type of studies, this paper addresses the challenges and limitations of conducting clinical studies in the primary care environment, intending to offer potential solutions and future directions.

2. Challenges and limitations of clinical studies

To address some of the aforementioned challenges, we will reflect on problems and proposed solutions that we faced in conducting the following studies: the Radboud Tooth Wear Project (RTWP), the Caries Detection in Children (CARDEC), Caries Cognition and Identification in Adults (CACIA) trials initiatives [10–14], and the practice-based studies about longevity of dental restorations [13–15]. The RTWP consists of multiple prospective observational trials with some nested RCTs conducted to evaluate treatments for tooth wear [10,11]. The CARDEC trials cover a series of RCTs and other nested studies designed to evaluate questions about caries diagnosis strategies and subsequent treatment in children [14,15] and adults [16], respectively. Finally, the practice-based initiative developed a series of pragmatic studies mainly focusing on the longevity of dental restorations [17–19].

The RTWP started in 2009, aiming to provide patients with moderate to severe tooth wear optimal individualized and minimally invasive care. Based on the presence of a functional or esthetical demand for treatment (pain, shortened teeth, problems with chewing, etc.) it was decided to monitor the progression of tooth wear or to prescribe a restorative rehabilitation using several direct and indirect composite materials. All 200 patients were evaluated every two years. The strength of this project is that patients with specific individual risk factors, such as para-functional habits of grinding/clenching or patients with GORD (Gastro-Oesophageal Reflux Disease), were also included in the project, even though these ‘**high-risk**’ patients are often excluded from clinical trials. Not only the survival of the restorations was defined as a primary outcome, but also the **PROMS** patient-related outcome measures were investigated, such as effects of the treatment on chewing, speech, quality of life, etc. [12,13]. One of the limitations of the project was the enormous effort to treat all these patients together with the necessary (mid-) long-term recalls to be performed by the research group.

CARDEC and CACIA trials were designed using broad eligibility criteria, including consecutive samples of patients who looked for dental treatments in schools that promoted the RCTs [8,14,16]. Moreover, the main trials were focused on diagnostic strategies, and many other RCTs and cross-sectional studies on dental treatments related to primary care were nested in the main trials. Both initiatives have significantly impacted the advancement of knowledge in caries diagnosis and management of dental caries, especially in the primary care setting. However, the studies faced many challenges and had essential limitations. First, all participants who demanded care in a primary health centre were potentially included in the trials. Even though this represented a relatively **small sample size**, it reflected a specific population of that **single centre**. They would undoubtedly benefit from using multicentric approaches for both internal, with the increase of the sample size, for example, and external validities with participants from different regions and socioeconomic backgrounds. Moreover, although they were conducted in the primary care environment, they had a **low degree of pragmatism** since well-trained clinicians conducted the diagnostic strategies, and the treatments were performed following protocols based on the best available evidence [8,14,16].

On the other hand, the practice-based studies were conducted more

pragmatically in the primary care context of dental practices in the Netherlands. This approach permitted a considerable sample size, with participants from several regions [17–20]. However, other problems usually arise, such as lower **accuracy and reproducibility in collecting clinical outcomes**, **difficulty retrieving data from patient files**, and **difficulty adjusting the outcomes for important confounders**. Furthermore, there are **technical and legal problems with retrospective data gathering**, and the need for patient approval is difficult to attain. Also, most of the recording dental data systems need to be more accurate for annotations on diagnosis and reasons for interventions, and a big effort must be made to standardize the recording of dental procedures and the data extraction.

In general, other challenges and limitations of clinical studies in dentistry can be emphasized, and they have also been addressed in previous publications. Taking studies on the longevity of dental restorations as an example, the focus over the decades of the included dental practices has shifted from the comparison between types of materials and techniques at the tooth level towards a focus on patient-level (including caries risk, tooth wear, parafunctional habits, and lifestyle) and the influence of dentist in decision-making [21]. In a previous paper, an overview of all types of study designs and outcomes for evaluating the survival of dental restorations [22] is presented. The advantages and disadvantages of randomized trials, prospective and retrospective longitudinal studies, and practice-based, pragmatic, and cohort studies are discussed. The paper recommends that clinical trials should have rational control groups, including confounders such as patient risk factors in the data and analysis, and the use of outcome parameters that are relevant to both professionals and patients. The focus, however, should shift from examining the survival of restorations to emphasizing **CROs and patient-centred outcomes**.

Moreover, possible solutions to overcome some limitations will bring new challenges. For example, in practice-based research or more extensive multicentric trials, the **clinical assessment of many patients by dentists is challenging to manage and standardize**. As a result, larger studies may be compromised by insufficiently trained practitioners or examiners to assess the outcomes. Moreover, involving many well-trained and calibrated clinicians would be too costly.

