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CLINICAL ORAL IMPLANTS RESEARCH

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Proceedings of the Seventh ITI Consensus Conference

International Team for Implantology



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Volume 34, Supplement 26, September 2023

Proceedings of the Seventh ITI Consensus Conference

Guest Editors: D Wismeijer, I Sailer, C Stilwell



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EDITORIAL

Preface

The International Team for Implantology (ITI) is a non-profit association of professionals in implant dentistry. The mission of the ITI is "to serve the dental profession by providing a growing global network for life-long learning in implant dentistry through comprehensive quality education and innovative research for the benefit of the patient." Key to the ITI is fostering learning, discussion, and exchange.

Every 5 years, the ITI conducts a consensus conference to review the current state of evidence in areas of topical interest in dental implantology. The 7th ITI Consensus Conference was held in Lisbon from May 2, 2023 to May 4, 2023. The Consensus Conference Steering Committee selected the topics under discussion by approaching various editors of scientific journals and asking them which topics would be of interest to the field in the coming years. Based on their input as well as ideas proposed by the members of the Steering Committee, the following five topics were selected: surgical techniques, technology, oral medicine, patient benefits, and implant placement and loading protocols. The Steering Committee approached experienced researchers on these topics to form a Supervisory Group that, in turn, selected the leaders of five groups, each of which focused on one of the five topics listed above.

Thirteen main authors were selected by the Steering Committee and Supervisory Group and systematic reviews were prepared by these authors and their teams (62 authors and co-authors in total) in preparation for the conference (Table 1). The manuscripts were submitted to the Clinical Oral Implants Research journal months before the Consensus Conference and went through a peer review process prior to the meeting in Lisbon to assure the quality of the papers.

During the 3 days of the Consensus Conference, based on the 13 review papers, five groups made up of 82 invited participants prepared Consensus Statements, Clinical Recommendations, and Recommendations for Future Research. They were asked to formulate their Clinical Recommendations based on questions asked by clinicians. The groups were also asked to deliver Patient Perspectives on their topics, hence, to provide evidence-based or expert consensus-based answers formulated in patient-friendly language to questions that could be expected from patients on the respective topics. On May 4 in the afternoon, an additional group of 45 participants was invited to be part of the discussion on the patient-focused questions related to the clinical recommendations made as part of the Patient Perspectives to ensure that there was sufficient input from clinicians.

For the 7th ITI Consensus Conference, the ITI took a novel approach to informing and engaging the broader implant dentistry community on the development and execution of the Conference and the publication of the proceedings. To cover this, five members of the international Young ITI were assigned the role of Consensus Conference Reporter, and each allocated to a specific group.

The Reporters' task was to create engaging content (articles, interviews, videos, etc.) in three phases: run-up to the Conference, the Conference itself, and post-Conference until the publication of the findings. This content focused on general topics such as the reason behind and the value of consensus conferences, benefits to daily practice, specific insights into the processes and procedures of conducting systematic reviews as well as the work toward the Conference itself and publication of the findings. The aim was to inform and enthuse a broad dental audience beyond the academic community about the ITI Consensus Conference and thereby to increase the reach and impact of the findings. The content is available on the ITI Blog (blog.iti.org) and the ITI's social media channels.

New to the organization of this Consensus Conference was the effort made to calculate the carbon footprint involved. While consensus conferences play an important role in providing dental professionals, policymakers, and the public with current, evidence-based information, scientists as a group should also serve as a role model. We felt we should analyze our behavior and show how we take the environment into consideration when traveling to scientific conferences or generating new scientific information. Calculating the carbon footprint of a conference is not easy as there are many aspects to consider, but, using three different online tools focusing primarily on air travel and hotel emissions, we estimated a ballpark figure of 485 tons of CO_2 emissions generated for the 7th ITI Consensus Conference.

Going forward, the ITI suggests that organizations active in the field of implant dentistry consider joining forces to conduct consensus conferences. This will help to reduce the overall carbon footprint of these scientific meetings. It will also bring greater clarity to the analysis of current scientific information for the benefit of the implant community and our patients.

ACKNOWLEDGMENTS

We would like to thank the members of the Steering Committee: D. Wismeijer (Chair), S. Chen, C. Stilwell, K. Benthaus, M. Mallaun, and P. Werder for the way the 7th ITI Consensus Conference was designed

Proceedings of the 7th ITI Consensus Conference.

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TABLE 1 The 13 systematic review papers that formed the basis for discussion during the 7th ITI Consensus Conference and the working groups.

	Authors	Title of review	Working group
Group 1: Surgical techniques Group leaders: T. Aghaloo, S. Jensen			
Paper 1	A. Monje, A. Roccuzzo, D. Buser, H.-L. Wang	Significance of buccal bone wall thickness on the fate of peri-implant hard and soft tissues: A systematic review	T. Aghaloo, K. Bertl, D. Buser, V. Chappuis, S. S. Jensen, R. E. Jung, A. Monje, A. Pispero, A. Roccuzzo, S. Shahdad, L. de Stavola, M. Stefanini, L. Tavelli, H.-L. Wang, G. Zucchelli
Paper 2	M. Stefanini, S. Barootchi, M. Sangiorgi, A. Pispero, M. G. Grusovin, L. Mancini, G. Zucchelli, L. Tavelli	Do soft tissue augmentation techniques provide stable and favorable peri-implant conditions in the medium and long term? A systematic review	
Group 2: Technology Group leaders: W. Derksen, T. Joda			
Paper 3	A. Ioannidis, K. Pala, F. Strauss, J. Hjerppe, R. E. Jung, T. Joda	Additively and subtractively manufactured implant-supported fixed dental prostheses: A systematic review	J. Chantler, W. Derksen, V. Fehmer, G. O. Gallucci, P. C. Gierthmühlen, A. Ioannidis, T. Joda, D. Karasan, A. Lanis, K. Pala, B. E. Pjetursson, M. Roccuzzo, I. Sailer, F. J. Strauss, T. C. Sun, S. Wolfart, N. U. Zitzmann
Paper 4	J. GM Chantler, C. DJ Evans, N. Zitzmann, W. Derksen	Clinical performance of single implant prostheses restored using titanium base abutments: A systematic review and meta-analysis	
Paper 5	B. E. Pjetursson, I. Sailer, E. Merino-Hilguero, B. C. Spiess, F. Burkhardt, D. Karasan	Systematic review evaluating the influence of the prosthetic material and prosthetic design on the clinical outcomes of implant-supported multi-unit fixed dental prosthesis in the posterior area	
Group 3: Oral medicine Group leaders: B. Al-Nawas, F. Lambert			
Paper 6	S. Roehling, M. Gahlert, M. Bacevic, H. Woelfler, I. Laleman	Clinical and radiographic outcomes of zirconia dental implants—A systematic review and meta-analysis	B. Al-Nawas, S. W. M. Andersen, M. M. Bornstein, M. Gahlert, A. Jokstad, J. Jung, Y.-D. Kwon, I. Laleman, F. Lambert, G. Oteri, S. Roehling, E. Schiegnitz, Y. Takeda H. Terheyden
Paper 7	I. Laleman, F. Lambert, M. Gahlert, M. Bacevic, H. Woelfler, S. Roehling	The effect of different abutment materials on peri-implant tissues—A systematic review and meta-analysis	
Paper 8	J. Jung, J.-I. Ryu, G.-J. Shim, Y.-D. Kwon	Effect of agents affecting bone homeostasis on short- and long-term implant failure	
Group 4: Patient benefits Group leaders: M. Araujo, M. Schimmel			
Paper 9	S. Abou-Ayash, M. Fonseca, S. Pieralli, D. R. Reissmann	Treatment effect of implant-supported fixed complete dentures and implant overdentures on patient-reported outcomes: A systematic review and meta-analysis	S. Abou-Ayash, M. Araujo, R. Buser, A. B. De Souza, S. Ebenezer, M. Fonseca, L. J. Heitz-Mayfield, L. Paterno Holtzman, P. Kamnoedboon, R. Levine, S. Maniewicz, F. Matarazzo, N. Mattheos, G. McKenna, P. Papaspyridakos, M. Schimmel, M. Srinivasan, C. Stilwell, H.-P. Weber
Paper 10	M. Srinivasan, P. Kamnoedboon, L. Angst, F. Müller	Oral function in completely edentulous patients rehabilitated with implant-supported dental prostheses: A systematic review and meta-analysis	
Paper 11	A. B. De Souza, P. Papaspyridakos, H.-P. Weber, K. Vazouras, F. Matarazzo	Effect of dental implant therapy on the preservation of orofacial tissues: A systematic review and meta-analysis	
Group 5: Implant placement and loading protocols Group leaders: D. Morton, D. Wismeijer			
Paper 12	J. G. Wittneben, P. Molinero-Mourelle, A. Hamilton, M. Alnasser, B. Obermaier, D. Morton, G. O. Gallucci, D. Wismeijer	Clinical performance of immediately placed and immediately loaded single implants in the esthetic zone: A systematic review and meta-analysis	P. Casentini, S. Chen, L. Gonzaga, A. Hamilton, R. Lazarin, W. Martin, P. Molinero-Mourelle, D. Morton, B. Obermaier, W. D. Polido, A. Tahmaseb, D. Thoma, D. Wismeijer, J. G. Wittneben, A. Zembic
Paper 13	A. Hamilton, L. Gonzaga, K. Amorim, J. G. Wittneben, L. Martig, D. Morton, W. Martin, G. O. Gallucci, D. Wismeijer	Selection criteria for immediate implant placement and immediate loading for single tooth replacement in the maxillary esthetic zone: A systematic review and meta-analysis	

and the research topics selected. We also thank the members of the Supervisory Group for their input when choosing the authors and leaders of the working groups: D. Wismeijer (Chair), I. Sailer, L. Heitz-Mayfield, M. Bornstein, and R. Jung. Special thanks go to the leaders of the working groups: T. Aghaloo, S. Jensen, T. Joda, W. Derksen, B. Al-Nawas, F. Lambert, M. Schimmel, M. Araujo, D. Morton, and D. Wismeijer for their efforts in guiding the authors in the preparation of the review papers and for leading the subsequent discussion in their respective working groups. Our thanks also go to the reporters for their input toward making the 7th ITI Consensus Conference process more understandable for those not directly involved with the proceedings: Matt Brennand Roper, Teresa Chanting Sun, Rafael Lazarin, Lucrezia Paterno Holtzman, and Yukihiro Takeda. Our thanks also go to consultants: Asbjørn Jokstad, Mario Roccuzzo, Giovanni

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CONFLICT OF INTEREST STATEMENT

The authors declare that they sit on the Board or the Education Committee of the International Team for Implantology (ITI) and were all involved in the organization of the Consensus Conference, which does not lead to any conflict of interest regarding the content of this article or the content of the conference.

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REVIEW ARTICLE

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Influence of buccal bone wall thickness on the peri-implant hard and soft tissue dimensional changes: A systematic review

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Abstract

Background: The significance on the association between the peri-implant buccolingual dimension (BLD) at the stage of implant placement and the occurrence of biological and esthetic complications is yet unknown.

Material and methods: Systematic screening of electronic sources was carried out to identify clinical and preclinical studies reporting on the baseline BLD and/or buccal bone thickness (BBT) values. A secondary objective was to assess the effect of simultaneous grafting at sites with deficient or no buccal bone wall (BBW) at baseline. The primary outcome variables were BBT, BLD, and buccal vertical bone loss (VBL) at re-evaluation. Moreover, radiographic, clinical, and patient-reported outcome measures (PROMs) were evaluated.

Results: Overall, 12 clinical and four preclinical studies met the inclusion criteria. Inconsistencies were found in defining the critical BBT across the clinical and preclinical data evaluated. The clinical evidence demonstrated that during healing, dimensional changes occur in the alveolar bone and in the BBW that may compromise the integrity of the peri-implant bone, leading to VBL and mucosal recession (MR), particularly in scenarios exhibiting a thin BBW. The preclinical evidence validated the fact that implants placed in the presence of a thin BBW, are more prone to exhibit major dimensional changes and VBL. Moreover, the clinical data supported that, in scenarios where dehiscence-type defects occur and are left for spontaneous healing, greater VBL and MR together with the occurrence of biologic complications are expected. Furthermore, the augmentation of dehiscence-type defects is associated with hard and soft tissue stability. PROMs were not reported.

Conclusions: Dimensional changes occur as result of implant placement in healed ridges that may lead to instability of the peri-implant hard and soft tissues. Sites presenting a thin BBW are more prone to exhibit major changes that may compromise the integrity of the buccal bone and may lead to biologic and esthetic complications.

KEYWORDS
biomaterials, bone implant interactions, bone regeneration, guided tissue regeneration, peri-implantitis, peri-implant disease

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1 | INTRODUCTION

Implant failures due to biological complications or unsatisfactory esthetic outcomes very often originate from implant malpositioning or errors during implant surgery (Monje et al., 2016). Interestingly, peri-implantitis and esthetic failures are more commonly noted in the buccal aspects (Monje & Nart, 2022). Implants placed in healed sites must have an adequate buccal bone wall thickness (BBT) to ensure that the implant is circumferentially embedded in vital bone at the completion of bone healing. Once initial bone healing and remodeling have taken place, the entire micro-rough implant surface must be osseointegrated and circumferentially covered by vital bone (Spray et al., 2000).

It is known that the outer layer of the buccal bone wall (BBW) is predominantly composed of cortical bone, which receives most of its vascular blood supply from the outside (the periosteum) and from the inside (the endosteum; Roush et al., 1989). The central portion of the alveolar ridge is characterized by cancellous bone with a good blood supply. When a flap is raised to gain access for implant placement, the blood supply from the periosteum is interrupted. In addition, by inserting the implant into the prepared implant bed, the endosteal blood supply is interrupted as well, when the buccal bone wall is mainly comprised of cortical bone. The interruption of the blood supply from the outside as well as from the inside results in necrosis of the buccal bone. This process is called "avascular necrosis" (Mankin, 1992) and leads to vertical bone loss (VBL), most often on the buccal aspect of the implant (Monje et al., 2019). This contributes to exposure of the micro-rough implant surface into the peri-implant sulcus, and consequently into the oral cavity—facilitating the potential access of bacteria and the perpetuation of pathological conditions (Roux & Orcel, 2000), as well as mucosal recession that leads to an unpleasing esthetic appearance (Monje et al., 2019). In consequence, the exposed micro-rough implant surface becomes a significant risk factor for biological complications as it can be set as the niche for pathogenic bacteria.

It has been suggested that dehiscence-like bone defects resulting from previous unsuccessful regenerative procedures (Schwarz et al., 2012) or during implant placement in pristine alveolar bone (Jung et al., 2017) may lead to instability of the soft and hard peri-implant tissues, resulting in a greater risk of developing biological complications (Monje et al., 2016). In fact, the presence of a thin BBW, often conditioned by the implant position (Grunder et al., 2005), has been shown to be related to a greater risk of peri-implant bone resorption during initial healing—resulting in a greater susceptibility to develop unfavorable peri-implant conditions (Monje et al., 2019), including mucosal recession (Farronato et al., 2020), peri-implantitis (Monje et al., 2019) and eventually implant failure (Spray et al., 2000). In contrast, one clinical study reported that alveolar bone dimensions did not show a negative impact on clinical and radiographic outcomes at 3-year follow-up (Temmerman et al., 2015). Considering the above, the aim of the present systematic review was to shed light on the influence of critical BBT and the overall dimensions of alveolar bone upon soft and hard tissue stability and to thus assess the need for simultaneous bone augmentation procedures according to the residual BBW. Findings derived from the present systematic review may assist in providing a clinical practice in implant dentistry more predictable in preventing esthetic and biological complications.

2 | MATERIAL AND METHODS

The study protocol was registered and received identification number CRD42021288604 in the PROSPERO International Prospective Register of Systematic Reviews, hosted by the National Institute for Health Research, University of York, Centre for Reviews and Dissemination.

Focused question 1: What is the peri-implant critical BBT that may compromise bone integration at the buccal aspect of dental implants placed in healed ridges?

2.1 | PECO question 1 for clinical research

- Patient: Partially or completely edentulous patients
- Exposure: Dental implants placed in native healed ridges exhibiting thin BBW or lack of BBW
- Comparison:
  - $Comparsion_1$: Thick BBW
  - $Comparison_2$: Presence of BBW
- Outcome:
  - $Outcome_{primary}$: VBL
  - $Outcome_{secondary\ (1)}$: BBT, BLD changes, and
  - $Outcome_{secondary\ (2)}$: Peri-implant proximal bone level
  - $Outcome_{secondary\ (3)}$: Peri-implant clinical parameters, clinical health and esthetics
  - $Outcome_{secondary\ (4)}$: Patient-reported outcome measures (PROMs)

Focused question 2: What is the effect in terms of dimensional, clinical, and radiographic outcomes of simultaneous bone augmentation in scenarios below the critical BBT in healed ridges?

2.2 | PICO question 2 for clinical research

- Patient: Partially or completely edentulous patients
- Intervention: Dental implants placed in native healed ridges exhibiting thin BBW or lack of BBW
- Comparison:
  - $Comparison_3$: Augmented BBW
- Outcome:
- $Outcome_{primary}$: VBL
- $Outcome_{secondary\ (1)}$: BBT, BLD changes, and
- $Outcome_{secondary\ (2)}$: Peri-implant proximal bone level
- $Outcome_{secondary\ (3)}$: Peri-implant clinical parameters, clinical health and esthetics

- Outcome$_{\text{secondary (4)}}$: Patient-reported outcome measures (PROMs)

2.3 | Eligibility criteria

Inclusion and exclusion criteria are listed in Table 1. It should be noted that whenever a study included implants placed immediately in fresh extraction sockets and healed sockets, only data from the latter were retrieved and included in the analysis.

2.4 | The preferred reporting items for systematic reviews and meta-analyses (PRISMA)

For describing and summarizing the results of our review, use was made of the 27-item PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement (Page et al., 2021).

2.5 | Search strategy

Two independent reviewers (AM and AR) performed the manual search and read the title and abstract of the entries obtained from the literature search. After completing the screening process, both reviewers assessed the full-text version of potentially eligible studies and established a final article selection. Disagreements between the reviewers were resolved by open discussion. If no consensus could be reached, a third author (HLW) was consulted. Any missing information that could contribute to the systematic review was requested from the corresponding author(s) via e-mail.

2.6 | Information sources

An electronic search of three databases (MEDLINE via PubMed, the Cochrane Library of the Cochrane Collaboration, and the New York Academy of Medicine Grey Literature) was conducted for studies published up to November 2021 (included), without language or year restrictions. The search strategy combined MeSH terms and text words with Boolean operators (OR, AND) filtered by "humans" and "animals" and sorted according to the most recent publications. For the PubMed database, the search terms applied were the following: (dental implant[MeSH Terms]) OR (abutment, dental[MeSH Terms])) OR (dental implantation, osseointegrated[MeSH Terms])) AND (implantation, osseointegrated dental[MeSH Terms])) OR (alveolar bone dimension[Title/Abstract])) OR (buccal bone[Title/Abstract])) OR (buccal bone thickness[Title/Abstract])) OR (critical buccal bone[Title/Abstract])) OR (facial bone[Title/Abstract])) AND (facial bone thickness[Title/Abstract])) AND (bone regeneration[MeSH Terms])) OR (bone augmentation[Title/Abstract])) OR (guided bone regeneration[Title/Abstract])) OR (bone reconstruction[Title/Abstract])) AND (bone dehiscence[Title/Abstract])) OR (alveolar bone loss[MeSH Terms])) OR (buccal bone level[Title/Abstract])) OR (facial bone level[Title/Abstract])) OR (peri-implant condition[Title/Abstract])) OR (peri-implant health[Title/Abstract])) OR (peri-implantitis[Title/Abstract]). In turn, the Cochrane database and the Grey Literature Database were screened for unpublished papers in the New York Academy of Medicine in accordance with the AMSTAR checklist. The list of references of the included studies and related review articles was further screened to check for additional relevant studies.

2.7 | Data extraction

The following data were extracted and recorded in duplicate by two independent reviewers (AM and AR): (1) citation and year of publication; (2) experimental group; (3) sample size; (4) BBT and/or BLD at baseline and at re-assessment; (5) method of assessment; (6) timing of assessment; (7) clinical and radiographic outcomes and; (8) take-home message.

2.8 | Risk of bias in individual studies

Methodological quality of the included observational studies (i.e., case series, prospective studies) was assessed based on the Newcastle-Ottawa Quality Assessment Scale for Cohort studies (Wells et al., 2014) while for RCTs, the risk-of-bias 2.0. tool was adopted (Sterne et al., 2019). With respect to animal studies, the SYRCLE's risk-of-bias tool was used (Hooijmans et al., 2014).

TABLE 1 Eligibility criteria for the systematic review.

Inclusion criteria	Exclusion criteria
Clinical single- or multiple-arm trials (CCT, RCT, CS)	Case reports (<10 cases)
Preclinical trials	In vitro research
Clinical, radiographic, histological and/or volumetric examination	Nonvalidated tools for examination
Baseline data on the buccal and/or alveolar bone dimension	Lack of data on the buccal/alveolar bone dimension
Baseline and follow-up data	Lack of baseline and/or follow-up data
Implants placed in healed ridges	Implants placed in fresh extraction sockets
Systemically healthy patients	Patients with disease conditions and/or heavy smokers (≥10 cigarettes/day)

3 | RESULTS

The PRISMA flowchart for literature selection is depicted in Figure 1. In summary, 1700 records were identified after duplicates were removed. Ninety of these records were assessed for full text. One more article was identified screening the references from included papers. Overall, 16 were included in the qualitative synthesis. Of these, 12 were human studies (Barone et al., 2015; Cardaropoli et al., 2006; Covani et al., 2004; Farronato et al., 2020; Jung et al., 2017; Li Manni et al., 2020; Marconcini et al., 2018; Nohra et al., 2018; Oda et al., 2021; Schwarz et al., 2012; Spray et al., 2000; Temmerman et al., 2015), while four were preclinical studies (Baffone et al., 2015; Bengazi et al., 2014; Monje et al., 2019; Vignoletti et al., 2019). The most frequent reason for exclusion based on the full-text evaluation was no baseline dimensional data or missing information (n = 41; Table 2). The heterogeneity of the sample across the included studies precluded the conduction of meta-analyses.

3.1 | Study and sample characteristics

3.1.1 | Clinical studies

The dominant study design was the prospective cohort (PC; Cardaropoli et al., 2006; Covani et al., 2004; Farronato et al., 2020; Nohra et al., 2018; Schwarz et al., 2012; Spray et al., 2000; Temmerman et al., 2015), followed by the randomized clinical trial (RCT; Barone et al., 2015; Jung et al., 2017; Li Manni et al., 2020; Marconcini et al., 2018; Table 3). Only one retrospective cohort (RC) study (Oda et al., 2021) was included. Overall, 3237 sites (implants) were included and evaluated. The vast majority of the studies tested dimensional changes under spontaneous healing, while two studies (Jung et al., 2017; Schwarz et al., 2012) further tested simultaneous guided bone regeneration (GBR) on deficient ridges. Moreover, two studies (Barone et al., 2015; Marconcini et al., 2018) compared alveolar bone changes according to the

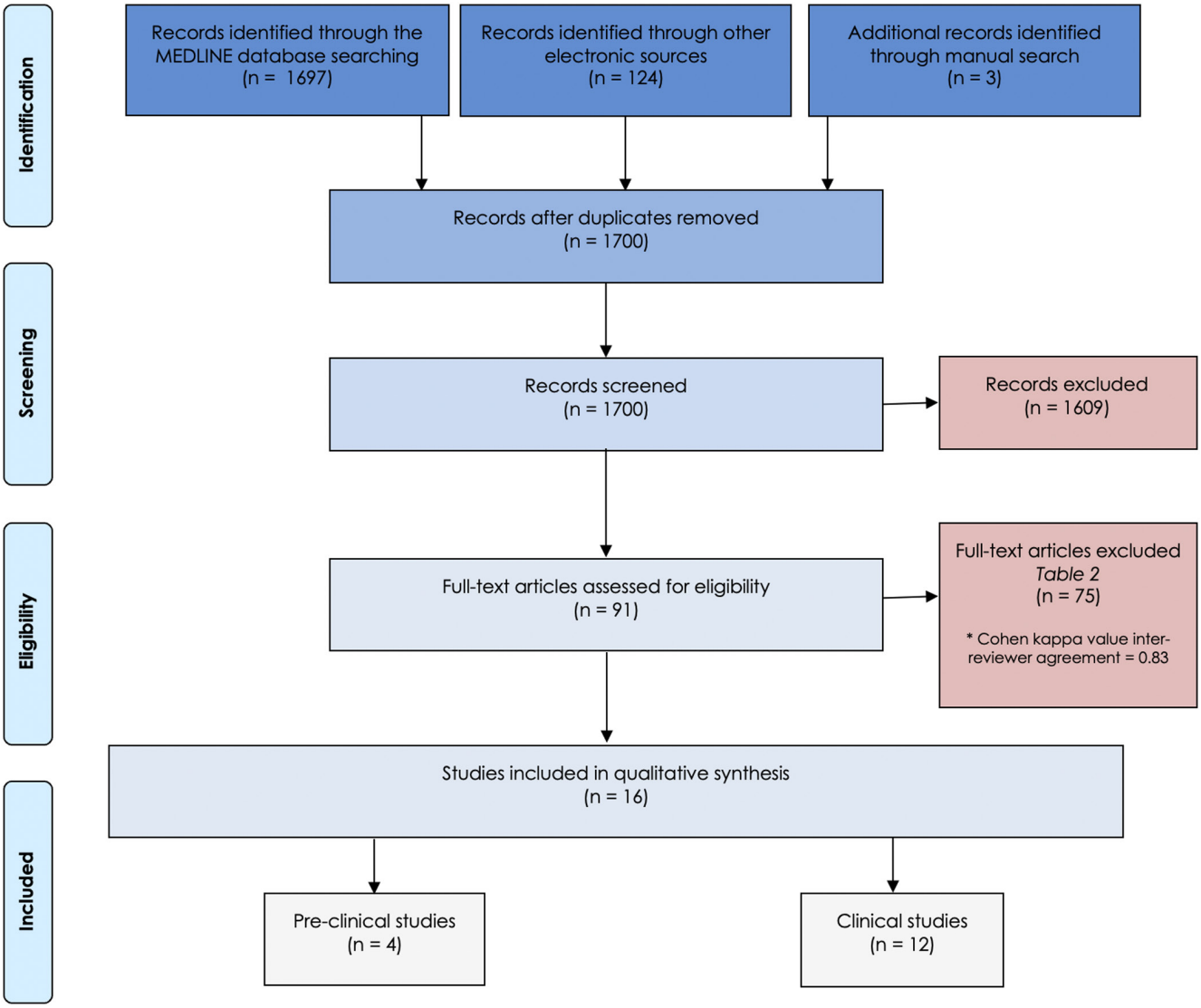


FIGURE 1 Flowchart of the systematic review

insertion torque recorded during implant placement. One study (Nohra et al., 2018) explored the effect of implant torque and BBT on bone remodeling. Li Manni et al. (2020) evaluated two different implant macro-designs. All the articles except one provided the BBT as baseline parameter. Covani et al. (2004) reported the baseline BLD. One PC study (Temmerman et al., 2015) grafted only when dehiscence or fenestrations were noted. Caliper, periodontal probe, and cone beam computed tomography (CBCT) were the methods used to assess the alveolar bone dimension at baseline. Seven studies assessed the radiographic outcome (Barone et al., 2015; Cardaropoli et al., 2006; Jung et al., 2017; Li Manni et al., 2020; Marconcini et al., 2018; Nohra et al., 2018; Temmerman et al., 2015)—5 of them reporting by means of periapical radiographs (Barone et al., 2016; Cardaropoli et al., 2006; Jung et al., 2017; Marconcini et al., 2018; Temmerman et al., 2015) and two using CBCT (Li Manni et al., 2020; Nohra et al., 2018). Furthermore, five studies reported clinical outcomes at latest follow-up assessment (Barone et al., 2015; Farronato et al., 2020; Jung et al., 2017; Marconcini et al., 2018; Schwarz et al., 2012). The length of study periods ranged from 4 to 72 months. Only one study described patient-reported outcomes (PROMs; Li Manni et al., 2020).

3.1.2 | Preclinical studies

The preclinical model testing the influence of the BBT on the fate of the peri-implant hard and soft tissues was the canine model in all the studies included (Table 4). Overall, 152 sites (implants) were included and evaluated. Spontaneous healing was the most reported intervention (Baffone et al., 2015; Bengazi et al., 2014; Monje et al., 2019; Vignoletti et al., 2019), while one study further assessed experimental peri-implantitis using a ligature-induced model (Monje et al., 2019). Baffone et al. (2015) evaluated the influence of ridge width and abutment width upon the alveolar dimensional changes. Bengazi et al. (2014) analyzed the influence of the anatomical site (molar/premolar) and the presence/absence of peri-implant keratinized mucosa upon the alveolar changes. Monje et al. (2019) in turn evaluated the influence of BBT (≥1.5 mm vs.

TABLE 2 Excluded articles and reasons for exclusion.

Reason for exclusion	Reference
Simultaneous grafting procedure with no control group	Fenner et al. (2009), Fienitz et al. (2012) Hur et al. (2017), Moses et al. (2005), Nemcovsky and Artzi (2002), Qahash et al. (2008)
Early placement protocol with simultaneous bone regeneration	Nir-Hadar et al. (1998), Rodriguez-Ortiz et al. (2021)
Grafted sockets with no baseline dimension	Crespi et al. (2021), Duong et al. (2020)
Immediate implant placement protocol	Barone et al. (2015), Chen et al. (2007), Novaes Jr. et al. (2012), Penarrocha-Oltra et al. (2012), Suaid et al. (2014)
Implant stability quotient with no dimensional data	Bozkaya et al. (2021)
No baseline dimensional data/missing information	Abrahamsson et al. (2004, 1999, 1996, 2014), Baffone et al. (2012, 2011), Becker et al. (2007, 2017), Bratu et al. (2009), Carcuac et al. (2020), Carmagnola et al. (1999), Carmo Filho et al. (2019), Cesaretti et al. (2015), Chacun et al. (2021), Checchi et al. (2017), Cooper et al. (2007, 2015), Di Raimondo et al. (2021), Finelle et al. (2015), Gehrke et al. (2018), Jemt and Lekholm (2003, 2005), Jonker et al. (2020), Kim et al. (2016), Koutouzis et al. (2013), Lee et al. (2016, 2019), Noelken et al. (2014), Nowzari et al. (2006), Oeschger et al. (2020), Palombo et al. (2021), Patil et al. (2020), Raes et al. (2018), Sanz-Martin et al. (2017), Schropp et al. (2015), Schwarz et al. (2007, 2016), Souza et al. (2018), Thoma et al. (2019), van Eekeren et al. (2017), Vera et al. (2012), Yi et al. (2017)
Implant removal procedures	Pons et al. (2021)
Survey analysis	Fiorellini et al. (2020)
Only descriptive data on dimensional features	Glibert et al. (2018)
Retracted article	Calvo-Guirado et al. (2016)
Ridge expansion procedures	Beolchini et al. (2015), Scipioni et al. (1997)
Outside scope	da Silva Pereira et al. (2000), Deporter et al. (1988), Dursun et al. (2012), Lin et al. (2009), Onem et al. (2012), Sarment and Meraw (2008), Schliephake et al. (2003), Tal et al. (2001), Wadamoto et al. (1996)
Case report	Yoda et al. (2017)
Only cortical thickness provided	Tanaka et al. (2018)

<1.5 mm) upon VBL of the BBW. Vignoletti et al. (2019) analyzed spontaneous healing in two early stages (2 and 8 weeks of follow-up). Two studies (Baffone et al., 2015; Bengazi et al., 2014) used calipers to measure the alveolar dimension at baseline, one study (Monje et al., 2019) used a tracking system, and another study (Vignoletti et al., 2019) used a periodontal probe. All the studies performed histological analysis at latest follow-up. Spontaneous healing was assessed over a range of 2–12 weeks, though an arm of one study (Monje et al., 2019) evaluated the dimensional changes in an experimentally induced peri-implantitis model at 5 months follow-up.

3.2 | Influence of baseline BLD upon BLD changes

3.2.1 | Clinical studies

Only two studies (Covani et al., 2004; Temmerman et al., 2015) reported on the baseline alveolar bone dimension, and only one of them documented the alveolar bone changes. Covani et al. (2004) demonstrated that after an average of 4 months after implant placement, the BLD was reduced by about 3 mm. None of the studies reported on the BBT changes.

3.2.2 | Preclinical studies

Only one study assessed the BLD changes at baseline. Baffone et al. (2015) showed that the narrower the baseline BLD, the thinner the BBW after 3 months of follow-up. Thus, implants installed in regular-sized alveolar ridges exhibited greater horizontal bone loss when compared to implants installed in narrower ridges. However, lesser vertical buccal bony crestal resorption was recorded compared to implants installed in reduced alveolar ridges.

3.3 | Influence of baseline BLD upon clinical and radiographic outcomes

3.3.1 | Clinical studies

No clinical study reported on the integrity of the BBW or the BBT using three-dimensional radiographic techniques. Only one study examined the radiographic findings (Temmerman et al., 2015), documenting a mean radiographic peri-implant marginal bone loss of approximately 0.8 mm (mean from mesial and distal linear measurements) at 3 years of follow-up with implants placed in narrow alveolar crests (4.5 mm).

3.3.2 | Preclinical studies

None of the preclinical studies reported on the clinical or radiographic outcomes.

3.4 | Influence of baseline BLD upon biological complications

3.4.1 | Clinical studies

None of the clinical studies reported on BLD and its association with biological complications.

3.4.2 | Preclinical studies

None of the preclinical studies reported on the occurrence of biological complications.

3.5 | Influence of baseline BLD upon PROMs

No clinical study assessed the association between BLD and PROMs.

3.6 | Influence of BBT upon buccal bone changes

3.6.1 | Clinical studies

All the included studies except one (Covani et al., 2004) reported on baseline BBT. Mean BBW ranged from 0 mm (Jung et al., 2017; Schwarz et al., 2012; dehiscence-like defect) to 1.84 mm (Spray et al., 2000). Few studies presented ranges instead of mean values (Barone et al., 2016; Farronato et al., 2020; Marconcini et al., 2018; Nohra et al., 2018; Temmerman et al., 2015). Overall, seven studies provided data referring to VBL or BBT at re-assessment (Cardaropoli et al., 2006; Jung et al., 2017; Li Manni et al., 2020; Nohra et al., 2018; Oda et al., 2021; Schwarz et al., 2012; Spray et al., 2000). Dimensional changes were noted in BBW ranging from approximately 0.3 mm to approximately 1.75 mm. Spray et al. (2000) in a large sample size study, showed that whenever ≥1.8 mm of BBW was present during implant placement, no VBL occurred (which demonstrates the integrity of the BBW), while in thinner BBW (<1.8 mm) assessed in the implant placement stage, a rising tendency was evidenced toward greater VBL values. Nohra et al. (2018) showed that implants presenting BBT <2 mm at baseline exhibited 8x greater VBL (2.34 mm vs. 0.31 mm) when compared to implants displaying BBT ≥2 mm. One study (Jung et al., 2017) further demonstrated progressive VBL of 0.17 mm when a dehiscence-like defect of 3.2 mm was left for spontaneous nonassisted healing.

3.6.2 | Preclinical studies

Two studies (Bengazi et al., 2014; Vignoletti et al., 2019) reported on the mean baseline BBT, while one study (Monje et al., 2019) clustered this variable into ranges. Mean BBT ranged from

TABLE 3 Clinical studies included in the qualitative analysis.

Author (year)	Study design	Experimental group	Sample size (implants)	Buccal bone wall thickness in implant placement stage (mm)	Alveolar bucco-lingual dimension (mm)	Vertical bone defect (mm)	Buccal bone wall thickness at re-assessment (mm)	Alveolar bucco-lingual dimension at re-assessment (mm)	Vertical bone loss (mm)	Method of assessment
Barone et al. (2016)	RCT	Spontaneous healing after implant placement with bone with high (50–100 Ncm) insertion torque (50 Ncm)	58	<1	NR	NR	NR	NR	NR	NR
				≥1	NR	NR	NR	NR	NR	NR
		Spontaneous healing after implant placement with regular insertion torque (50 Ncm)	58	<1	NR	NR	NR	NR	NR	NR
				≥1	NR	NR	NR	NR	NR	NR
Cardaropoli et al. (2006)	PC	Spontaneous healing	11	1.2 (1)	NR	NR	0.8 (0.3)	NR	NR	Caliper
Covani et al. (2004)	PC	Spontaneous healing	15	NR	8.8 (2.3)	NR	NR	5.8 (1.3)	NR	Probe
Farronato et al. (2020)	PC	Spontaneous healing	23	<0.5	NR	NR	NR	NR	NR	Caliper
			29	>0.5 < 1.5	NR	NR	NR	NR	NR	
			26	≥1.5	NR	NR	NR	NR	NR	
Jung et al. (2017)	RCT	Spontaneous healing (<5 mm in height dehiscence defect)	12	0	NR	3.2 (1.1)	NR	NR	0.17 (1.7)	Probe
		Simultaneous guided bone regeneration (<5 mm in height dehiscence defect)	10	0	NR	3.6 (1.3)	NR	NR	(+) 1.7 (2.2)	
Li Manni et al. (2020)	RTC	Spontaneous healing with circular-neck implant	17	1.34 (1.08)	NR	NR	1.03 (1.05)	NR	NR	CBCT
		Spontaneous healing with triangular-neck implant	17	1.34 (0.74)	NR	NR	1.08 (0.72)	NR	NR	
Marconcini et al. (2018)	RCT	Spontaneous healing after implant placement with bone with high (50–100 Ncm) insertion torque (50 Ncm)	58	<1	NR	NR	NR	NR	NR	NR
				≥1	NR	NR	NR	NR	NR	NR
		Spontaneous healing after implant placement with regular insertion torque (50 Ncm)	58	<1	NR	NR	NR	NR	NR	NR
				≥1	NR	NR	NR	NR	NR	NR
Nohra et al. (2018)	PC	Spontaneous healing with 3 different ranges of insertion torque	18	<2	NR	NR	NR	NR	2.34 (2.16)	Caliper
		Spontaneous healing with 3 different ranges of insertion torque	21	≥2	NR	NR	NR	NR	0.31 (0.63)	

		Clinical outcome					Radiographic outcome		
Time of re-assessment (months)	Length of study period (months)	Probing pocket depth (mm)	Bleeding on probing (%)	Mucosal recession (mm)	Suppuration (%)	Clinical attachment level (mm)	Method of assessment	Marginal bone level (mm)	Take home message
NR	12	NR	NR	1.07	NR	NR	Periapical radiograph	0.71 (0.39)	Sites with a thick buccal bone wall (≥1 mm) are less prone to buccal soft tissue recession than sites with a thin buccal bone wall
		NR	NR	0.78	NR	NR			
		NR	NR	0.35	NR	NR		1.11 (0.39) (12 m)	
		NR	NR	0.15	NR	NR			
6	12	NR	NR	NR	NR	NR	Periapical radiograph	1.9 (1.1)	Following implant placement in the healed alveolar ridge, remodeling of bone takes place, which is manifested in diminished dimensions, both horizontally and vertically, at the facial aspect of the implant
4	4	NR	NR	NR	NR	NR	NR	NR	Implants placed in healed ridges undergo dimensional changes due to bone resorption
NR	36	NR	NR	1.22	NR	NR	NR	NR	The buccal bone thickness at the time of implant placement may potentially affect buccal mucosal margin stability
		NR	NR	0.64	NR	NR	NR	NR	
		NR	NR	(+) 0.77	NR	NR	NR	NR	
6	18	2.9 (0.9)	0.07 (0.1)*	3.3	NR	NR	Periapical radiograph	0.3 (0.4)	Sites that are left for spontaneous healing reveal more vertical bone loss at the buccal aspect within the early stages of healing and less bone stability during follow-up
		2.6 (1.0)	0.07 (0.1)*	3.07	NR	NR		(+) 0.02 (0.4)	
12	12	NR	NR	NR	NR	NR	CBCT	0.42 (0.67)	Minimal dimensional changes are expected when a minimal buccal bone thickness is present in the posterior maxilla
		NR	NR	NR	NR	NR		0.22 (0.30)	
NR	36	NR	NR	1.53	NR	NR	Periapical radiograph	1.03 (0.12)	Sites with a thick buccal bone wall (≥ 1 mm) are less prone to buccal soft tissue recession than sites with thick buccal bone wall
		NR	NR	0.82	NR	NR			
		NR	NR	0.57	NR	NR		1.53 (0.29)	
		NR	NR	0.11	NR	NR			
12	12	NR	NR	NR	NR	NR	CBCT	0.36 (0.34)	Insertion torque and mucosal tissue thickness do not influence implant survival or marginal bone loss. Buccal bone thickness of ≥2 mm was associated with a minimal marginal bone remodeling
		NR	NR	NR	NR	NR		0.03 (0.42)	

TABLE 3 (Continued)

Author (year)	Study design	Experimental group	Sample size (implants)	Buccal bone wall thickness in implant placement stage (mm)	Alveolar bucco-lingual dimension (mm)	Vertical bone defect (mm)	Buccal bone wall thickness at re-assessment (mm)	Alveolar bucco-lingual dimension at re-assessment (mm)	Vertical bone loss (mm)	Method of assessment
Oda et al. (2021)	RC	Spontaneous healing	17	1.43	NR	NR	0.8	NR	NR	CBCT
Schwarz et al. (2012)	PC	Simultaneous guided bone regeneration	8	0	NR	0	NR	NR	NR	Caliper
			8	0	NR	1	0	NR	NR	
			8	0	NR	3.6 (1.5)	0	NR	NR	
Spray et al. (2000)	PC	Spontaneous healing	140	1.26 (0.87)	NR	>3	0.7 (1.70)*	NR	NR	Caliper and probe
			189	1.54 (1.11)	NR	2.1–3		NR	NR	
			415	1.67 (1.10)	NR	1.1–2		NR	NR	
			733	1.75 (1.41)	NR	0.1–1		NR	NR	
			716	1.83 (1.10)	NR	0		NR	NR	
			474	1.84 (1.41)	NR	0		NR	NR	
Temmerman et al. (2015)	PC	Spontaneous healing for buccal plates <1 mm and simultaneous guided bone regeneration when dehiscence/fenestration of implants placed 2 mm subcrestal	98	<1	<4.5	NR	NR	NR	NR	NR

Abbreviations: CBCT, cone beam computed tomography; NR, not reported; PC, prospective cohort; RC, retrospective cohort; RCT, randomized controlled trial.

[a]Refers to mean value of the modified sulcular bleeding index.

0.9 mm(Bengazi et al., 2014) to 2.29 mm (Vignoletti et al., 2019). All the included studies documented VBL at re-assessment, while two studies (Bengazi et al., 2014; Vignoletti et al., 2019) reported BBT at re-assessment (range from approximately 0.1 to 1.3 mm). Data from three studies (Bengazi et al., 2014; Monje et al., 2019; Vignoletti et al., 2019) demonstrated that VBL occurs regardless of the baseline BBT over a range of approximately 0.3–4 mm. Data from one study (Monje et al., 2019) showed that on average, a baseline BBW <1.5 mm is exposed to approximately 4 mm of VBL under spontaneous healing, while in scenarios where BBW is ≥1.5 mm, VBL is limited to about 0.1 mm. This tendency was sustained in experimentally induced peri-implantitis, showing a difference of approximately 0.9 mm in favor of BBW ≥ 1.5 mm. One study (Baffone et al., 2015) that did not report baseline BBT, found that narrower alveolar ridges tended to have thinner BBW at re-entry.

3.7 | Influence of baseline BBT upon clinical and radiographic outcomes

3.7.1 | Clinical studies

Overall, five studies (Barone et al., 2016; Farronato et al., 2020; Jung et al., 2017; Marconcini et al., 2018; Schwarz et al., 2012) reported on the clinical parameters, with mucosal recession (MR) being the most frequently documented parameter. No notable differences were observed in probing pocket depth (PPD) according to baseline BBT or to baseline vertical bone defect in dehiscence-type defects. In contrast, bleeding on probing was seen to increase in deeper vertical bone defects in dehiscence-type defects. Mucosal recession (MR) was significantly increased in the presence of thinner BBT or deeper vertical bone defects in dehiscence-type defects. In turn, seven studies (Barone et al., 2016; Cardaropoli et al., 2006; Jung et al., 2017; Li Manni et al., 2020; Marconcini et al., 2018; Nohra et al., 2018; Temmerman et al., 2015) further reported on marginal bone level (MBL) using radiographic analyses. The MBL values ranged from 0.2 to 1.9 mm under spontaneous healing. No comparisons could be made, due to the heterogeneity of the groups. Interestingly, Nohra et al. (2018) showed that implants presenting BBT < 2 mm at baseline exhibited 10× greater MBL (0.36 mm vs. 0.03 mm), respectively, when compared to implants displaying BBT ≥ 2 mm.

3.7.2 | Preclinical studies

Only one study (Monje et al., 2019) examined the clinical and radiographic parameters in experimental ligature-induced peri-implantitis. Greater PPD, MR, sulcular bleeding index (mSBI), and

		Clinical outcome					Radiographic outcome		
Time of re-assessment (months)	Length of study period (months)	Probing pocket depth (mm)	Bleeding on probing (%)	Mucosal recession (mm)	Suppuration (%)	Clinical attachment level (mm)	Method of assessment	Marginal bone level (mm)	Take home message
72	72	NR	NR	NR	NR	NR	NR	NR	Significant buccal bone loss occurs over the long-term in the edentulous maxilla
4	48	2.9 (0.7)	29.1 (21.3)	0.2 (0.3)	NR	3.1 (0.8)	NR	NR	Implants exhibiting residual defect height values >1 mm are at a greater risk of developing peri-implant disease and are associated to an increase in mucosal recession
		2.8 (0.7)	45.8 (30.5)	0.5 (0.7)	NR	3.3 (0.8)			
		2.7 (0.8)	54.1 (24.8)	0.4 (0.6)	NR	3.1 (1.2)			
Mandible (3–4)—Maxilla (3–8)	NR	NR	NR	NR	NR	NR	NR	NR	The greatest bone resorption occurs when the buccal plate at implant placement is <1.4 mm. Bone loss decreases with <1.7 mm baseline buccal plates. If bone is ≥1.8, changes are inexistent.
		NR	NR	NR	NR	NR	NR	NR	
		NR	NR	NR	NR	NR	NR	NR	
		NR	NR	NR	NR	NR	NR	NR	
		NR	NR	NR	NR	NR	NR	NR	
		NR	NR	NR	NR	NR	NR	NR	
3.6	NR	NR	NR	NR	NR	NR	Periapical radiograph	0.79	At sites with limited buccolingual dimensions (≤ 4.5 mm), implants can be successful if placed subcrestal

suppuration were noted under a baseline BBW < 1.5 mm when compared to BBW ≥ 1.5 mm. Mean bone loss was approximately 5 mm in both groups.

3.8 | Influence of baseline BBT upon biological complications

3.8.1 | Clinical studies

None of the clinical studies reported on BBT and its association with biological complications.

3.8.2 | Preclinical studies

One study (Monje et al., 2019) examined the progression of peri-implantitis in an experimental model. In general terms, a more acute inflammatory condition together with MR was noted in BBW < 1.5 mm.

3.9 | Influence of baseline BBT upon PROMs

A single study (Li Manni et al., 2020) noted no difference in PROMs according to the type of implant or the baseline BBT.