3. Tackling the challenges: some possible solutions

By sharing our experiences from previous clinical studies in the primary care environment, we present potential solutions and directions for new studies. Addressing the challenges mentioned above requires a comprehensive approach that involves changes in study design, data collection, analytical methods, and research practices. Above all, it involves changes in researchers’ mindsets.

Here we suggest potential solutions to the highlighted problems in conducting clinical research in dental primary care settings:

- *Conducting well-controlled observational studies in primary care environment:*

Cohort studies with participants with specific oral health problems, such as the RTWP study, should collect standardized and relevant data to address the prognosis and possible treatment for these conditions. Moreover, they should optimize tools to monitor these conditions effectively. Initiatives with a large number of participants that gather qualified data would enable researchers to design RCTs using subsets of the main cohort. Artificial intelligence (AI) is crucial in developing predictive models as well as accurate and reliable automated tools to diagnose and monitor oral health problems. This will be discussed in detail later.

- *Conducting more efficient and relevant clinical trials:*

Data from RCTs remains the highest level of evidence for questions

related to therapeutic or preventive interventions, also in primary care settings [8,23]. However, they need to become more efficient in logistics, costs, and time. In addition, they should focus on clinically relevant [8,9] or patient-centred outcomes [24]. These studies should involve centres in different cities and, preferentially, different countries. This procedure allows achieving a robust sample size, increasing the generalisability of the findings. Moreover, these multicentred studies must also focus on clinically relevant and patient-centred outcomes. Core outcome sets for prevalent oral health problems in primary care are very welcomed to support the researchers [25].

Improving the efficiency of RCTs inevitably involves the use of AI, which can play an important role in the inclusion of participants, standardisation of the methods for collecting the outcomes and optimisation of analysis and interpretation of findings.

- *Adoption of Pragmatic Study Designs to increase representativeness:*

Future studies should embrace and encourage using pragmatic designs that reflect real-world conditions and patient-centred outcomes. This is a necessary step forward for clinical trials. Pragmatic trials allow for flexibility and more accurately reflect the complexity of dental interventions in actual practice. A wise choice is to include the patients' perspectives and participation in study designs to identify and prioritize outcomes that matter most to them. Also, stimulating practice-based research is an important approach [26].

- *Collaborative Research Networks:*

Establishing collaborative research networks involving multiple dental practices and institutions is necessary to enable the necessary working force to address big questions in primary care dentistry. By sharing the resources and expertise, a network of researchers can tackle various oral health problems prevalent in primary care with different study designs that will achieve greater relevance in the findings with higher efficiency [27].

- *Increased Funding and Resources to address clinically relevant problems:*

Dental associations should advocate for increased funding for dental research in the primary care setting to overcome resource limitations. Increased financial support can facilitate the recruitment of qualified research personnel, the acquisition of necessary equipment, and the overall improvement of research infrastructure. These associations should also promote and organise collaborative research networks for relevant solutions to oral health problems.

- *Enhanced Data Retrieval:*

Adopting good electronic health record systems will facilitate accurate and standardized documentation of dental procedures, as well as from involved dental practices. Developing protocols and technologies that streamline data extraction from patient files, addressing both technical and legal challenges, should be promoted in the context of clinical research in dentistry. These systems allow recording and scoring of procedures, assessing risk factors, and documentation of the reasons for interventions. Also, a link between dental and medical patient records could allow the investigation of essential questions in the primary care environment. Additionally, AI-powered algorithms can assist in automating the extraction and standardization of data from patient files. Natural language processing can be used to interpret and extract relevant information from unstructured clinical notes, addressing technical and legal challenges.

- *Open science:*

Open science is an important movement for assessing the integrity

and transparency of all steps related to the scientific process. Moreover, this movement is also fundamental to speed up advances in knowledge [28] and increase representativeness. For example, open notebooks and data sharing can facilitate discoveries with resource savings [29]. Open science practices should be compulsory for clinical studies related to primary care.

- *Utilization of Technology and Artificial Intelligence:*

Leveraging advancements in dental technology, such as intraoral scanners and imaging systems, will enhance the efficiency and standardization of assessments and monitoring of oral health conditions. Incorporating digital tools for data collection and analysis, which reduces dependence on manual and operator-dependant methods is not only possible but also recommendable.

Moreover, as previously mentioned, AI will play a key role in developing more efficient and relevant studies in primary care dentistry. These benefits are related to many steps involved in clinical studies. AI algorithms can aid researchers in recruiting participants for clinical studies, mainly those involving many centres or clinical practices. Automated tools provided by a few critical pieces of information could identify eligible study participants, thereby increasing efficiency [30]. Moreover, AI can be a valuable tool to improve the participants' experience by reducing the need for patients to be present at research centres and decentralising research as much as possible [31].

AI can also power the development of algorithms to predict various oral health problems in primary care settings. These algorithms would be beneficial in both research and clinical practice, where patients at greater risk of specific outcomes would receive specialised (preventive) care in an attempt to prevent or reduce the damage caused by an oral health problem [32]. AI is an important tool for improving analytical methods in interventional and observational studies, even for investigating causality with a reduction of potential biases [33].

Finally, AI tools can automate and standardise the evaluation of outcomes investigated in the different studies. AI-powered automated tools are being developed to analyse different oral health outcomes, such as caries, tooth wear, and defects on dental restorations, using 2D and 3D images (X-rays, intra-oral images and intra-oral 3D scans). Computer vision algorithms can assist in assessing oral conditions, reducing reliance on manual evaluations and enhancing objectivity [34,35].

AI tools have the potential to play a significant role in overcoming several challenges associated with clinical research in dental settings. Implementing AI tools in dental research requires collaboration between researchers, clinicians, and AI experts. While AI offers promising solutions, it is essential to consider ethical considerations, data privacy, and ongoing validation to ensure the reliability and trustworthiness of AI-driven solutions in dental research.

4. Conclusions

In conclusion, clinical research in primary care should be conducted efficiently, always targeting relevant outcomes for the population and using strategies to enhance the representativeness and robustness of the findings. Several proposals can make these studies more feasible. However, AI will play a pivotal role in the coming years to make these objectives achievable in a more meaningful and efficient way.

CRediT authorship contribution statement

BAC Loomans: Conceptualization, Supervision, Writing – original draft. **FM Mendes:** Conceptualization, Writing – original draft. **S Vinayahalingam:** Writing – original draft. **T Xi:** Conceptualization, Writing – original draft. **NJM Opdam:** Conceptualization, Writing – original draft. **CM Kreulen:** Writing – original draft. **T Pereira-Cenci:** Conceptualization, Writing – original draft. **MS Cenci:** Conceptualization, Writing – original draft.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

We would like to acknowledge the Radboud Dental AI Hub to support the writing of this paper.