3.10 | Influence of bone regeneration on the buccal bone changes

3.10.1 | Clinical studies

One study (Jung et al., 2017) showed that VBL was significantly increased at 6 months of follow-up under conditions of spontaneous healing when compared to simultaneous bone regeneration.

3.10.2 | Preclinical studies

No preclinical study evaluated the impact of bone regeneration upon buccal bone changes.

TABLE 4 Preclinical studies included in the qualitative analysis.

Author (year)	Experimental model	Experimental design	Sample (implants)	Experimental group	Method of assessment	Buccal bone wall thickness in implant placement stage (mm)	Bucco-lingual alveolar bone dimension at implant placement (mm)	Buccal bone thickness at re-assessment (mm)	Bucco-lingual alveolar bone dimension at re-assessment (mm)
Baffone et al. (2015)	Labrador dog	Spontaneous healing	6	Narrow ridge—Narrow abutment (3.3 mm)	Caliper	NR	4.1 (0.6)	1 (0.7)	NR
			6	Wide ridge—Wide abutment (4.6 mm)		NR	5.4 (1.3)	1 (0.5)	NR
			6	Narrow ridge—Wide abutment (3.3 mm)		NR	3.7 (0.6)	0.7 (0.4)	NR
			6	Wide ridge—Narrow abutment (4.6 mm)		NR	6.2 (1.2)	1.5 (0.7)	NR
Bengazi et al. (2014)	Beagle dog	Spontaneous healing	6	Premolar—Alveolar mucosa	Caliper	0.9 (0.0)	NR	0.7 (0.3)	NR
			6	Premolar—Masticatory mucosa		0.9 (0.0)	NR	0.4 (0.6)	NR
			6	Molar- Alveolar mucosa		2.3 (0.3)	NR	2.2 (0.5)	NR
			6	Molar- Masticatory mucosa		2.4 (0.1)	NR	1.5 (0.8)	NR
Monje et al. (2019)	Beagle dog	Spontaneous healing	18	Thin buccal bone	Tracking system	<1.5	NR	NR	NR
			18	Thick buccal bone		≥1.5	NR	NR	NR
		Experimental peri-implantitis	18	Thin buccal bone		<1.5	NR	NR	NR
			18	Thick buccal bone		≥1.5	NR	NR	NR
Vignoletti et al. (2019)	Beagle dogs	Spontaneous healing	16	2-week healing	Probe	2.29 (0.15)	NR	1.96 (0.9)	NR
			16	8-week healing		2.29 (0.15)	NR	0.94 (0.79)	NR

3.11 | Influence of bone regeneration on the clinical and radiographic outcomes

3.11.1 | Clinical studies

A single study (Jung et al., 2017) demonstrated greater PPD (approximately 0.3 mm), MR (approximately 0.3 mm), and MBL (approximately 0.3 mm) when spontaneous healing was applied in dehiscence-type defects compared to augmented sites.

3.11.2 | Preclinical studies

No preclinical study explored the impact of bone regeneration on the clinical and radiographic outcomes of augmented sites.

3.12 | Influence of bone regeneration upon biological complications

3.12.1 | Clinical studies

One study (Schwarz et al., 2012) showed that the larger the dehiscence-type defect after regeneration, the greater the risk of biological complications (i.e., peri-implant mucositis) at four years of follow-up.

3.12.2 | Preclinical studies

No preclinical study explored the impact of bone regeneration on the occurrence of biological complications.

		Clinical outcome					Radiographic outcome		
Vertical bone loss (mm)	Time of re-assessment (months)	Probing pocket depth (mm)	Modified sulcular bleeding index (mean)	Mucosal recession (mm)	Suppuration (%)	Clinical attachment level (mm)	Method of assessment	Marginal bone level (mm)	Take home message
1.7 (1.7)	3	NR	NR	NR	NR	NR	NR	NR	Implants installed in regular- sized alveolar ridges have greater horizontal, but lesser vertical buccal bony crestal resorption compared to implants installed in reduced alveolar ridges.
1.3 (0.9)		NR	NR	NR	NR	NR	NR	NR	
0.9 (0.3)		NR	NR	NR	NR	NR	NR	NR	
1.5 (0.5)		NR	NR	NR	NR	NR	NR	NR	
1.7 (0.6)	3	NR	NR	NR	NR	NR	NR	NR	Greater buccal bony crest resorption and a more apical soft tissue marginal position should be expected when implants are surrounded with thin alveolar mucosa at the time of placement, independently of the thickness of the buccal bony crest
0.9 (0.6)		NR	NR	NR	NR	NR	NR	NR	
2.3 (0.9)		NR	NR	NR	NR	NR	NR	NR	
1.4 (0.5)		NR	NR	NR	NR	NR	NR	NR	
4.07	2	NR	NR	NR	NR	NR	NR	NR	Lower bone levels are expected when the critical buccal bone thickness is <1.5 mm. Experimental peri-implantitis is, in part, attributable to the greater vertical resorption of the buccal plate during initial remodeling. Clinical parameters are greater for implants placed in ridges under the critical buccal bone thickness when compared to implants placed ≥1.5 mm of buccal bone thickness
0.11		NR	NR	NR	NR	NR	NR	NR	
3.69	5	3.6	1.31	0.14	17	NR	CT	5.02	
2.83		3.21	1.1	(+)0.08	3	NR			
0.29 (0.18)	<1	NR	NR	NR	NR	NR	NR	NR	Pronounced buccolingual ridge alterations and vertical bone loss are noted at 2 and 8 weeks after implant placement in healed ridges
0.59 (0.58)	2	NR	NR	NR	NR	NR	NR	NR	

3.13 | Risk of bias

Risk of bias for clinical and preclinical studies are presented in Tables S1–S3. In summary, the 4 RCTs, evaluated with the risk-of-bias 2.0. tool, were scored at "some concerns" of bias. When considering the additional eight clinical non-RCTs, based on the COHORT version of the Newcastle-Ottawa Scale, five studies were graded at "high risk" of bias (3–6 stars), and five studies (eight stars) were scored at "low risk" of bias. Finally, with respect to the four animal studies included, two of them were scored "low" and 2 "unclear" risk of bias.

4 | DISCUSSION

4.1 | Main findings

Given the frequency of biological and esthetic complications in implant dentistry associated to buccal bone resorption, the question to be addressed is: What is the minimum BBT required to secure favorable outcomes conditioned to the dimensional changes after implant placement? The present systematic review yielded the following findings: (1) the clinical evidence demonstrated that during healing, dimensional changes occur in the alveolar bone and

in the BBW that may compromise the integrity of the peri-implant bone, leading to VBL and MR, particularly in scenarios exhibiting a thin BBW; (2) the preclinical evidence validated the fact that implants placed in the presence of a thin BBW are more prone to exhibit major dimensional changes; (3) clinical data indicated that in scenarios where dehiscence-type defects are left to heal spontaneously, greater VBL and MR together with the occurrence of biological and esthetic complications are to be expected; (4) in a ligature-induced peri-implantitis model, scenarios involving a thin BBW (BBT < 1.5 mm) at baseline were characterized by progression of the disease with more mucosal inflammation, MR and VBL when compared to a thick BBW (BBT ≥ 1.5 mm); and (5) the augmentation of dehiscence-type defects is associated to hard and soft tissue stability. However, the present systematic review (6) failed to identify a specific threshold for guaranteeing residual alveolar bone in the buccal wall after implant placement. Nonetheless, (7) it seems that preclinical and clinical evidence points towards BBT < 1.5–2 mm tended to show greater VBL, MR, and BBT reduction (Figure 2).

4.2 | Findings from clinical studies

Clinical data demonstrated changes in BBW after implant placement in healed ridges over a range of approximately 0.3–1.75 mm during up to 72 months of follow-up, with changes in the BLD of approximately 3 mm at 6 months of follow-up. Moreover, it was shown that completely intact BBW was guaranteed in scenarios that presented ≥1.8 mm at implant placement (Spray et al., 2000). On the other hand, scenarios characterized by approximately 1.2 mm during initial examination displayed >3 mm of VBL (Spray et al., 2000). Nohra et al., 2018

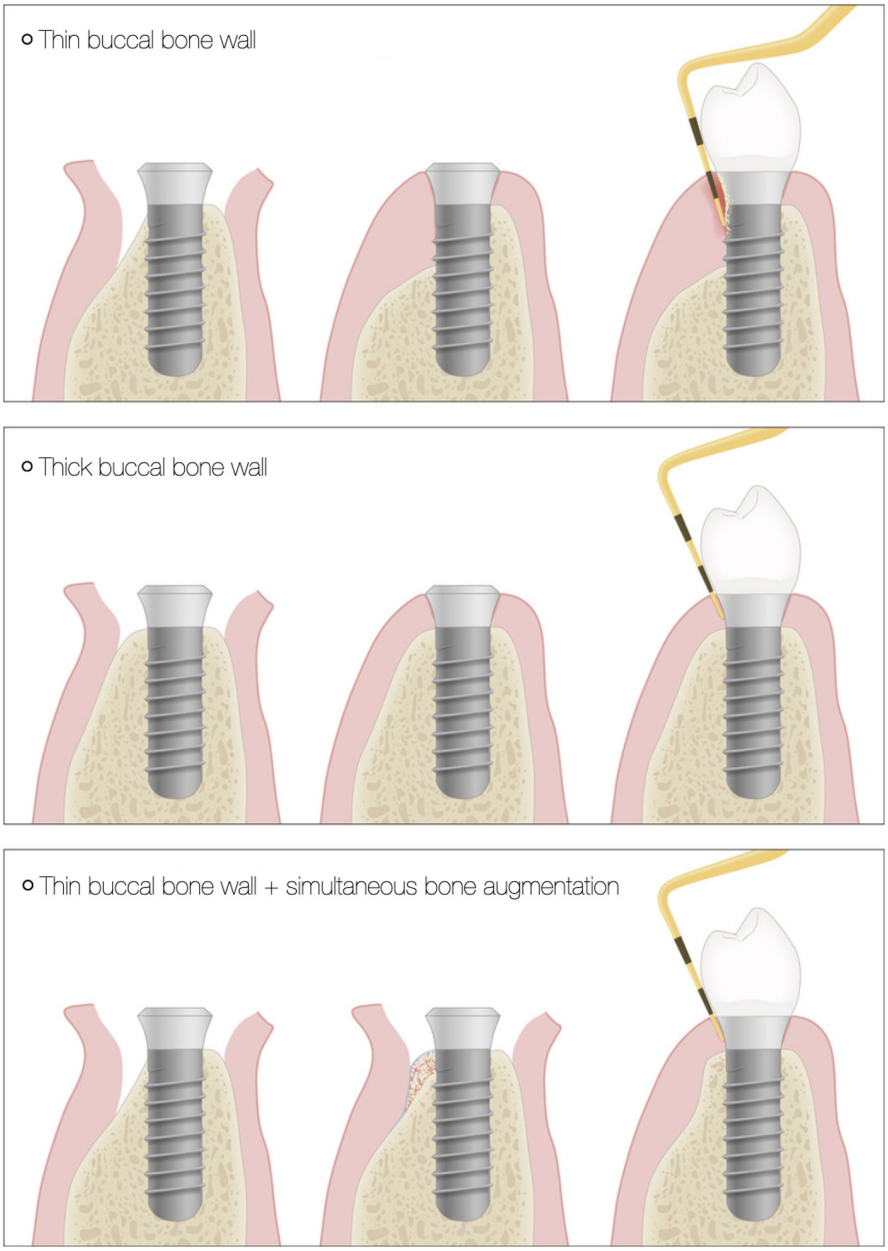


FIGURE 2 Schematic representation of avascular necrosis of the buccal bony wall according to the baseline BBT and the potential of bone augmentation to compensate scenarios characterized by a thin BBT.

showed that implants presenting BBT < 2 mm at baseline exhibited 8× and 10× greater VBL (2.34 mm vs. 0.31 mm) and MBL (0.36 mm vs. 0.03 mm), respectively, when compared to implants displaying BBT ≥ 2 mm. It is remarkable, however, that in subcrestal implants placed in reduced BLD (<4.5 mm), implant therapy can yield solid outcomes with minimal peri-implant bone loss as determined by periapical radiographs (Temmerman et al., 2015). Nonetheless, it should be noted that this study did not evaluate VBL at the buccal aspect during re-examination or assess the clinical parameters during the study period. Moreover, early dimensional changes yielded minimal changes in the posterior maxilla (Li Manni et al., 2020). In fact, confounders other than BBT could further impact upon the dimensional changes. For instance, the shape of the edentulous ridge dictates that the more apical the BLD is examined in a cross-sectional view, the wider it is when compared to the most coronal location since it follows a divergent morphology (Chen et al., 2021). This strategy may assist in compensating for the thin BBW at the most coronal aspect of the ridge. In turn, the anatomical area also may play a relevant role. The mandibular process is predominantly composed of cortical bone, which is poorly vascularized, while the maxillary bone is more cancellous and richer in blood supply. In fact, the thickness of the cortical layer at the coronal aspect of the mandibular ridge is approximately 1.4 mm (Chatvaratthana et al., 2017), versus approximately 2 mm at 3 mm below the crest in the molar area (Katranji et al., 2007)—being significantly thinner in the edentulous maxilla (Katranji et al., 2007). Moreover, Lindhe et al. (2013) showed that the cortical crest was wider in the mandible than in the maxilla, and widest in the symphysis region of the mandible. Further, it was demonstrated that the proportion of bone marrow was greater in the maxilla than in the mandible. Hence, it is hypothesized that the thickness of the cortical bone may dictate the extent of the remodeling process, being more critical in the mandibular anterior than in the posterior maxillary ridges.

Simultaneous augmentation was seen to mitigate dimensional changes, VBL, MR, and biological complications. One RCT (Jung et al., 2017) explored soft and hard tissue changes of dehiscence-type defects left for spontaneous healing and simultaneous horizontal bone augmentation using GBR. In fact, simultaneously grafted sites showed a significant gain in vertical bone, while nongrafted sites exhibited progressive VBL and greater MR. A four-year PC study (Schwarz et al., 2012) showed that successful lateral regeneration procedures during implant placement that secure complete buccal bone (BBT = 0.8 mm) are less prone to experience biological complications during the study period (4-year follow-up). Thus, data from these two studies highlight the role of simultaneous bone augmentation in scenarios characterized by a lack of buccal bone. The question of whether implants with thin BBW clinically benefit from regeneration was not addressed, however.

4.3 | Findings from preclinical studies

In light of measurement errors derived from radiographic methods (i.e., CBCT) to determine peri-implant bone dimensions, preclinical studies were further considered. insight on the actual significance Preclinical data afforded insight into the influence of BBT upon the dimensional changes. It was seen that dimensional changes may compromise BLD and BBW in healed alveolar ridges after implant placement. A range from approximately 0.1–1.4 mm in BBT changes was noted. Vertical bone loss ranged from approximately 0.3–4 mm. It is relevant to note that narrower alveolar ridges have a greater tendency to show a thin BBW at re-assessment (Baffone et al., 2015). Data from one study (Monje et al., 2019) showed that a baseline BBT < 1.5 mm is exposed on average to about 4 mm of VBL under spontaneous healing, while in scenarios where BBT is ≥1.5 mm, VBL is limited to approximately 0.1 mm. This tendency was sustained in experimentally induced peri-implantitis, showing a difference of approximately 0.9 mm in favor of BBT ≥ 1.5 mm. Moreover, two studies (Bengazi et al., 2014; Vignoletti et al., 2019) reported changes in BBT at re-assessment ranging from approximately 0.2 mm to approximately 1.5 mm. The abovementioned study (Monje et al., 2019) further provided information on the soft and hard tissues during experimental peri-implantitis. In general lines, a more acute inflammatory condition together with greater VBL and MR were noted in scenarios where the initial BBW was <1.5 mm. Another confounder in relation to the influence of initial BBT upon dimensional changes was the nature of the alveolar mucosa (Bengazi et al., 2014). Greater VBL changes occurred when implants were surrounded by thin nonkeratinized mucosa at the time of implant placement, in contrast to keratinized mucosa. Therefore, based on preclinical data, it seems that dimensional changes occur as a consequence of implant placement and that major resorption that may compromise the integrity of bone along the buccal aspect of the implant may lead to more aggressive peri-implantitis.

4.4 | Understanding the biological mechanism behind these findings

This systematic review evidenced the dimensional changes that occur after implant placement in healed alveolar ridges. This may reflect an avascular necrosis phenomenon as a consequence of damage to the alveolar bone (Chang et al., 1993; Roux & Orcel, 2000). The alveolar process is composed of cortical bone at the outer aspect, whereas the central portion of the mandible is characterized by a more cancellous structure. The cortical bone receives its blood supply branched from the outside through blood vessels of the periosteum, and from the inside of the endosteum (Roush et al., 1989). Therefore, when an implant is inserted with an open-flap procedure, the blood supply from both sources is disrupted (Roux & Orcel, 2000). Avascular necrosis following implant placement is initiated 12 h after disruption of the blood supply when the hematopoietic cells that are particularly sensitive to low oxygen levels die. This event is followed by the death of bone cells such as osteocytes and osteoblasts, leading to more noticeable osteoclast activity (Mankin, 1992). In consequence, the blood supply might not be sufficient to repair the bone at the buccal aspect. In response, osteoclasts activated by the RANKL/RANK pathway and mediated by a transcription factor (nuclear factor of activated T cells) induce buccal bone resorption (Roux

& Orcel, 2000). VBL together with buccal MR are thus attributable to this process. These changes may have a detrimental impact upon the integrity of the buccal bone and mucosal stability, compromising the functional and esthetic outcomes.

4.5 | Clinical implications

Considering that the clinical and preclinical data indicated that scenarios with an initial thin BBW (BBT ≤1.5 mm) may experience major dimensional changes that can compromise the integrity of the buccal bone and/or the stability of the soft tissues, simultaneous bone augmentation is encouraged (Figure 2). This may gain further importance in the mandibular bone (Figure 3) and in scenarios lacking keratinized mucosa. Other graftless clinical strategies to compensate BBW in narrower ridges include slightly submerging bone-level implants using transmucosal abutments. This concept is not applicable to tissue-level implants, owing to the increased depth of the mucosal tunnel that may lead to mucosal inflammation (Chan et al., 2019). The use of narrow-diameter implants (NDI) may be also a potential solution to approach situations of thin BBW. However, NDIs are mostly limited to premolar sites in both jaws and anterior implant sites in the mandible to achieve the desired emergence profile. For instance, the use of narrow-diameter bone-level implants in the posterior mandible may contribute to a convex emergence profile, which in turn may increase the risk of peri-implant biological complications (Katafuchi

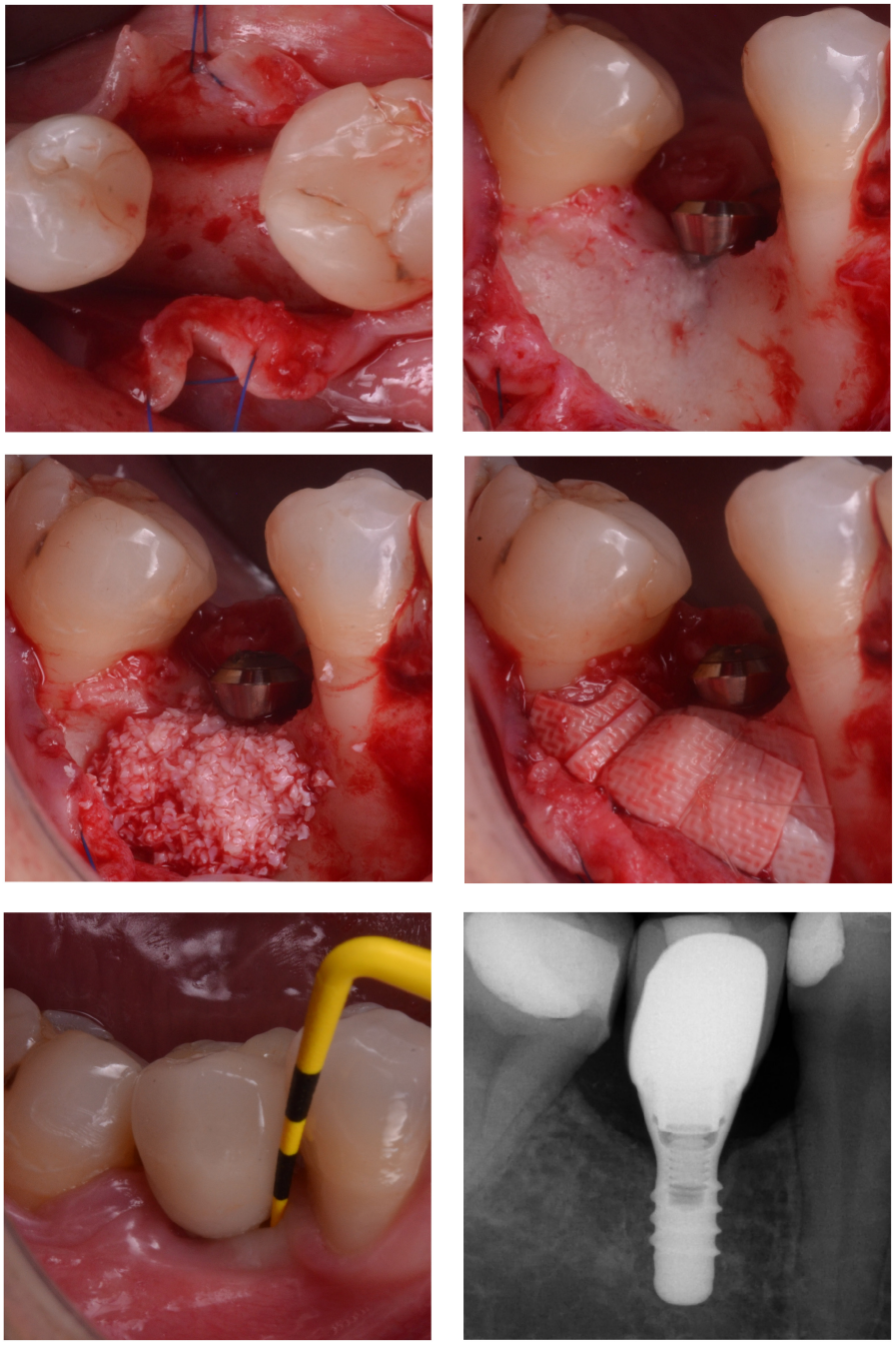


FIGURE 3 Case scenario of thin BBW in the posterior mandible; (a) occlusal view indicating the narrow alveolar dimension, (b) implant three-dimensional position must solely be dictated by the desired emergence profile, (c) grafting with autogenous bone and slowly reabsorbing bone in two layers, (d) cross-linked membrane is used to fulfill the principle of compartalization, (e) clinical outcomes show mucosal stability and peri-implant health, (f) bone levels remain stable during follow-up.

et al., 2018). Another option to reduce the risk of an exposed micro-rough surface to the peri-implant sulcus is the utilization of a so-called hybrid design (HD) implant (Tarnow, 1993). A HD implant has by definition a micro-rough surface in the endo-osseous portion for improved bone anchorage, and a machined surface in the neck/shoulder area for the trans- and supracrestal area to reduce the risk for biofilm colonization, and hence the development of biologic complications over time (Monje et al., 2021; Serrano et al., 2022) The essence and inspiration of all HD implants is the tissue-level implant by Straumann first utilized in 1986 (Sutter et al., 1988). Long-term studies seem to document the increased risk for peri-implantitis for non-HD implants, when the micro-rough is exposed to the supracrestal area (Derks et al., 2016; Windael et al., 2021). A 10-year study with 1482 implants showed an odds ratio for the development of peri-implantitis of more than 5 for implants that exceeded an early bone loss of more than 0.5 mm during the first year of function. The overall incidence of peri-implantitis was 11.8% on an implant level, on top of a failure rate of 5.26% (Windael et al., 2021). In contrast, a 10-year clinical with 511 tissue-level implants with an HD, the failure rate was at 1.2%, and the prevalence of peri-implantitis at 1.8% (Buser et al., 2012).

4.6 | Limitations and recommendations for future research

Due to the heterogeneity of the data (i.e., different methods of assessment and landmarks), no meta-analyses could be performed. Moreover, it must be highlighted that conclusions are mainly derived from preclinical and nonrandomized clinical trials. Therefore, cautiousness must be exercised when interpreting the findings. Based on deficiencies identified in this systematic review, there are several open questions, which should be addressed with appropriate preclinical and clinical studies. Most important, the details of postsurgical bone resorption induced by avascular necrosis should be further examined with preclinical studies using sequential histologic analysis during the first 8 weeks of healing. This would allow a better understanding of the biology behind this phenomenon including information on the sequence and involved cells. Then, it is also of interest to explore the differences between implant sites in the maxilla and in the mandible, since differences in density of the BBW might result in different threshold values between thin and thick. Moreover, studies are needed to assess the impact of bone augmentation in scenarios characterized by a thin BBW, in order to gain insight into the influence of bone augmentation upon long-term soft and hard tissue stability.

5 | CONCLUSIONS

Dimensional changes occur as result of implant placement in healed ridges that may lead to instability of the peri-implant hard and soft tissues. Sites presenting a thin BBW are more prone to exhibit major changes that may compromise the integrity of the buccal bone and may lead to biologic and esthetic complications. Hence, simultaneous bone augmentation of dehiscence-type defects or sites exhibiting a thin BBW may attenuate the buccal hard and soft tissue collapse that may jeopardize the long-term success and stability.

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CONFLICT OF INTEREST

The authors have no direct financial interests in the products and instruments listed in the paper.

DATA AVAILABILITY STATEMENT

The authors confirm that the data supporting the findings of this study are available within the article [and/or] its supplementary materials.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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REVIEW ARTICLE

CLINICAL ORAL IMPLANTS RESEARCH WILEY

Do soft tissue augmentation techniques provide stable and favorable peri-implant conditions in the medium and long term? A systematic review

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Abstract

Objectives: To review the available literature on the medium- and long-term effects of soft tissue augmentation (STA) at implant sites and to explore the effects of the different approaches on clinical-, patient-reported, and health-related parameters.

Materials and Methods: A comprehensive electronic and manual search was performed to identify prospective clinical studies that assessed the medium- and long-term (≥36 months) outcomes following STA, including number of sites maintaining peri-implant health and number of sites developing peri-implant disease, incidence of complications, stability of the clinical, volumetric, and radiographic parameters, and patient-reported outcome measures (PROMs).

Results: Fifteen studies were included in the qualitative analysis. STA was performed with either a bilaminar- or an apically positioned flap (APF) approach, in combination with autogenous grafts (free gingival graft [FGG] and connective tissue graft [CTG]) or substitutes (acellular dermal matrix [ADM] and xenogeneic cross-linked collagen matrix [CCM]). An overall high survival rate was observed. Most of the augmented implant sites maintained peri-implant health in the medium and long term, with the incidence of peri-implant mucositis and peri-implantitis ranging from 0% to 50% and from 0% to 7.14%, respectively. The position of the soft tissue margin following APF + FGG and bilaminar approaches involving CTG or CCM was found to be stable over time. No substantial changes were reported for plaque score/index, bleeding on probing/bleeding index, and probing depth between early time points and following visits. CTG-based STA procedures resulted in a stable or increased dimension of keratinized mucosa width (KMW) and mucosal thickness (MT)/volumetric outcomes over time, when compared with early follow-ups. Most of the included studies described stable marginal bone levels at the grafted implant sites over time. No substantial changes for patient-reported outcomes and professionally assessed esthetic results were reported at different time points.

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Conclusions: Implants that received STA showed overall high survival rate and relatively low incidence of peri-implantitis in the medium and long term. Augmented sites seem to maintain the level of soft tissue margin and marginal bone over time, while non-augmented implants may exhibit apical shift of the soft tissue margin. The overall favorable early outcomes obtained with STA are maintained in the medium and long term, with an increase in KMW and MT that may be expected over time at CTG-augmented sites.

KEYWORDS
connective tissue graft, dental implants, evidence-based dentistry, soft tissue augmentation, systematic review

1 | INTRODUCTION

Soft tissue augmentation (STA) is routinely performed at implants sites. Common indications for this procedure include treatment of implant esthetic complications, mucosal thickness augmentation, keratinized mucosa augmentation, and papilla reconstruction, among others (Avila-Ortiz et al., 2020; Zucchelli et al., 2020).

Studies investigating patient-reported outcome measures (PROMs) demonstrated that keratinized mucosa width (KMW) plays a key role on patient's comfort during brushing (Perussolo et al., 2018; Roccuzzo et al., 2016; Souza et al., 2016; Stefanini et al., 2021). In a 4-year longitudinal study, Perussolo et al. (2018) demonstrated that implants surrounded by an adequate KMW were associated with significantly less patient-reported discomfort during brushing and less marginal bone loss compared to implant sites characterized by <2 mm of KMW. In line with these findings, other authors advocated that an adequate band of keratinized and attached mucosa can have a protective effect on peri-implant health (Gharpure et al., 2021; Lin et al., 2013; Monje & Blasi, 2019; Sanz et al., 2022). Similarly, the role of mucosal thickness (MT) on implant-related outcomes has been extensively investigated (Gharpure et al., 2021; Jung et al., 2022; Puzio et al., 2020; Wang et al., 2021). It has been shown that MT can affect the color match of the peri-implant soft tissue with the adjacent natural gingiva and that it can also play a role on the stability of the marginal bone levels (Bhat et al., 2015; Garaicoa-Pazmino et al., 2021; Jung et al., 2008; Martinez-Rus et al., 2017; Tavelli, Barootchi, Avila-Ortiz, Urban, et al., 2021; Thoma et al., 2018). In addition, in line with recent evidence from long-term studies on root coverage procedures in natural dentition (Barootchi et al., 2022; Tavelli et al., 2019), it has been advocated that an augmented MT can contribute to the stability of the peri-implant soft tissue margin in the long term (Wang et al., 2021; Zucchelli et al., 2020).

Soft tissue augmentation can be performed with autogenous grafts or substitutes. An apically positioned flap (APF) in combination with a FGG is considered the technique of choice for posterior sites lacking keratinized and attached mucosa (Tavelli, Barootchi, Avila-Ortiz, Urban, et al., 2021; Zucchelli et al., 2020). MT augmentation, and overall STA at implant sites in the esthetic zone, is usually performed utilizing a bilaminar approach, with the flap that is coronally advanced to completely cover the graft, aiming for a healing by primary intention (Cosyn et al., 2016; Hosseini et al., 2020; Zucchelli, Felice, et al., 2018). Autogenous connective tissue graft (CTG), acellular dermal matrix (ADM), and xenogeneic collagen matrix (CCM) have been found effective in increasing MT at implant sites (Hutton et al., 2018; Schmitt et al., 2021; Thoma et al., 2016). When compared to CTG, soft tissue graft substitutes allow to avoid a second surgical site and to reduce the overall morbidity of the procedure (Stefanini et al., 2021; Tavelli, Barootchi, Stefanini, et al., 2022).

Nevertheless, comparisons among different STA procedures and graft materials have been mainly described in the short term, and their outcomes in the medium- and long-term periods need further investigation.

Therefore, the aim of this article was to conduct a systematic appraisal of the existing literature reporting the medium- and long-term results of peri-implant STA, exploring the effects of the different approaches on clinical-, patient-reported, and health-related parameters, together with the stability of these outcomes over time.

2 | MATERIALS AND METHODS

2.1 | Protocol registration and reporting format

The protocol for this review was designed according to the Cochrane guidelines (Higgins et al., 2021) and reported with the Preferred Reporting Items for Systematic reviews and Meta-Analysis Extension (PRISMA) (Page et al., 2021). The study protocol was registered in the PROSPERO database, hosted by the National Institute for Health Research, University of York, Center for Reviews and Dissemination.

2.2 | Objective

The goal of this review was to address the following focused question in regard to soft tissue augmentation at implant sites: "Which soft tissue augmentation techniques provide the most predictable and favorable clinical and health-related conditions in the medium-long term?"

2.3 | PICOT question

The following Population, Intervention, Comparison, Outcome, and Time (PICOT) framework (Stillwell et al., 2010) was used to guide the inclusion and exclusion of studies for the abovementioned focused question. In adult patients with one or more healthy dental implant(s), which soft tissue augmentation technique provides a better peri-implant health condition and stable outcomes over time as reported in RCTs or cohort studies (S) with at least a 36 months follow-up?

- Population (P): Adult patients (≥18 years old) who underwent soft tissue augmentation on at least one healthy dental implant.
- Intervention (I): Surgical treatment for soft tissue augmentation involving pedicle flaps or tunnel techniques in combination with autogenous grafts (free gingival graft [FGG] or connective tissue graft [CTG]) or substitutes (collagen matrices [CMs] or acellular dermal matrices [ADMs]) at healthy dental implants.
- Comparison (C): All possible comparisons among the eligible studies in terms of flap approaches and grafting materials, including non-treated sites (if available as a comparative arm) and non-grafted sites (such as the coronal advancement or apical positioning of flap alone).
- Outcome (O): The number of cases maintaining a condition of peri-implant health (Berglundh et al., 2018) and the number of cases developing biological complications ("as defined by the authors of the study" or as determined by the presence of bleeding on probing, an increase in probing depth, an increase in recession of the peri-implant soft tissue margin, and an increase in radiographic marginal bone loss) were set as the primary outcome. Changes in the position of the peri-implant soft tissue margin (defined as peri-implant soft tissue dehiscence [PSTD] depth when compared to the cemento-enamel junction [CEJ] of the homologous contralateral tooth, or midfacial recessions [Midf REC] when compared to the level of the soft tissue margin at crown delivery), changes in pocket depth, plaque index/score, bleeding on probing/bleeding index, changes in marginal bone levels (MBLs) assessed radiographically, professional esthetic assessment, and patient-reported outcome measures (PROMs) were also investigated.
- Time (T): Studies reporting outcomes in the medium (≥36 months) and long (≥60 months) term.

2.4 | Eligible studies

To specifically address the focused question, prospective interventional human studies were included in this systematic review's qualitative and quantitative assessment if they met the following criteria in at least one study arm: (i) soft tissue augmentation performed at healthy implant sites using FGG, CTG, or soft tissue graft substitutes; (ii) Evaluation and reporting of clinical outcomes of interest over a minimum of 36 months; (iii) Minimum of 10 participants at the first follow-up ≥36 months; and (iv) Eligible therapies included the use of apically positioned flap-based approach or bilaminar techniques.

Reasons for article exclusion included: (i) Retrospective studies, case reports, or animal studies; (ii) Inclusion of implants with a diagnosis of peri-implant disease (Berglundh et al., 2018); (iii) Soft tissue augmentation at edentulous areas or natural teeth; (iv) Simultaneous hard and soft tissue augmentation; and (v) Studies recruiting smokers only.

2.5 | Information sources and search strategy

To identify eligible articles, detailed search strategies were modelled for the following electronic databases: MEDLINE (via PubMed), EMBASE via OVID; the Cochrane Central Register of Controlled Trials; and Latin American & Caribbean Health Sciences Literature (LILACS), Web of Science, and Scopus. The grey literature, nonprofit reports, government research, or other materials were also electronically explored in ClinicalTrial.gov and OpenGrey. The search strategy was conducted to identify articles published up to September 1, 2022, and it was primarily designed for the MEDLINE database with a string of medical subject headings and free text terms, and then modified appropriately for other databases. No restrictions were set for date of publication, journal, or language. The search results were downloaded to a bibliographic database to facilitate duplicate removal and cross-reference checks. Details regarding the search strategy and the development of the search key terms for the databases, are displayed in the Appendix S1.

The reference lists of the retrieved studies for full-text screening and previous reviews in periodontal regeneration were screened. A manual search was also performed in the *Clinical Oral Implant Research*, *Journal of Periodontology*, *Journal of Clinical Periodontology*, *Journal of Dental Research*, *International Journal of Periodontics and Restorative Dentistry*, and *Clinical Implant Dentistry and Related Research*. Previous systematic reviews assessing medium and long-term outcomes of peri-implant soft tissue augmentations were also examined (Cairo et al., 2019; Fickl et al., 2021; Poskevicius et al., 2017; Rotundo et al., 2015; Sicilia et al., 2015; Tavelli, Barootchi, Avila-Ortiz, Urban, et al., 2021; Thoma et al., 2018, 2021).

2.6 | Article selection process

Two independent reviewers (L.T. and S.B.) screened the titles and abstracts (if available) of the entries identified in the literature search in duplicate and independently. Next, the full-text version of all studies that potentially met the eligibility criteria or for which there was insufficient information in the title and abstract to make a decision were obtained. Any article considered potentially relevant by at least one of the reviewers was included in the next screening phase. Subsequently, the full-text publications were also evaluated in duplicate and independently by the same review examiners. Disagreements between the review authors were resolved by open discussion. If no consensus

could be reached, a third author (L.M.) was consulted. All articles that did not meet the eligibility criteria were excluded, and the reasons for exclusion were noted. Inter-examiner agreement following full-text assessment was calculated via kappa statistics. Any missing information that could contribute to this systematic review was requested to the corresponding author(s) via email communication. In the case of multiple publications reporting on the same study or investigating the same cohort at different follow-up intervals (or secondary analysis of the same data), it was decided to pool together all relevant details as a single report with the most comprehensive data for inclusion in the qualitative and quantitative analyses.

2.7 | Data extraction and outcome measures

Two examiners (L.T. and S.B.) independently retrieved all relevant information from the included articles using a data extraction sheet specifically designed for this review.

Clinical outcomes of interest included probing depth (PD), PSTD depth, Midf REC, keratinized mucosa width (KMW), attached mucosa (AM), mucosal thickness (MT), bleeding on probing (BOP), plaque indices, inflammatory indices, presence/absence of bleeding on probing (BOP), and presence/absence of suppuration. Volumetric changes were considered if assessed through optical scanning (Tavelli, Barootchi, Majzoub, Siqueira, et al., 2021). Radiographic imaging outcomes included two-dimensional (using periapical radiographs) or three-dimensional (using cone-beam computed tomography [CBCT] or computed tomography [CT]) X-rays. Esthetic outcomes were evaluated through professional esthetic indices or a visual analog scale (VAS). PROMs involved quality-of-life assessments made by patients regarding different aspects of implant therapy, such as esthetic assessment, satisfaction, willingness for retreatment, etc., using standardized methods of assessment. Implant survival rate and incidence of peri-implant disease (mucositis and peri-implantitis) were assessed at the different time points.

Aside from the outcomes of interest, the following study characteristics were retrieved: (i) Year of publication, study design, geographic location, setting (university vs. private practice), and source of funding; (ii) Population characteristics, including age and gender of participants, number of participants and treated sites (baseline/follow-up), and inclusion of smokers; (iii) Timing of the STA procedure and type of surgical intervention (apically positioned flap [APF]-based procedure or bilaminar approaches), (iv) Soft tissue graft utilized; and (v) Follow-up time points. All values were extracted from the selected publications as mean ± standard deviations, when possible.

2.8 | Methodological quality and risk of bias assessment

The assessment of methodological quality and risk of bias (RoB) was independently evaluated by two authors (L.T. and S.B.). The recommendation of the Cochrane collaboration group was followed for assessing the RoB of randomized controlled clinical trials (RCTs) (RoB 2 tool) (Sterne et al., 2019). Risk of bias assessment for non-randomized case–control studies was performed using the ROBINS-I tool (Sterne et al., 2016), while the Joanna Briggs Institute Critical Appraisal tool (Moola et al., 2017) was utilized for quality assessment of case series. Any disagreement was discussed between the same authors. Another author (L.M.) was consulted in case no agreement was reached. No study was excluded based on the risk of bias within a study.

2.9 | Data analysis

When possible, weighted means (based on the treated sample size) with standard deviation were calculated for each outcome of interest based on the type of STA (bilaminar, APF-based approach, or non-augmented sites) and the type of graft utilized (FGG, CTG, or substitutes).

2.10 | Evidence quality rating and strength of recommendation

Evidence quality rating and strength of recommendation of STA procedures at implant sites were assessed in terms of levels of certainty in the body of evidence, net benefit rating (benefit-harm estimation), and strength of recommendation, as previously described (Avila-Ortiz et al., 2022; Tavelli, Chen, Barootchi, & Kim, 2022). Additional information are depicted in the Appendix S1.

3 | RESULTS

3.1 | Search results and study selection

The literature search flow diagram is shown in Figure 1. Following the removal of duplicates, 1329 records were identified based on titles and abstracts. A full-text assessment was performed for 47 articles. Based on our predetermined inclusion criteria, 15 studies were included in this review (Bianchi & Sanfilippo, 2004; Cosyn et al., 2016; Eeckhout et al., 2020; Eghbali et al., 2018; Fenner et al., 2016; Hanser & Khoury, 2016; Hosseini et al., 2020; Oh et al., 2020; Roccuzzo et al., 2016, 2019; Seyssens et al., 2020; Stefanini et al., 2016; Thoma et al., 2020, 2022; Zucchelli, Felice, et al., 2018). The two included articles from Thoma et al. (2020, 2022), as well as the articles from Cosyn et al. (2016) and Seyssens et al. (2020), reported data on the same cohort at different time points. The reason for the exclusion of the other 32 articles is reported in Table S4 of the Appendix S1. The inter-examiner reliability in the screening and inclusion process based on title and abstract, as assessed with Cohen's κ, corresponded to 0.89, while the inter-examiner reliability for full-text evaluation was 0.96.

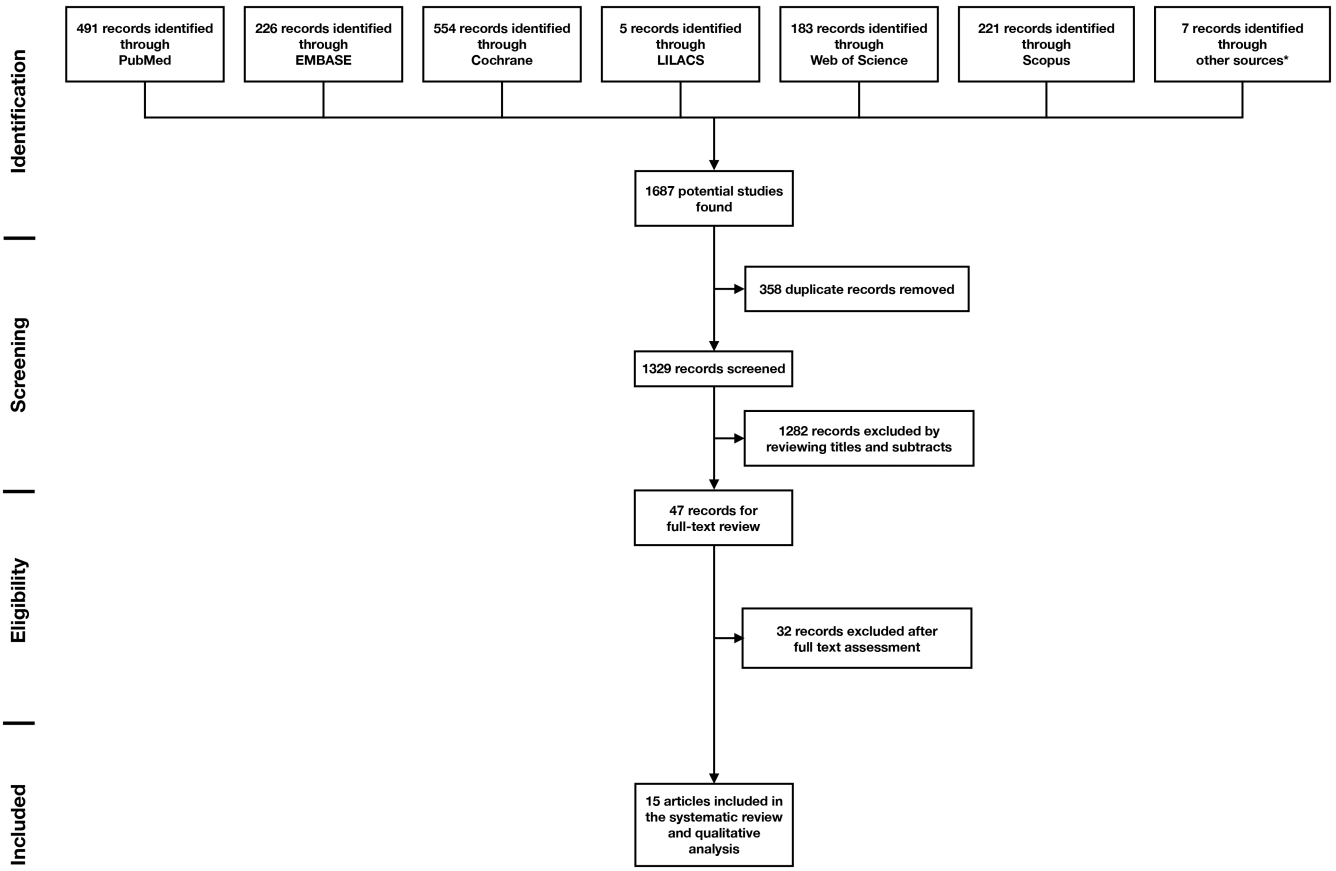


FIGURE 1 PRISMA flowchart.

3.2 | Characteristics of the included studies

Four of the included studies/publications (representing three cohorts) are RCTs (Bianchi & Sanfilippo, 2004; Oh et al., 2020; Thoma et al., 2020, 2022), five are non-randomized trials (Cosyn et al., 2016; Fenner et al., 2016; Hosseini et al., 2020; Roccuzzo et al., 2016; Seyssens et al., 2020), and the remaining six are case series (Eeckhout et al., 2020; Eghbali et al., 2018; Hanser & Khoury, 2016; Roccuzzo et al., 2019; Stefanini et al., 2016; Zucchelli, Felice, et al., 2018). All the studies were conducted in a single center. Five of them were performed in private practice (Cosyn et al., 2016; Hanser & Khoury, 2016; Roccuzzo et al., 2016, 2019; Seyssens et al., 2020), while the other studies took place in a university setting (Bianchi & Sanfilippo, 2004; Eeckhout et al., 2020; Eghbali et al., 2018; Fenner et al., 2016; Hosseini et al., 2020; Oh et al., 2020; Stefanini et al., 2016; Thoma et al., 2020, 2022; Zucchelli, Felice, et al., 2018).

In terms of indications for treatment, STA procedures were performed as a part of immediate implant therapy (Bianchi & Sanfilippo, 2004; Cosyn et al., 2016; Eghbali et al., 2018; Seyssens et al., 2020), for MT augmentation (Eeckhout et al., 2020; Fenner et al., 2016; Hanser & Khoury, 2016; Hosseini et al., 2020; Stefanini et al., 2016; Thoma et al., 2020, 2022), for KMW augmentation (Oh et al., 2020; Roccuzzo et al., 2016), and for addressing implant esthetic complications (PSTDs) (Cosyn et al., 2016; Hosseini et al., 2020; Roccuzzo et al., 2019; Seyssens et al., 2020; Zucchelli, Felice, et al., 2018). STA was executed at implant placement in four studies (Bianchi & Sanfilippo, 2004; Eeckhout et al., 2020; Hanser & Khoury, 2016; Stefanini et al., 2016), at second stage in one article (Hosseini et al., 2020), and delayed in 10 studies (Cosyn et al., 2016; Eghbali et al., 2018; Fenner et al., 2016; Oh et al., 2020; Roccuzzo et al., 2016, 2019; Seyssens et al., 2020; Thoma et al., 2020, 2022; Zucchelli, Felice, et al., 2018). Two studies performed soft tissue augmentation using APF + FGG (Oh et al., 2020; Roccuzzo et al., 2016), while in the other studies, STA was carried out using a bilaminar approach, involving a CTG, a porcine-derived acellular dermal matrix (PADM) or xenogeneic cross-linked collagen matrix (CCM) (Bianchi & Sanfilippo, 2004; Cosyn et al., 2016; Eeckhout et al., 2020; Eghbali et al., 2018; Fenner et al., 2016; Hanser & Khoury, 2016; Hosseini et al., 2020; Roccuzzo et al., 2019; Seyssens et al., 2020; Stefanini et al., 2016; Thoma et al., 2020, 2022; Zucchelli, Felice, et al., 2018). Three studies (two cohorts) assessed the outcomes of STA using graft substitutes (Eeckhout et al., 2020; Thoma et al., 2020, 2022). In terms of follow-up, three studies had a maximum period of observation of 3 years (Eeckhout et al., 2020; Stefanini et al., 2016; Thoma et al., 2020), one study reported data up to 4 years (Oh et al., 2020), seven articles described outcomes up to 5 years following STA (Cosyn et al., 2016; Eghbali et al., 2018; Hanser & Khoury, 2016; Hosseini et al., 2020; Roccuzzo et al., 2019; Thoma et al., 2022; Zucchelli, Felice, et al., 2018), Fenner et al. (2016) followed the study participants for 5–9 years (mean 7.2 years), Bianchi and Sanfilippo (2004) reported outcomes up to the 9-year follow-up and two studies provided data at 10 years (Roccuzzo et al., 2016; Seyssens et al., 2020). Further details are reported in Tables 1 and 2.