References

- [1] R.S. Gambhir, Primary care in dentistry - an untapped potential, *J. Fam. Med. Prim. Care* 4 (1) (2015) 13–18.
- [2] I.R. Blum, Primary dental care: an update for general dental practice, *Prim. Dent. J.* 12 (1) (2023) 2.
- [3] M.S. Cenci, M.C. Franco, D.P. Raggio, D. Moher, T. Pereira-Cenci, Transparency in clinical trials: adding value to paediatric dental research, *Int. J. Paediatr. Dent.* 31 (Suppl 1) (2020) 4–13.
- [4] R. Sarkis-Onofre, V. Poletto-Neto, M.S. Cenci, D. Moher, T. Pereira-Cenci, CONSORT endorsement improves the quality of reports of randomized clinical trials in dentistry, *J. Clin. Epidemiol.* 122 (2020) 20–26.
- [5] R. Sarkis-Onofre, V. Poletto-Neto, M.S. Cenci, T. Pereira-Cenci, D. Moher, Impact of the CONSORT Statement endorsement in the completeness of reporting of randomized clinical trials in restorative dentistry, *J. Dent.* 58 (2017) 54–59.
- [6] H. Saltaji, M.B. Ospina, S. Armijo-Olivo, S. Agarwal, G.G. Cummings, M. Amin, C. Flores-Mir, Evaluation of risk of bias assessment of trials in systematic reviews of oral health interventions, 1991–2014: a methodology study, *J. Am. Dent. Assoc.* 147 (9) (2016), 720–728 e1.
- [7] C.M. Pannuti, G.A. Romito, S.M. Paiva, Challenges of clinical research in dentistry, *Braz. Oral. Res.* 34 (Suppl 2) (2020) e092.
- [8] F.M. Mendes, M.M. Braga, A.L. Passaro, B.L.P. Moro, R.D. Freitas, T. Gimenez, T. K. Tedesco, D.P. Raggio, C.M. Pannuti, How researchers should select the best outcomes for randomised clinical trials in paediatric dentistry? *Int. J. Paediatr. Dent.* 31 (Suppl 1) (2020) 23–30.
- [9] C.M. Pannuti, D.J. Sendyk, Y.T.D. GraCas, S.L. Takai, V.P.A. SabOia, G.A. Romito, F.M. Mendes, Clinically relevant outcomes in dental clinical trials: challenges and proposals, *Braz. Oral. Res.* 34 (Suppl 2) (2020) e073.
- [10] B. Loomans, N. Opdam, A guide to managing tooth wear: the Radboud philosophy, *Br. Dent. J.* 224 (2018) 348–356.
- [11] L.A.M.J. Crins, N.J.M. Opdam, C.M. Kreulen, E.M. Bronkhorst, B.A.M. M. Sterenberg, M.C.D.N.J.M. Huysmans, B.A.C. Loomans, Randomized controlled trial on the performance of direct and indirect composite restorations in patients with severe tooth wear, *Dent. Mater.* 37 (2021) 1645–1654.
- [12] S.I. Kalaykova, B.A.M.M. Sterenberg, B.A.C. Loomans, M.C.D.N.J.M. Huysmans, Impact of restorative treatment of tooth wear upon masticatory performance, *J. Dent.* 88 (2019) 103159, <https://doi.org/10.1016/j.jdent.2019.06.006>.
- [13] R.M.F. van Sambeek, R. de Vos, L.A.M.J. Crins, E. Bronkhorst, S.B. Mehta, T. Pereira-Cenci, B.A.C. Loomans, Perception of oral health related quality of life and orofacial aesthetics following restorative treatment of tooth wear: a five-year follow-up, *J. Dent.* 136 (2023) 104626, <https://doi.org/10.1016/j.jdent.2023.104626>.
- [14] F.M. Mendes, L.R. Pontes, T. Gimenez, J.S. Lara, L.B. de Camargo, E. Michel-Crosato, C.M. Pannuti, D.P. Raggio, M.M. Braga, T.F. Novaes, C.C. Group, Impact of the radiographic examination on diagnosis and treatment decision of caries lesions in primary teeth—the Caries Detection in Children (CARDEC-01) trial: study protocol for a randomized controlled trial, *Trials* 17 (2016) 69.
- [15] B.L.P. Moro, C. Signori, R.D. Freitas, L.R.A. Pontes, T.L. Lenzi, T.K. Tedesco, D. P. Raggio, M.M. Braga, K.R. Ekstrand, M.S. Cenci, F.M. Mendes, C.c. group, C.I.A.c. g. Ca, The effect of two clinical criteria in the assessment of caries lesions around restorations in children (CARDEC-03): study protocol for a diagnostic randomized clinical trial, *F1000Res.* 9 (2020) 650.
- [16] C. Signori, B.L.P. Moro, J.L.S. Uehara, V.H.D. Romero, E.F. de Oliveira, M. M. Braga, F.M. Mendes, M.S. Cenci, C.I.A.C.G. Ca, Study protocol for a diagnostic randomized clinical trial to evaluate the effect of the use of two clinical criteria in the assessment of caries lesions around restorations in adults: the Caries Cognition and Identification in Adults (CaCIA) trial, *BMC. Oral. Health* 20 (1) (2020) 317.
- [17] M. Laske, Restoration longevity: practice based research in the Netherlands, *Ned. Tijdschr Tandheelkd* 126 (2019) 457–460.
- [18] M. Laske, N.J. Opdam, E.M. Bronkhorst, J.C. Braspenning, M.C. Huysmans, Longevity of direct restorations in Dutch dental practices. Descriptive study out of a practice based research network, *J. Dent.* 46 (2016) 12–17.
- [19] M. Laske, N.J.M. Opdam, E.M. Bronkhorst, J.C.C. Braspenning, M. Huysmans, Risk factors for dental restoration survival: a practice-based study, *J. Dent. Res.* 98 (4) (2019) 414–422.
- [20] C. Signori, M. Laske, F.M. Mendes, M. Huysmans, M.S. Cenci, N.J.M. Opdam, Decision-making of general practitioners on interventions at restorations based on bitewing radiographs, *J. Dent.* 76 (2018) 109–116.
- [21] F.F. Demarco, M.S. Cenci, A.F. Montagner, V.P. de Lima, M.B. Correa, R.R. Moraes, N.J.M. Opdam, Longevity of composite restorations is definitely not only about materials, *Dent. Mater.* 39 (1) (2023) 1–12.
- [22] N.J.M. Opdam, K. Collares, R. Hickel, S.C. Bayne, B.A. Loomans, M.S. Cenci, C. D. Lynch, M.B. Correa, F. Demarco, F. Schwendicke, N.H.F. Wilson, Clinical studies in restorative dentistry: new directions and new demands, *Dent. Mater.* 34 (1) (2018) 1–12.
- [23] R. Brignardello-Petersen, A. Carrasco-Labra, M. Glick, G.H. Guyatt, A. Azarpazhooh, A practical approach to evidence-based dentistry: understanding and applying the principles of EBD, *J. Am. Dent. Assoc.* 145 (11) (2014) 1105–1107.
- [24] M.F. Perazzo, J.M. Serra-Negra, R.T. Firmino, I.A. Pordeus, J.P.A. Martins, S. M. Paiva, Patient-centered assessments: how can they be used in dental clinical trials? *Braz. Oral. Res.* 34 (Suppl 2) (2020) e075.
- [25] R.N. Riordain, M. Glick, S. Mashhadani, K. Aravamudan, J. Barrow, D. Cole, J. R. Crall, J.E. Gallagher, J. Gibson, S. Hegde, R. Kaberry, E. Kalendarian, A. Karki, R. K. Celeste, S. Listl, S.N. Myers, R. Niederman, T. Severin, M.W. Smith, W. M. Thomson, G. Tsakos, M. Vujcic, R.G. Watt, S. Whittaker, D.M. Williams, Developing a standard set of patient-centred outcomes for adult oral health - an international, cross-disciplinary consensus, *Int. Dent. J.* 71 (1) (2021) 40–52.
- [26] F.F. Demarco, M.B. Correa, M.S. Cenci, F.J.T. Burke, N.J.M. Opdam, E.S.A.L. Faria, Practice based research in dentistry: an alternative to deal with clinical questions, *Braz. Oral. Res.* 34 (Suppl 2) (2020) e071.
- [27] G.H. Gilbert, O.D. Williams, J.J. Korelitz, J.L. Fellows, V.V. Gordan, S.K. Makhija, C. Meyerowitz, T.W. Oates, D.B. Rindal, P.L. Benjamin, P.J. Foy, P.C.G. National Dental, Purpose, structure, and function of the United States National dental practice-based research network, *J. Dent.* 41 (11) (2013) 1051–1059.
- [28] L. Besancon, N. Peiffer-Smadja, C. Segalas, H. Jiang, P. Masuzzo, C. Smout, E. Billy, M. Deforet, C. Leyrat, Open science saves lives: lessons from the COVID-19 pandemic, *BMC. Med. Res. Methodol.* 21 (1) (2021) 117.
- [29] K.D. Cobey, S. Hausteijn, J. Brehaut, U. Dirnagl, D.L. Franzen, L.G. Hemkens, J. Presseau, N. Riedel, D. Strech, J.P. Alperin, R. Costas, E.S. Sena, T. van Leeuwen, C.L. Ardern, I.O.L. Bacellar, N. Camack, M. Britto Correa, R. Buccione, M.S. Cenci, D.A. Fergusson, C. Gould van Praag, M.M. Hoffman, R. Moraes Bielemann, U. Moschini, M. Paschetta, V. Pasquale, V.E. Rac, D. Roskams-Edris, H.M. Schatzl, J.A. Stratton, D. Moher, Community consensus on core open science practices to monitor in biomedicine, *PLoS Biol.* 21 (1) (2023) e3001949.
- [30] A. Ismail, T. Al-Zoubi, I. El Naqa, H. Saeed, The role of artificial intelligence in hastening time to recruitment in clinical trials, *BJR. Open* 5 (1) (2023) 20220023.
- [31] K.A. Thomas, L. Kidzinski, Artificial intelligence can improve patients' experience in decentralized clinical trials, *Nat. Med.* 28 (12) (2022) 2462–2463.
- [32] L.T. Reyes, J.K. Knorst, F.R. Ortiz, T.M. Ardenghi, Scope and challenges of machine learning-based diagnosis and prognosis in clinical dentistry: a literature review, *J. Clin. Transl. Res.* 7 (4) (2021) 523–539.
- [33] S.J. Mooney, A.P. Keil, D.J. Westreich, Thirteen Questions About Using Machine Learning in Causal Research (You Won't Believe the Answer to Number 10!), *Am. J. Epidemiol.* 190 (8) (2021) 1476–1482.
- [34] H. Mohammad-Rahimi, S.R. Motamedian, M.H. Rohban, J. Krois, S.E. Uribe, E. Mahmoudinia, R. Rokhshad, M. Nadimi, F. Schwendicke, Deep learning for caries detection: a systematic review, *J. Dent.* 122 (2022) 104115.
- [35] A. Thurzo, W. Urbanova, B. Novak, L. Czako, T. Siebert, P. Stano, S. Marekova, G. Fountoulaki, H. Kosnacova, I. Varga, Where is the artificial intelligence applied in dentistry? Systematic review and literature analysis, *Healthcare (Basel)* 10 (7) (2022) 1269.