TABLE 1 Characteristics of the included studies at baseline and their interventions.

Publication	Study design	No. of centers, country, setting, funding	Clinical condition, treatment	Timing of intervention, flap approach	Age (years), male/female (*N*), inclusion of smokers	Patients at BL (*N*), implants at BL (*N*), implant type	Follow-up (months), patients at the last visit (*N*)
Bianchi and Sanfilippo (2004)	RCT	Single center, Italy, University, NA	Immediate implant therapy, CTG (bilaminar)	At implant placement	45.4, 58/58, yes	96, 96, Straumann Tissue Level (Straumann)	36–108 (19)
			No soft tissue augmentation	N/A		20, 20, Straumann Tissue Level (Straumann)	
Cosyn et al. (2016)	Non-RCT	Single center, Belgium, Private Practice, self-supported	Immediate implant therapy (esthetic complications), CTG (bilaminar)	Delayed	50, 12/10, no	7, 7, NobelActive (Nobel)	60 (17)
			Immediate implant therapy, no soft tissue augmentation	N/A		15, 15, NobelActive (Nobel)	
Eeckhout et al. (2020)	Case series	Single center, Belgium, University, self-supported	MT augmentation, Porcine-derived ADM (bilaminar)	At implant placement	51.4, 10/5, no	15, 15, NobelActive (Nobel)	36 (14)
Eghbali et al. (2018)	Case series	Single center, Belgium, University, self-supported	Immediate implant therapy, CTG (bilaminar)	Delayed	38, 19/18, no	37, 37, NobelActive (Nobel)	60 (32)
Fenner et al. (2016)	Non-RCT	Single center, Switzerland, University, self-supported	MT augmentation, CTG (bilaminar)	Delayed	48, N/A, yes	14, 14, Straumann Tissue Level (Straumann)	86.4[a] (28)
			No soft tissue augmentation	N/A		22, 22, Straumann Tissue Level (Straumann)	
Hanser and Khoury (2016)	Non-RCT	Single center, Germany, Private Practice, self-supported	MT augmentation, CTG (bilaminar)	At implant placement	37.8, 19/27, no	46, 52, Ankylos and XiVE (Dentsply Sirona)	60 (N/A)
Hosseini et al. (2020)	Non-RCT	Single center, Denmark, University, self-supported	MT augmentation and/or PSTD treatment, CTG (bilaminar)	At second stage	19, 8/11, yes	10, 10, Astra (Dentsply Sirona)	36, 60 (17)
			No soft tissue augmentation			15, 15, Astra (Dentsply Sirona)	
Oh et al. (2020)	RCT	Single center, USA, University, self-supported	KMW augmentation, FGG (APF)	Delayed	65.3, 2/9, no	15, 23, N/A	48 (11)
			KMW augmentation, FGG (APF) (delayed)[b]	Delayed	65, 2/3, no	5, 8, N/A	27[a] (5)
			No soft tissue augmentation	N/A	66, 3/4, no	15, 22, N/A	48 (7)
Roccuzzo et al. (2016)	Non-RCT	Single center, Italy, Private practice, self-supported	KMW augmentation, FGG (APF)	Delayed	52.4, 52/76, yes	N/A, 11, Straumann Tissue Level (Straumann)	120 (98)
			No soft tissue augmentation (implants with KM)	N/A		N/A, 63, Straumann Tissue Level (Straumann)	
			No soft tissue augmentation (implants without KM)	N/A		N/A, 24, Straumann Tissue Level (Straumann)	

(Continues)

TABLE 1 (Continued)

Publication	Study design	No. of centers, country, setting, funding	Clinical condition, treatment	Timing of intervention, flap approach	Age (years), male/female (*N*), inclusion of smokers	Patients at BL (*N*), implants at BL (*N*), implant type	Follow-up (months), patients at the last visit (*N*)
Roccuzzo et al. (2019)	Case series	Single center, Italy, Private Practice, self-supported	PSTD treatment, CTG (bilaminar)	Delayed	53.1, 3/13, yes	16, 16, Straumann Tissue Level (Straumann)	60 (13)
Seyssens et al. (2020)	Non-RCT	Single center, Belgium, Private Practice, self-supported	Immediate implant therapy (esthetic complications), CTG (bilaminar)	Delayed	50, 12/10, no	7, 7, NobelActive (Nobel)	120 (18)
			Immediate implant therapy, No soft tissue augmentation	N/A		15, 15, NobelActive (Nobel)	
Stefanini et al. (2016)	Case series	Single center, Italy, University, self-supported	MT augmentation, CTG (bilaminar)	At implant placement	NA, 8/12, no	20, 20, Straumann Tissue Level (Straumann)	36 (20)
Thoma et al. (2020)	RCT	Single center, Switzerland, University, sponsored	MT augmentation, CTG (bilaminar)	Delayed	43.4, N/A, yes	10, 10, N/A	36 (17)
			MT augmentation, CCM (bilaminar)	Delayed	44.1, N/A, yes	10, 10, N/A	
Thoma et al. (2022)	RCT	Single center, Switzerland, University, sponsored	MT augmentation, CTG (bilaminar)	Delayed	N/A, N/A, yes	10, 10, N/A	60 (15)
			MT augmentation, CCM (bilaminar)	Delayed	N/A, N/A, yes	10, 10, N/A	
Zucchelli, Felice, et al. (2018)	Case series	Single center, Italy, University, self-supported	PSTD treatment, CTG (bilaminar)	Delayed	N/A, N/A, yes	20, 20, N/A	60 (19)

Abbreviations: ADM, acellular dermal matrix (Mucoderm, Botiss); APF, apically positioned flap; BL, baseline; CCM, cross-linked collagen matrix (Geistlich Fibrogide, Geistlich Pharma); CTG, connective tissue graft; FGG, free gingival graft; KM/AM, keratinized and attached mucosa; KMW, keratinized mucosa width; MT, mucosal thickness; N/A, not available/not assessed; non-RCT, prospective non-randomized controlled clinical study; PSTD, peri-implant soft tissue dehiscence; RCT, Randomized controlled trial.

[a]Median observation period.

[b]Treatment arm not considered in the qualitative analysis (follow-up <36 months).

TABLE 2 Outcomes of interest of the included studies.

Publication	Clinical outcomes	Level of the soft tissue margin	Volumetric outcomes	Radiographic outcomes	Esthetic outcomes	PROMs	Complications
Bianchi and Sanfilippo (2004)	BOP, KMW, PAL, PD, and plaque score	EL alignment	N/A	DIB, bone peaks stability	Based on KMW and EL	Patient satisfaction with the esthetic outcomes	Survival rate
Cosyn et al. (2016)	BOP, PD, and plaque score	Midf REC	N/A	MBL	Mesial and distal papillary recession, PES	N/A	Survival rate, incidence of peri-implant diseases, biological, and prosthetic complications
Eeckhout et al. (2020)	BOP, PD, and plaque score	N/A	ΔD from 3D analysis	MBL	N/A	N/A	Survival rate, biological, and prosthetic complications
Eghbali et al. (2018)	BOP, PD, and plaque score	Midf REC	UMT	MBL	Mesial and distal papillary recession, PES	N/A	Survival rate, biological, and prosthetic complications
Fenner et al. (2016)	BOP, KMW, PD, and plaque index	Midf REC	N/A	MBL	Papilla index	Satisfaction (VAS)	Survival rate, biological, and prosthetic complications
Hanser and Khoury (2016)	PD	N/A	cMT	DIB	N/A	N/A	Survival rate
Hosseini et al. (2020)	Bleeding index, KMW, PD, and plaque score	Midf REC	cMT. LD changes at 1, 3, and 5 mm ΔD from 3D analysis	MBL	CIS, discoloration scores and papilla index	N/A	Survival rate, incidence of peri-implant diseases, biological, and prosthetic complications
Oh et al. (2020)	KMW	Midf REC	N/A	MBL	N/A	N/A	N/A
Roccuzzo et al. (2016)	BOP, PD, plaque score, and presence of plaque	Midf REC	N/A	MBL	N/A	Discomfort during brushing (yes/no), soreness upon hygiene maintenance (yes/no)	Survival rate, biological, and prosthetic complications
Roccuzzo et al. (2019)	BOP, PD, and presence of plaque	Midf REC	N/A	N/A	VAS	Satisfaction (VAS)	Survival rate, biological, and prosthetic complications
Seyssens et al. (2020)	BOP, papillary recession, PD, and plaque score	Midf REC	N/A	MBL BBT (from CBCT)	PES	N/A	Survival rate, incidence of peri-implant diseases, biological, and prosthetic complications
Stefanini et al. (2016)	KMW, PD	Vertical soft tissue level (Midf REC)	cMT	MBL	N/A	N/A	Incidence of peri-implant diseases

(Continues)

TABLE 2 (Continued)

Publication	Clinical outcomes	Level of the soft tissue margin	Volumetric outcomes	Radiographic outcomes	Esthetic outcomes	PROMs	Complications
Thoma et al. (2020)	BOP, KMW, PD, and plaque index	N/A	cMT and ΔD from 3D analysis	MBL	Papilla index and PES	OHIP-G14	N/A
Thoma et al. (2022)	BOP, KMW, PD, and plaque index	Midf REC	cMT and ΔD from 3D analysis	MBL	PES	OHIP-G14	Incidence of peri-implant diseases
Zucchelli, Felice, et al. (2018)	BOP, CAL, KMW, PD, and plaque score	PSTD depth, mean PSTD coverage, and complete PSTD coverage	cMT	N/A	PES/WES	Patient satisfaction with the esthetic outcomes (VAS)	Incidence of peri-implant diseases

Abbreviations: CAL, clinical attachment level; cMT, clinically assessed mucosal thickness using the transmucosal piercing method; DIB, distance from the implant shoulder to the first implant bone contact; EL, emergence line of the prosthetic crown from the soft tissue in relation to the EL of the mesial and distal adjacent teeth; KMW, keratinized mucosa width; LD changes, linear dimensional changes in the facial contour assessed with optical scanners; MBL, marginal bone loss; Midf REC, midfacial recession, defined as the apical shift of the peri-implant soft tissue margin from the prosthetic crown margin; N/A, not available/not assessed; OHIP-G14, oral health impact profile-G14; PAL, probing attachment level; PES, pink esthetic score; PSTD depth, depth of the peri-implant soft tissue dehiscence, measured as the distance between the peri-implant soft tissue margin and the cemento-enamel junction of the homologous contralateral tooth; UMT, mucosal thickness evaluated with an ultrasonic device; ΔD, mean distance between the surface/mean thickness of the reconstructed volume following superimposition of the digital models obtained with optical scanners.

3.3 | Risk of bias assessment

Among the RCTs, three studies were considered with a moderate risk of bias (Bianchi & Sanfilippo, 2004; Thoma et al., 2020, 2022) and one with a low risk of bias (Oh et al., 2020). Four non-RCTs were considered having a low risk of bias (Cosyn et al., 2016; Hosseini et al., 2020; Roccuzzo et al., 2016; Seyssens et al., 2020), with one case–control study that was rated with moderate risk of bias (Fenner et al., 2016). Four case series were judged with a low risk of bias (Eghbali et al., 2018; Roccuzzo et al., 2019; Stefanini et al., 2016; Zucchelli, Felice, et al., 2018), with the remaining two studies that were considered having moderate risk of bias (Eeckhout et al., 2020; Hanser & Khoury, 2016) (Tables S5–S7 of the Appendix S1).

3.4 | Qualitative analysis

The low number of RCTs and their heterogenous approaches and outcome measures did not allow to perform quantitative analyses.

Qualitative analyses on peri-implant health and biological complications, stability of the soft tissue margin, plaque score, BOP, PD, KMW, volumetric outcomes, MBLs, esthetic outcomes, and PROMs are depicted in detail in the Appendix S1.

3.4.1 | Implant survival rate and peri-implant health/disease

Overall, a high survival rate (ranging from 90.9% to 100%) was reported at augmented implant sites (Bianchi & Sanfilippo, 2004; Cosyn et al., 2016; Eeckhout et al., 2020; Eghbali et al., 2018; Fenner et al., 2016; Hanser & Khoury, 2016; Hosseini et al., 2020; Roccuzzo et al., 2019; Seyssens et al., 2020; Stefanini et al., 2016; Thoma et al., 2022; Zucchelli, Felice, et al., 2018) (Table 3). The incidence of peri-implant mucositis ranged from 0% to 50%, while the incidence of peri-implantitis was from 0% to 7.14% (Eghbali et al., 2018; Hosseini et al., 2020; Roccuzzo et al., 2019; Seyssens et al., 2020; Thoma et al., 2022; Zucchelli, Felice, et al., 2018). Statistical comparison among different STA procedures, as well as augmented versus non-augmented sites, was not feasible.

3.4.2 | Stability of the soft tissue margin

Twelve studies assessed the changes within the level of the soft tissue margin (Cosyn et al., 2016; Eghbali et al., 2018; Fenner et al., 2016; Hosseini et al., 2020; Oh et al., 2020; Roccuzzo et al., 2016, 2019; Seyssens et al., 2020; Stefanini et al., 2016; Thoma et al., 2020, 2022; Zucchelli, Felice, et al., 2018). The weighted mean the apical shift of the soft tissue margin following bilaminar augmentation with CTG was −0.06 mm on a mean observational period of 4.8 years (Cosyn et al., 2016; Eghbali et al., 2018; Fenner et al., 2016; Hosseini et al., 2020; Roccuzzo et al., 2019; Seyssens et al., 2020; Stefanini

TABLE 3 Qualitative analysis on implant survival rate and stability of the soft tissue margin and marginal bone levels.

Outcome of interest	Group	Weighted mean	*N* cohort/ sites
Implant survival rate (%)	BL + CTG	99.4	11/274
	NAS	100	4/75
Soft tissue margin (mm)	BL + CTG	−0.06	10/135
	BL + CCM	0.58	1/15
	APF + FGG	−0.54	1/18
	NAS	0.96	5/87
Marginal bone levels (mm)	BL + CTG	0.63	5/71
	BL + CTG[a]	0.18	4/57
	BL + CCM	0.71	1/15
	APF + FGG	0.28	2/22
	NAS	0.88	4/74
	NAS[a]	0.33	3/52

Note: Note that a negative value for soft tissue margin indicates an average trend toward coronal migration of the soft tissue margin.

Abbreviations: APF, apically positioned flap; BL, bilaminar technique; CCM, cross-linked collagen matrix; CTG, connective tissue graft; FGG, free gingival graft; NAS, non-augmented sites.

[a]Non considering the outlier study (Fenner et al., 2016).

et al., 2016; Thoma et al., 2020, 2022; Zucchelli, Felice, et al., 2018). Based on two studies from the same cohort (Thoma et al., 2020, 2022), the weighted mean of the apical shift of the soft tissue margin following bilaminar augmentation with XCM was 0.58 mm over 3–5 years. Non-augmented sites exhibited a weighted mean apical displacement of the soft tissue margin of 0.96 mm over a mean period of observation of 6.2 years (Cosyn et al., 2016; Fenner et al., 2016; Hosseini et al., 2020; Oh et al., 2020; Roccuzzo et al., 2016). The only study reporting this outcome for APF-based STA procedures, observed a mean coronal migration of the soft tissue margin of 0.54 mm within 4 years at sites augmented with APF + FGG (Oh et al., 2020) (Table 3).

3.4.3 | Stability of MBLs

Marginal bone level changes after STA were assessed and reported in 13 studies (Bianchi & Sanfilippo, 2004; Cosyn et al., 2016; Eeckhout et al., 2020; Eghbali et al., 2018; Fenner et al., 2016; Hanser & Khoury, 2016; Hosseini et al., 2020; Oh et al., 2020; Roccuzzo et al., 2016; Seyssens et al., 2020; Stefanini et al., 2016; Thoma et al., 2020, 2022). Except for one study reporting mean marginal bone loss of 2.2–2.5 mm after a follow-up of ≥5 years (Fenner et al., 2016), the other studies observed a marginal bone loss within 0.6 mm at augmented implant sites. The weighted mean marginal bone loss following STA with CTG-based bilaminar techniques was 0.63 mm over a mean period of 5 years, that dropped down to 0.18 mm over a mean period of 4.5 years if the abovementioned outlier study is not considered. The weighted mean marginal bone loss at non-augmented sites was 0.88 mm (mean follow-up of 6.6 years) considering the outlier study, and 0.33 mm (mean follow-up of 6.3 years) when excluding the study from Fenner et al. (2016). Sites augmented with APF + FGG showed a weighted mean marginal bone loss of 0.28 mm on a mean period of 7 years (Oh et al., 2020; Roccuzzo et al., 2016) (Table 3).

Clinical, esthetics, and volumetric outcomes, as well as PROMs of the individual studies are described in detail in the Appendix S1.

3.5 | Evidence quality rating

No serious complications or adverse reactions were reported following STA at implant sites. Clinical benefits of these procedures may include enhanced esthetic outcomes, stability of the soft tissue margin, and mucosal thickness over time, stability of marginal bone levels and improved PROMs. Therefore, the net benefit rating supporting soft tissue augmentation at implant sites should be considered strong, as the clinical benefits overweight the potential harms.

Based on the predetermined criteria recommended for rating the level of certainty, it can be stated that the body of evidence (and level of certainty) supporting the treatment effects of bilaminar STA with CTG in the medium and long term is moderate. Other approaches, such as APF + FGG and bilaminar techniques with PADM or CCM, are characterized by a low level of certainty when assessing their medium/long-term effect estimates.

Based on the net benefit rating and level of certainty rating, the strength of recommendation for STA at implant sites with the goal of promoting favorable and stable outcomes in the medium and long term, was deemed in favor.

4 | DISCUSSION

Modern periodontology and implantology aim for minimally invasive therapies with long-term stable outcomes. There are no doubts that biomaterials, together with advancements of surgical techniques and instruments, have had a major impact on STA at implant sites. Nevertheless, while long-term data of different approaches and graft materials following periodontal regeneration and root coverage in natural dentition are currently available, little is known on the medium- and long-term effects of STA at implant sites.

4.1 | Main findings

Based on 15 prospective studies from 13 cohorts, we observed that most of the dental implants that received STA were able to maintain peri-implant health over time. While isolated cases with peri-implant disease have been described, readers should bear in mind that peri-implant mucositis and peri-implantitis can be triggered by several factors, including but not limited to, history of periodontal disease, lack of compliance with supportive therapy, inadequate

design of the implant-supported crown, implant malpositioning not facilitating oral hygiene procedures, etc. (Berglundh et al., 2018; Heitz-Mayfield & Salvi, 2018). Nevertheless, it seems that an adequate soft tissue phenotype can contribute to reduce peri-implant inflammation and plaque accumulation, together with brushing discomfort (Oh et al., 2017; Roccuzzo et al., 2016; Tavelli, Barootchi, Avila-Ortiz, Urban, et al., 2021; Thoma et al., 2018). A recent network meta-analysis demonstrated that STA procedures were effective in promoting an improvement of the clinical and radiographic parameters related to peri-implant health in the short term (Tavelli, Barootchi, Avila-Ortiz, Urban, et al., 2021). Due to the lack of RCTs reporting medium- and long-term outcomes of STA, a quantitative analysis could not be performed in the present review. Findings from the individual studies showed that the early clinical and esthetic outcomes of STA observed at 6/12 months are maintained over time. These findings are of interest, as concerns could be raised on the long-term outcomes (e.g., PD, peri-implant health, stability of the soft tissue margin, etc) of STA procedures at implants exhibiting buccal bone dehiscence. When treating peri-implant soft tissue dehiscences, which are often characterized by deficient/lack of buccal bone (Tavelli, Barootchi, Majzoub, et al., 2022), a split-thickness flap elevation to facilitate graft nutrition and adhesion to the implant surface has been advocated (Stefanini et al., 2020; Zucchelli et al., 2013; Zucchelli, Tavelli, et al., 2021).

The esthetic outcomes of dental implants are strongly affected by the position of the soft tissue margin (Furhauser et al., 2005; Zucchelli et al., 2019; Zucchelli, Barootchi, et al., 2021). Therefore, it is not surprising that this parameter was often reported as the primary outcomes in the included studies. Eleven studies assessed the changes within the position of the soft tissue margin compared to baseline (Midf REC). Although this outcome provides a valuable information of the changes within the soft tissue level at implant sites, the stability of Midf REC does not necessarily correlate with satisfying esthetic outcomes, since the goal of implant therapy and STA at implant sites in the esthetic region should be obtaining the peri-implant soft tissue margin at the same level of the CEJ of the homologous contralateral tooth (Zucchelli et al., 2019; Zucchelli, Barootchi, et al., 2021; Zucchelli, Sharma, & Mounssif, 2018). The weighted average of Midf REC at implant sites augmented with CTG was 0.006 on a mean observational period of approximately 5 years. When compared the stability of the soft tissue margin at CTG-augmented versus non-augmented implant sites over 5 years, Hosseini et al. (2020) reported better results for the grafted dental implants. The benefits of STA with CTG for maintaining the level of the soft tissue margin in the long term was further demonstrated by Seyssens et al. (2020) that showed that all the implant placed without STA developed a Midf REC of at least 1 mm over 10 years. The authors advocated that lack of STA at immediately placed implants should be considered among the putative risk factors for Midf REC in the long term (Seyssens et al., 2020). Interestingly, it appears that sites augmented with autogenous grafts may also exhibit creeping attachment, increased KM, and greater MT over time (Oh et al., 2020; Stefanini et al., 2016; Zucchelli, Felice, et al., 2018). Zucchelli, Felice, et al. (2018) observed that an improvement in the level of the soft tissue margin (PSTD depth) from 1 to 5 years at implant sites previously treated for esthetic complications. When it comes to KMW, STA procedures were found to maintain the early outcomes over time (Thoma et al., 2020, 2022), or even resulting in an increased KMW (Stefanini et al., 2016; Zucchelli, Felice, et al., 2018). It can be assumed that the type of harvesting technique and CTG composition, together with local characteristics of the augmented implants and adjacent sites, may affect the initial and long-term KMW change/gain (Tavelli, Barootchi, Majzoub, Chan, et al., 2021; Zucchelli et al., 2020). In line with this speculation, Rojo et al. (2018) demonstrated that STA with a fibrous CTG from the tuberosity resulted in significantly higher KMW than STA using a subepithelial CTG obtained from the deepest layers of the palate.

Findings from this review also support the stability of early MT/volumetric gain up to 3–5 years following STA with CTG or graft substitutes. Nevertheless, readers should bear in mind that these conclusions are more robust for CTG than for graft substitutes, that have been described in two cohorts only (Eeckhout et al., 2020; Thoma et al., 2020, 2022), and therefore, more evidence is needed for ADM and CCM. Two studies utilizing a CTG obtained from the most superficial layer of the palate—as a FGG and then de-epithelialized—showed a progressively increased in MT compared to early time points (Stefanini et al., 2016; Zucchelli, Felice, et al., 2018), that can be once again explain with the nature of this type of CTG, mainly composed by lamina propria with minimal amount of adipose and glandular tissue (Bertl et al., 2015; Zucchelli et al., 2020). Interestingly, when assessing dimensional changes with optical scanning, Hosseini et al. (2020) reported that while CTG-augmented implants progressively gained volume up to 5 years, non-augmented sites exhibited volume loss at 3 and 5 years. The use of 3D digital optical scanning for assessing outcomes of STA has rapidly become popular among clinicians and researchers, replacing traditional transmucosal piercing in several instances (Tavelli, Barootchi, Majzoub, Siqueira, et al., 2021). Optical scanning has the advantage of being noninvasive and better tolerated by patients compared to transmucosal piercing that requires local anesthesia. Nevertheless, the superimposition of digital impression obtained with optical scanning describe the overall changes occurred within the facial contour only, without discriminating between hard and soft tissue, and without being able to provide information at single time points. In this view, ultrasonography has been shown to be a promising and noninvasive tool for assessing soft tissue thickness and buccal bone dimensions at natural teeth and dental implants, and may become the method of choice for the assessment of these parameters in clinical research (Tavelli, Barootchi, Majzoub, et al., 2022).

In terms of radiographic outcomes, it has been previously advocated that STA can have beneficial effects on the stability of MBLs. Most of the studies included in this review showed that previously augmented implant sites have stable marginal bone levels over time, with a mean marginal bone loss within 0.6 mm—except for one study (Fenner et al., 2016). Few studies also reported marginal bone gain over time (Eeckhout et al., 2020; Oh et al., 2020). Oh et al. (2020)

demonstrated that implant sites augmented with APF + FGG obtained significantly higher MBL stability over 4 years compared to non-augmented sites. The advocated positive effects of STA on the stability of MBLs may be related to facilitate oral hygiene procedures and the reduction of patient discomfort, that can result in less plaque accumulation and inflammation (Perussolo et al., 2018; Sanz et al., 2022; Souza et al., 2016).

Among the limitations of this review, the relatively limited number of available studies, their design, and lack of information on implant location have to be mentioned. Readers should be aware that the results of the present reviews are qualitative only, and therefore, strong conclusions cannot be drawn at the present time. Several medium/long-term RCTs describing STA with APF/bilaminar approaches with autogenous grafts and substitutes are needed to perform robust statistical analyses (e.g., mixed-modeling approach to network meta-analysis) comparing different techniques and graft materials and their impact on the medium/long-term peri-implant health.

5 | CONCLUSIONS

Based on the current available evidence, and within the limitations of this study, it can be concluded that implants that received STA procedures exhibited overall high survival rate and relatively low incidence of peri-implantitis in the medium and long term. Implant sites following STA displayed stable soft tissue margin over time, while non-augmented implants tend to exhibit an apical shift of the soft tissue margin in the medium and long term. The overall favorable outcomes of STA observed at early time points are maintained in the medium and long term, with sites augmented with CTG that may also show a progressive increase in KMW and MT. More evidence from medium- and long-term RCTs is needed to compare different surgical approaches and graft materials.

AUTHOR CONTRIBUTIONS

M. Stefanini: Design of the study, interpretation of data, article preparation and the initial draft, final reviewal of the work, and accountable for all aspects of the work. S. Barootchi: Acquisition and interpretation of data, article preparation and the initial draft, final reviewal of the work, and accountable for all aspects of the work. M. Sangiorgi: Acquisition and interpretation of data, article preparation and the initial draft, final reviewal of the work, and accountable for all aspects of the work. A. Pispero: Acquisition and interpretation of data, article preparation and the initial draft, final reviewal of the work, and accountable for all aspects of the work. M.G. Grusovin: Acquisition and interpretation of data, article preparation and the initial draft, final reviewal of the work, and accountable for all aspects of the work L. Mancini: Acquisition and interpretation of data, article preparation and the initial draft, final reviewal of the work, and accountable for all aspects of the work. G. Zucchelli: Design of the study, critical review of the draft, and contribution to the writing of the article. Final approval of the version to be published and accountable to the accuracy or integrity of the work. L. Tavelli: Design of the study, study registration, literature search, acquisition and interpretation of data, article preparation and the initial draft, final reviewal of the work, and accountable for all aspects of the work.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available in the Appendix S1 and Tables S1–S3.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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CONSENSUS REPORT

CLINICAL ORAL IMPLANTS RESEARCH WILEY

Group 1 ITI Consensus Report: The role of bone dimensions and soft tissue augmentation procedures on the stability of clinical, radiographic, and patient-reported outcomes of implant treatment

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Abstract

Objectives: The aims of Working Group 1 were to address the role (i) of the buccolingual bone dimensions after implant placement in healed alveolar ridge sites on the occurrence of biologic and aesthetic complications, and (ii) of soft tissue augmentation (STA) on the stability of clinical, radiographic, and patient-related outcomes of implant treatments.

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Materials and Methods: Two systematic reviews were prepared in advance of the Consensus Conference and were discussed among the participants of Group 1. Consensus statements, clinical recommendations, recommendations for future research, and reflections on patient perspectives were based on structured group discussions until consensus was reached among the entire group of experts. The statements were then presented and accepted following further discussion and modifications as required by the plenary.

Results: Dimensional changes of the alveolar ridge occurred after implant placement in healed sites, and a reduction in buccal bone wall thickness (BBW) of 0.3 to 1.8 mm was observed. In healed sites with a BBW of <1.5 mm after implant placement, increased vertical bone loss, and less favorable clinical and radiographic outcomes were demonstrated. Implants with buccal dehiscence defects undergoing simultaneous guided bone regeneration, showed less vertical bone loss, and more favorable clinical and radiographic outcomes, compared to non-augmented dehiscence defects during initial healing.

At healthy single implant sites, probing depths, bleeding and plaque scores, and interproximal bone levels evaluated at 1 year, remained stable for up to 5 years, with or without STA. When single implant sites were augmented with connective tissue grafts, either for soft tissue phenotype modification or buccal soft tissue dehiscence, stable levels of the soft tissue margin, and stable or even increased soft tissue thickness and/or width of keratinized mucosa could be observed from 1 to 5 years. In contrast, non-augmented sites were more prone to show apical migration of the soft tissue margin in the long-term. Favorable aesthetic and patient-reported outcomes after STA were documented to be stable from 1 to 5 years.

Conclusions: It is concluded that dimensional changes of the alveolar ridge occur after implant placement in healed sites and that sites with a thin BBW after implant placement are prone to exhibit less favorable clinical and radiographic outcomes. In addition, it is concluded that STA can provide stable clinical, radiographic, aesthetic, and patient-reported outcomes in the medium and long-term.

KEYWORDS
aesthetics, bone augmentation, dental implant, evidence-based dentistry, patient-reported outcome measures, soft tissue augmentation, surgical techniques, systematic review

1 | INTRODUCTION

The objectives of Group 1 of the 7th ITI Consensus Conference were to provide statements and recommendations for clinicians and researchers related to the effect of buccal bone wall thickness (BBW) and soft tissue augmentation (STA) procedures on the development of peri-implant disease, incidence of complications, stability of clinical, volumetric and radiographic parameters, and patient-reported outcome measures (PROMs) after implant therapy.

For Working Group 1, two systematic reviews were prepared and reviewed before the Consensus Conference. Based on the data of the systematic reviews and on thorough discussions among the participants of Group 1 and among the entire plenum, the Consensus Statements and Clinical Recommendations were carefully formulated. In addition, Recommendations for Future Research were also prepared by the working group. Finally, patient perspectives were formulated supported by the Consensus Statements from the systematic reviews and the Clinical Recommendations.

The two systematic reviews are listed below:

1. Influence of buccal bone wall thickness on the peri-implant hard and soft tissue dimensional changes: A systematic review. Alberto Monje, Andrea Roccuzzo, Daniel Buser, Hom-Lay Wang.
2. Do soft tissue augmentation techniques provide stable and favorable peri-implant conditions in the medium and long-term? A systematic review.

Martina Stefanini, Shayan Barootchi, Alberto Pispero, Maria Gabriella Grusovin, Leonardo Mancini, Giovanni Zucchelli, Lorenzo Tavelli.

2 | SYSTEMATIC REVIEW PAPER 1

2.1 | Manuscript title

Influence of buccal bone wall thickness on the peri-implant hard and soft tissue dimensional changes: A systematic review.

2.2 | Preamble

It is well established that the presence of alveolar bone is a prerequisite for osseointegration of dental implants. However, the exact amount of alveolar bone that is required to ensure the long-term stability of the peri-implant bone and to support the soft tissue has not yet been systematically evaluated. Lack of buccal bone has been documented to be a risk factor for the development of biologic and aesthetic complications. On the other hand, the potential preventive effect of bone augmentation of thin BBWs or dehiscence defects simultaneously with implant placement in healed sites on biologic and aesthetic complications has not been systematically evaluated.

The aim of the present systematic review was to evaluate the influence of BBW and the overall dimensions of alveolar bone upon soft and hard tissue stability and to assess the effectiveness of simultaneous bone augmentation procedures to prevent biological and aesthetic complications when implants were placed in healed sites.

The main goal was to correlate the BBW of implants placed in healed sites to the primary outcome parameter: vertical bone loss. Secondary outcome parameters included changes in buccal bone thickness, buccolingual ridge dimensions, peri-implant clinical parameters, crestal bone loss, and patient-reported outcome measures. In addition, the same primary and secondary outcome parameters were analyzed to evaluate the effect of bone augmentation of thin buccal bone walls and dehiscence defects simultaneous with implant placement in healed sites to prevent biological and aesthetic complications.

Out of 1700 identified records, 16 studies (12 clinical and 4 preclinical studies) could be included for the qualitative analysis. Preclinical studies were included in the analysis to potentially provide histologic data explaining the biologic background for clinically and radiographically observed peri-implant changes.

For the present consensus report, a BBW of <1.5 mm was considered a "thin" buccal bone wall. "Initial healing" after implant placement in healed sites was defined as ≤6 months. The available data did not allow to distinguish between open-flap and flapless approaches during implant placement. However, most of the implants documented in the included studies were placed with open-flap procedures.

2.3 | Consensus statements

2.3.1 | Consensus statement 1

The alveolar ridge is subjected to buccolingual dimensional reduction during initial healing after implant placement in healed sites. This statement was supported by two prospective clinical studies and one preclinical study. Reduction of BBW is observed after implant placement in healed sites (0.3 to 1.8 mm; up to 72 months). This statement was supported by 11 prospective clinical studies.

2.3.2 | Consensus statement 2

After implant placement in healed sites with a thin BBW, vertical bone loss occurs during initial healing. This statement was supported by five prospective, two retrospective clinical studies, and 1 preclinical study.

2.3.3 | Consensus statement 3

Implants with buccal dehiscence defects undergoing simultaneous guided bone regeneration, show less vertical bone loss, and more favorable clinical and radiographic outcomes, compared to non-augmented dehiscence defects during initial healing. This statement was supported by one RCT (22 patients, 28 implants).

2.3.4 | Consensus statement 4

Implants placed in healed sites exhibiting thin BBWs, not undergoing simultaneous bone augmentation, are prone to less favorable clinical (i.e., increased peri-implant probing pocket depth, bleeding on probing, suppuration or mucosal recession), and radiographic outcomes. This statement was supported by six prospective clinical studies and one preclinical study.

2.4 | Clinical recommendations

2.4.1 | Clinical recommendation 1

Do we need an intact buccal bone wall for long-term peri-implant health?

An intact buccal bone wall is necessary to avoid exposure to the implant surface designed to be inside the bone, such as a microrough surface. Therefore, simultaneous bone augmentation is recommended in cases of buccal dehiscence defects or a thin buccal bone wall to maintain long-term peri-implant health.

However, when soft tissue conditions are favorable, peri-implant health can be maintained in the presence of minor buccal bone deficiencies.

2.4.2 | Clinical recommendation 2

How thick should the buccal bone wall be after implant placement in healed sites?

A buccal bone wall thickness of >1.5 mm is recommended at the time of implant placement to promote long-term peri-implant health.

Aside from bone augmentation, this may, in selected cases, be achieved by reducing implant diameter, placing the implant deeper in the alveolar crest, or flattening the alveolar ridge (in the posterior region).

2.4.3 | Clinical recommendation 3

Is bone augmentation per se enough to achieve a satisfying aesthetic result?

In the majority of cases, simultaneous bone augmentation can achieve satisfactory aesthetic results. However, in cases with high aesthetic demands exhibiting a thin soft tissue phenotype or a soft tissue deficiency, an additional STA procedure is recommended.

2.5 | Patent perspectives

2.5.1 | Patient perspective 1

Question: Do I have enough bone for an implant to be placed?
Answer: To answer this, we first need to examine your mouth, take radiographs and plan the best position for the implant. At this point, we can determine if there will be enough bone around it. The bone needs to be 1.5 mm thick on the cheek/lip side of the implant and 1 mm thick on the palate/tongue side. So if the implant is 4 mm in diameter the bone needs to be 6.5–7 mm wide.

2.5.2 | Patient perspective 2

Question: Can I have a bone graft at the same time as the implant is placed?
Answer: Yes, it can be done at the same time, but it depends on how much grafting is required and how stable the implant is when it is placed. If we can place an implant in the correct position with good stability but still lack some bone thickness in places (see Section 2.5.1), then a bone graft can be performed at the same time.

2.5.3 | Patient perspective 3

Question: Will the bone graft come from my mouth or from elsewhere?
Answer: In most cases, we can collect bone from the same site where the implant is being placed. When a greater amount of bone is needed, we may need to go to a second surgical site inside your mouth. Often, however, the use of a bone substitute material, alone or in combination with your own bone, will avoid the need to use bone from other surgical sites.

2.5.4 | Patient perspective 4

Question: When do I get my crown after implant placement and bone grafting?
Answer: In a routine case, you will need to wait 2–3 months after implant placement and bone grafting for a fixed temporary crown. With a more complex situation, it may take up to 6 months. In addition, some aesthetic changes may take place during healing, so it may take 6–9 months for the final crown to be delivered.

2.5.5 | Patient perspective 5

Question: Will I need antibiotics after the implant surgery?
Answer: This is a controversial topic. If bone grafting is required, we would recommend antibiotics. These can either be given before surgery, after surgery, or both. For implant placement, it will depend on your medical risk factors.

2.6 | Recommendations for future research

2.6.1 | Recommendation 1 for future research

The influence of anatomical and procedural factors on the dynamics of buccal bone resorption during initial healing after implant placement in areas exhibiting different thicknesses of the buccal bone wall, such as mandible vs. maxilla, zone of keratinized mucosa, open flap vs. flapless procedure, submerged vs. transmucosal healing.

2.6.2 | Recommendation 2 for future research

Long-term clinical performance of different implant designs and implant surface characteristics in sites with thin buccal bone walls or dehiscence defects.

2.6.3 | Recommendation 3 for future research

The long-term effect of bone augmentation of thin buccal bone walls on clinical, aesthetic, and radiographic parameters.

3 | SYSTEMATIC REVIEW PAPER 2

3.1 | Manuscript title

Do soft tissue augmentation techniques provide stable and favorable peri-implant conditions in the medium and long-term? A systematic review.

3.2 | Preamble

STA is often performed around implants to treat aesthetic complications, improve mucosal thickness, increase keratinized mucosa width, and reconstruct papillae. Keratinized mucosa width has been associated with improved peri-implant health, as well as less marginal bone loss and reduced patient discomfort during brushing. However, the medium and long-term effects of STA around dental implants remain unclear in the literature. Although some studies report improvement in clinical parameters and PROMs in the short-term, questions remain regarding the stability of marginal soft tissue and bone levels.

The aim of this study was to systematically review prospective clinical reporting on medium and long-term stability of clinical, volumetric, and radiographic parameters, as well as the incidence of peri-implant disease, complications, and PROMs.

The main goal and primary outcome of the systematic review was to evaluate the stability of peri-implant health after STA at medium and long-term follow-up (≥36 months).

Secondary outcomes were as follows:

- Implant survival
- Incidence of complications
- Changes in the position of the peri-implant soft tissue margin
- Changes in peri-implant clinical parameters (plaque index/score, bleeding on probing/bleeding index, pocket depths)
- Radiographic marginal bone levels
- PROMs

The present systematic review is based on 15 clinical studies, including 4 randomized controlled trials (RCTs), 5 non-randomized clinical trials, and 6 case series. The study population included 447 patients with 461 implants, with a follow-up period ranging from 3 to 10 years (mean 8 years).

Sufficient data was not available to perform a meta-analysis of the primary outcome (stability of peri-implant health after STA at medium and long-term follow-up; ≥36 months). Only descriptive analyses were possible for the primary and secondary outcome measures, including the incidence of peri-implant disease, stability of marginal soft tissue, stability of crestal bone levels, and PROMs.

When interpreting the results, it is important to understand that medium-term follow-up is defined as 3–5 years, and long-term refers to >5 years. STA procedures were performed for different indications (soft tissue phenotype modification and treatment of soft tissue dehiscences), and due to the limited available evidence, it was difficult to draw significant conclusions about soft tissue substitutes.

3.3 | Consensus statements

3.3.1 | Consensus statement 1

Single implant sites may display stable peri-implant interproximal bone levels in the medium and long-term, whether or not soft tissue augmentation is performed. This statement is supported by 12 studies (3 RCTs and 9 prospective clinical studies).

3.3.2 | Consensus statement 2

At healthy single implant sites, probing depths, bleeding, and plaque scores evaluated at 1 year, remain stable for up to 5 years, with or without soft tissue augmentation. This statement is supported by 11 studies (2 RCTs and 9 prospective clinical studies).

3.3.3 | Consensus statement 3

Single implant sites augmented with connective tissue grafts, either for soft tissue phenotype modification or buccal soft tissue dehiscence, display a stable level of the soft tissue margin up to 5 years. This statement is supported by 10 studies (2 RCTs and 8 prospective clinical studies). Non-augmented sites may show apical migration of the soft tissue margin in the long-term. This statement is supported by five studies (1 RCT and 4 prospective clinical studies).

3.3.4 | Consensus statement 4

Single implant sites receiving connective tissue grafts, display stable, or even increased soft tissue thickness and/or width of keratinized mucosa, from 1 to 5 years. This statement is supported by five studies (1 RCT and 4 prospective clinical studies) for soft tissue thickness and three studies (1 RCT and 2 prospective clinical studies) for the width of keratinized mucosa.

3.3.5 | Consensus statement 5

Single implant sites after augmentation with connective tissue grafts or substitutes with favorable aesthetic outcomes (i.e., pink aesthetic score, visual analog scale) are maintained or even improved, from 1 to 5 years. This statement is supported by four studies (1 RCT and 3 prospective clinical studies) for connective tissue grafts and 1 RCT for substitutes (15 patients in total, 8 vs. 7 implants). Single implant sites without soft tissue augmentation may display a higher discoloration (ie. mucosal discoloration score) compared to sites with connective tissue grafts. This statement is supported by 1 prospective clinical study (17 patients in total, 28 implants, 20 vs. 8).

3.3.6 | Consensus statement 6

Single implant sites receiving soft tissue augmentation maintain stable patient-reported aesthetic outcomes, from 1 to 5 years. This statement is based on three studies (1 RCT and 2 prospective clinical

studies). Patient-reported brushing discomfort is reduced at implant sites where keratinized mucosa width was augmented with a free gingival graft. This statement is based on 1 prospective clinical study, including 98 patients and 98 implants followed up to 10 years.

3.4 | Clinical recommendations

3.4.1 | Clinical recommendation 1

Are soft tissue augmentation procedures recommended in the presence of inadequate keratinized mucosa at healthy implant sites?

In patients with difficulty in plaque control and/or reporting brushing discomfort, a free gingival graft is recommended in non-aesthetic implant sites, whereas a connective tissue graft is recommended in aesthetic implant sites.

3.4.2 | Clinical recommendation 2

Are soft tissue augmentation procedures recommended in the presence of a thin soft tissue phenotype at healthy implant sites?

Soft tissue augmentation procedures are recommended only when there is a patient aesthetic request. A connective tissue graft should be used when there is no keratinized mucosa, while soft tissue substitutes may also be selected as an alternative in the presence of keratinized mucosa.

3.4.3 | Clinical recommendation 3

Are soft tissue augmentation procedures recommended in the presence of a mid-facial soft tissue dehiscence at a restored implant with healthy peri-implant conditions?

In case of acceptable 3-dimensional implant position: Soft tissue augmentation with a connective tissue graft is recommended to improve aesthetic outcomes and promote long-term stability of the soft tissue margin.

In case of facial implant malposition: In the presence of patient aesthetic complaints and based on the severity of implant malposition, two treatment options should be considered: connective tissue graft with a new implant crown/abutment, or removal of the implant.

3.4.4 | Clinical recommendation 4

In the presence of a concave soft tissue profile and thin buccal bone, can soft tissue augmentation be performed alone?

In the presence of patient aesthetic complaint or difficulty in plaque control due to a concave soft tissue profile, a connective tissue graft is recommended.

3.5 | Patient perspectives

3.5.1 | Patient perspective 1

Question: How long will I have to be without a tooth?
Answer: Ideally, we will try to avoid leaving you without a tooth. We can offer both fixed and removable solutions and design them so there is no pressure on the surgical site. If you already have a tooth replacement, we can adjust it (usually by cutting it back by 2 mm) to avoid any pressure.

3.5.2 | Patient perspective 2

Question: Will I need to have a soft tissue graft?
Answer: It depends on the shape and volume of your jaw bone and gum where the implant is to be placed.

3.5.3 | Patient perspective 3

Question: Will you use part of my palate to increase the thickness of gum around the implant?
Answer: Most likely we will need to use soft tissue from your palate, either from behind the teeth or from the back of the upper jaw. In some specific cases, we may be able to use a soft tissue substitute.

3.5.4 | Patient perspective 4

Question: How long after implant placement and soft tissue grafting will I get the crown?
Answer: In some favorable cases it is possible to have a screw-retained temporary crown fitted immediately. If this is not possible, 3 months is usually the longest you will have to wait.

3.5.5 | Patient perspective 5

Question: Can bone and soft tissue grafting be performed in the same surgical procedure?
Answer: Yes, this can be done if the conditions are favorable and feasible.

3.6 | Recommendations for future research

3.6.1 | Recommendation 1 for future research

Long-term efficacy of soft tissue substitute materials to increase peri-implant soft tissue phenotype and to treat soft tissue dehiscences.

3.6.2 | Recommendation 2 for future research

Long-term stability of the level of the mucosal margin around dental implants with thin or missing buccal bone wall undergoing soft tissue augmentation.

AUTHOR CONTRIBUTIONS

All co-authors contributed to the wording of the consensus statements, clinical recommendations, patient perspectives, and recommendations for future research. Simon Storgård Jensen, Tara Aghaloo and Ronald E. Jung drafted the manuscript. All authors gave their final approval and agreed to be accountable for all aspects of the consensus report.

CONFLICT OF INTEREST STATEMENT

All co-authors reported no conflicts of interest with regards to the present consensus report.

DATA AVAILABILITY STATEMENT

None.

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REVIEW ARTICLE

CLINICAL ORAL IMPLANTS RESEARCH WILEY

Additively and subtractively manufactured implant-supported fixed dental prostheses: A systematic review

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Abstract

Aim: To compare and report on the performance of implant-supported fixed dental prostheses (iFDPs) fabricated using additive (AM) or subtractive (SM) manufacturing.

Methods: An electronic search was conducted (Medline, Embase, Cochrane Central, Epistemonikos, clinical trials registries) with a focused PICO question: In partially edentulous patients with missing single (or multiple) teeth undergoing dental implant therapy (P), do AM iFDPs (I) compared to SM iFDPs (C) result in improved clinical performance (O)? Included were studies comparing AM to SM iFDPs (randomized clinical trials, prospective/retrospective clinical studies, case series, in vitro studies).

Results: Of 2′184 citations, no clinical study met the inclusion criteria, whereas six in vitro studies proved to be eligible. Due to the lack of clinical studies and considerable heterogeneity across the studies, no meta-analysis could be performed. AM iFDPs were made of zirconia and polymers. For SM iFDPs, zirconia, lithium disilicate, resin-modified ceramics and different types of polymer-based materials were used. Performance was evaluated by assessing marginal and internal discrepancies and mechanical properties (fracture loads, bending moments). Three of the included studies examined the marginal and internal discrepancies of interim or definitive iFDPs, while four examined mechanical properties. Based on marginal and internal discrepancies as well as the mechanical properties of AM and SM iFDPs, the studies revealed inconclusive results.

Conclusion: Despite the development of AM and the comprehensive search, there is very limited data available on the performance of AM iFDPs and their comparison to SM techniques. Therefore, the clinical performance of iFDPs by AM remains to be elucidated.

KEYWORDS
additive manufacturing, CAD-CAM, Computer-Aided Design, Computer-Aided Manufacturing, dental implants, Dental Prosthesis, Implant-Supported, single tooth, 3 Dimensional Printing, 3 D Printing, Three-Dimensional Printing

1 | INTRODUCTION

With the advent of digital technologies in implant dentistry, conventional surgical and prosthetic approaches have been increasingly replaced or complemented by digital workflows (Jung et al., 2009; Muhlemann et al., 2018; Schneider et al., 2021). These technologies pursue toward a common goal: the optimization of current treatment options in implant dentistry (Al-Dwairi et al., 2019; Joda

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et al., 2017, 2021; Kunavisarut et al., 2022; Muhlemann et al., 2022; Pan et al., 2019).

Conventional prosthetic workflows have shown predictable long-term results, but involve more manual effort and treatment time, and are more technique-sensitive (Joda & Bragger, 2016). To overcome these limitations, digital workflows, using computer-aided design (CAD) as well as computer-aided manufacturing (CAM) for the fabrication of the prostheses, have been introduced (Mormann et al., 1990; Muhlemann et al., 2018). The CAM process for the different restorative materials relies on two methods: (1) SM: subtractive manufacturing or (2) AM: additive manufacturing (Pyo et al., 2020).

Subtractive manufacturing methods involve the milling of a manufacturing material to obtain an interim or final restoration. SM has become a well-established technology in implant dentistry producing accurate implant-supported fixed dental prostheses (iFDPs; De Angelis et al., 2020; Gintaute et al., 2021; Muhlemann et al., 2020). Nevertheless, there are some limitations such as the large amounts of waste due to material residues generated during the grinding of the material block. In addition, the SM technology is limited to some extent by the complexity of the structures, as the number of milling axes and number and shape of the milling instruments limit the possible design and affect the reproduction of an object (Methani et al., 2020; Revilla-Leon, Besne-Torre, et al., 2019). Furthermore, during the milling processes of ceramics, the material's high strength can lead to an increased wear of the milling instruments (Methani et al., 2020).

Additive manufacturing, commonly referred to as 3D printing, describes the process of successive adding and joining materials layer by layer to build a digitally designed three-dimensional object by means of a 3D printer (Jockusch & Ozcan, 2020). The AM technology allows the inclusion of different material properties or colors in the same workpiece (Methani et al., 2020; Stansbury & Idacavage, 2016). Moreover, AM may bring the advantage of reduced material waste and enables the recycling of unused material (Galante et al., 2019). There are different technologies and materials used for AM. The quality of a product, as well as the production time and costs, can be affected by various factors such as the technology used, its resolution, processing parameters (e.g. the energy source, layer thickness, or building orientation), material composition, and required post-processing treatments. (Alharbi et al., 2016; Osman et al., 2017; Tian et al., 2021).

In in vitro studies, both AM and SM methods have shown similar precision for the fabrication of tooth-supported fixed dental prostheses (Ioannidis et al., 2021; Son et al., 2021; Wang et al., 2019). A previous systematic review comparing SM to AM for iFDPs reported inconclusive results, in part due to a limited number of studies applying AM (Muhlemann et al., 2021). Due to the significant and ongoing interest in additive manufacturing, it is crucial to analyze and summarize the latest state of evidence in order to arrive at more definitive conclusions about this fabrication method. The aim of the present systematic review was, therefore, to compare and report on the performance of iFDPs fabricated using AM or SM techniques.

2 | MATERIALS AND METHODS

2.1 | Protocol development registration and reporting format

A detailed protocol was developed and followed according to the PRISMA (Preferred Reporting Items for Systematic Review and Meta-Analyses) statement (Page et al., 2021) and the 2021 Cochrane Handbook (Higgins et al., 2021). The protocol was registered in PROSPERO with the identification number CRD42021293470.

2.2 | Eligibility criteria

According to the PICO-framework, a focused question was utilized to facilitate the inclusion and exclusion of studies.

2.2.1 | Focused question

In partially edentulous patients with missing single (or multiple) teeth undergoing dental implant therapy (P), do AM iFDPs (I) compared to SM iFDPs (C) result in an improved clinical performance (O)?

Population (P): Partially edentulous patients with missing single (or multiple) teeth undergoing dental implant therapy.

Intervention (I): AM iFDPs.

Comparison (C): SM iFDPs.

Outcome (O): Clinical performance including clinical, radiographic, aesthetic outcomes, survival and complication rates as well as patient-reported outcomes.

2.3 | Search strategy

An electronic search was conducted on Medline (PubMed) Embase, Cochrane Central, and Epistemonikos (for relevant systematic reviews addressing the topic). An electronic search was also performed on ClinicalTrial.gov and Cochrane Central Register of Controlled Trials for registered ongoing trials. The electronic search was conducted up to November 1, 2022 and designed and adapted to each type of database (Table 1). In addition, reference lists of retrieved studies for full-text screening and previous reviews on the topic were screened.

2.4 | Inclusion criteria

Randomized clinical trials (RCT), prospective and retrospective clinical studies, case series with at least 10 patients, and in vitro studies, all comparing AM to SM single- or multi-unit iFDPs.

TABLE 1 Search strategy.

Medline	"dental implants"[MeSH Terms] OR "dental implants, single tooth"[MeSH Terms] OR "dental implants, single tooth"[MeSH Terms] OR "Dental Implantation, Endosseous"[MeSH Terms] OR "Dental Prosthesis" [MeSH Terms] OR "Dental Prosthesis, Implant-Supported" [MeSH Terms] OR "Denture, Partial, Fixed" [MeSH Terms] OR "Crowns" [MeSH Terms] OR "dental restoration failure" [MeSH Terms] OR "Tooth, Artificial" [MeSH Terms] OR "Dental abutments" [MeSH Terms] OR "restoration*" [All Fields] OR "suprastructure*" [All Fields] OR "crown*" [All Fields] OR "fixed dental prosthes*" [All Fields] OR "fixed partial denture*" [All Fields] OR "abutment*" [All Fields] OR "dental implant*"[All Fields] OR "Denture, Partial, Temporary" [MeSH Terms] AND Dental Technology [MeSH Terms] OR Computer-Aided Design [MeSH Terms] OR Computer-Aided Manufacturing [MeSH Terms] OR Manufacturing, Computer Aided [MeSH Terms] OR Design, Computer Aided [MeSH Terms] OR "CAD-CAM" [All Fields] AND Printing, Three Dimensional [MeSH Terms] OR Printings, Three-Dimensional [MeSH Terms] OR Three-Dimensional Printings [MeSH Terms] OR 3-Dimensional Printing [MeSH Terms] OR 3 Dimensional Printing [MeSH Terms] OR 3-Dimensional Printings [MeSH Terms] OR Printing, 3-Dimensional [MeSH Terms] OR Printings, 3-Dimensional [MeSH Terms] OR 3-D Printing [MeSH Terms] OR 3 D Printing [MeSH Terms] OR 3-D Printings [MeSH Terms] OR Printing, 3-D [MeSH Terms] OR Printings, 3-D [MeSH Terms] OR Three-Dimensional Printing [MeSH Terms] OR Three Dimensional Printing [MeSH Terms] OR 3D Printing [MeSH Terms] OR 3D Printings [MeSH Terms] OR Printing, 3D [MeSH Terms] OR Printing, 3D [MeSH Terms] OR "3-dimensional print*" [All Fields] OR "3d print*" [All Fields] OR "three-dimensional print*" [All Fields] OR "3-dimensional print*" [All Fields] OR "additive" [All Fields] OR "additive manufacturing" [All Fields] OR "additively manufact*"[All Fields] OR "CAD-CAM mill*" [All Fields]
Embase	"tooth implant"/exp OR "tooth implantation"/exp OR "implant-supported denture"/exp OR "tooth prosthesis"/exp OR "dental abutment"/exp OR "partial denture"/exp OR "prosthesis design"/exp OR "suprastructure*" OR "crown*" OR "fixed dental prosthes*" OR "fixed partial denture*" OR "abutment*" OR "dental implant*" AND "dental technology"/exp OR "computer aided design"/exp OR "computer aided design/computer aided manufacturing"/exp OR "CAD/CAM software"/exp OR "CAD-CAM" AND "three dimensional printing"/exp OR "three dimensional computer aided design"/exp OR "stereolithography"/exp OR "three dimensional printing" OR "additively manufact*" OR "3-dimensional print*" OR "additive" "OR additive manufacturing" OR "three-dimensional print*" OR "CAD-CAM mill*"
Central	[mh "dental implant"] OR "dental implant*" AND [mh "Computer-Aided Design"] OR [mh "Computer-Aided Manufacturing"] OR [mh "Manufacturing, Computer Aided"] OR [mh "Design, Computer Aided"] OR "CAD-CAM" OR "subtractive manufacturing" OR "subtractive manufact*" AND [mh "Printing, Three Dimensional"] OR [mh "Printings, Three-Dimensional"] OR [mh "Three-Dimensional Printings"] OR [mh "Three-Dimensional Printing"] OR [mh "Three Dimensional Printing"] OR "additive" OR "additive manufacturing" OR "additively manufact*"
Epistemonikos	"dental implants"[MeSH Terms] OR "dental implants, single tooth"[MeSH Terms] OR "dental implants, single tooth"[MeSH Terms] OR "Dental Implantation, Endosseous"[MeSH Terms] OR "Dental Prosthesis" [MeSH Terms] OR "Dental Prosthesis, Implant-Supported" [MeSH Terms] OR "Denture, Partial, Fixed" [MeSH Terms] OR "Crowns" [MeSH Terms] OR "fixed dental prosthes*" [All Fields] OR "fixed partial denture*" [All Fields] OR "abutment*" [All Fields] OR "dental implant*"[All Fields] OR "Denture, Partial, Temporary" [MeSH Terms] AND Computer-Aided Design [MeSH Terms] OR Computer-Aided Manufacturing [MeSH Terms] OR Manufacturing, Computer Aided [MeSH Terms] OR Design, Computer Aided [MeSH Terms] OR "CAD-CAM" [All Fields] AND Printing, Three Dimensional [MeSH Terms] OR Printings, Three-Dimensional [MeSH Terms] OR Three-Dimensional Printings [MeSH Terms] OR 3-Dimensional Printing [MeSH Terms] OR 3 Dimensional Printing [MeSH Terms] OR 3-Dimensional Printings [MeSH Terms] OR Printing, 3-Dimensional [MeSH Terms] OR Printings, 3-Dimensional [MeSH Terms] OR 3-D Printing [MeSH Terms] OR 3 D Printing [MeSH Terms] OR 3-D Printings [MeSH Terms] OR Printing, 3-D [MeSH Terms] OR Printings, 3-D [MeSH Terms] OR Three-Dimensional Printing [MeSH Terms] OR Three Dimensional Printing [MeSH Terms] OR 3D Printing [MeSH Terms] OR 3D Printings [MeSH Terms] OR Printing, 3D [MeSH Terms] OR Printing, 3D [MeSH Terms] OR "3-dimensional print*" [All Fields] OR "3d print*" [All Fields] OR "three-dimensional print*" [All Fields] OR "3-dimensional print*" [All Fields] OR "additive" [All Fields] OR "additive manufacturing" [All Fields] OR "additively manufact*"[All Fields] OR "CAD-CAM mill*" [All Fields]

2.5 | Exclusion criteria

- Fully edentulous cases.
- Studies focusing on the manufacturing procedures of frameworks or abutments.

2.6 | Study selection

Based on the inclusion/exclusion criteria, two calibrated authors (JH; KP) screened independently the titles, abstracts, and full texts to check for eligibility. No restrictions were set for the date of publication, but the language for text eligibility was restricted to English, German, Spanish, Finnish, Turkish, Italian, and Portuguese. The identified articles were inserted into the Rayyan® Online Software (Qatar Computing Research Institute) and the duplicated articles were deleted. The inter-agreement among the authors was based on Cohen's Kappa score. Any disagreements were resolved by discussion with a third author (AI). All articles that did not meet the eligibility criteria were excluded and the reasons for exclusion were noted.

2.7 | Data extraction

Consistent with the latest handbook by the Cochrane group (Higgins et al., 2021) a paper form using processing software was used for the data extraction tables. The tables were pilot-tested

by two extractors. Data were independently extracted by two reviewers (JH, KP) using data extraction tables (Excel Microsoft Corporation). In case of missing data, the authors of the included studies were contacted via email to provide the missing or additional data.

3 | RESULTS

3.1 | Search

A total of 2′184 articles were identified through the electronic search (Figure 1). After the removal of 414 duplicates, 1′770 titles were screened, and 23 records were evaluated on the basis of their abstract and on the information available in the trial registry. Based on full-text analysis 15 articles were excluded (Table 2). Two relevant trial registrations (German Clinical Trial Register ID: DRKS00029049 and Brazilian Registry of Clinical Trials ID: RBR-4msyxn) were further excluded, as the final reports were not available. A total of 6 articles remained and were finally included. The inter-rater agreement during the selection of the abstracts (screening phase) between reviewers was $\kappa = 0.839$.

3.2 | Description of included studies and study characteristics

The included studies were published between 2016 and 2022 (Table 3, Figure 2). No clinical studies could be found and, therefore, only in vitro studies were included. A total of 6 in-vitro studies including screw- or cement-retained single-unit iFDPs were analyzed. Performance was evaluated by assessing marginal and internal discrepancies and mechanical properties (fracture loads, bending moments). Materials included for the AM iFDPs were ceramics (zirconia) and polymers (PMMA, resin composite). For the SM iFDPs, zirconia, lithium disilicate reinforced glass ceramic, resin-modified ceramic, composite, and polymer materials (PMMA, Pekkton) were investigated in the included studies. The used AM methods were digital light processing (DLP) and stereolithography (SLA). SM refers to milling processes with multi-axis milling machines.

No clinical studies comparing AM to SM iFDPs were found. The identified in vitro investigations comparing these two manufacturing methods for iFDPs focused on (1) the marginal and internal discrepancies, and (2) the fracture loads and bending moments.

The data were analyzed qualitatively and given that no clinical study was included no demographics were reported. Considering

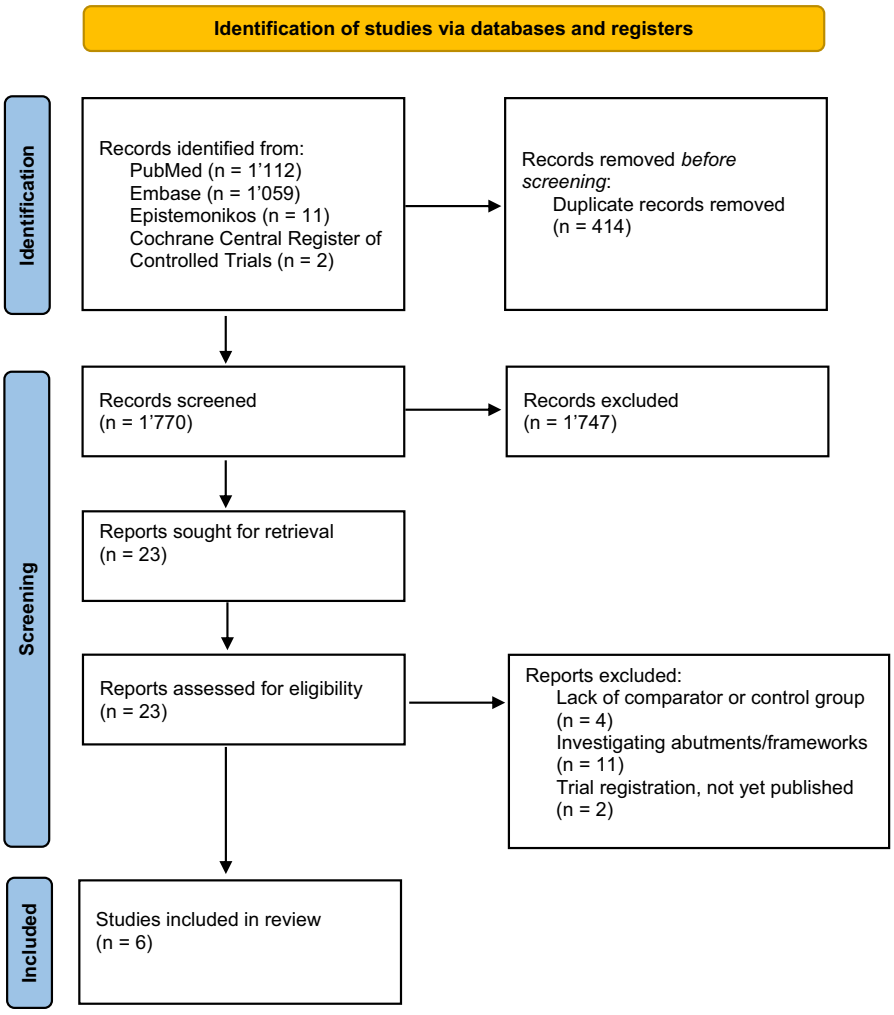


FIGURE 1 Flow chart of the systematic review.

TABLE 2 List of excluded studies.

Author/Publication Year	Journal	Reason for exclusion
Kim et al. (2017)	Materials	Investigating abutments/ frameworks
Akcin et al. (2018)	The Journal of Prosthetic Dentistry	Investigating abutments/ frameworks
Obermeier et al. (2018)	Clinical Oral Investigations	Lack of comparator or control group
Svanborg et al. (2018)	The International Journal of Oral and Maxillofacial Implants	Investigating abutments/ frameworks
Ghodsi et al. (2019)	European Journal of Dentistry	Investigating abutments/ frameworks
Presotto et al. (2019)	The Journal of Prosthetic Dentistry	Investigating abutments/ frameworks
Barbin et al. (2020)	Journal of the Mechanical Behaviour of Biomedical Materials	Investigating abutments/ frameworks
Gonzalo et al. (2020)	Materials	Investigating abutments/ frameworks
Kim and Lee (2020)	BioMed Research International	Lack of comparator or control group
Williams et al. (2020)	Journal of Oral and Maxillofacial Surgery	Lack of comparator or control group
Yildirim (2020)	The Journal of Prosthetic Dentistry	Investigating abutments/ frameworks
Graf et al. (2021)	The Journal of Advanced Prosthodontics	Lack of comparator or control group
Revilla-Leon et al. (2021)	The Journal of Prosthetic Dentistry	Investigating abutments/ frameworks
Hsu et al. (2022)	Polymers	Investigating abutments/ frameworks
Revilla-Leon et al. (2022)	Journal of Prosthodontics	Investigating abutments/ frameworks

that only in vitro studies were included, no risk of bias analysis was deemed necessary.

3.3 | Data extraction and management

Two reviewers (KP and JH) extracted data from the included studies using a pre-piloted data extraction form and checked them against each other. We resolved any disagreements by discussion or with a third review author (AI). We extracted data on: Author, date of publication, study design, manufacturing technique in AM and SM, testing method, marginal and internal discrepancies, fracture load, and bending moments.

3.4 | Marginal and internal discrepancies

Three of the included studies examined the marginal and internal discrepancies between AM and SM iFDPs. One of these studies assessed interim iFDPs, while two examined definitive iFDPs.

An in vitro study compared cemented interim single-unit iFDPs, which were manufactured either using a 4-axis milling machine (SM) or DLP (AM) (Park et al., 2016). The used materials were Pekkton (SM) and PMMA (AM). The marginal and internal discrepancies between the prostheses and the standardized implant abutments were examined at 20 reference points. The mean marginal discrepancies (±standard deviations) amounted to 58.02 (±19.75) μm (SM) and 56.85 (±22.24) μm (AM). For both groups, the largest internal discrepancies were measured in the occlusal area with mean values (±standard deviations) of 197.87 (±42.18) μm for SM and 167.81 (±41.86) μm for AM. Statistically significant differences between AM and SM for the intermarginal and occlusal areas were reported, while the marginal, axio-gingival, and axio-occlusal discrepancies did not reach statistically significant levels.

The second study examining the marginal and internal discrepancies, compared three study groups (Revilla-Leon, Methani, et al., 2020). In the SM group, definitive single-unit SM zirconia iFDPs were tested. The second group consisted of definitive single-unite AM zirconia iFDPs (AM full-contour). In the third group, the

TABLE 3 Characteristics of included studies.

Author/Publication Year	Journal	Study design	Number of specimens per group	Material test group (AM)	Manufacturing technique test group (AM)	Materials control group (SM)	Manufacturing techniques control group (SM)	Testing method	Primary outcome	Results
Studies about marginal and internal discrepancies										
Park et al. (2016)	The Journal of Prosthetic Dentistry	In vitro	40	PMMA (E-Dent; Envision TEC)	Digital light processing (Perfactory PixCera; Envision TEC)	Pekkton (Pekkton Ivory; Cendres&Metaux)	4-axis milling machine (Cendres&Metaux SA)	Silicon replica method	Marginal and internal discrepancies	Mean discrepancy (μm) (±SD) marginal SM 58.02 (±19.75) AM 56.85 (±22.24) intermarginal SM 96.70 (±25.38) AM 108.50 (±35.21) axio-gingival SM 67.02 (±17.97) AM 67.54 (±20.29) axio-occlusal SM 81.41 (±30.64) AM 79.57 (±28.35) occlusal SM 197.87 (±42.18) AM 167.81 (±41.86) total SM 109.59 (±71.53) AM 96.05 (±50.23)
Revilla-Leon, Methani, et al. (2020)	The Journal of Prosthetic Dentistry	In vitro	10	Zirconia stabilized with 3% yttria (3DMix ZrO2 paste; 3DCeram Co)	Stereolithography (CERAMAKER 900; 3DCeram Co)	CARES Zirconia-dioxide (Institut Straumann AG)	5-axis milling machine (CARES Straumann centralized)	Silicon replica method	Marginal and internal discrepancies	Median discrepancy (μm) (±SD): marginal SM 37.5 (±50) AM full-contour 146.0 (±103.2) AM splinted 79.5 (±49.2) internal SM 73.0 (±44.7) AM full-contour 79.0 (±46) AM splinted 85.0 (±48)
Studies about marginal and internal discrepancies and mechanical properties										
Donmez et al. (2022)	Journal of Dentistry	In vitro	10	Composite resin Saremco Print, Crowntec (SP)	Digital light processing (MAX UV; ASIGA)	Composite resins (Brilliant, Crios) (BC), (Cerasmart 270) (CS)/Resin-modified ceramic (Vita Enamic) (VE)	4-axis milling machine (inLab MC XL; Dentsply Sirona)	Stereomic-roscopical measuring of marginal gap; static loading	Marginal discrepancy; fracture load	Mean marginal discrepancy (μm) (±SD) after cementation: SM BC 63.3 (±2.8) SM VE 65.5 (±2.7) SM CS 62.6 (±3.5) AM 52.4 (±2.3) Mean fracture loads (N) (±SD): SM BC 1′333.23 (±144.73) SM VE 1′359.25 (±159.63) SM CS 1′274.32 (±135.8) AM 1′413.91 (±140.49)

(Continues)

TABLE 3 (Continued)

Author/Publication Year	Journal	Study design	Number of specimens per group	Material test group (AM)	Manufacturing technique test group (AM)	Materials control group (SM)	Manufacturing techniques control group (SM)	Testing method	Primary outcome	Results
Studies about mechanical properties										
Martin-Ortega et al. (2022)	The Journal of Prosthetic Dentistry	In vitro	10	Photopolymer interim dental resin (SHERAprint-cb; Shera)	Digital light processing 3D printer (SHERAprint30; Shera)	PMMA (Vivodent CAD Multi; Ivoclar)	5-axis milling machine (PrograMill CAM V4; Ivoclar)	Aging, static loading	Fracture load	Mean fracture loads (N) (±SD): anterior SM 988 (±55) AM 636 (±277) posterior SM 424 (±68) AM 321 (±129)
Sudbeck et al. (2022)	Dental Materials	In vitro	12	3D Printed resin (Next Dent)	Digital light processing (D 20II, Rapidshape)	Composite resin (Crios Coltene) (CC)/ Resin-modified ceramic (Vita Enamic) (VE)/ PMMA (Ceramill A-Temp) (PM) with and without titanium base	5-axis milling machine (Ceramill Motion 2, Amann Girrbach)	Aging, dynamic, and static loading	Bending moment	Mean bending moment (Ncm)/ fracture load (N) after aging (±SD): with titanium base SM CC 775 (±189)/1′565 (±381) SM VE 676 (±108)/1′365 (±218) SM PM 622 (±109)/1′258 (±219) AM 520 (±131)/1′050 (±264) without titanium base SM CC 510 (±325)/1′029 (±657) SM VE 611 (±124)/1′236 (±250) SM PM 456 (±22)/921 (±44) AM 563 (±96)/1′138 (±194)
Zandinejad et al. (2019)	Journal of Prosthodontics	In vitro	10	Zirconia stabilized with 3% yttria (3DMix ZrO2 paste; 3DCeram Co.) (Zr)	Stereolithography (CeraMaker 900; 3DCeram Co.)	Zirconia (Lava Plus Zirconia W1, 3 M Co.) (ZR)/Lithium disilicate (IPS e.max CAD; Ivoclar Vivadent) (LiSi)	5-axis milling machine (CARES Straumann centralized)	Static loading	Fracture load	Median fracture loads (N): SM Zr 1′292 (±189) SM LiSi 1′289 (±142) AM Zr 1′243.4 (±265.5)

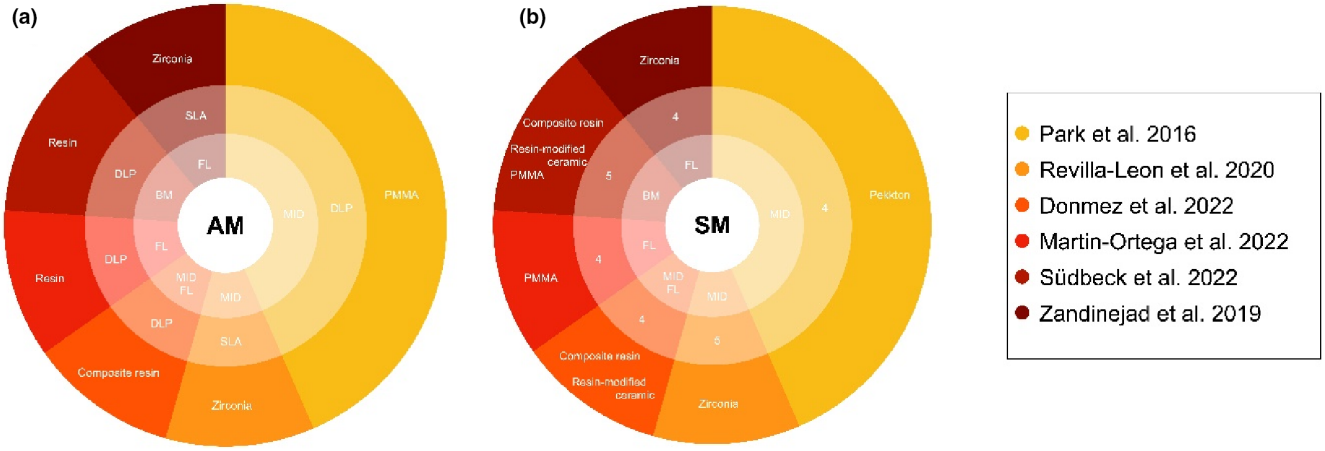


FIGURE 2 Graphical overview of the characteristics of the included in vitro studies for the groups AM (a) and SM (b). For the AM groups, the restorative materials, the fabrication method (DLP, SLA) and the measurement methods (BM = bending moments, FL = fracture loads, MID = marginal and internal discrepancy) are indicated from the outside to the inside. For the SM groups, the restorative materials, the number of milling axes (4, 5) and the measuring methods (BM, FL, MID) are indicated from the outside to the inside.

full-contour design was divided into two files: one representing the enamel part of the iFDP and the second one the dentin part. Only the latter was further processed to be fabricated by AM technologies to build the third group under investigation (AM splinted). For the AM of the zirconia parts, SLA was applied. The SM and AM fabricated zirconia parts were placed onto individualized zirconia abutments to measure the marginal and internal discrepancies. The silicon replica technique was used to determine the marginal discrepancies at 25 points and the internal discrepancies at 50 points per specimen. Median marginal discrepancies (±standard deviations) of 37.5 (±50) μm (SM), 146.0 (±103.2) μm (AM full-contour), and 79.5 (±49.2) μm (AM splinted) were found. In the internal areas, discrepancies of 73.0 (±44.7) μm (SM), 79.0 (±46) μm (AM full-contour), and 85.0 (±48) μm (AM splinted) were detected. The differences of marginal discrepancies were significantly different when comparing AM full-contour to AM splinted and SM, and when comparing AM splinted to SM. As for the internal discrepancies, the differences between the groups were statistically significant when comparing SM to AM full-contour and splinted and when comparing AM full-contour to AM splinted.

In another in vitro study, the marginal discrepancy for definitive single-unit iFDPs, where the prostheses were cemented to standardized titanium abutments, was investigated using stereomicroscopy (Donmez & Okutan, 2022). For the fabrication of the SM iFDPs, three different definitive restorative materials were used, including two composites and one resin-modified ceramic material. The iFDPs were milled using a 4-axis milling machine. For the AM group, DLP was used for the fabrication of definitive composite resin iFDPs. Marginal discrepancy measurements were performed at 60 points per iFDP before and after cementation with self-adhesive resin cement. The mean marginal discrepancies (±standard deviations) after cementation amounted to 62.6–65.5 μm in the SM groups and 52.4 (±2.3) μm in the AM group. The results showed significantly lower marginal discrepancy values for the AM specimens compared to the SM groups.

3.5 | Mechanical properties: fracture loads and bending moments

Four of the included studies examined the mechanical properties of SM and AM iFDPs—all single-unit—measuring the fracture loads (four studies) and the bending moments (one study). One of the studies evaluated interim iFDPs, while two assessed definitive iFDPs. One study evaluated both definitive and interim materials.

An included study (Donmez & Okutan, 2022) compared the fracture resistance of an AM composite resin with three different SM materials: two composites and a resin-modified ceramic. The used AM technique was DLP. The definitive prostheses were cemented to titanium abutments using a self-adhesive resin cement and then statically loaded with a vertical force. In the SM groups mean fracture loads of 1′274–1′359N were found, whereas the AM group showed a mean value (±standard deviations) of 1′413.91 (±140.49) N. All the iFDPs fractured without an abutment fracture and the results showed no significant differences between the groups.

A further study (Martin-Ortega et al., 2022) evaluated the fracture loads of anterior and posterior polymer-based screw-retained interim iFDPs. The SM PMMA iFDPs were fabricated using a 5-axis milling machine. The AM fabrication process for the polymer iFDPs was DLP. All prostheses were cemented to standardized metallic implant abutments and screw-retained to the implants. Prior to loading, all specimens were subjected to thermo-cyclic aging. The mean fracture loads (±standard deviations) were 988 (±55) (SM) and 636 (±277) N (AM) for the anterior iFDPs, whereas the posterior groups showed values of 424 (±68) (SM) and 321 (±129) N (AM). The fracture load testing resulted in fractures of the iFDPs, while the abutments remained intact. The failure modes consisted of multiple fractures in the anterior group and mostly single longitudinal fractures in the posterior group. The results showed significantly higher failure load values for the SM iFDPs in both the anterior and posterior groups.

In both manufacturing methods, the anterior iFDPs had higher mean fracture load values than the posterior iFDPs.

Another included study (Zandinejad et al., 2019) compared the fracture loads of definitive SM (5-axis milling machine) zirconia and lithium disilicate iFDPs to SLA AM zirconia iFDPs. All prostheses were cemented to standardized zirconia abutments. The antagonist for the loading test consisted of a Co-Cr prosthesis. The median fracture loads (±standard deviations) were 1′292 (±189) N (SM Zirconia), 1′289 (±142) N (SM lithium disilicate), and 1′243 (±265.5) N (AM). No significant differences were found among the groups. All fractures occurred at the abutment level with the fracture line near the interface of the implant analog and the zirconia abutment. Therefore, all iFDPs were intact at the end of the loading test.

One study (Sudbeck et al., 2022) reporting on mechanical properties evaluated the bending moments and fracture loads of polymer-based iFDPs with or without a standardized titanium base before and after aging. For the specimens with a titanium base, the prostheses were cemented onto the titanium base and screw-retained to the implant. For the specimens without a titanium base, the iFDPs were directly screwed to the implant. The manufacturing methods included milling with a 5-axis milling machine and DLP. The tested materials included composite resin, resin-modified ceramic, PMMA, and a 3D-printed resin. Before aging, the iFDPs with a titanium base showed no significant differences in bending moments for any of the restorative materials tested. iFDPs without a titanium base exhibited higher bending moments when fabricated using 3D printed resin and milled composite resin compared to the other materials before aging. After aging, in the titanium base group, 3D printed resin resulted in lower bending moments than milled composite resin. Without a titanium base, there was no significant impact of the restorative material on the results after aging. The results for the fracture loads showed no significant differences between the materials when titanium base abutments were not used. With a titanium base abutment AM iFDPs had the lowest fracture load values.

4 | DISCUSSION

4.1 | Main findings

The current systematic review sought to compare and report on the performance of AM and SM iFDPs. No clinical studies could be found that directly compared the two methods of fabrication. Based on the included in vitro studies, the present systematic review revealed:

1. A lack of studies comparing the performance of AM and SM iFDPs.
2. No significant differences between AM and SM interim iFDPs for marginal discrepancies. The internal discrepancies were statistically significantly lower with AM compared to SM only in intermarginal and occlusal areas.
3. Inconsistent results when comparing marginal and internal discrepancies of SM versus AM definitive iFDPs.
4. Lower fracture loads and bending moment values for AM compared to SM interim iFDPs.
5. Similar fracture loads for AM and SM definitive iFDPs.
6. Insufficient data to draw strong conclusions.
7. Considerable heterogeneity across the studies limiting a thorough comparison. Confounding variables included the type of prosthesis (definitive or interim), the varying materials, the different locations, and the lack of detailed information regarding material compositions, production, and post-processing parameters.

4.2 | Marginal and internal discrepancies

When examining the marginal and internal discrepancies between a prosthesis and an abutment, the marginal fit plays a pivotal role. Consequently, the accuracy in the marginal area is a relevant aspect of the longevity of indirect prostheses and thus the clinical success of iFDPs. A lack of marginal fit may expose the prosthesis/abutment interface to the oral environment, increasing the possibility of bacterial colonization and triggering peri-implant inflammation, which can eventually may lead to marginal bone loss (Broggini et al., 2003). Furthermore, a poor fit can predispose to plaque accumulation, intensifying the ensuing inflammatory response. Clinically, the marginal gap between the restorative material and the abutment is usually filled up with resin cement (Ioannidis et al., 2020; Pitta et al., 2021). It is known that this interface area can be further affected by aging processes (Ioannidis et al., 2020). In the literature, a mean marginal discrepancy of <120 μm has been reported as clinically acceptable (Jemt & Book, 1996), while other authors have reported a misfit of up to 200 μm as an acceptable discrepancy (Boeckler et al., 2005). The present review found similar marginal accuracies of interim iFDPs between SM and AM when using Pekkton and PMMA as restorative materials (Park et al., 2016). This suggests that AM could be a viable alternative to SM for iFDPs. The study had a high number of specimens per group, which increased the statistical power and enabled the detection of small differences. When it comes to definitive iFDPs, the present review found conflicting results on the marginal and internal discrepancies between AM and SM fabrication methods. Whereas some results favored the SM method (Revilla-Leon, Methani, et al., 2020), another study showed significantly lower marginal discrepancies for the AM fabricated prostheses (Donmez & Okutan, 2022). The differences in outcomes might be attributed to the use of different restorative materials and manufacturing technologies. Resin-based and resin-modified ceramic materials showed lower marginal discrepancies for AM specimens than for SM groups. Resin-based materials can be fabricated with SM or AM technologies at a high precision (Jockusch & Ozcan, 2020; No-Cortes et al., 2022; Revilla-Leon & Ozcan, 2019). In contrast, the study showing non-clinically acceptable marginal and internal accuracies for full-contour prostheses fabricated by AM technologies used zirconia as restorative material (Revilla-Leon, Methani, et al., 2020). The latter study showed only acceptable marginal and internal discrepancies for the AM process for the group testing the AM intermediate secondary

abutment (AM splinted). The anatomically full-contoured and the splinted prostheses did not differ regarding the design of the cervical area. However, the total volume of the AM splinted prostheses was substantially smaller. Other studies confirm the acceptable marginal accuracy when small-volume prostheses are fabricated (Ioannidis et al., 2021). Accordingly, the authors speculated that differences in the material bulk or volume design might lead to varying directions and volumetric shrinkage behavior during the post-processing, causing the accuracy differences between the 2 AM groups (Revilla-Leon, Methani, et al., 2020). This might be further explained by the fact that zirconia prostheses manufactured in full contour showed a high standard deviation in discrepancies in the marginal area.

The included studies indicate that marginal discrepancies might pose a challenge in the manufacturing process of the iFDPs. Although the discrepancies found may be partially clinically acceptable, the results of AM groups tended to be more variable (Revilla-Leon, Methani, et al., 2020). This might be explained by the further development of SM. AM, on the contrary, has only been recently introduced in dentistry for the fabrication of prostheses. A further aspect that needs to be taken into consideration when interpreting the present findings is the method of assessment. Whilst some studies performed a two-dimensional cross-sectional analysis, others performed a direct analysis of the marginal area using a stereomicroscope. Arguably, a 3D analysis of the complete prosthesis might be necessary to generate accurate information regarding the marginal and internal fit (Boitelle et al., 2018). Additionally, more information about the production parameters, debinding, sintering, and post-processing procedures for the SM and AM techniques would have been needed to further interpret the data. This is of importance since these factors can influence the final accuracy of the prostheses and therefore determine the marginal and internal fit (Komissarenko et al., 2018; Tian et al., 2021). Detailed information on the material composition for the print materials was mostly lacking. At this stage, there is insufficient data to draw strong conclusions on the marginal fit of AM compared to SM iFDPs.

4.3 | Fracture loads and bending moments

The mechanical properties play a pivotal crucial in the clinical success of iFDPs. Factors such as fracture loads and bending moments are important and determine whether a prosthesis can withstand the physiological occlusal forces. The present review found lower fracture loads and bending moment values for AM compared to SM interim iFDPs (Martin-Ortega et al., 2022). While interim AM iFDPs in the anterior region might withstand physiological forces, posterior ones could have a higher risk for fractures (Martin-Ortega et al., 2022). The AM iFDPs showed higher standard deviations compared to the SM ones. In other words, there was more variability in the results. AM iFDPs showed failure modes with several smaller fragments, whereas the iFDPs in the SM groups mainly fractured in two to four pieces (Sudbeck et al., 2022). Two of the included studies evaluated screw-retained iFDPs (Martin-Ortega et al., 2022; Sudbeck et al., 2022). It should be noted that the screw access channel might have affected the manufacturing accuracy as well as the mechanical properties. Also, artificial aging led to a decrease in bending moment values (Sudbeck et al., 2022).

As for definitive iFDPs, the present review found a similar fracture load for AM and SM iFDPs. These findings should, however, be interpreted with caution because of the varying manufacturing methodology applied, including printer, printing protocol, and restorative materials. For example, in one of the included studies, all specimens were fractured at the abutment level but none at the level of the prosthesis (Zandinejad et al., 2019). Therefore, the results cannot provide a real comparison between the tested manufacturing methods, but demonstrate that all included restorative materials were able to withstand physiological occlusal forces. In fact, previous studies (Martin-Ortega et al., 2022; Park et al., 2019) have evaluated the mechanical properties of AM prostheses but the varying methodology applied, for example, manufacturing technique, materials used, and methods of assessment, made it difficult to draw definitive conclusions (Giugovaz et al., 2022). In addition, aging processes were often lacking in the included studies. The influence of aging processes could have a significant impact on the fracture load and should therefore be included in further study designs to have a more complete picture (Sudbeck et al., 2022). Detailed information on the material compositions, printing parameters, sintering processes, and postprocessing procedures was often lacking.

Fracture loads and bending moments are primarily material parameters and are highly influenced by the mechanical properties of the restorative material (Donmez et al., 2022). The manufacturing process (AM and SM) may have a secondary effect on the mechanical properties of the iFDPs. However, the extent to which the manufacturing process affects the resulting bending moments or fracture loads remains unclear. Therefore, the direct comparisons of mechanical performance are a result of the material properties themselves and the associated manufacturing processes.

4.4 | Further aspects regarding AM procedures

The AM techniques used in the included studies were SLA and DLP. The main difference between stereolithography and digital light processing is the light source. The differences in manufacturing techniques might have contributed to the differences found across the studies. A narrative review evaluating AM techniques in prosthodontics considered SLA the most accurate technique (Alharbi et al., 2017). The precision of the SLA method is determined by different factors such as the precision of the laser beam position, the exposure size in x–y planes, and the resolution in the *z*-axis (Alharbi et al., 2017). The precision of the DLP method is determined by different factors such as the optical specifications of the DMD, lens quality, pixel size, and resolution (Alharbi et al., 2017). Additionally, there are differences in accuracy between the available 3D printers. There are also different parameters, including the layer thickness

and printing orientation, that can have an influence on the printing results (Alharbi et al., 2017).

Another important point to consider when interpreting the present findings is the restorative material used as this can influence the clinical outcomes. In this sense, it should be mentioned that the AM process is not equally evolved for all materials. While studies show good results with the use of metals, the AM of ceramics and polymers still has some limitations (Hesse & Ozcan, 2021; Jockusch & Ozcan, 2020; Revilla-Leon, Meyer, & Ozcan, 2019). The AM processes of included studies (SLA and DLP) can be used to produce ceramic parts by mixing ceramic powders and photosensitive resin. Green parts are then fabricated using the vat photopolymerization. Subsequently, during the debinding and sintering processes the organic materials in photosensitive resin are eliminated, and the ceramic particles are fused together to create denser ceramic objects (Revilla-Leon, Meyer, et al., 2020). An in vitro study comparing the fracture resistance and flexural strength of SM and AM zirconia bars resulted in significantly lower values for the AM parts indicating that the mechanical properties of printed zirconia might still be a limiting factor. AM zirconia seems to be more sensitive to shrinkage during the sintering process. A review evaluating the AM of dental ceramics reported favorable volumetric shrinkage for SM compared to AM (Al Hamad et al., 2022). That review also reported that an increase in the zirconia content of a suspension could lead to reduced volumetric shrinkage, whereas it might have challenging effects on factors such as the viscosity and layer thickness. This aspect could be further evaluated to overcome the limitations for AM zirconia prostheses. As for the use of polymers, based on the included studies it appears that AM of interim resin iFDPs is a reliable method and different kinds of geometries can be manufactured. Mechanically AM resin material seems to be more prone to fractures compared to other resin materials. One of the limiting factors may be the lower elastic modulus for the polymers used in AM procedures. A recent review concluded that there was a lack of dental polymers, which could remain in the oral cavity for a longer period than 12 months (Goodridge et al., 2012; Jockusch & Ozcan, 2020; Sudbeck et al., 2022).

Further studies are needed to compare AM and SM procedures and thus increase the evidence. Similar materials should be used for both manufacturing processes to enable clearer comparisons. Additionally, detailed documentation of material compositions and manufacturing processes is required for comparisons with other studies. Other in vitro studies are necessary to investigate the potential advantages of AM, such as the inclusion different material properties or colors in the same workpiece. This aspect was not addressed in the current studies and could offer more possibilities than the SM process. Randomized clinical trials are needed to compare the clinical performance of AM and SM iFDPs.

The low number of studies included, and the absence of clinical studies limit the translation of findings to the clinic. Interestingly, the present systematic review indicate that interim AM iFDPs in the anterior region might be clinically acceptable in terms of fit and mechanical properties, making them a viable alternative to SM processes and resulting in reduced material waste. However, the use of AM iFDPs is still insufficiently investigated and should not be widely used in clinical practice outside of clinical trials.

The major strength of the present review is the comprehensive search and the adherence to the methodological standards through all stages of the review process. The comprehensive search was achieved by means of searching additional clinical trial registers. The present review, however, also has limitations, particularly the lack of clinical studies, as no clinical study could be found comparing AM and SM iFPDs, and thus only in vitro in studies were included. Hence, the outcomes of the review could not answer the original question posed. In addition, the absence of a grey literature search and the language restriction to English, German, Spanish, Finnish, Turkish, and Portuguese may have prevented the inclusion of additional studies. Finally, relevant factors including the material compositions and (post-) processing parameters, were not always available limiting the comparability between the studies.

5 | CONCLUSION

At present, there is very limited in vitro and no clinical data available comparing additively manufactured (AM) fixed implant-supported dental prostheses (iFDPs) with those fabricated using subtractive manufacturing (SM) techniques. Heterogeneity across the available and included in vitro studies delivered insufficient data to draw conclusions on the marginal and internal discrepancies and the mechanical performance. Therefore, the performance and comparison of AM iFDPs with those fabricated by SM procedures remain to be elucidated.

AUTHOR CONTRIBUTIONS

All authors have made substantial contributions to conception and design of the study. FJS, JH, KP were involved in data collection and data analysis. AI, KP, and FJS interpreted the data and drafted the manuscript. All authors critically revised the draft and approved the final version.

CONFLICT OF INTEREST STATEMENT

This study was financially supported by the Clinic for Reconstructive Dentistry, Center of Dental Medicine, University of Zurich, Zurich, Switzerland.

DATA AVAILABILITY STATEMENT

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

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REVIEW ARTICLE

CLINICAL ORAL IMPLANTS RESEARCH WILEY

Clinical performance of single implant prostheses restored using titanium base abutments: A systematic review and meta-analysis

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Abstract

Purpose: The aim of this review was to evaluate the survival rates of restorations utilizing titanium base abutments (TBA) for restoring single-unit implant prostheses.

Materials and Methods: This review was conducted following the preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines. The focus question was: In patients who require the restoration of a single dental implant utilizing a titanium base abutment, what are the determining factors and outcomes relating to implant prosthesis prognosis and survival? A comprehensive search of databases (PubMed, EMBASE, and Cochrane Library) was conducted on 16 April 2023 and updated on 5 May 2023. Randomized clinical trials (RCT), retrospective studies and prospective studies, reporting on the use of TBA for single implant prostheses, were reviewed. A Cochrane collaboration risk of bias assessment analysis was performed for randomized clinical studies, and the Newcastle–Ottawa Scale tool was applied for non-randomized studies. A meta-analysis was performed on clinical trials reporting on survival rates of both TBA and other abutments. Other clinical studies, reporting on TBA only, were included for descriptive statistics.

Results: The search provided 1159 titles after duplicates were removed. Six RCTs were included to perform a meta-analysis and compare the survival of the TBA to other abutments [OR 0.74; 95% CI: 0.21–2.63, heterogeneity; I^2 0%; $p = .99$]. Twenty-three prospective and retrospective studies fulfilled the criteria and were included in the meta-analysis after 12 months of function. A total of 857 single implant-supported prostheses fabricated with a TBA were included. TBA abutments have an estimate 98.6% survival rate after 1 year in function (95% CI: 97.9%–99.4%). The mean follow-up period was 31.2 ± 16.9 months.

Conclusions: Single implant prosthesis restored with titanium base abutments showed favourable short-term survival rates.

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KEYWORDS
customized abutment, dental abutment, single dental implant, titanium abutment, titanium base abutment, zirconia abutment

1 | INTRODUCTION

Single fixed implant-supported prostheses, also referred to as implant-supported single crowns (iSC), have predictable clinical outcomes with high survival and success rates, and are a reliable option to replace the single missing tooth (Alqutaibi et al., 2021; Buser et al., 1997; Jung et al., 2012; Sailer, Zembic, et al., 2009). Advancements in technology and dental materials have resulted in different fabrication options for the single implant prosthesis (Joda, Ferrari, Gallucci, et al., 2017; Kapos & Evans, 2014; Karoussis et al., 2004). A dental implant-abutment fabricated utilizing a porcelain fused to metal reconstruction, has been the 'standard' to which newer techniques are compared (Alqutaibi et al., 2021; Lemos et al., 2019; Rammelsberg et al., 2020; Schmitt & Zarb, 1993; Schwarz et al., 2012). Clinicians have sought alternative techniques to abutment fabrication in attempts to reduce labour and material costs (Joda & Brägger, 2015).

Industrialized processes in the fabrication of a dental prostheses have led implant manufacturing companies to develop componentry which can be integrated into the complete digital dentistry workflow (Al-Thobity, 2022). The evolution of computer-aided design (CAD) and computer-assisted manufacturing (CAM; CAD/CAM) have enabled clinicians to access a wider variety of dental materials (Joda, Ferrari, & Brägger, 2017; Kapos et al., 2009; Mühlemann et al., 2020). CAD/CAM manufacturing facilitated the creation of the titanium base abutment (TBA). These abutments are importantly unique and different to customizable abutments as it is associated with a digital library. The digital library is provided by the manufacturer and allows the prosthesis designer to have a genuine digital replica of the abutment.

Titanium base abutments, for single unit restorations, commonly have anti-rotation features in the connection area to the endosseous implant, as well as surface irregularities along the retentive attachment segment to enhance resistance form for crown fixation. These abutments have specific geometric shapes and are unique to each manufacturer (Al-Thobity, 2022). In general, the geometry of TBA has four components; a prefabricated implant-abutment connection; a flat abutment shoulder; a retentive attachment segment; and a transmucosal segment. The TBA is available in a variety of retentive attachment and transmucosal heights and contours, which are stored in a digital library with open STL files containing the required TBA geometries. Once TBA is selected and the full crown or intermediate coping is designed using a (CAD) software, the resulting STL file of the restoration is sent for milling. The fitting surface of the milled restoration to the TBA should require very little adjustment and has an intimate fit prior to cementation. The restoration can then be contoured and finalized prior to being adhesively cemented to the TBA extra-orally.

The TBA offers several advantages for implant prostheses which include avoiding direct contact of zirconia in the connection area to the titanium implant (Sailer, Philipp, et al., 2009); a low metal profile, the emergence profile and improving mucosal colour (Carrillo de Albornoz et al., 2014; Jung et al., 2012); preventing the abutment–implant interface from damage or oxidative change during technical fabrication (Joda, Ferrari, Gallucci, et al., 2017); cementation of the restoration extra-orally and use as screw-retained implant prostheses (de Holanda Cavalcanti Pereira et al., 2022; Joda, Ferrari, & Brägger, 2017); and a lower cost of fabrication (Joda, Ferrari, Gallucci, et al., 2017).

Alternative names of such prefabricated abutments found in the literature include: Ti-base abutments; titanium-bonding bases; titanium insert; cementing cap; hybrid abutments (Al-Thobity, 2022). Furthermore, individual implant companies create confusion by referring to TBA with proprietary names. There is a lack of consistent terminology, and no suitable term has been published in the Glossary of Prosthodontic Terms. Moving forwards, a universal definition is required to enable historical information to be compared to newer strategies. Figure 1 categorizes the TBA abutment as a stock abutment with an integrated digital library. A single implant prosthesis fabricated with a TBA can be fabricated with one or two additional layers and is either screw- or cement-retained. The primary aim of this systematic review was to analyse the survival rates, and biological, technical and aesthetic outcomes of TBAs, when restoring a single implant prosthesis.

2 | MATERIALS AND METHODS

This systematic review is based on the preferred reporting items for systematic reviews and meta-analyses (PRISMA) checklist structure (Moher et al., 2010).

A protocol was developed aiming to answer the focused question 'In patients who require the restoration of a single dental implant utilising a titanium base abutment, what are the determining factors and outcomes relating to implant prosthesis prognosis, survival?'

This question considered the following population, intervention, comparison and outcome (PICO) criteria:

- Population: Partially edentulous patients with at least one implant in the maxilla and/or mandible needing restoration.
- Intervention: Titanium dental implants restored with a TBA for a single-implant prosthesis.
- Comparison: Titanium dental implants restored with customized abutments incorporating any abutment material and design including cast to abutments; altered stock abutments; and

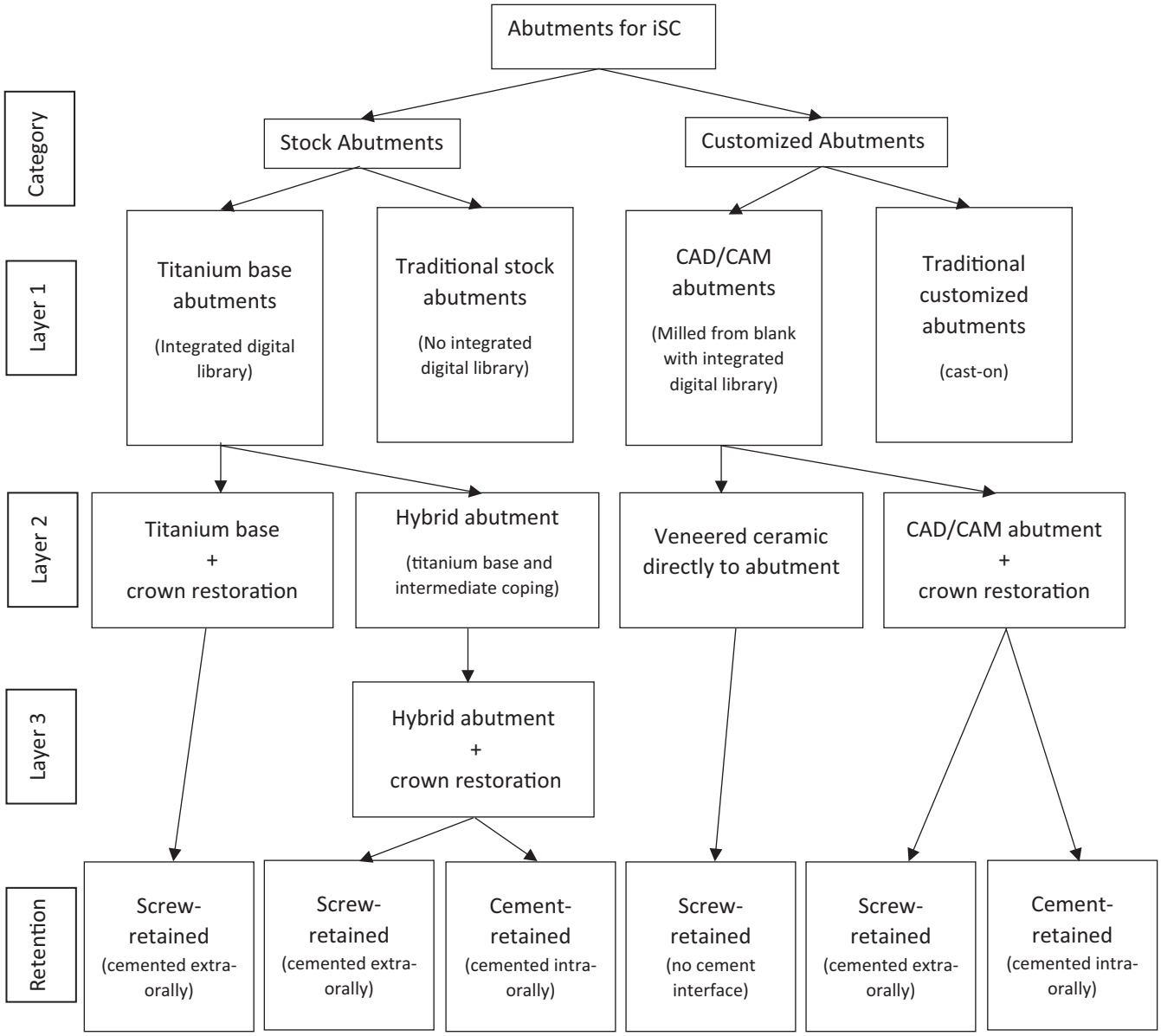


FIGURE 1 Flow diagram describing the layers to iSC. Other traditional stock and customized abutments historically used for screw-retained or cement-retained single implant crown restorations that are not stored in digital libraries are not further displayed.

customized CAD/CAM abutments fabricated from titanium, chrome-cobalt, or zirconia.

- Outcomes: survival rates, and technical complications, biological complications and aesthetic outcomes.

2.1 | Search strategy for identification of studies

Evaluation criteria were defined in accordance with the PICO criteria. A systematic electronic literature search from PubMed, EMBASE and Cochrane Library databases was performed. The complete search strategy aimed to identify all types of publications in English from 01 January 2000 up to 16 April 2023 and included the terms detailed in Table 1. The search was completed by JC and CE. Population-based search terms including dental implant, oral implant, endosseous implant, jaw, partially edentulous and single missing tooth. Considering the intervention that was performed the following terms were used; implant restoration or prosthesis; titanium abutment; Ti-base; Variobase®; universal abutment; implant hybrid restoration; two-piece abutment; titanium insert; titanium cementing abutment; hybrid zirconia abutment. The comparison group was searched using the terms—customized abutment, zirconia abutment, cast to abutment, gold abutment, CAD/CAM anatomical abutment. The outcomes searched were implant prognosis, implant survival, implant success, prosthetic complications, prosthetic survival, prosthetic success, patient satisfaction, clinical satisfaction, biological complications, aesthetics, technical complications and treatment time.

A free electronic search was updated on 5 May 2023 by WD of '(implant OR implants OR dental OR oral) AND (variobase OR ti-base

TABLE 1 Systematic search strategy.

Focus question: In patients who require the restoration of a dental implant utilizing a titanium base abutment, what are the determining factors and outcomes relating to implant and prosthesis prognosis, survival	
Search strategy	
Population	1. Dental implant OR oral implant OR endosseous implant 2. Jaw OR partially edentulous OR partial edentulous OR single missing tooth
Intervention or exposure	3. Implant restoration OR implant prosthesis 4. Titanium abutment OR Titanium base OR Ti Base OR Variobase® OR universal abutment OR implant hybrid restoration OR two-piece abutment OR titanium insert OR titanium cementing abutment OR hybrid zirconia abutment
Comparison	5. Customized abutment OR zirconia abutment OR cast-to abutment OR gold abutment OR CAD/CAM OR anatomical abutment OR UCLA abutment OR abutment
Outcome	6. Implant prognosis OR implant survival OR implant success OR prosthetic complications OR prosthetic survival OR prosthetic success 7. Patient satisfaction OR clinical satisfaction OR biological complications OR biological outcomes OR aesthetics OR technical complications OR treatment time
Search combination	1 OR 2 OR 3 OR 4 AND 5 AND (6 OR 7)
Database search	
Language	English
Electronic	PubMed, EMBASE and Cochrane Central Register of Controlled Trials (CENTRAL)
Selection criteria	
Inclusion criteria	1. Clinical studies on adults only (18+) 2. Published between 2000 and 2023 3. Studies at all levels of evidence, except expert opinion 4. Incorporate the use of a titanium base abutment 5. If there are multiple publications on the same patient cohort, only the publication with the longest follow-up time was included. 6. Sufficient reporting on the detailed clinical outcomes (survival) of TBA
Exclusion criteria	1. Not meeting all inclusion criteria 2. Studies in languages other than English 3. Studies with multiple units 4. Studies with mean follow-up time <1 year 5. Absence of clear methodology indicating type of abutment 6. Studies reporting on ceramic or subperiosteal implants 7. Poor reporting on drop-outs and number of patients at follow-up

OR titanium base abutment OR bonding base OR hybrid abutment OR titanium base) AND (Clinical OR RCT OR prospective OR outcome)'. The search results were exported and organized utilizing specialized bibliographic software, where any duplicate articles were removed (EndNote X9, Version 3.3, Wintertree Software Inc). Two independent observers independently scanned the abstracts and later, the preselected full-text articles. For studies meeting the inclusion criteria, full-text manuscripts were obtained and evaluated further. All studies meeting the inclusion criteria were subject to further data extraction. Data were extracted using structured data extraction forms. Any disagreement was discussed, and an additional review author, WD, was consulted when necessary. Outcome parameters, descriptive summaries of the relevant study characteristics and influence parameters (study design, number of patients, number of single inserted dental implants) of the respective included studies were extracted. The primary outcome was the survival rate of TBA and secondary outcomes were biological outcomes, prosthetic complications and aesthetic clinical outcomes.

2.2 | Eligibility criteria

2.2.1 | Study types

Clinical studies on dental implants restored with a single-implant prosthesis under functional loading, including at least 10 treated patients and published in English journals were evaluated. The studies must have had subjects over the age of 18, published between 2000 and 2023, evaluating a TBA with a superstructure manufactured using a digital implant-abutment library and CAD/CAM techniques. If there were multiple publications on the same patient cohort, only the publication with the longest follow-up time was included.

The following study designs were included:

- Prospective: randomized-controlled; non-randomized controlled; and cohort studies
- Retrospective: controlled; case–control; and single cohort.

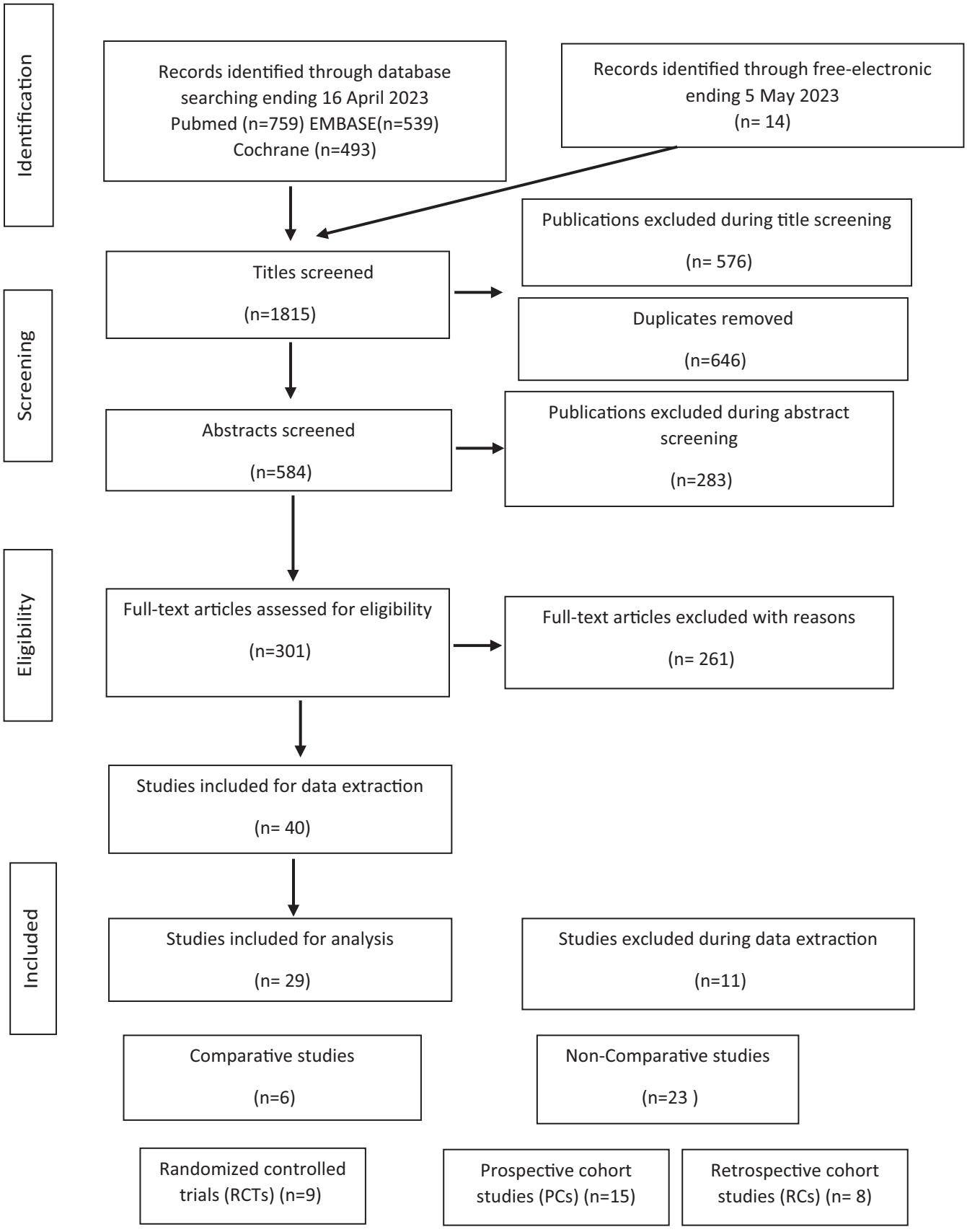


FIGURE 2 PRISMA flow diagram.

TABLE 2 Included papers.

	Number	Studies
Randomized controlled studies (RCTs)	6	Mühlemann et al. (2020) Erhan Çömlekoğlu et al. (2018) Mangano and Veronesi (2018) Vazouras et al. (2022) Rathe et al. (2022) Wolfart et al. (2021)
Prospective cohort studies	15	Linkevicius et al. (2018) Gierthmuehlen et al. (2020) Bodereau et al. (2020) Krawiec et al. (2021) Joda, Ferrari, & Brägger (2017) Strauss et al. (2022) Finelle et al. (2021) Trimpou et al. (2022) Lilet et al. (2022) Derksen & Wismeijer (2022) Linkevicius et al. (2022) Naumann et al. (2023) Joda et al. (2018) Salem et al. (2022) Strasding et al. (2023)
Retrospective cohort studies	8	Chen and Pan (2019) Diéguez-Pereira et al. (2020) Lerner et al. (2020) Menchini-Fabris et al. (2020) Guncu et al. (2022) De Angelis et al. (2020) Iglhaut et al. (2021) Gehrke et al. (2023)
Total	29	

TABLE 3 Excluded papers at data extraction.

Study	Reason for exclusion
Meijndert et al. (2021)	Full methodology of abutment design not reported
Rathe et al. (2021)	Same patient pool to a more recent study as Rathe et al. (2022)
Asgeirsson et al. (2019)/Stucki et al. (2021), Thoma et al. (2017)	Same patient pool to a more recent study Strauss et al. (2022)
Saponaro et al. (2023)	Single unit prostheses results not separated from multiple unit prostheses
Mangano et al. (2019)	Same patient pool to a more recent study Lerner et al. (2020)
Joda and Brägger (2015)	Same patient pool to a more recent study Joda, Ferrari, & Brägger (2017)
Akin and Chapple (2022)	Full methodology of abutment design not reported
Rattanapanich et al. (2019)	Abutment utilized does not have a digital library
Kunavisarut et al. (2022)	Follow-up period not sufficient
Derksen et al. (2021)	Same patient pool to a more recent study Derksen and Wismeijer (2022)

2.2.2 | Exclusion criteria

The following studies were excluded: (1) not meeting all inclusion criteria; (2) studies in languages other than English; (3) studies with multiple units; (4) studies with mean follow-up time less than 12 months; (5) absence of clear methodology indicating type of abutment; (6) studies reporting on ceramic or subperiosteal implants; (7) poor reporting on dropouts and number of patients at follow-up.

2.3 | Data analyses

Two reviewers (JC and CE) independently extracted the data of the included articles. The authors were calibrated prior to the data extraction to ensure consistency within the process. When an article was published as an RCT but did not directly compare TBA to other abutments, it was categorized as a prospective study. The study characteristics as author, year, study setting, study design, mean follow-up time, total number of included patients at baseline and at

TABLE 4 Descriptive characteristics of randomized clinical trials.

Study	Number of patients (baseline)	No TBA follow-up (baseline)/ control customisable abutment (baseline)	Abutment location	Follow-up (months)	Intervention and control abutment types
Mühlemann et al. (2020)	74 (76)	38 (39)/36 (37)	Posterior maxilla and mandibular	12	TBA with zirconia suprastructure (t) compared to gold cast-to PFM (c)
Erhan Çömlekoğlu et al. (2018)	16 (16)	16 (16)/16 (16)	Anterior maxilla	24	Immediate finalized placement (t) of abutments and dis/ reconnections (c)
Mangano and Veronesi (2018)	50 (50)	25 (25)/25 (25)	Posterior maxilla and mandible	12	Digital procedure TBA (t) vs. analogue procedure PFM (c)
Vazouras et al. (2022)	25 (25)	25(25) TBA/25 (25) titanium/25 (25) pink anodized	Anterior maxilla	12	Crossover design; grey titanium abutment; pink anodized titanium abutment; TBA with zirconia crown
Rathe et al. (2022)	22 (24)	22 (24)/22 (24)	All locations	60	Compared TBA (t) to one piece CAD/CAM titanium abutments (c)
Wolfart et al. (2021)	39 (41)	27 (28)/26 (28)	Posterior maxilla and mandible	24	Screw retained TBA compared to cement retained

Abbreviations: *c* control; PFM: porcelain fused to metal crowns; *t* test; TBA: titanium base abutments.

follow-up, number of patients dropped outs were recorded. The restoration design features extracted was either one piece cemented to a TBA or two pieces cemented to a TBA; material cemented to TBA; type of cement utilized; and TBA geometry.

2.4 | Outcome measures

Restoration survival was defined as a prosthesis with an abutment, and restorative crown or intermediate coping remaining in situ, for the entire observation period without replacement. Failure in this present systematic review was considered when the prosthesis was reported to be lost, removed and/or remade however, did not include reasons such as implant loss. Biological outcomes such as marginal bone level (MBL) loss, bleeding on probing and periodontal pocket depths (PPD) were recorded. Technical outcome of debonding was defined as loss of retention of the restorative material to the TBA. Chippings that were repairable and/or polishable, screw loosening and abutment fracture were considered as a technical complication and the data were extracted through descriptive measures. Aesthetic outcomes were recorded as PES and WES scores. Prosthetic loading was reported and classified according the ITI Treatment Guide Vol. 3 (Buser et al., 2019). The loading classification reported by the 4th ITI Consensus Conference was utilized for this review (Weber et al., 2009).

2.5 | Quality assessment of the included studies

JC and CE made the quality assessment of the included studies. The quality assessment for RCTs was performed with the Cochrane classification of assessing risk and non-randomized studies were performed with the Newcastle–Ottawa Scale (NOS). According to the NOS, studies with scores <5 were considered as low quality, 5–7 were considered as moderate quality and scores >7 were considered as high quality.

2.6 | Statistics

The included RCTs of similar design permitted a meta-analysis assessing the survival rate of a prosthesis restored with a TBA and comparing the TBA to other abutments. A meta-analysis was also used to compare survival rates and MBL loss of TBA to other abutments. In the present systematic review, survival rates were calculated by dividing the number of events (failed restorations) by the total number of restorations. For each study, event rates for the TBA were calculated by dividing the total number of events by the total number of TBA exposed after 1 year in function. Titanium base abutments were also compared to other abutments by calculating the number of events and dividing it by the total number of abutments exposed presented as odds ratios. For each outcome, the DerSimonian–Laird random effects models were used to constructed pooled estimates across studies. For the analysis of

survival of TBA after 1 year of function, a correction factor of 0.5 was added in situations where the observed survival was 100%; that is, zero failures were observed. The handling of adding the correction factor of 0.5 was done according to the default settings of the OpenMetaAnalyst software as implemented as defaults in the metafor package (Wallace et al., 2012). The statistical heterogeneity among studies was assessed using the Q test based on a chi-square test (Cochran, 1954) and reported along with the I^2 index (Higgins et al., 2003), which represents the percentage of variation in the pooled estimate that was attributable to heterogeneity between the studies.

Marginal bone level loss was presented in millimetres: means ± standard deviations. Forest plots were created to illustrate the results of the meta-analysis across the different studies. Statistical significance was defined as p-value <.05.

3 | RESULTS

3.1 | Inclusion and exclusion of articles and data extraction

A flow diagram (Figure 2) reports the screening and selection of studies. The electronic search identified 1159 papers in total after all the duplicates were removed. Three hundred and one full-text articles obtained for screening and independently. A final 29 articles were found to qualify for inclusion in the review. The study designs of these articles were 15 prospective cohort studies (52%), eight retrospective (28%) and six RCT (21%; Table 2). The excluded articles at time of data extraction are tabulated in Table 3. Table 4 provides descriptive detail of the RCT studies and Table 5 outlines the details of all the 29 eligible studies. The mean and standard deviation of the follow-up period of 29 studies were 31.2 ± 16.9 months with the minimum being 12 months and maximum 72 months.

A total of 857 TBAs were assessed. Implants most commonly used per study were from the following manufacturers—Straumann (n = 11), Exacone (n = 2) and Camlog (n = 4). Other implant brand (n = 11) include; NucleOSS; Genesis; Biomet 3i; Biohorizons; Klockner; Nobel Biocare; Xive;Virtonex; Duocone; MIS; and Thommen Inciell. Stage C prosthetic loading of the implants was reported in 24 studies. The implant loading protocol reported varied from Stage 1 to 4: stage 1 (n = 4); stage 2 (n = 1); stage 3 (n = 3); stage 4 (n = 12) not reported (n = 10).

3.2 | Quality assessment of the included studies

The quality assessment and selected risk of bias for RCTs studies were classified according to the Cochrane classification of assessing risk of bias summarized in Figure 3. There were four studies which had a low risk of bias in all fields (Higgins et al., 2011). Two of the six studies had some concerns in one or two fields. The unweighted summary plot of RCTs is depicted in Figure 4.

Prospective and retrospective cohort studies were assessed utilizing the Newcastle–Ottawa Scale (NOS). Most of the studies were judged to have moderate methodological quality, NOS score 5, 6, 7 or 8 out of a total of 9 points. A maximum score of nine stars could be assigned to the investigations that conformed to the nine criteria as follows: (1) representativeness of exposed cohort, (2) selection of non-exposed cohort, (3) ascertainment of exposure, (4) demonstration of outcome of interest not present at the start of study, (5–6) comparability in use of abutment and endosseous implant, (7) assessment of outcome, (8) follow-up longer than 12 months and (9) adequacy of follow-up (Table 6).

3.3 | Survival rates

The odds ratio of a TBA compared to other abutments was 0.74 with the 95% confidence interval ranging from 0.21 to 2.63 and p-value .64. The I^2 heterogeneity was 0% and p-value = .99. The full description of the meta-analysis is tabulated in Table 7 and illustrated in a forest plot (Figure 5). The estimate survival rate of a TBA was 98.6% after 12 months of use; 95.0%CI: 97.9%–99.4%; heterogeneity I^2 = 0%, p = .99 (Figure 6 and Table 8).

3.4 | Biological outcomes

Radiographic data on MBL were reported in five of the six RCT studies. All studies utilized an intraoral radiograph to evaluate periimplant MBLs. Data pooled from five studies found there was not a significant difference between the TBA and other customizable abutments (Mean difference: 0.095; 95% CI: −0.07 to 0.261; heterogeneity: p = .26, I^2 = 23.44%) (Figure 7 and Table 9). The customizable abutments included were gold cast-to, preformed titanium and zirconia abutments. Statistical analysis of the included studies did not display a significant difference in MBL change between different implant-abutment protocols. Other biological complications PDD and BOP were commonly reported; however, there was not enough consistency within the studies to allow for comparison (Table 10).

3.5 | Technical outcomes

The studies reviewed analysed a variety of TBA designs, the specifications of each are outlined in Table 11. The TBA varied in attachment height, width, material thickness, anti-rotation features, transmucosal heights and cement space. Seventeen studies utilized a zirconia; 14 studies utilized lithium disilicate; and single study utilized PEEK, resin-modified hybrid ceramic and titanium as the restorative material at the TBA. All of the studies utilized a resin cement to adhere the titanium base abutment to zirconia or lithium disilicate.

TABLE 5 Methodological characteristics of the studies included.

Study	Patients at follow up (patients at baseline)	Number of TBA	Follow-up (months)	Material cemented to TBA	Cement	Survival of restoration of TBA at 12 months	Survival of implant at 12 months (%)	Implant placement/ loading protocol
(Erhan Çömlekoğlu et al., 2018)	16 (16)	8	24	Zirconia	Self-curing resin cement	7/8	100	4/C
Rathe et al. (2022)	24 (24)	24	60	Titanium	Dual cure resin cement	24/24	100	NR/C
(Strauss et al., 2022)	22 (24)	22	60	Zirconia	Dual cure resin cement	21/22	96	4/C
Iglhaut et al. (2021)	20 (20)	20	43.2	Zirconia	NR	20/20	100	NR/C
Linkevicius et al. (2018)	(54) 55	54	12	LDS	Resin cement	54/54	100	4C
Vazouras et al. (2022)	23 (25)	18	12	Zirconia	Dual cure resin cement	16/18	96	NR/C
Linkevicius et al. (2022)	29 (30)	29	12	Zirconia	NR	29/29	98	NR/NR
Linkevicius et al. (2022)	26 (30)	30	12	Zirconia	NR	26/26	100	NR/NR
Wolfart et al. (2021)	(40) 41	28	24	LDS	Self-curing resin cement	28/28	100	4C
Gierthmuehlen et al. (2020)	26 (27)	39	12	LDS	Self-curing resin cement	39/39	100	NR/C
Gierthmuehlen et al. (2020)		6		LDS	Self-curing resin cement	6/6	100	NR/C
Krawiec et al. (2021)	40 (40)	40	12	LDS	Self-curing resin cement	40/40	100	3B
Chen and Pan (2019)	32 (32)	32	72	Zirconia	NR	32/32	100	2C
Bodereau et al. (2020)	10 (10)	10	42	Zirconia	Self-adhesive resin cement	10/10	100	4C
Derksen and Wismeijer (2022)	30 (32)	45	36	Zirconia	Self-curing resin cement	44/45	96	4C
Mühlemann et al. (2020)	59 (60)	38	12	Zirconia	Self-curing resin cement	38/38	97	2C
Joda, Ferrari, & Brägger (2017)	44 (44)	50	36	LDS	Self-curing resin cement	50/50	100	NR/NR
Lerner et al. (2020)	90 (90)	106	36	Zirconia	Resin cement	101/105	99	NR/C
F. Mangano and Veronesi (2018)	50 (50)	25	12	Zirconia	NR	23/25	100	3C
Naumann et al. (2023)	10 (10)	10	36	LDS	Resin cement	9/10	100	NR/C
Naumann et al. (2023)	10 (10)	10	36	LDS	Resin cement	10/10	100	NR/C
Menchini-Fabris et al. (2020)	54 (54)	54	36	LDS	Self-adhesive resin cement	54/54	100	1C
Finelle et al. (2021)	17 (17)	17	24	LDS	Resin cement	19/19	100	4C
De Angelis et al. (2020)	19 (19)	19	36	LDS	Resin cement	19/19	100	4C

Implant brand (type)	Ti-base type	Bone level (BL) / tissue level (TL)	Transmucosal height	Attachment height	Connection	Prostheses with 1 cement layer (1) or 2 cement layers (2)
Camlog (conelog)	Conelog Ti Base	BL	2 mm	4.7 mm	Conical (7.5°)	1
Camlog (conelog)	Conelog Ti Base	BL	0.8 mm	4.7 mm	Conical (7.5°)	2
Straumann (bone level, 6x NC, 18x RC)	Medentika	BL	6 × 1 mm 18 × 0.8 mm	3.5 mm	Conical (15°)	1
Straumann (BLT)	Variobase	BL	1.5 mm	3.5 mm	Conical (7°)	1
MIS	Ti-Base	BL	0.5 mm	4.0 mm	Conical (12°)	1
Keystone (genesis)	NS	BL	<1 mm	NS	Conical connection (° NS)	2
NucleOSS (T6 standard bone level implant)	Titanium base	BL	0.7 mm	NS	Conical (First part 20°, 15°)	1
NucleOSS (T6 standard bone level implant)	Titanium base	BL	2.4 mm	NS	Conical (First part 20°, 15°)	1
Camlog screw-line promote plus	Camlog (flat ti-base	BL (0.4 mm machined)	0.3 mm	4.7 mm	Butt-joint	1
Nobel replace	Universal base tri-channel	BL (details NS)	1.5 mm	NS	Butt-joint	1
Xive S Plus	Dentsply Sirona ti-base	BL	NS	NS	Butt-joint	1
Thommen (Innicell®SPI Element MC)	Dentsply Sirona ti-base	BL	NS	NS	Butt-joint	1
Biomet 3i Certain R	Dentsply Sirona ti-base	BL	NS	NS	Butt-joint	2
BioHorizons (Tapered Internal Laser-Lok)	BioHorizons Ti Base Abutment	BL	1 mm	4 mm	45° internal hex	1
Straumann (tissue-level SP & TE)	Variobase RN	TL	NA	4 mm	Synocta, 45° external bevelled shoulder	1
Straumann (tissue-level SP)	Variobase RN	TL	NA	NS	Synocta 45° external bevelled shoulder	1
Straumann (tissue-level SP)	Variobase RN/WN	TL	NA	4,0–4.5 mm	Synocta 45° external bevelled shoulder	
Exacone	Ti-base on top of friction fit abutment	NA	NA	4.0 & 6.0 mm	Friction fit	2
Exacone	Ti-base on top of other friction fit abutment	NA	NA	4.0 & 6.0 mm	Friction fit	2
Camlog (conelog)	Conelog Ti Base	BL	2 mm	4.7 mm	Conical (7.5°)	2
Camlog (conelog)	Conelog Ti Base	BL	2 mm	4.7 mm	Conical (7.5°)	1
Outlink	TL	External Hex	NS	NS	External Hex	1
Straumann	Variobase	TL/BL	NS	NS	Conical (7°) / Synocta 45° external bevelled shoulder	1
Straumann	NR	BL	NS	NS	Conical (7°)	1

(Continues)

TABLE 5 (Continued)

Study	Patients at follow up (patients at baseline)	Number of TBA	Follow-up (months)	Material cemented to TBA	Cement	Survival of restoration of TBA at 12 months	Survival of implant at 12 months (%)	Implant placement/loading protocol
De Angelis et al. (2020)	19 (19)	19	36	Zirconia	Resin cement	19/19	100	4C
Trimpou et al. (2022)	21 (21)	21	12	Zirconia	Resin cement	21/21	100	1A
Lilet et al. (2022)	19 (20)	20	12	LDS	NR	19/19	100	1C
Guncu et al. (2022)	118 (118)	192	32	Zirconia	Self-curing resin cement	180/192	100	NR/NR
Joda et al. (2018)	10 (10)	10	36	LDS	NR	10/10	100	NR/NR
Salem et al. (2022)	30 (30)	30	24	10 Zirconia, 10 Resin modified, 10 PEEK with composite veneer	Self-curing resin cement	30/30	100	4C
Strasding et al. (2023)	55 (60)	54	12	26 LDS 28 Zirconia	Self-curing resin cement	54/54	98.3	4C+3C
Gehrke et al. (2023)	75 (75)	109	12	NR	NR	108/109	100	1A+4C

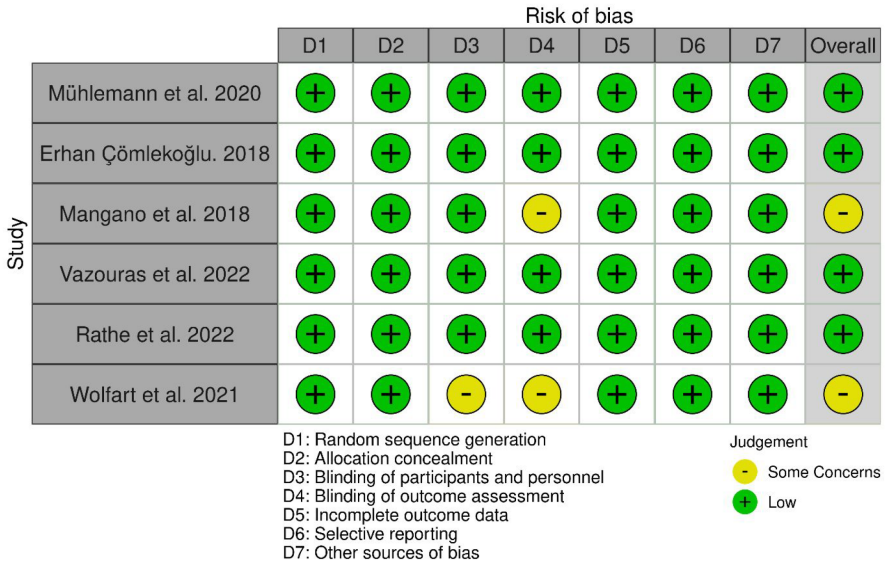


FIGURE 3 Risk of bias assessment according to the Cochrane Collaboration recommendations (Higgins et al., 2003).

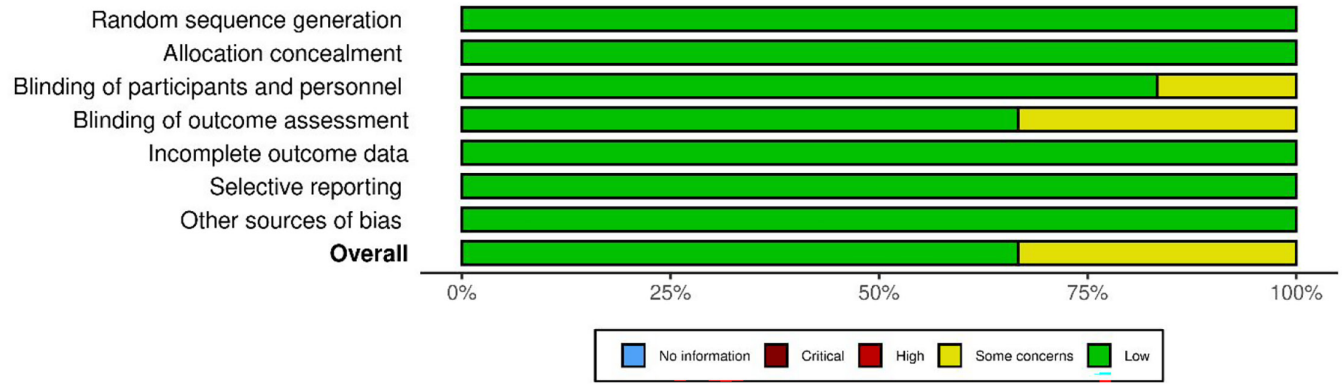


FIGURE 4 Unweighted summary plot of randomized clinical trials McGuinness and Higgins (2020).

Implant brand (type)	Ti-base type	Bone level (BL) / tissue level (TL)	Transmucosal height	Attachment height	Connection	Prostheses with 1 cement layer (1) or 2 cement layers (2)
Straumann	Ti base Dentsply Sirona	BL	NS	NS	Conical (7°)	1
Camlog (progressive line)	NR	BL	NS	NS	Conical (7.5°)	2
Straumann	Variobase®	BLX	NS	NS	Conical (7°)	1
Straumann	Variobase®	BL	NS	3.5 mm + 5.5 mm	Conical (7°)	1
Straumann	Variobase®	TL	NA	4 mm	Synocta 45° external bevelled shoulder	1
Virtonex	Titanium base	BL	NA	4 mm	Conical (7°)	2
Straumann	Variobase®	BL	NS	NS	Conical (7°)	1
DuoCone	Titanium Base	BL	1.5, 2.5, 3.5 mm	NR	Morse Taper	1

The cementation protocol, whether the abutment was sandblasted or primed, was not consistently reported.

Eight studies assessed aesthetic outcomes (Table 12). Three of the 29 studies assessed the PES and WES scores together with the mean ± standard deviation been reported respectively (8.5 ± 1.4 and 8.4 ± 2.0) (Bodereau et al., 2020; Krawiec et al., 2021). Two studies provided aesthetic outcomes utilizing PES only (Erhan Çömlekoğlu et al., 2018; Vazouras et al., 2022). Lithium disilicate superstructure prostheses maintained their colour over 12 months, but became duller and exhibited increased surface roughness (Gierthmuehlen et al., 2020). Vazouras et al. did comment that a zirconia superstructure as second layer exposed less titanium and increased the aesthetic outcomes of the implant prosthesis (Vazouras et al., 2022).

4 | DISCUSSION

The current systematic review investigated the survival rates of TBA with particular interest in biological complications, technical complications and aesthetic considerations. The present systematic and meta-analysis demonstrated a high survival rate after 12 months. The main technical problem leading to a remake of the restoration was debonding to the TBA. A limited number of RCTs assessed all the clinical outcomes; however, data were also extracted from prospective and retrospective studies to perform a meta-analysis on survival of TBA abutments and comparison to other abutments for prostheses survival and MBL loss.

Previous analysis on the difference between titanium and zirconia abutments under mechanical, biological and aesthetic aspects has not been statistically significant (Halim et al., 2022). The previously reported high short-term survival rate of 97.6% for monolithic and veneered single implant prosthesis (Pjetursson et al., 2021) was affirmed by this present systematic review. There has been a paucity of literature to support the clinical use of TBA and clinicians have been utilizing them through clinical 'experimentation'. This review is the first to focus exclusively on clinical studies regarding the performance of TBA in hope to clarify their use in clinical practice.

The concept of an early crestal bone remodelling response to establishing a biologic width or zone away from the implant-abutment micro gap is a well-accepted concept in implant dentistry (Hermann et al., 2001). Mattheos, Vergoullis, et al. (2021) recently revised the interrelationship of this complex in the literature as the implant supracrestal complex. This describes the anatomical complex of human tissue, technical component and bacteria extending through the transmucosal part of the implant prosthesis, and possible interrelationship between biological and technical complications (Mattheos, Vergoullis, et al., 2021). A consistent and reproducible connection of the implant-abutment to the endosseous implant reduced micromovement of the implant prosthesis and can lead to fewer biologic complications (Hamilton et al., 2013). A high incidence of BOP and PPD was reported in one of the included studies using non-genuine componentry as the genuine abutments were not available at the beginning of their study. The authors compared their abutments to the genuine TBA and noted an increased diameter and reduced height. This led to a design with a close vertical and horizontal distance between the restoration and the marginal bone around the two-piece implants including a cement gap, which was deemed responsible for a biologic reaction with increased bone remodelling (Stucki et al., 2021). The accuracy of fit of the crown restoration to the TBA is paramount in ensuring a minimal cement gap exists in the transmucosal portion. Pitta et al. analysed the bending movements between TBA and CAD/CAM customized abutments and found that the ultimate fracture point in both groups was through the abutment screw, but such high forces are unlikely to occur clinically (Pitta et al., 2021).

TABLE 6 Quality assessment of prospective and retrospective cohort studies based on Newcastle–Ottawa Scale (NOS).

	Selection				Comparability		Outcome			Score
Study (Author, year)	Representativeness of cases	Selection of controls (RCT—Control group of exposure from the same cohort)	Ascertainment of exposure	Demonstration outcome of interest not present at the start of the study	TBA	Implant fixture	Assessment of outcome	Follow-up long enough	Adequacy of follow-up	Total
Bodereau et al. (2020)					*	*		*	*	4
Chen and Pan (2019)			*	*	*	*	*	*	*	7
De Angelis et al. (2020)			*	*	*	*		*	*	6
Diéguez-Pereira et al. (2020)			*	*	*			*	*	5
Finelle et al. (2021)			*		*			*	*	4
Guncu et al. (2022)			*	*	*			*	*	5
Gierthmuehlen et al. (2020)			*	*	*	*		*	*	6
Joda, Ferrari, & Brägger (2017)			*	*	*	*		*	*	6
Krawiec et al. (2021)			*	*	*	*		*	*	6
Lerner et al. (2020)			*	*	*	*		*	*	6
Lilet et al. (2022)			*	*	*	*		*	*	6
T. Linkevicius et al. (2018)		*	*	*	*	*		*	*	7
Menchini-Fabris et al. (2020)		*	*	*	*	*		*	*	7
Strauss et al. (2022)			*	*	*	*		*	*	6
Trimpou et al. (2022)			*	*	*	*		*	*	6
Derksen and Wismeijer (2022)			*	*	*	*		*	*	6
Tomas Linkevicius et al. (2022)			*	*	*	*		*	*	6
Naumann et al. (2023)			*	*	*	*		*	*	6
Joda et al. (2018)			*	*	*	*	*	*	*	6
Salem et al. (2022)			*	*	*	*		*	*	6
Strasding et al. (2023)			*	*	*	*		*		5
Gehrke et al. (2023)			*	*	*	*	*	*	*	7

*Are assigned to the investigations that conform to the quality assessment criteria.

TABLE 7 Comparison of abutment survival for TBA and other abutments survival after 1 year of function.

	TBA survival		Other abutment survival		Odd ratio (OR)				Heterogeneity	
Study	Events	Total	Events	Total	OR	95% CI		*p*-value	I^2 (%)	*p*-value
Overall	136	141	126	128	0.74	0.21	2.63	.64	0	.99
Mühlemann et al. (2020)	38	38	36	36	1.06	0.02	54.56			
Erhan Çömlekoğlu et al. (2018)	7	8	8	8	0.29	0.01	8.37			
Mangano and Veronesi (2018)	23	25	23	25	1.00	0.13	7.18			
Vazouras et al. (2022)	16	18	7	7	0.44	0.02	10.34			
Wolfart et al. (2021)	28	28	28	28	1.00	0.02	52.15			
Rathe et al. (2022)	24	24	24	24	1.00	0.02	52.44			

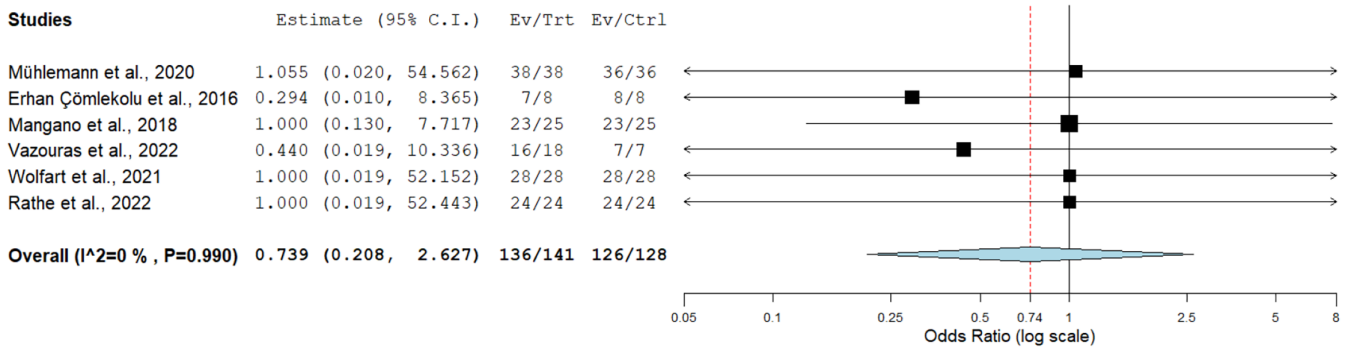


FIGURE 5 Forest plot meta-analysis of titanium base abutments survival compared to other abutments.

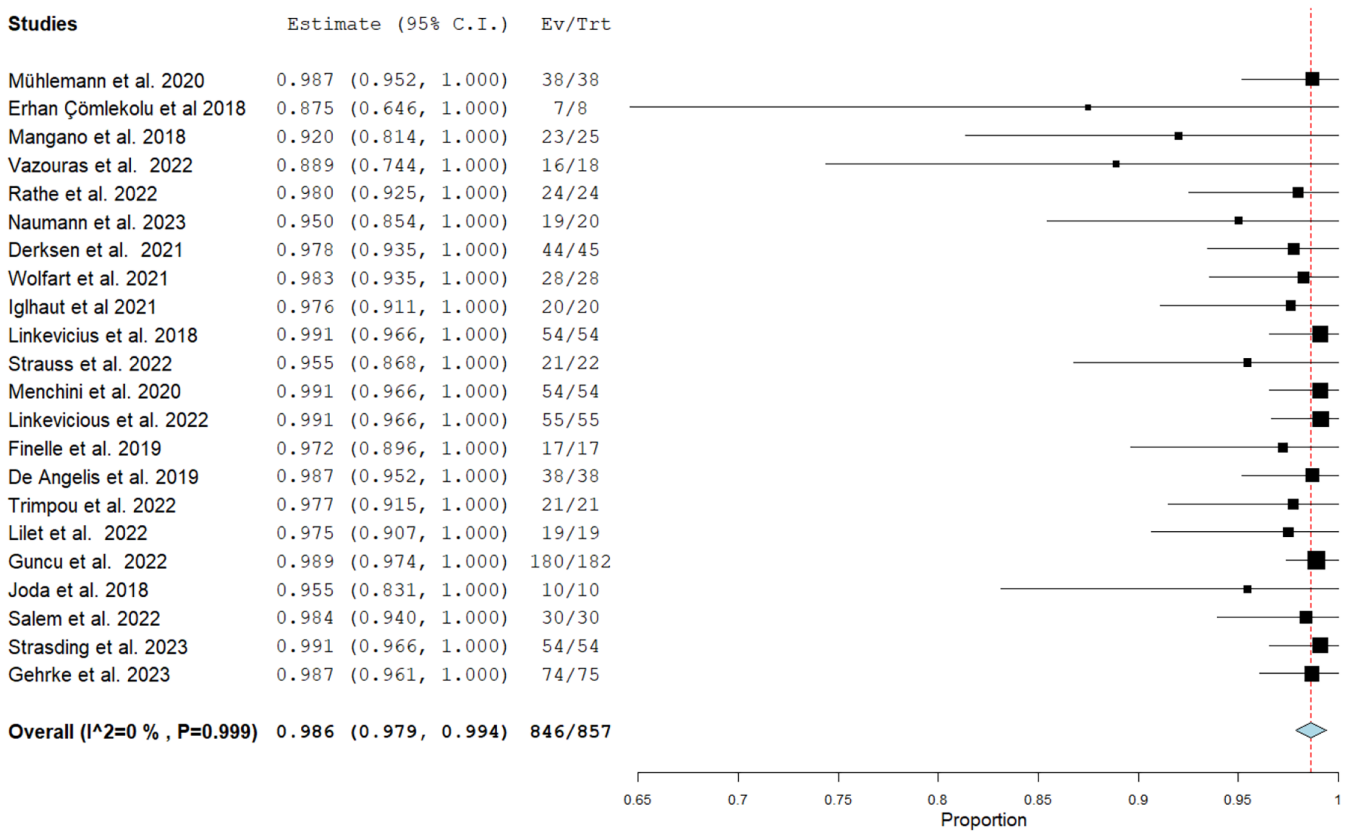


FIGURE 6 Forest plot meta-analysis of titanium base abutments abutment survival.

TABLE 8 Titanium base abutments (TBA) survival after 1 year of function.

	TBA survival						Heterogeneity	
Study	Events	Total	Estimate	95% CI		*p*-value	I^2 (%)	*p*-value
Overall	846	857	0.99	0.98	0.99	<.01	0	.99
Mühlemann et al. (2020)	38	38	0.99	0.83	1.00			
Erhan Çömlekoğlu et al. (2018)	7	8	0.88	0.46	0.98			
Mangano and Veronesi (2018)	23	25	0.92	0.73	0.98			
Vazouras et al. (2022)	16	18	0.89	0.65	0.97			
Rathe et al. (2022)	24	24	0.98	0.75	1.00			
Naumann et al. (2023)	19	20	0.95	0.72	0.99			
Derksen and Wismeijer (2022)	44	45	0.98	0.86	1.00			
Wolfart et al. (2021)	28	28	0.98	0.78	1.00			
Iglhaut et al. (2021)	20	20	0.98	0.71	1.00			
Linkevicius et al. (2018)	54	54	0.99	0.87	1.00			
Strauss et al. (2022)	21	22	0.95	0.74	0.99			
Menchini-Fabris et al. (2020)	54	54	0.99	0.87	1.00			
Linkevicius et al. (2022)	55	55	0.99	0.87	1.00			
Finelle et al. (2021)	17	17	0.97	0.68	1.00			
De Angelis et al. (2020)	38	38	0.99	0.83	1.00			
Trimpou et al. (2022)	21	21	0.98	0.72	1.00			
Lilet et al. (2022)	19	19	0.98	0.70	1.00			
Guncu et al. (2022)	180	182	0.99	0.96	1.00			
Joda et al. (2018)	10	10	0.96	0.83	1.01			
Salem et al. (2022)	30	30	0.98	0.94	1.02			
Strasding et al. (2023)	54	54	0.99	0.97	1.01			
Gehrke et al. (2023)	74	75	0.99	0.96	1.01			

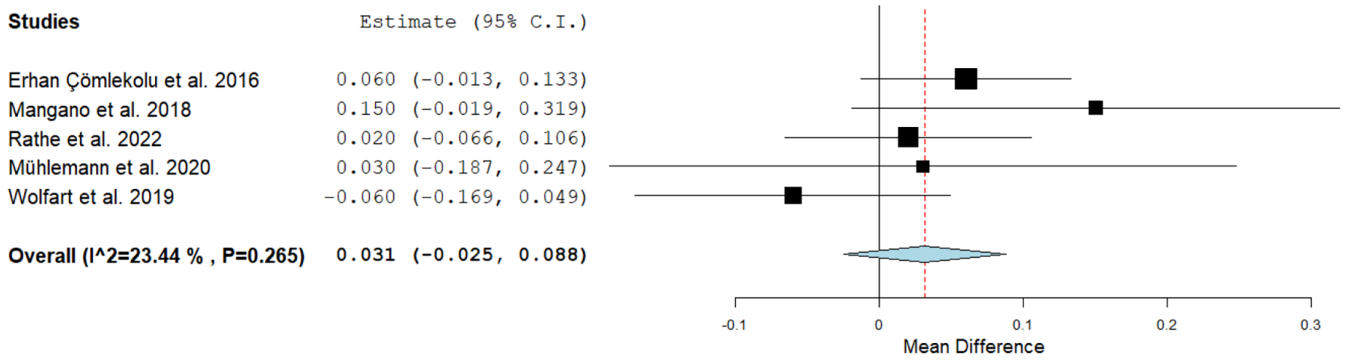


FIGURE 7 Forest plot meta-analysis of marginal bone level.

Manufacturers of TBA can standardize the cement gap within their prescribed digital library, while allowing for adequate ventilation of cement. The age of the milling tools (Payaminia et al., 2021); CAD milling strategies (Zimmermann et al., 2018); and surface treatment protocol (Arce et al., 2018) are factors that can influence the accuracy of the internal fitting surface of the implant prosthesis. Industrialization of the process standardizes these parameters, unlike traditional manual processes where the dental technician can easily influence the intimacy of fit. Selecting and implementing validated workflows to produce such restorations with proprietary manufacturing files is essential. Crown separation from the TBA was observed as the major complication and was categorized as a failure in this review, as the implant prosthesis was required to be remade. Due to the inconsistent follow-up periods reported on TBA, the results were taken after 12 months in function and 10 TBAs were reported to have a loss of retention. This result seems to be similar to the reported 1.97% annual complication rate of loss of retention in a similar systematic review (Pjetursson et al., 2021).

Cemented crowns have a higher risk for peri-implant diseases compared to screw-retained restoration because excess cement

TABLE 9 Comparison of marginal bone levels (MBL) (mm).

Study	TBA			Other abutments			MD	95% CI				Heterogeneity	
MBL	Number	Mean	SD	Number	Mean	SD	MD	Lower	Upper	*p*-value	Weighted (%)	I^2 (%)	*p*-value
Overall							0.03	−0.03	0.88	.28		23.44	.265
Mangano and Veronesi (2018)	25	−0.39	0.29	25	−0.54	0.32	0.15	−0.02	0.32		19.60		
Erhan Çömlekoğlu et al. (2018)	16	−0.12	0.10	16	−0.18	0.11	0.06	−0.01	0.13		23.53		
Rathe et al. (2022)	24	−0.07	0.13	24	−0.09	0.17	0.02	−0.06	−0.11		23.15		
Mühlemann et al. (2020)	38	−0.19	0.90	36	−0.22	0.66	0.03	−0.33	0.38		11.45		
Wolfart et al. (2021)	26	−0.13	0.16	27	−0.07	0.24	−0.06	−0.17	0.05		22.28		

Note: All values were taken at the same follow-up time of 12 months.

Abbreviations: MD, mean difference; SD, standard deviation.

is not accessible and cement penetrates in submucosal regions particularly with soft tissue healing periods shorter than 4 weeks (Staubli et al., 2017). When crown margins are located more than 1–2 mm submucosally the complete removal of cement remnant is unlikely (de Brandão et al., 2013; C. Lemos et al., 2016; Staubli et al., 2017). Titanium base abutments within the selected studies reported transmucosal heights ranging from 0.3 to 2.4 mm with a highly polished interface cement gap of 50–100 μm (Mattheos, Janda, et al., 2021). The location of the flat shoulder being near the implant-abutment interface has raised the concern that adhesive resin cement around TBA is associated with an increased risk of breakdown, biofilm formation and subsequent biological complications (Heitz-Mayfield & Salvi, 2018; Nissan et al., 2006, 2011). The differing transmucosal heights allow for clinicians and dental technicians to shift the location of the cement gap distanced from the implant-abutment interface (Linkevicius et al., 2018). Linkevicius et al. assessed the difference between different transmucosal heights of TBA short (0.7 mm) versus high (2.4 mm), and reported positive changes in MBL of +0.13 mm and + 0.37 mm for the short and high abutments, respectively, from the time of placement to 1-year follow-up. Due to the lack in statistical difference, the authors concluded that the height of the transmucosal segment of the TBA may not affect biological outcomes (Linkevicius et al., 2022). Gehrke et al. also assessed TBA with differing transmucosal heights (1.5 mm, 2.5 mm and 3.5 mm). Radiographic MBL was assessed on the mesial and distal and the authors reported less MBL loss when transmucosal abutment heights of 2.5 mm were utilized. The authors also investigated different abutment diameters, 3.5 and 4.5 mm, but without significantly different outcomes (Gehrke et al., 2023). The surface topography of the transmucosal segment of the implant prosthesis has not shown to be significant in affecting the TBA outcome (Rompen et al., 2006). In vitro studies on cement surfaces demonstrated that the cement gap should be smooth and an oxygen inhibition layer removed to increase cell viability of human gingival fibroblasts (Rohr et al., 2022; Rohr et al., 2020).

Titanium base abutments classified as CAD/CAM stock abutments offer the opportunity to select the height of the transmucosal segment so that the abutment shoulder with the corresponding restoration and cement margin is distant from the marginal bone, while allowing an emergence profile that facilitates an aesthetic outcome and cleanability. Above the abutment shoulder, the selected restorative material, such as zirconia, lithium disilicate or polymer-infiltrated ceramics, can be customized based on the desired clinical emergence profile (de Melo Moreno et al., 2022). When comparing differing materials around the emergence profile of an implant-abutment prosthesis complex, zirconia has reduced plaque retention and demonstrates a better quality of soft tissue attachment when used as an abutment material (Enkling et al., 2022). This may play a role in the reduction of soft tissue inflammation and bleeding on probing values when compared to titanium over-time (Sanz-Sánchez et al., 2018). Individualization of sulcus contours is a highly desirable and TBA have the benefits

TABLE 10 Biological outcomes.

Study	Implant survival rates at 12 months (%)	Biological outcomes
Erhan Çömlekoğlu et al. (2018)	100	MBL after 24 months was greater in t group than c PPD and BOP insignificant differences between the groups
Tomas Linkevicius et al. (2022)	98.3	MBL short TBA 0.6 mm, high TBA 0.45 mm PPD and BOP insignificant differences between groups
Derksen and Wismeijer (2022)	97.8	BOP, PPD, MBL not commented on
Mühlemann et al. (2020)	97.4	MBL, BOP, PPD No significant differences between the groups were detected
Wolfart et al. (2021)	100	GI and MBL (loss between 0.03 and 0.15 mm) no significant differences between groups PI: TBA (96.6%) and cemented (64.3%) at 12 months At 12 months, BOP screw retained 14.2% and cement retained 17.9% Cement detected on radiograph at baseline in cemented group (6.9%)
Rathe et al. (2022)	100	MBL, BOP no significant differences between the groups PPD c group showed significant deepening than t group
Mangano and Veronesi (2018)	100	BOP c group 8% t group 4% MBL c group 0.54 ± 0.32 mm t group 0.39 ± 0.29 mm not statistically significant
Bodereau et al. (2020)	100	BOP, PPD, MBL not commented on
Chen and Pan (2019)	100	No BOP or suppuration MBL 31 implants had low amounts of bone loss, 1 implant lost 2.1 mm
Diéguez-Pereira et al. (2020)	100	BOP, PPD, MBL not commented on
Gierthmuehlen et al. (2020)	100	No BOP, PPD and MBL not commented on
Iglhaut et al. (2021)	100	No Significant difference between groups PPD TBA group 3.45 ± 0.57 mm c group 3.50 ± 0.95 mm BOP TBA group 30.8% c group 26.7%
Joda, Ferrari, and Brägger (2017)	100	PPD 3.5 ± 0.6 mm BOP 19.5 ± 1.9% PI 20.6 ± 2.2% MBL 2.0 ± 0.0 mm
Krawiec et al. (2021)	100	MBL 0.19 ± 0.29 mm (thin biotype) 0.24 ± 0.24 mm (thick biotype) PPD 2.17 ± 0.53 mm (thin biotype) 2.04 ± 0.37 mm (thick biotype)
Lerner et al. (2020)	100	BOP 1.9%
T. Linkevicius et al. (2018)	100	MBL 1.25 ± 0.80 mm (thin biotype) 0.98 ± 0.42 mm (medium biotype) 0.43 ± 0.37 mm(thick biotype)
Meijndert et al. (2021)	96.7	MBL 0.07 ± 0.12 mm No significant differences in bleeding index or GI
Strauss et al. (2022)	91.7	MBL 0.32 ± 0.36 mm PPD 3.3 ± 0.08 mm BOP 31.1 ± 26.4%
Naumann et al. (2023)	100	MBL, PPD, BOP no individually commented on
Vazouras et al. (2022)	90.9	Peri-implant soft tissue thickness
Menchini-Fabris et al. (2020)	100	NR
Finelle et al. (2021)	100	Gingival recession 0.53 ± 0.35 mm MBL 0.79 ± 0.51 mm
Joda et al. (2018)	100	No biological outcomes PI, PPD and BOP recorded but unable to distinguish test and control groups.
Salem et al. (2022)	100	PI, BOP PPD, MDL assessed and given a score No biological complications
Strasding et al. (2023)	98.3	BOP: 0.27 ± 0.30% PI 0.17 ± 0.2% PPD 3.6 ± 0.8 mm.
Gehrke et al. (2023)	100	MBL comparing abutment diameter 3.5 mm −0.57 ± 0.53 mm (mesial) and − 0.66 ± 0.53 (distal) 4.5 mm −0.78 ± 0.75 mm (mesial) and − 0.75 ± 0.76 (distal) MBL comparing transmucosal abutment height 1.5 mm −1.13 ± 0.39 mm (mesial) and − 1.15 ± 0.43 (distal) 2.5 mm −0.62 ± 0.61 mm (mesial) and − 0.66 ± 0.60 (distal) 3.5 mm −0.25 ± 0.64 mm (mesial) and − 0.26 ± 0.65 (distal)

Abbreviations: BOP, bleeding on probing; c, control; GI, Gingival Index; MBL, marginal bone loss; NR, not reported.; PI, Plaque Index; PPD, pocket probing depth; t, test.

TABLE 11 Technical outcomes.

Study	Criteria	Abutment fracture	Screw loosening	Prosthesis complication
Wolfart et al. (2021)	NA	No	Yes 1 TBA restoration (3%)	No chipping or restoration fail Similar rate of loss of contact points between groups Both groups, TBA cemented extra orally and TBA cemented intra orally, lost proximal contact points 18% Both groups, TBA cemented extra orally and TBA cemented intra orally, lost occlusal contacts 32%
Erhan Çömlekoğlu et al. (2018)	NA	No	No	Two temporary crowns decemented from TBA: group t
Derksen and Wismeijer (2022)	NA	No	2 TBA abutment (4.9%)	1 screw loosening, 1 debonding from TBA
Tomas Linkevicius et al. (2022)	USPHS	No	No	None reported
Mühlemann et al. (2020)	USPHS	Yes (Not reported which group)	Yes (Not reported which group)	4 minor veneering chipping in c group. Technical complication rate of 11.1% (includes incidences of chipping of veneering ceramic, fracture of crown, fracture of abutment, fracture of abutment screw, loosing of abutment screw, loss of occlusal filling and debonding from abutment) Proximal contact point, 3 crowns lost in t group and 1 crown in the c group Occlusal contact point, 4 crowns in t group and 6 in c group Occlusal wear; more in c group than t.
Mangano and Veronesi (2018)	NA	No	No	Veneering chipping in 1 TBA No technical complications in c group
Chen and Pan (2019)	NA	No	No	Veneering porcelain chipping 6.2% Crown debonding 9.3%
Gierthmuehlen et al. (2020)	USPHS	No	No	No chipping, cracks, fractures, debondings or marginal deterioration Surface roughness 9 crowns 20.5%
Joda, Ferrari, & Brägger (2017)	FIPS	No	No	No technical complications
Lerner et al. (2020)	NA	No	No	Loss of connection between hybrid abutment and fixture 1.8% Crown decemented from two-piece abutment 0.9% Marginal adaptation, interproximal contact points and occlusal contacts scored from 1 to 5 Marginal adaptation 4.41 ± 0.7 Interproximal Contacts 4.46 ± 0.6 Occlusal Contact 3.89 ± 0.8
Strauss et al. (2022)	USPHS	No	Yes (1 incidence)	3 cases of minor veneering chipping, 1 major veneering chipping (replacement of restoration) 1 abutment loosening
Naumann et al. (2023)	FIPS	No	No	1 debonding of TBA
Vazouras et al. (2022)	NA	Yes	No	Zirconia abutment fracture cemented to TBA (2 cases)
Joda et al. (2018)	FIPS	No	No	FIPS 8.0 ± 0.8, no technical complications
Salem et al. (2022)	FIPS	No	No	1 resin matrix crown debonding from intermediate coping, 1 PEEK/composite minor chipping
Strasding et al. (2023)	USPHS	No	No	3 patients minor chipping LDS restorations
Gehrke et al. (2023)	NA	Yes (1 incidence)	No	1 abutment fracture

Abbreviations: NA, not applicable; t, test; TBA, titanium base abutments.

of a CAD/CAM customized abutment. While this may suit some clinical situations, in more aesthetic regions of the mouth, the clinician needs the ability to customize the emergence profile to match the individual clinical situation. Aesthetic success is the goal of restoratively driven treatment planning for dental implant therapy. When achieved, it contributes to higher patient-reported

TABLE 12 Aesthetic outcomes.

Study	Indices	Aesthetic outcomes
Erhan Çömlekoğlu et al. (2018)	PES	No difference between groups Mean ± SD: c: 9.25 ± 0.93 t: 9.94 ± 1.12
Mühlemann et al. (2020)	NA	PFM (c) group colour matched significantly inferior to Zirconia TBA (t) group
Vazouras et al. (2022)	PES, ΔE	PES: TBA 10.88 ± 0.88; grey titanium 9.68 ± 1.41; pink 10.12 ± 1.13 ΔE: TBA 6.46 ± 1.43; grey titanium 11.25 ± 2.98; pink 9.90 ± 2.51
Wolfart et al. (2021)	NA	Colour match and colour retention were better in TBA group than cemented
Bodereau et al. (2020)	PES, WES	Mean ± SD: WES 7 ± 1.5, PES 7.5 ± 0.8
Krawiec et al. (2021)	PES, WES	Thick biotype PES: 9.56 0 ± .53 WES: 9.89 ± 0.33 Thin biotype PES: 9.48 ± 0.70 WES: 9.7 ± 0.54
Lerner et al. (2020)	NA	Scored 1–5: Chromatic and aesthetic integration 4.15 ± 0.7
Meijndert et al. (2021)	PES, WES	Median PES 6, WES 8

Abbreviations: c, control; NA, not applicable; SD, standard deviation; t, test.

outcomes (Vazouras et al., 2022). The ability for clinicians to highly customize the emergence profile to suit the individual clinical situation is essential. The general consensus within the included studies state that regardless of soft tissue thickness, TBAs provide similar aesthetic outcomes to full zirconia abutments (Asgeirsson et al., 2019; Chen & Pan, 2019; Erhan Çömlekoğlu et al., 2018; Mangano & Veronesi, 2018).

One of the limitations of the current review is the minimal amount of information available with short 1-year follow-up periods on the clinical outcomes of TBA when compared to other abutments. The recent literature has not kept pace with the rapid expansion and development of different types of 'genuine' company TBAs. There has also been a rapid proliferation of 'non-genuine' alternatives of TBAs for clinical use with varying geometries; different transmucosal heights and retentive features. The author recognizes that there is a bias in collating many variable abutments, confounded with a short follow-up period. More research is required to assess different geometry designs, cementation protocols for the dental technician and varied tolerances of TBA fit to their survival rates. A further comparison between TBA and the anatomical customized abutments should be further completed to ascertain which clinical scenarios the abutment is indicated when more clinical data become available.

5 | CONCLUSION

Based on the findings of this systematic review, single implant prostheses restored with a TBA have high short-term survival rates. Similar early survival rates and marginal bone level changes are shown when TBA are compared to other abutments. However, limited data are available to guide the clinician on the tolerance of fit to a TBA and the implications of variable TBA geometry have on survival.

AUTHOR CONTRIBUTIONS

JC, CE and WD conceived ideas; JC, CE and WD collected the data; JC, CE and WD analysed the data; JC, CE, NZ and WD led the writing.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

None.

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REVIEW ARTICLE

CLINICAL ORAL IMPLANTS RESEARCH WILEY

Systematic review evaluating the influence of the prosthetic material and prosthetic design on the clinical outcomes of implant-supported multi-unit fixed dental prosthesis in the posterior area

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Abstract

Objective: The objectives of the study were to assess the survival, failure, and technical complication rates of implant-supported fixed dental prosthesis (iFDPs) with pontic or splinted crown (iS_pC) designs in the posterior area and compare the influence of prosthetic materials and prosthetic design on the outcomes.

Methods: Electronic and manual searches were performed to identify randomized-, prospective-, and retrospective clinical trials with follow-up time of ≥12 months, evaluating the clinical outcomes of posterior iFDPs with pontic or iS_pCs. Survival and complication rates were analyzed using robust Poisson's regression models.

Results: Thirty-two studies reporting on 42 study arms were included in the present systematic review. The meta-analysis of the included studies indicated estimated 3-year survival rates of 98.3% (95%CI: 95.6–99.3%) for porcelain-fused-to-metal (PFM) iFDPs, 97.5% (95%CI: 95.5–98.7%) for veneered zirconia (Zr) iFDPs with pontic, 98.9% (95%CI: 96.8–99.6%) for monolithic or micro-veneered zirconia iFDPs with pontic, and 97.0% (95%CI: 84.8–99.9%) for lithium disilicate iFDPs with pontics. The survival rates for different material combination showed no statistically significant differences. Veneered restorations, overall, showed significantly ($p < .01$) higher ceramic fracture and chipping rates compared with monolithic restorations. Furthermore, there was no significant difference in survival rates (98.3% [95%CI: 95.6–99.3%] vs. 99.1% [95%CI: 97.6–99.7%]) and overall complication rates between PFM iFDPs with pontic and PFM iS_pCs.

Conclusions: Based on the data identified by this systematic review, PFM, veneered Zr, and monolithic Zr iFDPs with pontic and iS_pCs showed similarly high short-term survival rates in the posterior area. Veneered restorations exhibit ceramic chipping more often than monolithic restorations, with the highest fracture rate reported for veneered Zr iFDPs.

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KEYWORDS
ceramics, dental crown, dental implants, fixed bridge, implant-supported dental prosthesis, meta-analysis, systematic review, zirconia

1 | INTRODUCTION

Computer-aided design and computer-aided manufacturing (CAD/CAM) procedures are well established today and have replaced conventional manual fabrication of fixed tooth- and implant-supported restorations to a large extent. While in the past, manually fabricated porcelain-fused-to-metal (PFM) restorations were mainly considered, a recent change of fabrication technology was accompanied by the introduction of new or improved restorative materials suitable for CAD/CAM technology (Alghazzawi, 2016; Davidowitz & Kotick, 2011; Miyazaki et al., 2009). These new material options range from highly esthetic dental ceramics like reinforced glass–ceramics (e.g., lithium disilicate glass ceramic) to high strength dental ceramics like different zirconia (Zr) generations varying both in translucency but also in fracture resistance (Silva et al., 2017; Spitznagel et al., 2018). In addition, hybrid materials were developed representing a combination of ceramics and resins, fundamentally differing in which part represents the matrix or the filler component (Silva et al., 2017; Spitznagel et al., 2018).

The clinical indications of these CAD/CAM materials for rehabilitation of partial edentulous areas with implant-supported restorations are determined by considering the compatibility of material properties, namely strength and the esthetics, with restoration characteristics such as restoration location (anterior/posterior) and restoration design. An implant-supported fixed restoration can be a single crown (iSC) or a multi-unit fixed dental prosthesis (iFDP). The latter one can be designed as splinted crowns (iS_pCs) and iFDPs with pontic units. In anterior regions, and for single-unit restorations, ceramics like reinforced glass ceramics were recommended, while first generations of Zr ceramics were considered the second choice to treat these indications due to reduced esthetics by means of high opacity. However, for iFDPs, especially located in load-bearing posterior areas, solely Zr was to be recommended for clinical application in case of requesting an all-ceramic solution as it offered sufficient strength (Sailer et al., 2018). Prior to the introduction of Zr generations with increased translucency by modification of the lattice composition toward an increased portion of the cubic phase, poor esthetics of early generation Zr materials had to be improved by the application of veneering ceramics, even in posterior areas. Systematic reviews focusing on veneered Zr (v-Zr) implant-supported restorations have shown, however, that chipping of veneering ceramic was the predominant technical problem. In contrast to the rather low annual occurrence of this complication that was analyzed to be 0.6% for v-Zr iSCs (Pjetursson et al., 2018), the respective annual complication rate when focusing on iFDPs made from the same material complex has been reported to be up to 13.9%. Finally, this means that every second iFDP (50%) made from v-Zr experienced this complication over a 5-year observation period (Sailer et al., 2018).

To overcome this limitation of v-Zr restorations, major improvements of the esthetic appearance of Zr were made in the last years (Ghodsi & Jafarian, 2018). With the increase of stabilizer content, mainly yttria, and the addition of coloring agents the developers have accomplished to significantly improve the translucency and the esthetics of Zr ceramics (Ghodsi & Jafarian, 2018; Zhang & Lawn, 2018). Unfortunately, this increase in translucency is necessarily accompanied with a decrease in fracture strength of new-generation Zr ceramics (Schönhoff et al., 2021). For this reason, most manufacturers offer a variety of Zr materials significantly differing regarding their optical properties, that is, translucency and mechanical properties (Schönhoff et al., 2021).

These material developments and esthetic improvements resulted in a shift toward new treatment and material concepts for iSCs and iFDPs. Nowadays, in most clinical situations, such restorations can be fabricated without use of any veneering ceramic, that is, in a monolithic approach, or applying a rather thin (<0.5 mm) facially layer of a veneering ceramic (i.e., micro-veneered zirconia; micro-v-Zr) (Pjetursson et al., 2021) to improve the esthetic appearance or, in most cases, to exactly match given coloration of adjacent natural or reconstructed teeth. For the connection of these restorations to the implant, prefabricated standardized abutments like titanium-base (ti-base) abutments are predominantly used today. In this concept, subtractively manufactured and finalized restorations are adhesively cemented to the ti-base abutments outside the oral cavity before being screw-retained to the supporting implants.

Monolithic or micro-v-Zr restorations can be applied in both, anterior and posterior regions and as an alternative to reinforced glass–ceramic materials for single-unit restorations. However, in order to provide sufficient fracture resistance in cases revealing multiple adjacent missing teeth, Zr remains to be the ceramic material of choice without any non-metallic material alternative. Depending on the anterior or posterior location of a restoration, different types of Zr according to the afore-mentioned material modification and available generations need to be carefully selected by the dentist or the dental technician. This, however, can be considered a challenging task since both naming of products (mostly containing superlatives of the term “translucency” such as high-, extra-, or super-translucent) and description of material properties and composition are mostly not particularly transparent.

First clinical studies demonstrated very promising outcomes of monolithic/micro-veneered implant restorations out of glass–ceramic or Zr used in combination with ti-base abutments. A previous systematic review (Pjetursson et al., 2021) has focused on failure and complication rates of veneered and monolithic all-ceramic iSCs. In this work, lower rates for ceramic chipping were found when the outcome of monolithic iSCs analyzed (Pjetursson et al., 2021). According to the findings of this review, new concepts for iSCs could be defined and validated, while the outcomes of iFDPs still need to be addressed

in further investigations prior to define consistent conclusions and solution approaches. Comparisons of materials, designs and concepts should be made in order to define the most appropriate material according to the design of the iFDPs. Furthermore, a clear distinction between iS_pC and iFDP with pontic designs of iFDPs should be established in order to provide substantiated clinical implications.

Therefore, the primary aim of the present systematic review was to evaluate the survival rates as well as the incidence of technical complications of iFDPs inserted in the posterior area exploring the influence of different prosthetic materials. Furthermore, the secondary aim was to analyze the influence of the design of implant-supported multi-unit reconstructions, differentiating iFDPs with pontics from splinted crown (iSpCs) designs.

2 | MATERIALS AND METHODS

2.1 | Study design

The study protocol of this systematic review was designed according to the Cochrane guidelines (Cumpston et al., 2019) and reported following the guidelines for Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (Moher et al., 2009). This report followed the appropriate EQUATOR (http://www.equator-network.org) guidelines. Furthermore, to improve searching databases for clinical questions, the PICO framework was applied (Schardt et al., 2007). PICO stands for patient/population (P), intervention (I), comparison (C), and outcome (O). For this systematic review, the "PICO" question was defined as follows:

- Population: Patients with multiple adjacent missing teeth in the posterior maxilla and/or mandible.
- Intervention: Reconstruction with implant-supported multi-unit fixed restorations.
- Comparison: Different restoration materials and prosthetic designs (iFDPs with pontics and iSpCs).
- Outcome: Survival, failure, and complication rates of the restorations.

The focus question was: "In patients that have multiple adjacent missing teeth in the posterior area what is the influence of the prosthetic material selection and restoration design (iFDPs with pontics vs. iS_pCs, veneered vs. monolithic) on the survival and complication rates of implant-support restorations?"

As this study is a literature-based systematic review, ethical committee approval is not required.

2.2 | Information sources and search strategy

Detailed and database-specific search strategies were developed to systematically access MEDLINE via PubMed (http://www.ncbi.nlm.nih.gov/pubmed), EMBASE (https://www.embase.com), and the Cochrane Central Register of Controlled Trials (CENTRAL) (http://www.thecochranelibrary.com). The search strategy was conducted to identify papers published until October 10, 2022, and it was primarily designed for the MEDLINE database, and subsequently modified appropriately to consider the syntax of the remaining included databases. Some free-text terms were additionally tagged with an asterisk as truncation symbol to improve the search sensitivity. No filters were applied for date of publication, journal, or language. The search results were downloaded and imported to a bibliographic database software (EndNote X9, Thomson Reuter) to facilitate duplicate removal and cross-reference checks. Details regarding the search strategy and the key word structures are displayed in Figure 1.

2.3 | Eligibility criteria

The inclusion criteria for the clinical investigations were as follow:

- Human studies
- Randomized controlled clinical trials (RCTs), controlled clinical trials, prospective cohort studies, or retrospective case series including at least 10 patients.
- A minimum follow-up time of 12 months after loading the final reconstructions.
- Restoration design (iFDPs with pontic or iS_pCs) and location (anterior or posterior) clearly described and data from iFDPs reported separately from other types of restorations.
- Detailed information on the restoration material used.
- If multiple publications on the same patient cohort were available, only the publication with the longest follow-up time and/or the most comprehensive data was included.
- Posterior iFDPs made of PFM, high-performance polymer materials, monolithic, or veneered all-ceramic materials.
- Sufficient reporting on the clinical outcomes (survival and technical complications) of the restorations.
- Reconstructions supported by titanium dental implants.

The studies not fulfilling the above listed criteria were excluded.

2.4 | Selection of studies

Two reviewers (E.M. and F.B.) screened the titles and abstracts of the entries identified in the literature search independently. Thereafter, the full-text version of all studies that potentially met the eligibility criteria or for which there was insufficient information in the title and abstract were obtained. Any publication considered potentially relevant by at least one of the reviewers was included in the next screening phase. Subsequently, the full-text publications were also evaluated in duplicate and independently by the same review examiners. Conflicts between their decisions were resolved by an open discussion in the presence of a third reviewer (D.K.). In case of no consensus established,

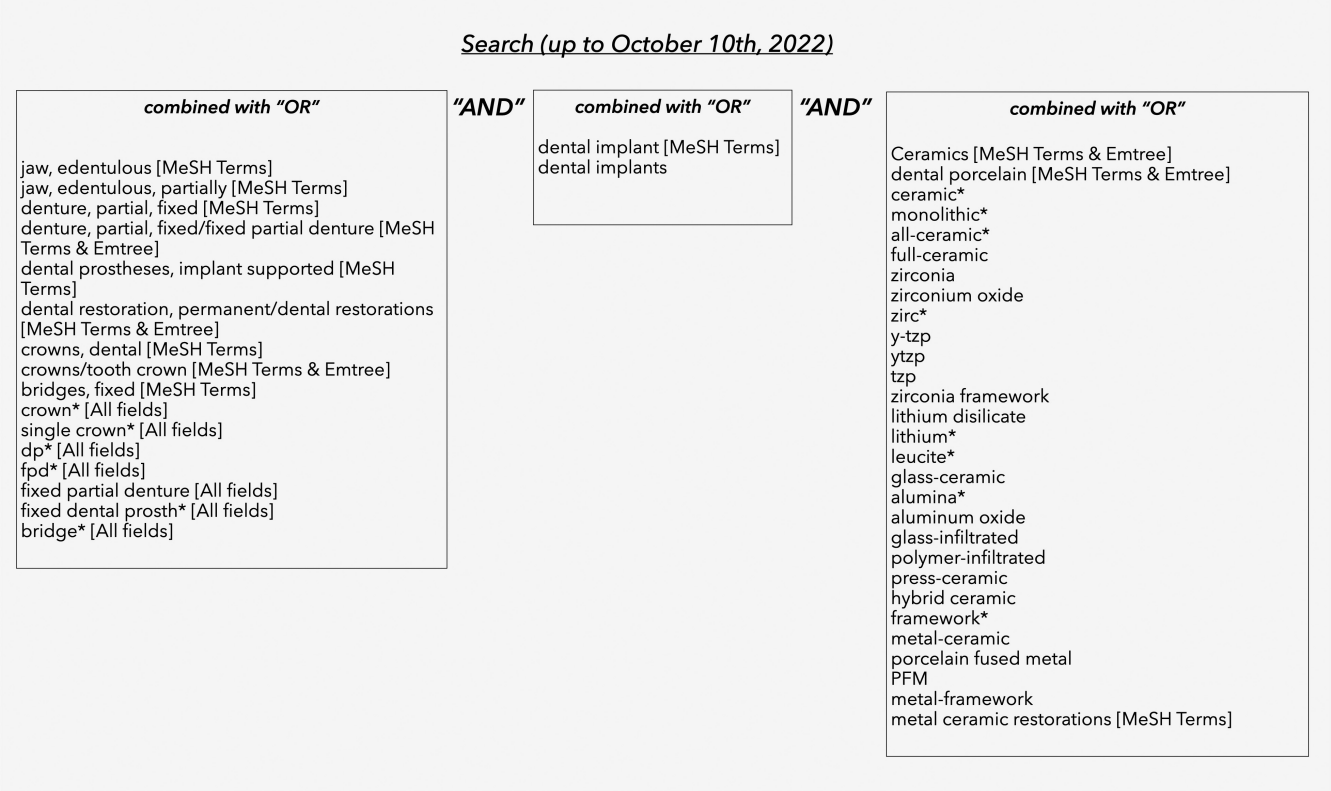


FIGURE 1 Summary of the search terms that were used for the electronic literature searches. The blocks are addressing the restoration type, the restoration support, and the restoration material.

a fourth reviewer (B.E.P.) was consulted. All evaluated full-text publications that did not meet the eligibility criteria were excluded, and the reasons for exclusion were noted. In the case of multiple publications reporting on the same patient cohort, only the publication with the longest follow-up time and/or the most comprehensive data was included in the qualitative and quantitative analyses.

2.5 | Data extraction

Two examiners (B.E.P. and D.K.) independently extracted all relevant information from the included articles using a data extraction sheet specifically designed for this review. Aside from the outcomes of interest, the following study characteristics were retrieved: name of first author, publication year, study setting, study design, mean follow-up time, total exposure time, total number of included patients, number of patients at the end of the follow-up period, number of patients that dropped out of the study, number of implants, abutments, and restorations at the baseline and at the end of the follow-up period were recorded. The restoration characteristics and the number of iFDPs based on restoration design (iFDPs with pontic or iS_pCs), retention type (screw retention or cement), and region (anterior or posterior) was extracted. The material characteristics namely the restoration material (veneered, micro-veneered or monolithic), abutment, framework, and veneering ceramic materials specifications, brands, and fabrication methods were recorded.

2.6 | Outcome measures

The clinical outcome measures for implants were as follow:

- Implant survival was defined as implants survived with or without complications. Implants lost were grouped according to time of failure, before or after loading.

The clinical outcome measures for restorations were as follow:

- Overall survival rate defined the number of restorations that were in-situ at the final follow-up visit with or without complications occurring.
- Overall failure and complication rate was defined as the overall rate of failures and biological and technical complications occurring. Giving the number of restorations free of all complications over the entire observation period.
- Overall failure due to ceramic fractures was defined as restorations failing due to ceramic fractures, such as framework fractures or catastrophic veneer fractures, leading to the remake of the restoration.

- Total number of ceramic fractures or chippings was defined as the incidence of ceramic fractures and chippings irrelevant of the extension of the fracture.
- Major ceramic chipping—repair, was defined as ceramic chippings that needed more treatment than polishing but remake was not required.
- Minor ceramic chipping was defined as surface roughness and polishable ceramic fractures.
- Loss of retention was defined as de-cementation or fracture of the luting cement of cement-retained restorations.
- Screw loosening or screw fracture was defined as screw-related complications yet not leading to the failure of the restoration.

2.7 | Risk of bias assessment of the included studies

The quality of the included studies was assessed by two reviewers (E.M. and F.B.) applying the Cochrane Collaboration's tool for assessing risk of bias. The Cochrane tool for assessing risk of bias in non-randomized studies of interventions (ROBINS-I) was implemented to evaluate the risk of bias of all included studies (prospective and retrospective) in seven different domains: (D1) bias due to confounding; (D2) bias in the selection of participants into the study; (D3) bias in classification of interventions, (D4) bias due to deviations from intended interventions; (D5) bias due to missing data; (D6) bias in measurement of outcomes; (D7) bias in selection of the reported result.

2.8 | Statistics

In the present systematic review, failure and complication rates were calculated dividing the number of events (failures or complications; numerator) by the total restoration exposure time (denominator).

In most cases, the numerator can be directly extracted from the publication data. The total exposure time was calculated by summarizing:

- Exposure time of restorations that could be followed for the whole observation time.
- Exposure time up to a failure of the restorations that were lost during the observation time.
- Exposure time up to the end of observation time for restorations in patients that were lost to follow-up due to reasons such as death, change of address, refusal to participate, non-response, chronic illnesses, missed appointments, and work commitments.

For each study, event rates for the restorations were calculated dividing the total number of events by the total restorations exposure time in years. For further analysis, the total number of events was considered to be Poisson distributed for a given sum of restoration exposure, and Poisson regression were used with a logarithmic link-function and total exposure time per study as an offset variable (Kirkwood & Sterne, 2003). To assess heterogeneity of the study specific event rates, the Spearman goodness-of-fit statistics and associated *p*-value were calculated. To reduce the effect of heterogeneity robust standard errors were calculated to obtain 95% confidence intervals of the summary estimates of the event rates.

The 3-year survival proportions were calculated via the relationship between event rate and survival function S, $S(T) = \exp(-T * \text{event rate})$, by assuming constant event rates (Kirkwood & Sterne, 2003). The 95% confidence intervals for the survival proportions were calculated by using the 95% confidence limits of the event rates. Multivariable Poisson regression was used to investigate formally whether event rates varied by material utilized, the design of the restoration (iFDPs with pontic/iS$_p$Cs). All analyses were performed using Stata®, version 15.1 (Stata Corp).

3 | RESULTS

3.1 | Screening process

Literature search resulted in a total of 4.424 records (Figure 2). After duplicate removal, 3470 references were screened by title. Out of these, 157 full-text articles were assessed for eligibility and subsequently 32 studies were identified to be eligible for inclusion (Figure 2). The detailed reasons for exclusion of the full-text articles were provided in Table S1.

3.2 | Included studies

The present systematic review included 32 studies reporting on 42 study arms or cohorts with implant-supported restorations in the posterior area. 22 of the included cohorts reported on iFDPs with pontic (Table 1). The remaining 20 cohorts, however, reported on iS$_p$Cs (Table 2). Eight of the included cohorts reported on PFM iFDPs with pontic ($n = 449$), seven cohorts reported on v-Zr iFDPs with pontic ($n = 353$), six cohorts reported on monolithic or micro-v-Zr iFDPs with pontic ($n = 210$) and one cohort reported on lithium disilicate iFDPs with pontic ($n = 50$; Table 1). Of the 20 included cohorts reporting on iS$_p$Cs, 13 evaluated PFM iS$_p$Cs ($n = 527$), two cohorts v-Zr iS$_p$Cs ($n = 33$), two cohorts monolithic Zr iS$_p$Cs ($n = 34$), and the remaining three cohorts reported on reinforced glass–ceramic (lithium disilicate) iS$_p$Cs ($n = 100$; Table 2).

Nine of the included studies were RCTs, 15 were prospective cohort studies and the remaining eight studies were retrospective case series (Tables 1 and 2). Only one of the included RCTs made comparison directly related to the aim of the present systematic review comparing PFM iFDPs with pontic to v-Zr iFDPs with pontic (Esquivel-Upshaw et al., 2020). However, this study provided important information regarding chipping of the veneering ceramic, without reporting on survival and other technical complications. The remaining eight RCTs' research questions were not directly

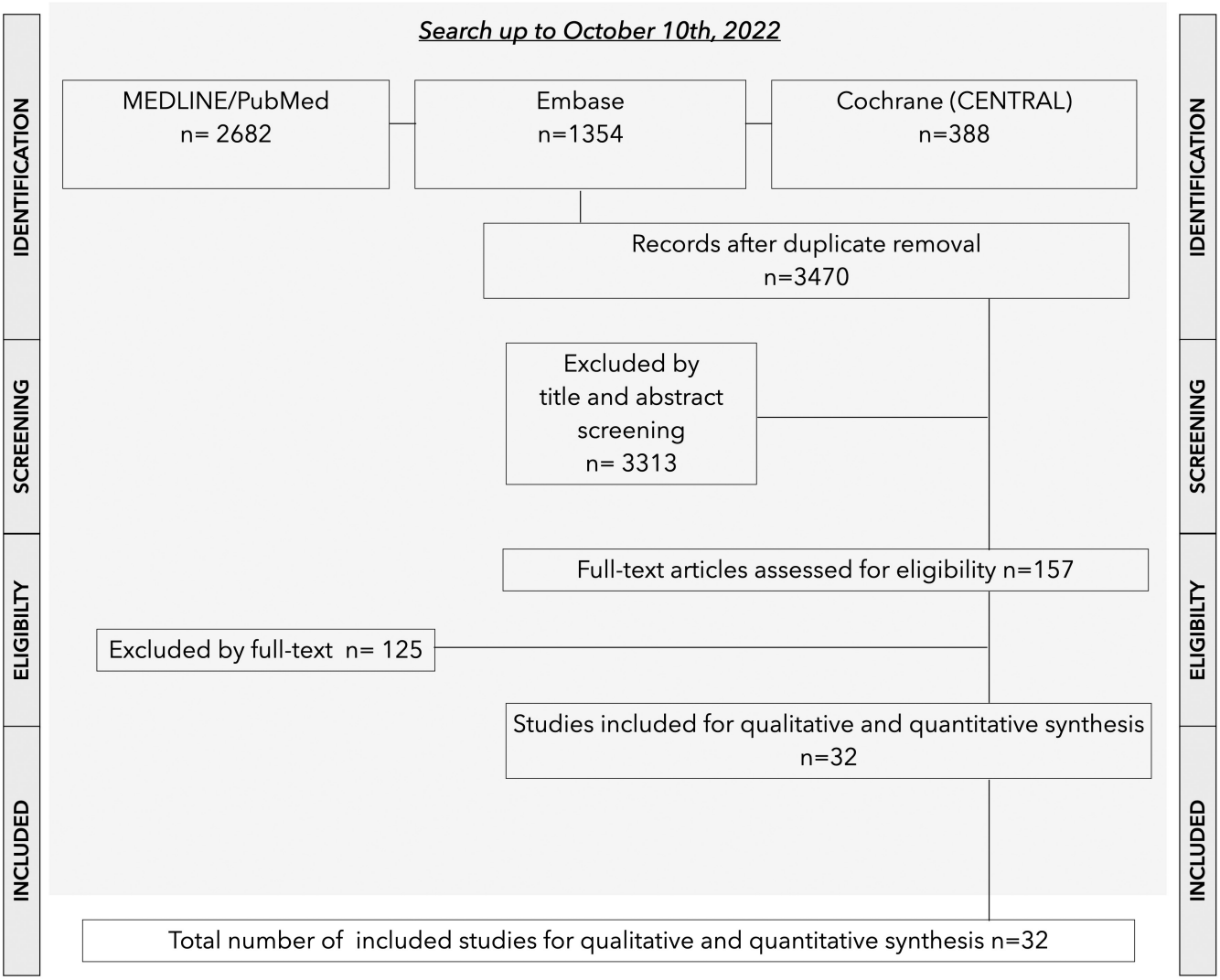


FIGURE 2 PRISMA flowchart.

comparable to the focused question of the present systematic review, such as comparing different Zr systems (Larsson & Vult von Steyern, 2016) different implant lengths (Fonseca et al., 2022; Guljé et al., 2019; Romeo et al., 2014), digital vs. conventional impression techniques (Derksen et al., 2021), splinted vs. non-splinted crowns (Al-Sawaf et al., 2020; Clelland et al., 2016) and the time point of implant loading (Cesaretti et al., 2016). As none of the included RCTs exactly addressed the focused question of the present systematic review, they were addressed as prospective studies and analyzed as such.

The studies reporting on PFM P-FDPs were published between 2001 and 2022 (median 2016). The studies on v-Zr iFDPs were published between 2012 and 2020 (median 2017), monolithic and micro-v-Zr iFDPs studies were published between 2018 and 2021 (median 2020) and reinforced glass–ceramic iFDP studies were published between 2018 and 2021 (median 2020; Tables 1 and 2).

The reporting on the proportion of patients followed for the observation period of the study (drop-out rate) was available in 28 included studies out of 32. The drop-out rate ranged between 0% and 25% with a mean of 5% (median 1%). None of the 28 studies reported a dropout rate of more than 25% (Tables 1 and 2).

From the overall included restorations, 69% were cement-retained and 31% screw-retained. The respected ratio for PFM iFDPs was 62% cemented and 38% screw-retained, for v-Zr iFDPs, 93% were cement-retained and only 7% screw-retained, for monolithic Zr iFDPs, 48% were cement-retained, and 52% screw-retained and all of the reinforced glass–ceramic iFDPs were cemented (Tables 1 and 2).

Twenty-two of the included studies were conducted in an institutional environment, such as university, 8 in private practice setting and the remaining 2 studies did not report the study setting (Tables 1 and 2).

3.3 | Survival and failure rates for implant-supported iFDPs with pontics

Six studies including 332 implant-supported PFM iFDPs with pontics with a mean follow-up period of 4.7 years provided data on the

TABLE 1 Study, patient, and restoration characteristics of the included studies on implant-supported iFDPs with pontics.

Study			Patient					Implants		FDPs				
Author, Year	Design	Setting	Initial [*n*]	End of follow-up [*n*]	Drop-out [*n*]	Drop-out [%]	Mean age [years]	Initial [*n*]	Failed [*n*]	Initial [*n*]	Drop-out [*n*]	Screw-retained [*n*]	Cemented [*n*]	Number of units per iFDPs with pontics
PFM Zr iFDPs with pontics														
Esquivel-Upshaw et al. (2020)	Pro [RCT]	U	96	96	0	0	Nr	128	Nr	64	Nr	0	64	3
Nejatidanesh et al. (2020)	Pro [RCT]	U	114	104	10	9	59	127	Nr	62	4	0	62	3 or 4
Ravidà et al. (2019)	Retro	U	53	Nr	Nr	Nr	63.4	106	0	53	Nr	41	12	3
Shi et al. (2017)	Pro	U	125	118	7	6	60.7	328	1BF & 3 AF	152	8	0	152	3
Vanlioglu et al. (2012)	Retro	U	95	95	0	0	41.2	70	Nr	34	0	0	34	3
Ozkan et al. (2007)	Pro	U	63	63	0	0	46.9	114	0	56	Nr	Nr	Nr	3 or 4
Duncan et al. (2003)	Pro	U	32	32	0	0	43.2	13	0	6	0	Nr	Nr	3 or 4
Aparicio et al. (2001)	Retro	U	25	25	0	0	54	38	2BF	22	0	22	0	Nr
Veneered Zr iFDPs with pontics														
Esquivel-Upshaw et al. (2020)	Pro [RCT]	U	96	96	0	0	Nr	130	Nr	65	Nr	0	65	3
Nejatidanesh et al. (2020)	Pro [RCT]	U	114	104	10	9	59	95	Nr	52	6	0	52	3 or 4
Ferrini et al. (2018)	Pro	U	24	24	0	0	63.6	48	0	24	0	24	0	3 or 4
Shi et al. (2017)	Pro	U	125	118	7	6	60.7	288	2AF	127	6	0	127	3
Larsson and Vult von Steyern (2016)	Pro [RCT]	U	3	3	0	0	Nr	10	Nr	4	Nr	0	4	3 to 5
Monaco et al. (2015)	Pro	U	131	Nr	Nr	Nr	53	Nr	Nr	44	Nr	Nr	Nr	Nr
Pozzi et al. (2012)	Pro	U	27	27	0	0	54.2	81	3BF	37	0	0	37	3 or 4
Monolithic Zr iFDPs with pontics														
De Angelis et al. (2021)	Pro [RCT]	U	32	25	7	22	56.9	Nr	Nr	25	Nr	25	0	Nr
Derksen et al. (2021)	Pro [RCT]	U	38	38	0	0	Nr	48	0	24	0	24	0	3
Pol et al. (2020)	Pro [RCT]	U	54	51	3	6	60.5	120	1BF	59	4	0	59	3
Koenig et al. (2019)	Pro	U	47	46	1	2	54.3	28	0	14	Nr	13	1	3
Cheng et al. (2018)	Pro	U	27	Nr	Nr	Nr	50.7	24	0	12	0	5	7	3
Degidi, Nardi, Gianluca, and Piattelli (2018)	Pro	U	76	72	4	5	45.3	156	0	76	4	Na	Na	3
Monolithic LiSi2 iFDPs with pontics														
Degidi et al. (2021)	Pro	U	50	49	1	2	45.5	100	0	50	1	0	50	3

Abbreviations: AF, failed implant after loading; BF, failed implant before loading; iFDP, implant-supported fixed dental prostheses with pontics; iFDP, implant-supported fixed dental prostheses with pontics; LiDi2, lithium disilicate; Na, not applicable; Nr, not reported; PFM, porcelain-fused-to-metal; PP, private practice setting; Pro [RCT], RCTs that were considered as prospective study for data analysis; Pro, prospective clinical study; RCT, randomized controlled trial; Retro, retrospective clinical study; U, university setting; Zr, zirconia.

TABLE 2 Study, patient, and restoration characteristics of the included studies on implant-supported SpCs.

Study			Patient					Implants		SpCs				
Author, Year	Design	Setting	Initial [*n*]	End of follow-up [*n*]	Drop-out [*n*]	Drop-out [%]	Mean age [years]	Initial [*n*]	Failed [*n*]	Initial [*n*]	Drop-out [*n*]	Screw-retained [*n*]	Cemented [*n*]	Number of units per SpCs
PFM Zr SpCs														
Fonseca et al. (2022)	Pro [RCT]	U	10	10	0	0	59	40	0	20	0	20	0	2
Guljé et al. (2021)	Pro [RCT]	U	95	85	10	11	54.5	209	3 BF & 2 AF	95	10	95	0	2 or 3
Daher et al. (2019)	Pro	U	26	24	2	8	49.2	160	7	48	0	48	0	3 or 4
Hsu et al. (2019)	Retro	U	135	104	31	23	49.8	201	2AF	97	Nr	0	97	2, 3 or 4
Ravidà et al. (2019)	Retro	U	52	Nr	Nr	Nr	60.2	156	13	52	Nr	40	12	3
Cesaretti et al. (2016)	Pro [RCT]	PP	30	30	0	0	Nr	49	1BF & 2AF	22	0	Nr	Nr	2 or 3
Clelland et al. (2016)	Pro [RCT]	U	18	15	3	17	56	32	0	15	Nr	14	1	2 or 3
Romeo et al. (2014)	Pro [RCT]	U	24	18	6	25	54.3	54	1BF	24	6	0	24	2 or 3
Vanlioglu et al. (2012)	Retro	U	95	95	0	0	41.2	18	Nr	18	0	0	18	2
Pieri et al. (2012)	Pro	PP	25	25	0	0	64.5	61	2	28	0	13	15	2 or 3
Nissan et al. (2011)	Pro	U	38	38	0	0	58	221	0	76	0	38	38	2 or 3
Ozkan et al. (2007)	Pro	U	63	63	0	0	46.9	28	Nr	14	0	Nr	Nr	2
Duncan et al. (2003)	Pro	U	32	32	0	0	43.2	32	0	15	0	Nr	Nr	2 or 3
Veneered Zr SpCs														
Roh et al. (2019)	Pro	U	8	Nr	Nr	Nr	Nr	30	0	12	0	0	12	2, 3 or 4
Larsson and Vult von Steyern (2016)	Pro [RCT]	U	15	14	1	7	Nr	51	Nr	21	0	0	21	2 or 3
Monolithic Zr SpCs														
Derksen et al. (2021)	Pro [RCT]	U	38	38	0	0	Nr	42	0	21	0	21	0	2
Roh et al. (2019)	Pro	U	11	Nr	Nr	Nr	Nr	30	0	13	0	0	13	2, 3 or 4
Monolithic LiSi2 SpCs														
Al-Sawaf et al. (2020)	Pro [RCT]	U	20	20	0	0	59	22	0	11	0	0	11	2
Degidi et al. (2019)	Pro	U	24	23	1	4	39.3	48	0	24	1	Na	Na	2
Degidi, Nardi, Sighinolfi, and Piattelli (2018)	Pro	U	67	63	4	6	43	134	1BF	65	2	Na	Na	2

Abbreviations: AF, failed implant after loading; BF, failed implant before loading; LiDi2, lithium disilicate; Na, not applicable; Nr, not reported; PFM, porcelain-fused-to-metal; PP, private practice setting; Pro, prospective clinical study; RCT, randomized controlled trial; Retro, retrospective clinical study; SpC, splinted crowns; U, university setting; Zr, zirconia.

TABLE 3 Annual failure rates and 3-year survival rates of implant-supported iFDPs with pontics.

Author, Year	iFDPs with pontics [*n*]	Mean follow-up [year]	Failures [*n*]	Total iFDPs with pontics exposure time	Estimated annual failure rate[a] (per 100 SpCs years)	Estimated survival after 3 years[a] [%]
PFM Zr iFDPs with pontics						
Nejatidanesh et al. (2020)	62	5	0	290	0%	100%
Shi et al. (2017)	152	5.2	8	790	1.0%	97.0%
Vanlioglu et al. (2012)	34	7	1	238	0.4%	98.7%
Ozkan et al. (2007)	56	2	0	168	0%	100%
Duncan et al. (2003)	6	3	0	18	0%	100%
Aparicio et al. (2001)	22	3	0	68	0%	100%
Total	332	4.7	9	1572		
Summary estimate (95% CI)[a]					0.57% (0.22–1.49%)	98.3% (95.6–99.3%)
Veneered Zr iFDPs with pontics						
Nejatidanesh et al. (2020)	52	5	1	230	0.4%	98.7%
Ferrini et al. (2018)	24	3	0	72	0%	100%
Shi et al. (2017)	127	5	6	535	1.1%	96.7%
Larsson and Vult von Steyern (2016)	4	10	0	40	0%	100%
Monaco et al. (2015)	44	1.8	2	77	2.6%	92.5%
Pozzi et al. (2012)	37	3.6	0	134	0%	100%
Total	288	3.8	9	1088		
Summary estimate (95% CI)[a]					0.83% (0.44–1.54%)	97.5% (95.5–98.7%)
Monolithic Zr iFDPs with pontics						
De Angelis et al. (2021)	25	2	0	75	0%	100%
Derksen et al. (2021)	24	1	0	24	0%	100%
Pol et al. (2020)	59	1	0	56	0%	100%
Koenig et al. (2019)	14	1.8	0	25	0%	100%
Cheng et al. (2018)	12	2	1	22	4.5%	87.3%
Degidi, Nardi, Gianluca, and Piattelli (2018)	76	5	1	353	0.3%	99.2%
Total	210	2.6	2	555		
Summary estimate (95% CI)[a]					0.36% (0.12–1.08%)	98.9% (96.8–99.6%)
Monolithic LiSi2 iFDPs with pontics						
Degidi et al. (2021)	50	2	1	99	1.0%	97.0%
Total	50	2	1	99		
Summary estimate (95% CI)[a]					1.01% (0.02–5.5%)	97.0% (84.8–99.9%)

Abbreviations: CI: confidence interval; iFDP, implant-supported fixed dental prostheses with pontics; LiDi2: lithium disilicate; [*n*]: number; PFM: porcelain-fused-to-metal; Zr: zirconia.

[a]Based on robust Poisson regression.

survival of the iFDPs with pontic. Six studies reporting on 288 restorations with a mean follow-up time of 3.8 years provided data on the survival of v-Zr implant-supported iFDPs with pontic. Four studies on 210 iFDPs with pontic after a mean follow-up time of 2.6 years provided data on the survival of monolithic or micro-veneered implant-supported iFDPs with pontic and one study with 50 restorations and a mean follow-up time of 2 years gave information on the survival rate of implant-supported reinforced glass–ceramic (lithium disilicate) iFDPs with pontics (Table 3).

The meta-analysis revealed an estimated annual failure rate of 0.57% (95% CI: 0.22–1.49%), translating into a 3-year survival rate of 98.3% (95% CI: 95.6–99.3%) for PFM iFDPs with pontic, annual failure rate of 0.83% (95% CI: 0.44–1.54%) and 3-year survival rate of 97.5% (95% CI: 95.5–98.7%) for v-Zr iFDPs with pontic, annual

TABLE 4 Annual failure rates and 3-year survival rates of implant-supported SpCs.

Author, Year	SpCs [*n*]	Mean follow-up [year]	Failures [*n*]	Total SpCs exposure time	Estimated annual failure rate[a] (per 100 SpCs years)	Estimated survival after 3 years[a] [%]
PFM Zr SpCs						
Fonseca et al. (2022)	20	2	0	40	0%	100%
Daher et al. (2019)	48	3	2	139	1.4%	95.8%
Hsu et al. (2019)	97	6.3	1	611	0.2%	99.5%
Cesaretti et al. (2016)	22	3	0	66	0%	100%
Clelland et al. (2016)	18	3	0	45	0%	100%
Romeo et al. (2014)	24	4.3	1	99	1.0%	97.0%
Vanlioglu et al. (2012)	18	7	1	126	0.8%	97.6%
Pieri et al. (2012)	28	2	0	56	0%	100%
Nissan et al. (2011)	76	5.3	0	402	0%	100%
Ozkan et al. (2007)	14	2	0	42	0%	100%
Duncan et al. (2003)	15	3	0	45	0%	100%
Total	380	4.4	5	1671		
Summary estimate (95 % CI)[a]					0.30% (0.11–0.80%)	99.1% (97.6–99.7%)
Veneered Zr SpCs						
Roh et al. (2019)	12	1	0	12	0%	100%
Larsson and Vult von Steyern (2016)	21	10	0	210	0%	100%
Total	33	6.7	0	222		
Summary estimate (95 % CI)[a]					0% (0–1.65%)	100% (95.2–100%)
Monolithic Zr SpCs						
Derksen et al. (2021)	21	1	0	21	0%	100%
Roh et al. (2019)	13	1	0	13	0%	100%
Total	34	1	0	34		
Summary estimate (95 % CI)[a]					0% (0–10.3%)	100% (73.5–100%)
Monolithic LiSi2 SpCs						
Al-Sawaf et al. (2020)	11	3	0	33	0%	100%
Degidi et al. (2019)	24	2	0	46	0%	100%
Degidi, Nardi, Sighinolfi, and Piattelli (2018)	65	3	2	188	1.1%	96.9%
Total	100	2.7	2	267		
Summary estimate (95 % CI)[a]					0.75% (0.31–1.79%)	97.8% (94.8–99.1%)

Abbreviations: CI, confidence interval; iSpC, implant-supported splinted crowns; LiDi2, lithium disilicate; [*n*], number; PFM, porcelain-fused-to-metal; Zr, zirconia.

[a]Based on robust Poisson regression.

failure rate of 0.36% (95% CI: 0.12–1.08%) and 3-year survival rate of 98.9% (95% CI: 96.8–99.6%) for monolithic or micro-veneered Zr iFDPs with pontic and annual failure rate of 1.01% (95% CI: 0.02–5.5%) and 3-year survival rate of 97.0% (95% CI: 84.8–99.9%) for reinforced glass–ceramic iFDPs with pontic (Table 3).

Formally investigating the relative failure rates of different types of implant-supported iFDPs with pontic by applying PFM iFDPs with pontic as reference, no statistically significant difference between the restoration materials was observed (Table 4). However, when the survival rates of monolithic Zr (98.9%) and monolithic reinforced glass–ceramic (97.0%) iFDPs with pontic where directly compared, the meta-analysis resulted in a tendency, however, not statistically significant, toward lower survival rates of reinforced glass–ceramic iFDPs with pontic ($p = .063$).

Investigating the number of implant-supported iFDPs with pontic that failed due to ceramic fractures such as fracture of the framework or catastrophic fracture of the veneering material, implant-supported reinforced glass–ceramic iFDPs with pontic demonstrated significantly ($p < .0001$) higher annual fracture rate (1.0%) compared with the other material groups (Table 6).

Meta-analysis comparing the overall failure and fracture rates of veneered and monolithic Zr implant-supported iFDPs with pontic demonstrated no significant difference ($p = .728$). Moreover, none of the 288 veneered Zr restorations analyzed failed due to framework

TABLE 5 Summary of annual failure rates, relative failure rates, and survival estimates for iFDPs with pontics with implant-supported PFM iFDPs as reference.

iFDPs material	iFDPs [*n*]	Total iFDPs exposure time	Mean follow-up [year]	Estimated annual failure rate[a] (95% CI)	3-year survival summary estimate[a] (95 % CI)	Relative failure rate[b] (95% CI)	*p*-value[b]
PFM iFDPs	332	1572	4.7	0.57% (0.22–1.49%)	98.3% (95.6–99.3%)	1.00 (Ref.)	
Veneered Zr iFDPs	288	1088	3.8	0.83% (0.44–1.54%)	97.5% (95.5–98.7%)	1.44 (0.50–4.20)	.495
Monolithic Zr iFDPs	210	555	2.6	0.36% (0.12–1.08%)	98.9% (96.8–99.6%)	0.63 (0.16–2.43)	.501
Monolithic LiDi2 iFDPs	50	99	3	1.01% (0.02–5.5%)	97.0% (84.8–99.9%)	1.76 (0.73–4.27)	.209

Abbreviations: CI, confidence interval; iFDP, implant-supported fixed dental prostheses with pontics; LiDi2, lithium disilicate; [*n*], number; PFM, porcelain-fused-to-metal; Zr, zirconia.

[a]Based on robust Poisson regression.

[b]Based on multivariable robust Poisson regression including all types of iFDPs.

fracture, and none of the 210 monolithic Zr iFDPs with pontic investigated failed due to catastrophic fracture of the veneering material. Combined, the annual framework fracture rate for monolithic Zr 0.36%, and the catastrophic ceramic fracture rate of 0.46% for v-Zr iFDPs with pontic did not show significant difference (Table 8).

3.4 | Survival and failure rates for implant-supported S_pCs

Eleven studies including 380 implant-supported PFM iS_pCs in the posterior area, with a mean follow-up period of 4.4 years, provided information regarding the survival of the restorations: two studies including 33 restorations with a mean follow-up time of 6.7 years provided information on the survival of v-Zr iS_pCs, 2 studies including 34 iS_pCs and a mean follow-up time of 1 year provided data on the survival of monolithic Zr iS_pCs and 3 studies reporting on 100 iS_pCs and a mean follow-up time of 2.7 years provided information on the survival rate of reinforced glass–ceramic (lithium disilicate) iS_pCs (Table 5).

The meta-analysis revealed an estimated annual failure rate of 0.30% (95% CI: 0.11–0.80%), translating into a 3-year survival rate of 99.1% (95% CI: 97.6–99.7%) for PFM iS_pCs, annual failure rate of 0% (95% CI: 0–1.65%), and 3-year survival rate of 100% (95% CI: 95.2–100%) for v-Zr S_pCs, annual failure rate of 0% (95% CI: 0–10.3%) and 3-year survival rate of 100% (95% CI: 73.5–100%) for monolithic Zr iS_pCs and annual failure rate of 0.75% (95% CI: 0.31–1.79%), and 3-year survival rate of 97.8% (95% CI: 94.8–99.1%) for reinforced glass–ceramic iS_pCs (Table 5).

The failures due to ceramic fractures were not investigated statistically due to the insufficient number of veneered and monolithic Zr implant-supported iS_pCs. None of the included Zr iS_pCs failed due to framework fracture or veneering/surface material fracture (Table 7).

Meta-analysis comparing implant-supported PFM iFDPs with pontic vs. implant-supported PFM iS_pCs did not reveal any significant difference ($p = .334$) when comparing the annual failure rates. However, significantly ($p = .042$) more PFM iFDPs with pontic were lost due to fracture of the veneering ceramic compared with PFM iS_pCs. The overall numbers for both configurations, however, were low (Table 9).

3.5 | Overall complication rates

Only a few of the included studies reported the total number of complications or the number of restorations free of all complications over the entire observation period. The annual complication rate of 1.93% was reported for implant-supported PFM iFDPs with pontic ($n = 149$). Significantly higher ($p = .010$) annual complication rate of 11.76% was reported for monolithic Zr iFDPs with pontic ($n = 96$; Table 6). The high overall complication rate calculated for monolithic Zr iFDPs with pontic is mainly affected by one study (Pol et al., 2020)

TABLE 6 Overview of failures and technical complications of iFDPs made with different materials.

Complications & Failures	PFM iFDPs		Veneered Zr iFDPs		Monolithic Zr iFDPs		Monolithic LiDi2 iFDPs	
	Number of iFDPs [*n*]	Estimated annual failure/complication rates[a] (95% CI)	Number of iFDPs [*n*]	Estimated annual failure/complication rates[a] (95% CI)	Number of iFDPs [*n*]	Estimated annual failure/complication rates[a] (95% CI)	Number of iFDPs [*n*]	Estimated annual failure/complication rates[a] (95% CI)
Overall failures due to ceramic fractures	385	0.36[a] (0.02–0.63)	288	0.46[a] (0.18–1.16)	210	0.36[a] (0.12–1.08)	50	1.0[a] (0.03–5.50)
Failure due to framework fractures	385	0.16[a] (0.03–0.67)	288	0[a] (0–0.34)	210	0.36[a] (0.12–1.08)	50	1.0[a] (0.03–5.50)
Failure due to catastrophic veneer fractures	385	0.25[a] (0.09–0.70)	288	0.46[a] (0.18–1.16)	134	0[a] (0–1.81)	0	Nr
Total number of ceramic chippings or fractures	393	2.20[a] (1.56–3.11)	353	4.95[a] (3.72–6.60)	210	0.18[a] (0.02–1.83)	0	Nr
Minor ceramic chippings	254	0.89[a] (0.49–1.65)	288	2.85[a] (2.16–3.76)	210	0.18[a] (0.02–1.83)	0	Nr
Major ceramic chippings–repair	254	0.90[a] (0.36–2.23)	288	1.65[a] (0.54–5.06)	210	0[a] (0–0.66)	0	Nr
Loss of retention	363	1.56[a] (0.40–6.13)	179	2.75[a] (1.38–5.46)	185	1.46[a] (0.21–10.27)	0	Nr
Screw loosening or fractures	267	2.36[a] (0.09–63.5)	188	8.33[a] (3.12–17.26)	172	0[a] (0–0.73)	0	Na

Abbreviations: AF, failed implant after loading; BF, failed implant before loading; CI, confidence interval; iFDP, implant-supported fixed dental prostheses with pontics; LiDi2, lithium disilicate; Na, not applicable; Nr, not reported; PFM, porcelain-fused-to-metal; PP, private practice setting; Pro, prospective clinical study; RCT, randomized controlled trial; Retro, retrospective clinical study; U, university setting; Zr, zirconia.

[a]Based on robust Poisson regression.

TABLE 7 Overview of failures and technical complications of SpCs made with different materials.

Complications & Failures	PFM SpC		Veneered Zr SpCs		Monolithic Zr SpCs		Monolithic LiDi2 SpCs	
	Number of SpCs [*n*]	Estimated annual failure/complication rates[a] (95% CI)	Number of SpCs [*n*]	Estimated annual failure/complication rates[a] (95% CI)	Number of SpCs [*n*]	Estimated annual failure/complication rates[a] (95% CI)	Number of SpCs [*n*]	Estimated annual failure/complication rates[a] (95% CI)
Overall complication rate	231	4.30[a] (2.86–6.45)	0	Nr	0	Nr	10	3.03[a] (0.08–15.76)
Overall failures due to ceramic fractures	527	0.04[a] (0.005–0.32)	33	0[a] (0–1.65)	34	0[a] (0–10.28)	100	0.75[a] (0.31–1.79)
Failure due to framework fractures	451	0.05[a] (0.006–0.39)	33	0[a] (0–1.65)	34	0[a] (0–10.28)	100	0.75[a] 0.31–1.79)
Failure due to catastrophic ceramic fractures	527	0.04[a] (0.005–0.32)	33	0[a] (0–1.65)	34	0[a] (0–10.28)	100	0[a] (0–1.37)
Total number of ceramic chippings or fractures	513	1.79[a] (1.04–3.10)	33	9.01[a] (8.87–9.15)	34	0[a] (0–10.28)	100	3.37[a] (0.94–12.13)
Minor ceramic chippings	290	1.71[a] (1.19–2.46)	33	9.01[a] (8.87–9.15)	34	0[a] (0–10.28)	100	3.37[a] (0.94–12.13)
Major ceramic chippings - repair	290	0.08[a] (0.009–0.71)	33	0[a] (0–1.65)	34	0[a] (0–10.28)	100	0[a] (0–1.37)
Loss of retention	288	0.81[a] (0.43–1.51)	12	0[a] (0–26.46)	34	0[a] (0–10.28)	76	0[a] (0–1.37)
Screw loosening or fractures	493	2.81[a] (1.14–6.93)	12	Na	13	0[a] (0–24.71)	100	0[a] (0–1.37)

Abbreviations: CI, confidence interval; LiDi2, lithium disilicate; Na, not applicable; Nr, not reported; PFM, porcelain-fused-to-metal; SpC, splinted crown; Zr, zirconia.

[a]Based on robust Poisson regression.

TABLE 8 Comparison of annual failure and complication rates for veneered and monolithic implant-supported iFDPs.

Failures/complications	Veneered Zr iFDPs		Monolithic Zr iFDPs		
	iFDPs [*n*]	Estimated annual failure rate[a] (95% CI)	iFDPs [*n*]	Estimated annual failure rate[a] (95% CI)	*p*-value[a]
Overall failures due to ceramic fractures	288	0.46[a] (0.18–1.16)	210	0.36[a] (0.12–1.08)	.728
Failure due to framework fractures	288	0[a] (0–0.34)	210	0.36[a] (0.12–1.08)	<.0001
Failure due to catastrophic ceramic fractures	288	0.46[a] (0.18–1.16)	134	0[a] (0–1.81)	<.0001
Total number of ceramic chippings or fractures	353	4.95[a] (3.72–6.60)	210	0.18[a] (0.02–1.83)	<.0001
Minor ceramic chippings	288	2.85[a] (2.16–3.76)	210	0.18[a] (0.02–1.83)	.015
Major ceramic chippings–repair	288	1.65[a] (0.54–5.06)	210	0[a] (0–0.66)	<.0001
Loss of retention	179	2.75[a] (1.38–5.46)	185	1.46[a] (0.21–10.27)	.527
Screw loosening or fractures	188	8.33[a] (3.12–17.26)	172	0[a] (0–0.73)	<.0001

Abbreviations: CI, confidence interval; iFDP, implant-supported fixed dental prostheses with pontics; Na, not applicable; Nr, not reported; Zr, zirconia.

[a]Based on robust Poisson regression.

reporting on 60 restorations with high incidence of cement-related complications such as loss of retention, misfit, and marginal gaps. Annual overall complication rate of 4.30% was reported for implant-supported PFM iS$_p$Cs and of 3.03% for lithium disilicate iS$_p$Cs. Meta-analysis formally comparing the overall annual complication rate of PFM iFDPs with pontic (1.93%) with the annual complication rate of PFM iS$_p$Cs (4.30%) did not reach statistically significant difference ($p = .078$; Table 9).

3.6 | Technical complications

Forty of the included cohorts, reporting on 1636 implant-supported iFDPs, analyzed the incidence of ceramic chipping and fractures of the ceramic surface. The estimated average annual chipping rate when comparing the different material groups ranged from 0% to 9.01%. No surface chippings were reported for monolithic Zr iS$_p$Cs ($n = 34$), followed by an annual chipping/fracture rate of 0.18% for monolithic Zr iFDPs with pontic ($n = 201$), 1.79% for PFM S$_p$Cs ($n = 513$), 2.20% for PFM S$_p$Cs ($n = 393$), 3.37% for reinforced glass–ceramic iS$_p$Cs ($n = 100$), 4.95% for v-Zr iFDPs with pontic ($n = 353$), and 9.01% v-Zr S$_p$Cs ($n = 33$; Tables 6 and 7). Meta-analysis formally analyzing the chipping/fracture rates of veneered Zr vs. monolithic Zr showed significantly ($p < .01$) higher complication rates for the total number of ceramic fractures and chippings, major chipping requiring repair and minor ceramic chippings that can be polished (Table 8). Furthermore, comparing ceramic fracture/chippings for PFM iFDPs with pontic vs. PFM S$_p$Cs showed that significantly ($p = .05$) more iS$_p$Cs experienced minor ceramic chippings and significantly ($p = .04$) more iFDPs with pontic, however, exhibited major ceramic chippings requiring repair (Table 9).

The estimated annual rate of loss of retention or fracture of the luting cement for iFDPs with pontic ranged from 1.46% to 2.75% with no statistically significant differences when comparing the different material groups or iFDPs with pontic with iS$_p$Cs. Furthermore, the annual rate of screw-loosening ranged from 0% to 8.33% with the highest complication rate reported for v-Zr iFDPs with pontic (Tables 6 and 8). For screw-loosening no significant difference (p = 0.744) was reported between iFDPs with pontic and iS$_p$Cs (Table 9).

3.7 | Risk of bias assessment of the included studies

All included RCTs were considered as prospective studies therefore 32 studies were assessed according to ROBINS-I tool. Only two of the included studies presented overall serious risk of bias and the remaining presented either overall low risk of bias (Derksen et al., 2021) or overall moderate risk of bias (Table S2).

4 | DISCUSSION

The findings of the present systematic review showed that all included reconstructions, regardless of their design (iFDPs with pontics or iS$_p$C$_s$) or material selection ranging from PFM to all-ceramic alternatives, exhibited favorable short-term outcomes and can, therefore, be considered clinically applicable. No significant differences regarding the survival rates were found ($p > .209$). Failure due to framework fracture or fractures of the entire reconstruction in case of monolithic reconstructions were mostly observed for reinforced glass–ceramic iFDPs, resulting in an annual failure rate of 1.0 compared to <0.46 for PFM and Zr reconstructions (monolithic, micro-veneered, veneered). Chipping was shown to be most prevalent for veneered Zr iFDPs with pontics highlighted by an annual failure rate of 4.95 (minor: 2.85, major: 1.65) for iFDPs with pontics compared to annual failure rates ranging from 0.18 to 2.20 for other included material solutions. This finding was even more significant when focusing on splinted crowns (annual failure rate of 9.01), however associated with questionable validity due to a reduced amount of included reconstructions ($n = 33$). Furthermore, meta-analyses indicated superiority of monolithic Zr iFDPs compared to veneered Zr-based reconstructions with respect to chipping of the veneering

TABLE 9 Comparison of annual failure and complication rates for PFM iFDPs with pontic and PFM SpCs.

Failures/complications	PFM SpCs		PFM SpCs		
	iFDPs [*n*]	Estimated annual failure rate[a] (95% CI)	SpCs [*n*]	Estimated annual failure rate[a] (95% CI)	*p*-value[a]
Overall failure rate	332	0.57[a] (0.22–1.49)	380	0.30[a] (0.11–0.80)	.334
Overall complication rate	149	1.93[a] (0.80–4.67)	231	4.30[a] (2.86–6.45)	.078
Overall failures due to ceramic fractures	385	0.36[a] (0.02–0.63)	527	0.04[a] (0.005–0.32)	.042
Failure due to framework fractures	385	0.16[a] (0.03–0.67)	451	0.05[a] (0.006–0.39)	.353
Failure due to catastrophic ceramic fractures	385	0.25[a] (0.09–0.70)	527	0.04[a] (0.005–0.32)	.105
Total number of ceramic chippings or fractures	393	2.20[a] (1.56–3.11)	513	1.79[a] (1.04–3.10)	.522
Minor ceramic chippings	254	0.89[a] (0.49–1.65)	290	1.71[a] (1.19–2.46)	.053
Major ceramic chippings–repair	254	0.90[a] (0.36–2.23)	290	0.08[a] (0.009–0.71)	.039
Loss of retention	363	1.56[a] (0.40–6.13)	288	0.81[a] (0.43–1.51)	.366
Screw loosening or fractures	267	2.36[a] (0.09–63.5)	493	2.81[a] (1.14–6.93)	.744

Abbreviations: CI, confidence interval; iFDPs, implant-supported fixed dental prostheses with pontics; PFM, porcelain-fused-to-metal; SpC, splinted crown.

[a]Based on robust Poisson regression.

ceramic ($p < .0001$), both for the prevalence of minor ($p = .015$) and major ($p = .0001$) delamination. Significantly less chipping of the veneering ceramic was found for monolithic iFDPs as compared to veneered reconstructions. Taking the limitation of short-term observations into account, the present review supports the application of monolithic high-strength ceramics such as Zr for implant-supported iFDPs in the posterior regions.

In the last decades, PFM was considered the gold standard material option for the fabrication of iFDPs, most specifically in the posterior region where high occlusal forces occur. Metal frameworks were successfully evaluated in clinical settings to exhibit the required fracture resistance crucial for good long-term clinical stability, without specific alloys proving to be particularly advantageous or disadvantageous (Sailer et al., 2018). For esthetic reasons, the metal frameworks had to be covered with veneering ceramic to reach a natural appearance. Although the excellent longevity of PFM implant restorations is well documented, along with the increase in digital fabrication technologies this material option seems to lose importance also because of time-consuming production (conventional or associated with increased tool wear in case of subtractive manufacturing) and post-processing (opaquing, veneering) mostly requires various manual steps (Karasan et al., 2023). Besides esthetics and efforts, another reason for a reduced prevalence of PFM reconstructions might be seen in increased costs associated with precious, gold-containing alloys (Jokstad et al., 2021). New digital fabrication technologies allowed for the introduction of new restorative materials with improved esthetical properties and acceptable clinical stability (Pjetursson et al., 2021). New high strength ceramics like a variety of Zr generations became available for the fabrication of dental restorations, as this ceramic necessarily needs to be processed with CAD/CAM technologies (Pjetursson et al., 2022). As an alternative, CAD/CAM glass ceramics with improved fracture strength like lithium disilicate were developed (Pjetursson et al., 2022). Due to their specific properties, these new restorative materials allowed for single- and multi-unit tooth- and implant-supported reconstructions at much lower costs compared to traditional PFM reconstructions (Pjetursson et al., 2021).

The main technical complication for PFM tooth- or implant-supported reconstructions is considered chipping of the veneering ceramic. Chipping can be superficial and of minor clinical importance (to be overcome by e.g., polishing the fracture zone), or extended (e.g., up to the framework material) and therefore being of major clinical importance, potentially resulting in failure (Pjetursson et al., 2007, 2014; Sailer et al., 2007). Several factors were found to attribute to the phenomenon of chipping of the veneering ceramic. Veneering ceramics are a rather weak glass–ceramic materials, directly dependent to be increased in strength by a supporting framework material and structure. The shape of the framework is crucial for the support of the veneering ceramic and, hence, must be carefully adapted to the individual clinical situation by the dental technician. Moreover, both framework and veneering material need to be specifically tailored regarding their chemical and physical properties (such as e.g., coefficient of thermal expansion, CTE) in order to prevent tension along the material interface during environmental exposure in the oral cavity or during manufacturing (e.g., sintering, cooling etc.). Finally, the technique of the veneering process, that is, the baking and sintering of the veneering ceramic onto the framework material was described to be a relevant factor to overcome the incidence of chip-off fractures. On one hand, the sintering process must be performed under high vacuum to eliminate the air inclusions in the veneering ceramic resulting from the veneering process. On the other hand, the temperature increase during the sintering of the veneering ceramic must be adapted to the framework material as well as the decrease after the baking, to reduce strain in the veneering ceramic. Clinically, occlusal and functional forces are of importance and can increase the risk for chipping. Even if it might

be concluded that the occurrence of chipping fractures of veneered bi-layer reconstructions can be overcome by a long list of rules to be considered during material development and processing, feasibility of these highly technique-sensitive steps in daily clinical routine can be considered at least questionable.

Reviews addressing the outcomes of both tooth- and implant-supported restorations have shown, that chipping of the veneering ceramic is one major technical complication of veneered restorations, independent of the framework material (Pjetursson et al., 2017, 2018, 2021; Sailer et al., 2016, 2018). The combination of two types of materials revealing thin layers and a large-scale material interface remains to be the weak link at veneered restorations. At Zr-based restorations, chipping of the veneering ceramic was even shown to be the most prevalent technical problem, occurring in up to 50% of the restorations over an observation period of 5 years, and despite all improvements of materials and methods, never managed to be significantly reduced to the amount observed at other types of framework materials (Pjetursson et al., 2017, 2018, 2021; Sailer et al., 2016, 2018). The present review confirms these previous observations.

As mentioned earlier, new digital technologies and material improvements meanwhile allow for a monolithic, fully anatomic, design of the restorations. The application of either no veneering ceramic or only very thin layers (micro-veneering) for highly individual esthetic adaptation to, for example, natural adjacent teeth are required (Pieralli et al., 2018; Pjetursson et al., 2021; Rabel et al., 2018). At least for the short term, the present review showed that these more recent types of monolithic or micro-veneered restorations exhibited significantly less complications regarding chipping of the veneering ceramic when in function compared to bi-layered restorations, independent of the framework material (Pjetursson et al., 2021). Hence, monolithic or micro-veneered CAD/CAM ceramics like Zr should be preferred over veneered restorations independent of the framework material for multi-unit posterior implant reconstructions, from a technical but also from an economical point of view (Mühlemann et al., 2018). Regrettably, presently available data in the literature did not allow to distinguish between different Zr generations along with their significantly differing optical properties accompanied by diametrically differing mechanical properties. This needs to be considered by practitioners, since times in which it was clearly defined what is meant when speaking about Zr ceramics in dentistry (i.e., 3Y-TZP) meanwhile belong to the past. With the introduction of not only more translucent but also more fragile 4Y- or even 5Y-TZP and corresponding multilayer materials incorporating all these generations within a single blank, the term "zirconia" rather addresses a material group such as "metals" than a single ceramic material with specific and well-known mechanical properties. Therefore, the findings of the present work, when reporting about monolithic or (micro-) veneered Zr reconstructions should be handled with care and be associated with the most robust material generations (3Y-TZP). Transferring these outcomes to new generations materials (4Y-TZP, 5Y-TZP or multilayer materials), not part of the included literature, might result in misinterpretation and consecutive failure.

It is interesting to note, that not only occurrence of technical complications directly associated with mechanical properties of the evaluated materials (like fractures of the veneering ceramic) were found to be different when comparing the different types of included reconstructions. When focusing on technical complications like loss of retention (annual failure rate of 1.46 vs. 2.75) or screw-loosening (annual failure rate of 0 vs. 8.33), monolithic Zr iFDPs with pontics likewise performed better compared to veneered Zr iFDPs with pontics, even if the relevant material interface (i.e., implant-abutment interface or reconstruction-abutment interface) opposes the same material substrates away from the veneered areas. One explanation for this finding could be the exponential improvement in accuracy of CAD/CAM technologies in recent years, positively affecting the outcome of more recent (monolithic approaches) compared to less recent (veneered reconstructions) literature.

Another interesting observation made in the present review is that in clinical situations with posterior partial edentulism, no differences in the outcomes of iS_pCs compared to iFDPs with pontic could be found. From a short-term perspective, hence, the number of implants might be reduced to replace several adjacent missing posterior teeth. As a result, the invasiveness and morbidity, and finally the costs of the treatments may be reduced. The treatment using iFDPs with pontics instead of iS_pCs should at least be considered at treatment planning as a valid option to be discussed with the patient. For further confirmation and definition of new treatment concepts, however, longer observation periods and an increased portion of randomized controlled clinical studies with larger cohorts are needed. Also, implants of reduced length or narrow diameter need to be tested in the mentioned indications before final conclusions can be drawn.

To the knowledge of the authors, the present systematic review is the first one available in the literature comparing the outcomes of the different types of iFDPs, that is, iFDPs including non-implant-supported pontics vs. splinted single crowns. Both groups of reconstructions could be analyzed separately and compared. For PFM reconstructions, overall failure due to ceramic fracture occurred less frequently in case of iSpCs ($p = .042$) compared to the iFDPs with pontics, reaching statistical significance for major ceramic chippings ($p = .039$) and a tendency toward an increased prevalence of minor ceramic chippings ($p = .053$). One reason for this might be the reduced span of non-supported areas in between the single units of an iSpC compared to iFDPs with pontics associated with reduced flexibility of the framework structure, jeopardizing the integrity of a veneering layer brittle in nature. These findings must be interpreted with caution as the included iS_pC as the included material consist of a mixture of two implants with two splinted crowns and three implants with three splinted crowns (average 2.4 unites) compared with at least 3 units for the iFDPs with pontics.

The main limitation of the review should be considered the fact that the clinical follow-up of the analyzed restorations was rather short and that the total number of included iFDPs is rather small for some of the included material groups. Therefore, the process of this systematic review should be repeated in several years, when the

follow-up time of the included studies reaches five or more years or more, and more research is published focusing on the topic of posterior iFDPs with pontics and iS_pCs.

5 | CONCLUSIONS

Implant-supported multi-unit restorations in the posterior area showed high 3-year survival rates ranging from 97% to 100%, regardless of the materials used. Prosthetic design, whether iS_pCs or iFDPs with pontic units, does not significantly impact clinical outcomes. Monolithic and micro-veneered Zr iFDPs with pontic units exhibit superior performance in ceramic fracture and chipping rates compared to PFM and veneered Zr. However, there is a lack of data regarding monolithic lithium disilicate. Furthermore, monolithic and micro-veneered Zr iS_pCs outperformed PFM, veneered Zr, and monolithic lithium disilicate in terms of annual ceramic fracture and chipping rates.

To minimize technical complications, monolithic zirconia is recommended for posterior iFDPs. However, it is important for clinicians and dental technicians to consider the specific properties of different zirconia types, as not all have been extensively validated in clinical studies. The studies included in this analysis primarily focused on 3Y-TZP zirconia with a flexural strength exceeding 1000 MPa, as well as multi-layered alternatives that combined 3Y-TZP and 5Y-TZP. Additionally, restoring multiple posterior missing teeth with iFDPs with pontic units can be a cost-effective and less invasive approach, provided the mechanical properties of the restorative material and implants are considered.

AUTHOR CONTRIBUTIONS

B. Pjetursson: Design of the study, interpretation of data, manuscript preparation and the initial draft, final review of the work; accountable for all aspects of the work. I. Sailer: Acquisition and interpretation of data, manuscript preparation and the initial draft, final review of the work; accountable for all aspects of the work. E. Merino-Higuera and F. Burkhardt: Acquisition of data, final review of the work; accountable for all aspects of the work. B. Spies: Manuscript preparation and the initial draft, final review of the work; accountable for all aspects of the work. D. Karasan: Design of the study, literature search, acquisition and interpretation of data, manuscript preparation and the initial draft, final review of the work; accountable for all aspects of the work.

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CONFLICT OF INTEREST STATEMENT

The authors have no specific conflict of interest related to the present systematic review. The authors do not have any financial interests, either directly or indirectly, in the products or information enclosed in the paper.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available in the Tables S1 and S1.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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CONSENSUS REPORT

CLINICAL ORAL IMPLANTS RESEARCH WILEY

Group 2 ITI Consensus Report: Technological developments in implant prosthetics

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Abstract

Objectives: Group-2 reviewed the scientific evidence in the field of «Technology». Focused research questions were: (1) additive versus subtractive manufacturing of implant restorations; (2) survival, complications, and esthetics comparing prefabricated versus customized abutments; and (3) survival of posterior implant-supported multi-unit fixed dental prostheses.

Materials and Methods: Literature was systematically screened, and 67 publications could be critically reviewed following PRISMA guidelines, resulting in three systematic reviews. Consensus statements were presented to the plenary where after modification, those were accepted.

Results: Additively fabricated implant restorations of zirconia and polymers were investigated for marginal/internal adaptation and mechanical properties without clear results in favor of one technology or material. Titanium base abutments for screw-retained implant single crowns compared to customized abutments did not show significant differences concerning 1-year survival. PFM, veneered and monolithic

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zirconia implant-supported multi-unit posterior fixed dental prostheses demonstrated similar high 3-year survival rates, whereas veneered restorations exhibited the highest annual ceramic fracture and chipping rates.

Conclusions: For interim tooth-colored implant single crowns both additive and subtractive manufacturing are viable techniques. The clinical performance of additively produced restorations remains to be investigated. Implant single crowns on titanium base abutments show similar clinical performance compared to other type of abutments; however, long-term clinical data from RCTs are needed. The abutment selection should be considered already during the planning phase. Digital planning facilitates 3D visualization of the prosthetic design including abutment selection. In the posterior area, monolithic zirconia is recommended as the material of choice for multi-unit implant restorations to reduce technical complications.

KEYWORDS
clinical research, clinical trials, material sciences, patient centered outcomes, prosthodontics

1 | INTRODUCTION

The rapid technological progress influences our society like no other—and in dentistry this is no different. Due to the continuous development in the IT sector, completely new possibilities have emerged today. The MedTech industry is developing and marketing (digital) applications and tools faster than they can be scientifically investigated. Moreover, the technological turnover is so rapid that updates and follow-on products are already commercially available before the first generation of this technology could be sufficiently investigated.

Additive manufacturing in terms of 3D printing is one such example. A multitude of device manufacturers and an even greater variability of materials are on the market. Another example is the so-called titanium base abutment. As a prefabricated implant prosthetic component in combination with monolithic restorations, they have become indispensable in implantology, if the many case reports published on social media are to be believed. Last but not least, however, we clinicians are concerned about the long-term results to the whole of our patients. Is it just fancy and hip to use new technologies or is there scientific evidence? To what extent can these technologies be used without hesitation in daily practice today?

Working Group-2 «Technology» of the 7th ITI Consensus Conference has addressed these questions. The aim was to systematically examine the available scientific literature on the three core topics: (Ioannidis et al., 2023) additive versus subtractive manufacturing of implant restorations; (Chantler et al., 2023) survival and complications rates as well as esthetic outcomes comparing prefabricated versus customized abutments; and (Pjetursson et al., 2023) clinical performance of implant-supported fixed dental prostheses with different prosthetic designs and restorative material for treatment of multiple missing teeth in the posterior area. In the context of the above-mentioned core topics, Group-2 also addressed the patient perspective. Possible answers to questions that patients may ask the dentist in daily routine were formulated. The answers to these questions are based on both the consensus statements and the clinical recommendations of Group-2.

2 | SYSTEMATIC REVIEW PAPER 1

2.1 | Manuscript title

Additively and subtractively manufactured implant-supported fixed dental prostheses (iFDPs): A systematic review.

2.2 | Preamble

With the advent of digital technologies in implant dentistry, there has been an increasing shift from conventional to digital workflows, which employ computer-aided design (CAD) and computer-aided manufacturing (CAM). The CAM process relies on subtractive (SM) or additive manufacturing (AM). Subtractive manufacturing methods entail milling of a restorative material to obtain interim or definitive restorations and have become a well-established technology to produce iFDPs. Conversely, AM—commonly known as 3D printing—describes the process of successive adding and joining materials layer-by-layer to build a digitally designed three-dimensional object. Additive manufacturing results in less material waste, enables the production of more complex geometries and allows the combination of different material properties in a single workpiece. Given the significant and ongoing interest in AM, it is crucial to analyze and summarize the latest state of evidence. Therefore, the aim of the present systematic review was to compare and report on the performance of iFDPs produced with AM versus SM CAM techniques.

An electronic search was performed with the focused PICO-question: In partially edentulous patients with missing single or

multiple teeth undergoing dental implant therapy (P), do AM iFDPs (I) compared to SM iFDPs (C) result in an improved clinical performance (O). The electronic search was conducted up to November 1, 2022. No clinical trial met the inclusion criteria, whereas six in vitro studies proved to be eligible out of a total of 2′184 titles. Performance of a total of 184 single implant crowns was evaluated in the included studies by assessing marginal and internal adaptation as well as mechanical properties, as fracture loads and bending moments. Additive manufacturing iFDPs were made of zirconia and polymers. For SM iFDPs, zirconia, lithium-disilicate, resin-modified ceramics, and different types of polymer-based materials were used. Due to the considerable heterogeneity among the included studies, no meta-analysis could be performed.

2.3 | Consensus statements

2.3.1 | Consensus statement 1 (*technology*)

Subtractive manufacturing (SM) technologies have been widely used for the fabrication of tooth-colored iFDPs, while AM techniques are increasingly being explored. At the present time, there are no comparative clinical data and six comparative in vitro studies.

2.3.2 | Consensus statement 2 (*marginal and internal adaptation*)

Additive and subtractive CAM techniques have the potential to influence the marginal and internal adaptation of tooth-colored iFDPs on both prefabricated and customized abutments. Current data are insufficient to draw comparative conclusions.

Based on three in vitro studies, directly comparing AM versus SM.

2.3.3 | Consensus statement 3 (*mechanical properties*)

Both additive and subtractive CAM techniques can influence the mechanical properties (fracture loads and bending moments) of tooth-colored iFDPs. Current data are insufficient to draw comparative conclusions.

Based on four in vitro studies, directly comparing AM versus SM.

2.4 | Clinical recommendations

2.4.1 | Clinical recommendation 1

Which CAD/CAM technology can be recommended for the production of an interim implant-supported fixed dental prosthesis?

For interim tooth-colored single implant crowns both additive- and subtractive manufacturing are viable techniques; however, for interim multi-unit iFDPs SM is currently recommended to minimize complications.

2.4.2 | Clinical recommendation 2

Which CAD/CAM technology can be recommended for the production of a definitive implant-supported fixed dental prosthesis?

For CAD/CAM definitive single- and multi-unit iFDPs subtractive manufacturing is recommended. Clinicians and dental technicians are encouraged to follow the rapid development of AM technology and related materials as significant improvements are expected in the near future.

2.4.3 | Clinical recommendation 3

Is CAD/CAM technology simple to use, once the devices are installed?

To achieve the intended results, it is necessary that both AM and SM technologies are applied with careful consideration requiring technical expertise and ongoing training. It is essential to follow specific manufacturing protocols and to maintain the devices.

2.5 | Patient perspectives

2.5.1 | Patient perspective 1

Question: I have heard about a new technology 3D printing. Would you recommend this technology for my implant crown?
Answer: 3D-printed implant crowns can be recommended for temporary use. When it comes to implant bridges, we are still in the development phase. For definitive implant restorations, 3D printing cannot be recommended at the present time.
Based on expert opinion.

2.5.2 | Patient perspective 2

Question: I have heard that there is also the option of milling implant crowns. Are 3D-printed implant crowns cheaper and faster than milled ones?
Answer: As both technologies require manual post-processing adjustments, 3D printed restorations are not necessarily cheaper or faster. As the technology for printing implant bridges evolves it may prove to be faster than milling but it is too early to say or to recommend.
Based on expert opinion.

2.5.3 | Patient perspective 3

Question: Do 3D-printed implant crowns look good?
Answer: As with any other temporary implant restoration, with manual adjustments an esthetic result can be achieved.
Based on expert opinion.

2.5.4 | Patient perspective 3

Question: Have 3D resins proven to be safe?
Answer: 3D printing materials for dental restorations are officially approved for use in the mouth. However, we can only recommend them for provisional/temporary implant restorations as only the results for shorter term use in the mouth are available.
Based on expert opinion.

2.6 | Recommendations for future research

2.6.1 | Recommendation 1 for future research

Randomized controlled trials on AM versus SM are needed to evaluate the clinical performance of iFDPs in terms of long-term survival, technical and biological complications, esthetics, and PROMs under different indications: interim/definitive; anterior/posterior; single-/multi-units.

2.6.2 | Recommendation 2 for future research

The potential of AM to produce iFDPs combining different optical and mechanical properties in a workpiece should be explored with the aim to achieve esthetic integration and reduce the inherent human intervention.

2.6.3 | Recommendation 3 for future research

Given the wide use of zirconia in prosthetic implant dentistry, research should focus on AM of this material. To integrate this new technology into clinical practice, it is crucial to conduct in vitro and clinical trials that compare the performance of additively versus subtractively manufactured monolithic zirconia iFDPs.

3 | SYSTEMATIC REVIEW PAPER 2

3.1 | Manuscript title

Clinical performance of single screw-retained implant prostheses restored using titanium base abutments: A systematic review and meta-analysis.

3.2 | Preamble

Most dental implant abutments have a prefabricated implant connection and are either used as a stock or customized abutment. Titanium base abutments (TBA) have been proposed as a stock abutment for the restoration of single dental implants. The abutment allows the clinician to utilize a complete digital workflow. The TBAs are available with variable geometries of the transmucosal and the retentive attachment segments that are captured within an associated digital library. This allows for the restorative cemented crown or intermediate layer (coping) to be fabricated from. The combination of a prefabricated base and customizable restorative crown, enables the clinician to optimize the emergence profile with the benefits of a traditional stock and customizable abutment. The long-term efficacy of this abutment has been a topical debate since its inception. The majority of studies do not include direct comparisons between TBA and other categories of abutments. The aim of this systematic review and meta-analysis was to analyze the clinical performance of TBA compared to other abutments for single implant crown (iSC). The primary outcome was to compare the 1-year survival rates of TBA versus other abutments. Secondary outcomes were as follows: biological outcomes including marginal bone loss, PPD, BOP; and technical complications such as loss of retention of the abutment to the restorative material (debonding), veneer chipping, abutment fracture, screw loosening, or screw fracturing; and esthetic outcomes. A PICO strategy was executed following the PRSIMA guidelines. The electronic search was conducted in the databases PubMed/MEDLINE, Scopus, and Cochrane Library to identify publications in English from January 1, 2000 to May 5, 2023. The search provided 1′159 titles, whereas six RCTs fulfilled the inclusion criteria and were considered for data extraction of the meta-analysis. Fifteen prospective and eight retrospective cohort studies were collated for descriptive results. A total of 857 iSCs fabricated with a TBA were analyzed.

3.3 | Consensus statements

3.3.1 | Consensus statement 1

Implant-supported single crowns (iSC) on titanium base abutments show similar short term survival rates (1 year) to iSC restorations with other type of abutments.

Based on a meta-analysis including six RCTs.

3.3.2 | Consensus statement 2

The geometric designs of titanium base abutments vary considerably in transmucosal height, width, and contours. Current data does not provide solid guidelines for abutment selection criteria.

Based on 21 prospective cohort studies and eight retrospective studies.

3.3.3 | Consensus statement 3

Technical complications of titanium base abutments occur at a low rate. Separation of the suprastructure from the titanium base abutment is the most frequent reported complication.

Based on 21 prospective cohort studies and eight retrospective studies.

3.4 | Clinical recommendations

3.4.1 | Clinical recommendation 1

When should the implant abutment be selected?

Since abutments have important biological implications, the abutment selection should be considered during the implant-prosthetic treatment planning phase prior to implant placement. Digital planning facilitates 3D visualization of the final prosthetic design and pre-operative abutment selection. The final selection is made after the maturation of the soft tissues.

3.4.2 | Clinical recommendation 2

Which titanium base abutment shoulder height should be selected for bone level conical-connection implants?

The selection of the titanium base abutment is conducted so that the shoulder is located sufficiently distanced from the bone and in a submucosal position with sufficient space for an optimal emergence profile.

3.4.3 | Clinical recommendation 3

Which factors do contribute to retention of suprastructures to the titanium base abutments?

Overall retention of the restorative material on the titanium base abutment is determined by: the retentive-attachment height and shape, resistance features and the adhesive cementation protocol. Clinicians are encouraged to maximize overall retention considering the available restorative space.

3.4.4 | Clinical recommendation 4

Can titanium base abutments be used for all single implant crowns?

When a titanium base abutment is considered for use but the standardized shapes do not allow for an adequate emergence profile contour or provide inadequate resistance and retentive features, the use of a customized abutment is recommended.

3.5 | Patient perspectives

3.5.1 | Patient perspective 1

Question: What material will my implant crown be made of?
Answer: Nowadays we usually use monolithic ceramic materials for the suprastructure, meaning it is made entirely of one material, such as zirconia. These crowns are designed on a computer using CAD.
Based on scientific evidence.

3.5.2 | Patient perspective 2

Question: How will the crown be attached to my implant?
Answer: The crown is connected to the implant via a component called an abutment. There are many different types and designs of abutments including ones that are ready made and others that are custom made. Most abutments are made of a ceramic or metal material. The choice of abutment will depend on your specific situation.
Based on scientific evidence.

3.5.3 | Patient perspective 3

Question: Is there a difference in cost between the different types of abutments?
Answer: Ready-made components such as titanium abutments are usually less expensive. However, in some situations a customized abutment is required to achieve the best result.
Based on scientific evidence.

3.6 | Recommendations for future research

3.6.1 | Recommendation 1 for future research

Randomized controlled trials on titanium base abutments versus customized abutments to analyze the clinical performance in terms of long-term survival, technical and biological complications, esthetics, and patient-reported outcome measures (PROMs).

3.6.2 | Recommendation 2 for future research

In vivo studies investigating the influence of a submucosally located restorative-abutment-junction on the marginal bone level and supra-implant soft tissues.

4 | SYSTEMATIC REVIEW PAPER 3

4.1 | Manuscript title

Systematic review evaluating the influence of the prosthetic material and prosthetic design on the clinical outcomes of implant-supported multi-unit fixed dental prosthesis in the posterior area.

4.2 | Preamble

The primary aim of this systematic review was to evaluate the survival rates as well as the incidence of technical complications of implant-supported partial fixed dental prosthesis in the posterior area exploring the influence of different prosthetic materials. The secondary aim, the influence of the design, differentiating reconstructions in formation as «bridge» including non-supported pontic units or «splinted crowns» was analyzed. The study protocol of this systematic review was designed according to the Cochrane and PRISMA guidelines for systematic reviews and meta-analyses. An electronic and manual search was performed up to October 10, 2022 to identify randomized controlled trials (RCTs), prospective and retrospective clinical trials with a follow-up of at least of 12 months, evaluating the clinical outcomes of implant-supported posterior multi-unit fixed dental prostheses. Survival and complication rates were analyzed using robust Poisson's regression models. A total of 32 studies (24 prospective cohort studies and 8 retrospective case series) reporting on 42 patient cohorts were included. The extracted data was used for meta-analysis to estimate 3-year survival and complication rates.

4.3 | Consensus statements

4.3.1 | Consensus statement 1

Implant-supported multi-unit restorations, that is, splinted crowns or fixed dental prostheses with pontic units, in the posterior area are both well-documented and reliable treatment options exhibiting high 3-year survival rates ranging from 97% to 100% regardless of the materials used. The material combinations analyzed were porcelain-fused-to-metal, veneered, micro-veneered and monolithic zirconia, and monolithic lithium disilicate.

Based on 22 prospective cohort studies and seven retrospective case series.

4.3.2 | Consensus statement 2

The prosthetic design—whether using splinted implant crowns or iFDPs with pontic units—for the restoration of multi-unit posterior edentulous sites, does not significantly influence 3-year clinical outcomes in terms of survival and technical complications rates.

Based on 10 prospective cohort studies and six retrospective case series.

4.3.3 | Consensus statement 3

Monolithic and micro-veneered zirconia implant-supported multi-unit restorations with pontic units exhibit superior performance compared to porcelain-fused-to-metal and veneered zirconia in the posterior area in terms of annual ceramic fracture and chipping rates. No applicable data is currently available for monolithic lithium disilicate implant-supported multi-unit restorations with pontic units.

Based on 11 prospective cohort studies and six retrospective case series.

4.3.4 | Consensus statement 4

When splinted implant crowns are made of monolithic and micro-veneered zirconia, they exhibit superior performance when compared to porcelain-fused-to-metal, veneered zirconia, and monolithic lithium disilicate in the posterior area in terms of annual ceramic fracture and chipping rates.

Based on 12 prospective cohort studies and three retrospective case series.

4.4 | Clinical recommendations

4.4.1 | Clinical recommendation 1

What prosthetic design is recommended to treat multiple missing teeth in posterior edentulous sites with a fixed implant restoration?

Both splinted implant crowns and implant-supported multi-unit restorations with pontic units can be recommended to replace multiple posterior missing teeth.

4.4.2 | Clinical recommendation 2

How many implants you need to support a fixed restoration to replace at least three missing teeth in the posterior area?

To minimize invasiveness and treatment cost, it can be recommended to reduce the number of implants by restoring multiple posterior missing teeth with iFDPS with pontic units as long as the mechanical properties of the restorative material and the implants can be respected (e.g., three-unit iFDPs on two implants instead of three splinted implant crowns).

4.4.3 | Clinical recommendation 3

What restorative material of choice for posterior multi-unit fixed implant-supported restorations?

In the posterior area, monolithic zirconia is recommended as the material of choice for implant-supported posterior multi-unit restorations in order to reduce technical complications such as ceramic

fracture and chipping. The evidence supporting this recommendation is based on studies reporting on 3Y-TZP zirconia with a flexural strength >1000 mPa or multi-layered (3Y-TZP/5Y-TZP) alternatives.

4.4.4 | Clinical recommendation 4

What must be considered when using zirconia for implant-supported multi-unit fixed dental prostheses?

The clinician and the dental technician need to be well-informed and should select the restorative material for every indication as a team. Even though zirconia is the best-documented ceramic material for posterior multi-unit restorations, it has to be considered that various types and generations exist. The significant differences in optical and mechanical properties have not all been validated in clinical studies.

4.5 | Patient perspectives

4.5.1 | Patient perspective 1

Question: I am missing my upper-right back teeth. Can I have fixed teeth again?
Answer: Yes, if the circumstances are right we can provide you with a fixed solution on implants. Depending on what you would like, your anatomy, health, and budget, we can determine how many teeth need to be replaced and how many implants will be needed.
Based on scientific evidence.

4.5.2 | Patient perspective 2

Question: I have lost three teeth and want to replace them all. How many implants do you think I will need?
Answer: We have the choice between placing two or three implants to support three fixed teeth. In general, we recommend placing just two implants to support a three-unit bridge. This will make the surgical procedure easier, reduce the cost, and the expected outcome is the same.
Based on scientific evidence.

4.5.3 | Patient perspective 3

Question: I guess the material needs to be quite strong if there is a non-supported tooth in the middle. What material do you use to make a bridge like that?
Answer: Today, the material of choice for this type of bridge is monolithic zirconia. Since it is made entirely out of high strength ceramic, there is less chance of the surface breaking or fracturing.
Based on scientific evidence.

4.5.4 | Patient perspective 4

Question: Does monolithic zirconia look like a natural tooth?
Answer: Today's zirconia comes closer to imitating the look of a natural tooth. We can also further improve the parts that are visible when you smile by applying a thin layer of color to the surface of the zirconia.
Based on scientific evidence.

4.6 | Recommendations for future research

4.6.1 | Recommendation 1 for future research

Randomized controlled trials with long-term follow-up are needed comparing different types of monolithic zirconia (e.g., 3Y-TZP zirconia, multi-layered 3Y-TZP/5Y-TZP), restoration designs (splinted, non-splinted, pontic-containing, cantilevers), and differences in pontic span length.

4.6.2 | Recommendation 2 for future research

Randomized controlled trials comparing different retention types for multi-implant monolithic zirconia restorations on bone level conical connection implants, for example, intermediate abutments versus direct-to-implant retention (such as with a titanium base abutment), specifically addressing the number and distribution of implants.

4.6.3 | Recommendation 3 for future research

Randomized controlled trials comparing cement-retained versus angulated solutions for multi-implant monolithic zirconia restorations.

4.6.4 | Recommendation 4 for future research

Those RCTs should report on survival and complication rates, esthetics, PROMs, as well as cost- and time-efficiency.

AUTHOR CONTRIBUTIONS

W. Derksen: Conceptualization; Methodology; Writing – original draft; Writing – review & editing; Supervision; Project administration; Validation. T. Joda: Conceptualization; Methodology; Supervision; Project administration; Writing – review & editing; Writing – original draft; Validation. J. Chantler: Investigation; Writing – review & editing; Formal analysis; Data curation. V. Fehmer: Writing – review & editing. G. O. Gallucci: Writing – review & editing. P. C. Gierthmuehlen: Writing – review & editing. A. Ioannidis: Investigation; Formal analysis; Data curation; Writing – review & editing. D. Karasan: Writing – review & editing. A. Lanis: Writing – review & editing. K. Pala:

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REVIEW ARTICLE

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Clinical and radiographic outcomes of zirconia dental implants—A systematic review and meta-analysis

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Abstract

Objectives: For the present review, the following focused question was addressed: In patients with root-analog dental implants, what is the effect of implants made of other materials than titanium (alloy) on implant survival, marginal bone loss (MBL), and technical and biological complications after at least 5 years.

Materials and Methods: An electronic (Medline, Embase, Web of Science) search was performed to identify observational clinical studies published from January 2000 investigating a minimum of 20 commercially available zirconia implants with a mean follow-up of at least 60 months. Primary outcome was implant survival, secondary outcomes included peri-implant MBL, probing depths (PDs), and technical and biological complications. Meta-analyses were performed to evaluate implant survival, MBL, and PD.

Results: From 5129 titles, 580 abstracts were selected, and 111 full-text articles were screened. Finally, 4 prospective and 2 retrospective observational clinical cohort studies were included for data extraction. Meta-analyses estimated after 5 years of loading mean values of 97.2% (95% CI 94.7–99.1) for survival (277 implants, 221 patients), 1.1 mm (95% CI: 0.9–1.3) for MBL (229 implants, 173 patients), and 3.0 mm (95% CI 2.5–3.4) for PDs (231 implants, 175 patients).

Conclusions: After 5 years, commercially available zirconia implants showed reliable clinical performance based on survival rates, MBL, and PD values. However, more well-designed prospective clinical studies and randomized clinical trials investigating titanium and zirconia implants are needed to confirm the presently evaluated promising outcomes.

KEYWORDS
biological complications, dental implants, implant survival, marginal bone loss, meta-analysis, probing depths, technical complications, yttria stabilized tetragonal zirconia, zirconium oxide

1 | INTRODUCTION

For many decades, titanium has been used for the fabrication of dental implants and abutments. In recent years, esthetic outcomes – especially in the anterior region – have become very important. The dark grayish color of titanium implants and abutments can be a major drawback regarding white and pink esthetics (Glauser et al., 2004; Jung et al. 2008). However, not only the focus on esthetics but also the biological awareness of clinicians and patients has changed. Metals like commercially pure titanium or specific

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titanium–zirconium alloy show very good soft and hard tissue integration capacities and excellent clinical performance (Roehling et al., 2015). However, concerns have been raised regarding the potential of titanium to induce hypersensitivity or inflammatory reactions in the host tissues which could lead to various biological complications. In addition, an association between plaque, biocorrosion, presence of titanium particles, and biological implant complications has been reported (Mombelli et al., 2018).

In clinical studies, alumina and zirconia have been investigated as implant materials other than titanium or titanium–zirconium. Alumina implants were established on the market at the end of the 1960s and were clinically used until the beginning of the 1990s (De Wijs et al., 1994). At the beginning of 2004, zirconia was established on the market as an implant material and is currently the only material that is used for the fabrication of ceramic dental implants with 1- and 2-piece designs. Based on superior biomechanical properties, zirconia implants can withstand oral occlusal forces (Kohal et al., 2015). So far, systematic reviews investigating the clinical performance of zirconia implants estimated mean survival rates between 95% and 97.2% only for follow-up periods of 1 and 2 years (Pieralli et al., 2017; Roehling et al., 2018). However, even though meta-analyses are limited to 1 and 2 years of follow-up, clinical studies investigating zirconia implants after functional loading periods of 5 years and more have most recently been published (Brunello et al., 2022; Gahlert et al., 2022). So far, no systematic reviews and meta-analyses evaluating the clinical and radiographic performance of zirconia implants after follow-up periods of more than 2 years are available.

The intended focused question for this invited review (2023 ITI consensus conference) was: 'In clinical studies, what other materials compared to commercially pure titanium, or a specific titanium alloy allow peri-implant soft and hard tissue integration?' However, due to the large heterogeneity of the available abutment and implant studies (several randomized controlled clinical trials available investigating abutments, while this is not the case for the commercially available implant materials), it was not possible to combine both topics. Consequently, the focused question was answered in two separate systematic reviews. The present manuscript reports data on implant materials, while information regarding abutment materials will be the subject of another systematic review (Laleman et al.).

For the present systematic review, the focused question to be addressed was as follows:

In patients with root-analog dental implants, what is the effect of implants made of other materials than titanium or a specific titanium alloy on implant survival, marginal bone loss (MBL), and technical and biological complications after at least 5 years?

2 | MATERIALS AND METHODS

This systematic review was conducted according to the Preferred Reporting Items for Systematic review and Meta-Analysis Protocols (PRISMA-P (Page et al., 2021)) statement using the Population, Intervention, Comparison and Outcome (PICO) method (Schardt et al., 2007). The protocol for this systematic review was registered on PROSPERO (CRD42022376487).

2.1 | Search strategy

An electronic, systematic search of Medline via Pubmed, Embase via Elsevier and Web of Science via Clarivate databases was performed in July 2022. The specific search terms are found in Appendix S1.

Additional hand searches were performed and included the following: bibliographies of previous reviews on the subject and bibliographies of all included full-text articles. Moreover, a manual search of the reference lists of relevant articles published in *Clinical Oral Implants Research*, *International Journal of Oral & Maxillofacial Implants*, *Clinical Implant Dentistry and Related Research*, *Journal of Periodontology*, and *Journal of Clinical Periodontology* was performed.

2.2 | Eligibility criteria

2.2.1 | Implant studies

For the part of the systematic review focusing on the implants, the following inclusion criteria were defined:

- Human, observational trials (prospective and retrospective) investigating implants made of materials other than commercially pure grade 4 titanium or specific titanium alloys published from January 2000.
- Implant types and surface topographies investigated in the included studies have not been removed from the market, respectively, replaced on the market by a further developed, next generation of the same type of implant.
- At least 20 implants were evaluated at follow-up.
- Follow-up for at least 60 months after implant placement.
- Reported details regarding implant survival.
- Reported details regarding peri-implant marginal boneloss.
- Language: English.

Studies not meeting the inclusion criteria were excluded from the review. Moreover, clinical studies investigating individually designed zirconia implants or multiple publications on the same patient population, as well as investigations based on charts, questionnaires, or interviews as well as case reports were excluded. Due to time limitations and invited systematic review, only articles published in the English language could be included in the present manuscript.

2.2.2 | Selection of studies

After the elimination of duplicates, the reviewers (SR, IL) independently screened titles, abstracts, and full texts meeting the selection criteria. For the screening of titles and abstracts, the free web and mobile

app Rayyan (http://rayyan.qcri.org) was used (Ouzzani et al., 2016). Unclear titles were included in the abstract screening. If titles or abstracts did not provide sufficient information for selection, full texts were obtained. Any disagreement regarding inclusion and exclusion was resolved by discussion between the reviewers. To evaluate the agreement between the reviewers, Cohen's kappa coefficient (κ) was calculated for the title and abstract selection (Landis & Koch, 1977).

2.2.3 | Data extraction and outcome measures

The primary outcome was implant survival. Secondary outcomes included peri-implant MBL, peri-implant probing depths (PDs) as well as technical and biological complications.

Implant survival was defined as the implant remaining in situ for the observation period.

MBL was calculated as the difference between implant placement and the last follow-up examination.

PDs were monitored at the last follow-up examination.

Technical complications were defined as implant or abutment fracture, fracture of the implant prosthesis, chipping of the veneering ceramic, and loosening of the implant prosthesis.

The biological complications included bone loss of more than 2 mm over the observation periods, soft tissue complications (swelling, fistulas, mucositis), and peri-implantitis.

The timing of implant placement was classified as defined by Hammerle et al., 2004:

- Type 1: Immediate implant placement following tooth extraction.
- Type 2: Early implant placement after complete soft tissue healing (4–8 weeks).
- Type 3: Early implant placement after partial bone healing (12–16 weeks).
- Type 4: Late implant placement after complete bone healing (more than 16 weeks).

Implant loading protocols were classified as follows by (Weber et al., 2009):

- Immediate loading: Functional loading of implants earlier than 1 week subsequent to implant placement.
- Early loading: Functional loading of implants between 1 week and 2 months subsequent to implant placement.
- Conventional loading: Functional loading after more than 2 months subsequent to implant placement.

Implant failures were classified as follows:

- Early implant failures: Implant loss before prosthetic loading (Broggini et al., 2007).
- Late implant failures: Implant loss after prosthetic loading (Broggini et al., 2007).
- Implant fractures.

Data extraction by the reviewers was independently performed for all included studies (SR, IL) using data extraction tables. Disagreement regarding data extraction was resolved by discussion. In case of missing or unclear information, the corresponding authors of the articles were contacted via email. If the information was still not sufficient for inclusion and evaluation, the study was excluded from the present review.

From the included clinical full-text articles, the following data were extracted: author(s), year of publication, design of study (retrospective study design [RE]/prospective study design [PR]/randomized clinical trial [RCT]), number of included patients and implants, implant material (yttria-stabilized zirconia [YTZP]/alumina-toughened zirconia [ATZ]/titanium), implant design (1-piece/2-piece), implant system, implant surface treatment, surface roughness, market availability of investigated zirconia implant surface (yes/no), type of implant placement (Type 1/2/3/4), use of bone augmentation during surgery (yes/no), use of immediate temporization directly after implant placement (yes/no), immediate loading (yes/no), time period between implant placement and final prosthetic reconstruction (weeks), type of prosthetic restoration on implants and abutments (single crown [SC]/fixed dental partials [FDPs]/removable hybrid dentures [RHDs]), retention modes prosthetics (abutments and prostheses, cement-retained [CR]/screw-retained [SR]), number of drop outs, number of early/late implant failures and implant fractures, mean observation period (months), implant survival (%), and mean peri-implant MBL (mm). Moreover, technical and biological complications as well as PDs were recorded.

2.2.4 | Quality assessment and risk of bias

Two reviewers (IL and SR) independently screen the included cohort studies and assessed for quality and reporting using the Newcastle–Ottawa scale, which includes 8 key domains. One star is awarded for each domain in which the criteria are fulfilled, except for 'comparability' which can be awarded two stars.

2.3 | Statistical analysis

For survival rates after 60 months, MBL and mean PD, a random-effect meta-analysis was performed using metaprop and metan in Stata statistical software version 17.0 (StataCorp LLC). The amount of heterogeneity across studies was assessed with the I^2 measure (Higgins et al., 2003). For the survival rates, exact binomial 95% confidence intervals were calculated. Since the survival rates are at 1 in some studies, we enabled the Freeman–Tukey double arcsine transformation to include such studies in the pooled estimate and to guarantee the pooled estimate to be within the [0, 1] interval (Nyaga et al., 2014). For MBL and PD, 95% confidence intervals for means were calculated using standard errors derived from the reported standard deviations.

Forest plots were used for the graphic presentation of survival rates, MBL and mean PD in each study with confidence intervals along with the overall pooled prevalence. In the graphs, the weight of each study to the meta-analyses is represented by the area of a box whose center represents the size of the effect estimated from that study. The confidence interval for the effect from each study is also shown. The summary effect is shown by the middle of a diamond whose left and right extremes represent the corresponding confidence interval.

3 | RESULTS

The electronic database search resulted in 7718 publications (Pubmed: 4972; Embase: 1981; Web of Science: 1665, Figure 1). After the removal of duplicates, 5129 titles were available and screened resulting in 580 abstracts for further evaluation. After screening the abstracts, a total of 111 publications were selected for full-text evaluation. After analysis of the included full-text articles, a total of 6 clinical studies fulfilled the inclusion criteria and were included in the present qualitative and quantitative analyses (Figure 1, Tables 1–4). In total, 93 reports had to be excluded (Table 5). The inter-examiner agreement was $\kappa = 0.82$.

3.1 | Study characteristics

The literature search has shown that in clinical studies, only zirconia and alumina have been used as alternative implant materials instead of commercially pure titanium, or a specific titanium alloy. Since alumina implants have been removed from the market in the 1990s, only studies investigating zirconia as an implant material were included in the present review.

Based on the eligibility criteria, only observational studies were included for data extraction and further statistical analysis. Altogether, 6 observational clinical cohort studies with prospective ($n = 4$) and retrospective ($n = 2$) designs investigating 1-piece (5 studies, 229 implants) and 2-piece zirconia implant designs (1 study,

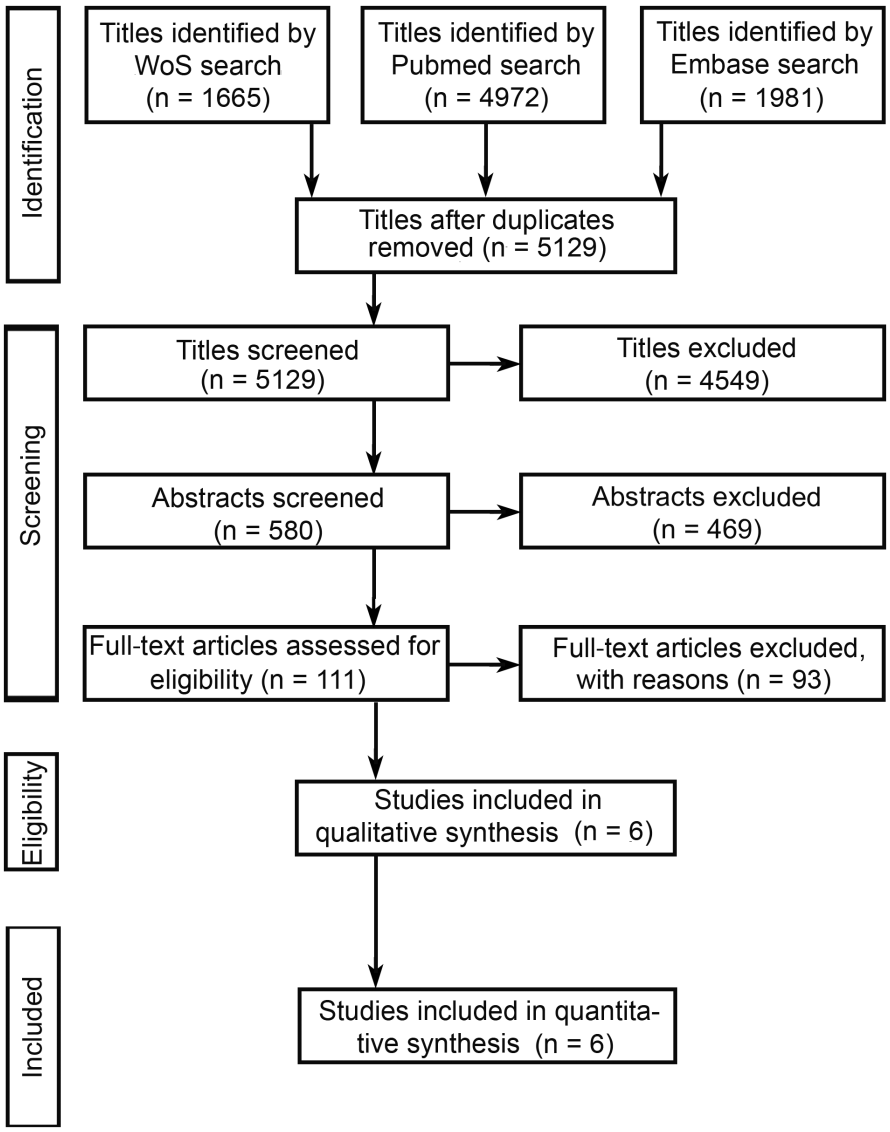


FIGURE 1 Search strategy and selection process for the included studies.

TABLE 1 Characteristics of clinical studies investigating implant survival.

Author/year	Study Design	Patients (n)	Impl. (n)	Material	Impl. Design	Setting	Company/implant type	Surface treatment	Surface roughness (μm)
Brunello et al., 2022	RE	48	48	YTZP	2	Univ.	Patent, Zircon-Medical, former ZV3, Zirkon Vision GmbH	Air particle abrading, sintering	Ra 7.0
Gahlert et al., 2022	PR	44	44	YTZP	1	Priv. pract. and Univ.	Straumann/PURE Ceramic Implant	Sandblasting, large-grit and acid etching	Sa 7.0
Borgonovo et al., 2021	RE	12	29	YTZP	1	Univ.	Bredent/WhiteSky	Sandblasting	Ra 0.9–1.0
Balmer et al., 2020	PR	60	71	YTZP	1	Univ.	Vita Zahnfabrick/ceramic. implant Vitaclinic	Sandblasting and acid etching	Ra 1.2
Kohal et al., 2020	PR	40	53	ATZ	1	Univ.	Metoxit AG/Ziraldent FR 1	Sandblasting, Sintering with pore-building polymers	Ra 1.8
Grassi et al., 2015	PR	17	32	YTZP	1	Priv. pract. and Univ.	Bredent/WhiteSky	Sandblasting	Sa 1.17

Abbreviations: 1, 1-piece implant design; 2, 2-piece implant design; ATZ, alumina-toughened zirconia; Impl. Design, Implant Design; Impl, Implants; PR, prospective study design; Priv. pract.: Private practice; RE, retrospective study design; Ti, Titanium; Univ.: University; YTZP, yttria-stabilized zirconia; NR, not reported.

48 implants) were included in the analysis ([Balmer et al., 2020; Borgonovo et al., 2021; Brunello et al., 2022; Gahlert et al., 2022; Grassi et al., 2015; Kohal et al., 2020], [Table 1]). The risk of bias assessment of these studies is shown in Table 6. The investigated implant diameters ranged between 3.5 mm and 5.5 mm. Implant placement was performed immediately after tooth extraction (type 1), after soft tissue (type 2) or osseous healing (types 3 and 4). Immediate temporization after implant placement was performed in 4 studies, whereas immediate loading was allowed in only 1 study. All the included investigations allowed simultaneous bone augmentation procedures and the time periods between implant placement and insertion of the final prosthetic reconstruction ranged between 8 and 26 weeks, whereas SCs and FDPs were investigated. All the investigated prosthetic reconstructions – abutments as well as SCs and FDPs – were cement retained. The evaluated implants were either placed in a university setting (4 studies, 199 implants [Balmer et al., 2020; Borgonovo et al., 2021; Brunello et al., 2022; Kohal et al., 2020]) or in a multicenter setting consisting of university and private practice (2 studies, 76 implants [Gahlert et al., 2022; Grassi et al., 2015], Tables 1 and 2).

3.2 | Implant survival

Altogether, data from 277 implants placed in 221 patients were included in the analysis regarding implant survival. The meta-analysis estimated 5-year mean survival rates of 97.1% (CI 91.6–100.0) and 97.3% (CI 94.2–99.3) for retrospective and prospective studies, respectively. Considering all the included studies, the 5-year mean survival rate was 97.2% (CI 94.7–99.1), whereas a low degree of heterogeneity was evaluated for the included studies ($I^2 = 0.0\%$, $p = .5$, Figure 2).

A total of 38 patients (17.4%) and 40 zirconia implants (14.5%) were reported as dropouts for reported follow-up periods between 60 and 120 months (Table 3). The overall failure rate was 3.8%, whereas 8 implants were classified as early (3.4%) and 1 implant as late failure (0.4%). The reported survival rates ranged between 93.8% and 100% (Table 3). Only 1 study investigated 48 2-piece zirconia implants. After implant placement and unloaded healing of 10–12 weeks, fiberglass abutments as well as single crowns were cemented. After a mean follow-up period of 111.1 months (±2.2), 32 implants were evaluated, and the authors reported a survival rate of 93.8% (Brunello et al., 2022).

3.3 | Peri-implant MBL

Overall, 229 implants placed in 173 patients were evaluated (Table 3). Regarding prospective studies, the meta-analysis estimated a mean 5-year MBL of 1.0 mm (CI 0.8–1.3). Only 1 retrospectively designed study reported MBL (Borgonovo et al., 2021). Considering all included studies, the evaluated mean 5-year MBL was 1.1 mm (CI 0.9–1.3). A low degree of heterogeneity was found between the studies ($I^2 = 4.9\%$, $p = .4$, Figure 3).

TABLE 2 Surgical and prosthetic characteristics of included clinical studies.

Author/year	Material	Type implant placement	Simultaneous bone augmentation	Immediate temporization	Immediate loading	Time period placement – Final reconstruction (weeks)	Prosthetics	Retention modes prosthetics (abutments/ prostheses)
Brunello et al., 2022	YTZP	2,3,4	Yes	No	No	Maxilla: 12 Mandible: 10	SC	CR/CR
Gahlert et al., 2022	YTZP	2,3,4	Yes	No	No	26	SC	–/CR
Borgonovo et al., 2021	YTZP	2,3,4	Yes	Yes	No	24	SC/FDP	–/CR; –/CR
Balmer et al., 2020	YTZP	2,3,4	Yes	Yes	No	Maxilla: 16 Mandible: 8	SC/FDP	–/CR; –/CR
Kohal et al., 2020	ATZ	NR	Yes	Yes	No	Maxilla: 16 Mandible: 8	SC/FDP	–/CR; –/CR
Grassi et al., 2015	YTZP	1,4	Yes	Yes	Yes	14	SC	–/CR

Abbreviations: ATZ, alumina-toughened zirconia; CR, cement-retained; FDP, fixed dental partials; RHD, removable hybrid denture; SC, single crowns; SR, screw-retained; Ti, titanium; YTZP, yttria-stabilized zirconia.

TABLE 3 Primary and secondary outcomes of included clinical studies.

Author/year	Impl. (*n*)	Material	Fol. Up after placement (months)	Drop outs implants (*n*)	Early failures (*n*)	Late failures (*n*)	Fractures (*n*)	Survival rate (%)	Mean MBL (mm ± SD)	Mean probing Dephts (mm ± SD)
Brunello et al., 2022	48	YTZP	111.1	16	2	1	0	93.8	NR	3 ± 0.6
Gahlert et al., 2022	44	YTZP	60	8	1	0	0	97.7	0.99 ± 0.58	NR
Borgonovo et al., 2021	29	YTZP	120	3	0	0	0	100	0.92 ± 0.97	3.26 ± 1.46
Balmer et al., 2020	71	YTZP	60	7	1	0	0	98.4	0.7 ± 0.6	3.3 ± 0.6
Kohal et al., 2020	53	ATZ	60	5	3	0	0	94.3	0.81 ± 0.77	0.64 ± 0.87
Grassi et al., 2015	32	YTZP	61.2	1	1	0	0	96.8	1.23 ± 0.29	0.53 ± 0.47

Abbreviations: ATZ, alumina-toughened zirconia; NR, not reported; SD, standard deviation; Ti, titanium; YTZP, yttria-stabilized zirconia.

TABLE 4 Technical and biological complications of implants.

Author/year	Impl. (*n*)	Drop outs implants (*n*)	Decementation (*n*)	Abutment fracture (*n*)	Bone loss >2 mm (*n*)	Soft tissue complications (*n*)	Peri-implantitis (*n*)
Brunello et al., 2022	48	16	1	6	NR	13	0
Gahlert et al., 2022	44	8	NR	NA	0	0	0
Borgonovo et al., 2021	29	3	NR	NA	0	NR	0
Balmer et al., 2020	71	7	NR	NA	NR	0	1
Kohal et al., 2020	53	5	NR	NA	4	0	0
Grassi et al., 2015	32	1	NR	NA	0	0	0

Abbreviations: NA, not applicable due to 1-piece implant design; NR, not reported.

TABLE 5 Excluded studies.

Reason for exclusion	Number	Studies
Wrong study design	47	Abduo et al. (2021), Amorfini et al. (2018), Asgeirsson et al. (2019), Ayyadanveettil et al. (2021), Bae et al. 2008), Bienz et al. (2021), Borges et al. (2014), Bradley et al. (2021), Canullo (2007), Chen & Pan (2019), Chen et al. (2008), Cionca et al. (2016), de Oliveira Silva et al. (2020), Di Alberti et al. (2013), Duncan et al. (2022), Eisner et al. (2018), Fabbri et al. (2021), Ferrari et al. (2016), Fonseca et al. (2021), Gallucci et al. (2011), Glauser et al. (2004), Hosseini et al. (2013), Kniha et al. (2018a), Laass et al. (2019), Lops et al. (2013), Lops et al. (2015), Lorenz et al. (2019), Nilsson et al. (2017), Nothdurft & Pospiech (2010), Nothdurft (2019), Nothdurft et al. (2014), Olander et al. (2022), Passos et al. (2016), Pol et al. (2020), Rinke et al. (2015), Rohr et al. (2021), Schepke et al. (2017), Spies et al. (2017), Spies et al. (2019), Thoma et al. (2016), Thoma et al. (2018), van Brakel et al. (2012), Vanlioglu et al. (2012), Vanlioglu et al. (2014), Wilson & Blum (2019), Yoon et al. (2019), Zembic et al. (2015)
Follow-up too short	38	Aldebes et al. (2022), Balmer et al. (2018), Balmer et al. (2022), Becker et al. (2017), Borgonovo et al. (2010), Borgonovo et al. (2011), Borgonovo et al. (2012), Borgonovo et al. (2013), Borgonovo et al. (2015), Bormann et al. (2018), Brandenberg et al. (2017), Brüll et al. (2014), Cannizzaro et al. (2010), Cionca et al. (2015), Gahlert et al. (2013), Gahlert et al. (2016), Gargallo-Albiol et al. (2022), Hagi (2021), Holländer et al. (2016), Jung et al. (2016), Kniha et al. (2018b), Kohal et al. (2013), Kohal et al. (2018), Kohal et al. (2012), Kunavisarut et al. (2020), Oliva et al. (2007), Osman & Ma (2014), Osman et al. (2014), Payer et al. (2013), Payer et al. (2015), Rodriguez et al. (2018), Ruiz Henao et al. (2021), Rutkowski et al. (2022), Siddiqi et al. (2015), Spies et al. (2015), Spies et al. (2016a), Spies et al. (2016b), Vilor-Fernández et al. (2021)
Too few patients	2	Bittencourt et al. (2021), Steyer et al. (2021)
Investigated zirconia implants not commercially available	3	Cionca et al. (2021), Koller et al. (2020), Roehling et al. (2016)
Data not clear for evaluation	1	Oliva et al. (2010)
Not English	1	Li et al. (2017)

One study did not provide any information regarding MBL (Brunello et al., 2022), 5 studies used periapical radiographs to determine MBL between implant placement and the last follow-up investigation (Balmer et al., 2020; Borgonovo et al., 2021; Gahlert et al., 2022; Grassi et al., 2015; Kohal et al., 2020).

3.4 | Probing depths

Altogether, 231 implants placed in 175 patients were evaluated, whereas the PD values ranged between 2.2 mm 3.3 mm for follow-up periods between 60 and 120 months (Table 3).

The meta-analysis estimated 5-year mean PD values of 3.0 mm (CI 2.6–3.5) and 2.9 mm (CI 2.2–3.7) for retrospective and prospective studies, respectively. Regarding all included studies, the mean 5-year mean PD value was 3.0 mm (CI 2.5–3.4), whereas a substantial degree of heterogeneity was evaluated for the included studies ($I^2 = 69.4\%$, $p = .0$, Figure 4).

One prospective study provided information regarding the presence and incidence of bleeding. However, no information was reported regarding PD (Gahlert et al., 2022).

3.5 | Biological complications

All the included studies provided data regarding biological complications. Of the 277 initially placed implants, information was available for 235 implants at the time point of the last clinical and

TABLE 6 Quality assessment and risk of bias of included observational cohort studies.

Author/year	Representative of the exposed cohort	Selection of the non- exposed cohort	Ascertainment of exposure	Outcome of interest not present at commencement of study	Comparability of cases and controls (maximum 2 stars)	Assessment of outcome	Sufficient follow-up time for outcomes to occur	Adequacy of follow-up	Total
Brunello et al., 2022	*	*	*		*	*	*		6
Gahlert et al., 2022	*	*	*	*	*	*	*	*	8
Borgonovo et al., 2021	*	*	*		*	*	*	*	7
Balmer et al., 2020	*	*	*	*	*	*	*	*	8
Kohal et al., 2020	*	*	*	*	*	*	*	*	8
Grassi et al., 2015	*	*	*	*	*	*	*	*	8

radiographic investigation (range between 60 and 120 months). Two studies reported on peri-implant infections around zirconia implants (Table 4). Brunello and coworkers investigated a patient population that received 48 2-piece zirconia implants. After a follow-up period of 9 years, information was available for 29 implants. The authors reported that before the 2-year follow-up, 10 implants were diagnosed with peri-implantitis and peri-implant mucositis, respectively. After appropriate treatment, these infections could be successfully treated and no further cases of peri-implantitis could be observed until the last follow-up. However, at the 9-year follow-up, signs of inflammation (bleeding on probing) were observed around 13 implants (Brunello et al., 2022). In another study, peri-implantitis was diagnosed around 1 out of 71 initially placed 1-piece zirconia implants after 5 years of investigation, whereas the implant was included in a cumulative therapy, starting with non-surgical procedures (Balmer et al., 2020). Only 1 study reported MBL of more than 2 mm around 4 out of 53 initially placed implants; however, none of the implants lost more than 3 mm of bone. Interestingly, the authors also evaluated some bone gain after 5 years of investigation around 5 implants (Kohal et al., 2020). Regarding biological complications that were present at the last follow-up, the overall complication rate was 7.7%, whereas the incidences for soft tissue complications, bone loss of more than 2 mm, and peri-implantitis were 5.5%, 1.7% and 0.4%, respectively (Table 4).

3.6 | Technical complications

Only 1 study investigating 48 2-piece zirconia implants provided information regarding technical complications (Table 4). After a mean observation period of 43.7 months, the authors reported the documentation of 1 fiberglass abutment and 1 crown fracture followed by the loosening of the new crown. In addition, 6 fractures of the fiber-glass abutment were registered after a mean observation time of 53.7 months, whereas all fractured abutments could successfully be replaced by new ones (Brunello et al., 2022).

Regarding implant fractures, information was available for 235 implants. Considering all included studies, no zirconia implant fractures were reported (Table 3).

4 | DISCUSSION

In the present systematic review, implant materials other than commercially pure titanium or a specific titanium alloy were evaluated. With regards to zirconia implants, the meta-analysis estimated similar survival rates, MBL and PD values after 5 years compared with published data on titanium implants. Although technical complications regarding implant components were similar, the biological complications showed a minor occurrence of zirconia compared with reported data for titanium as implant material.

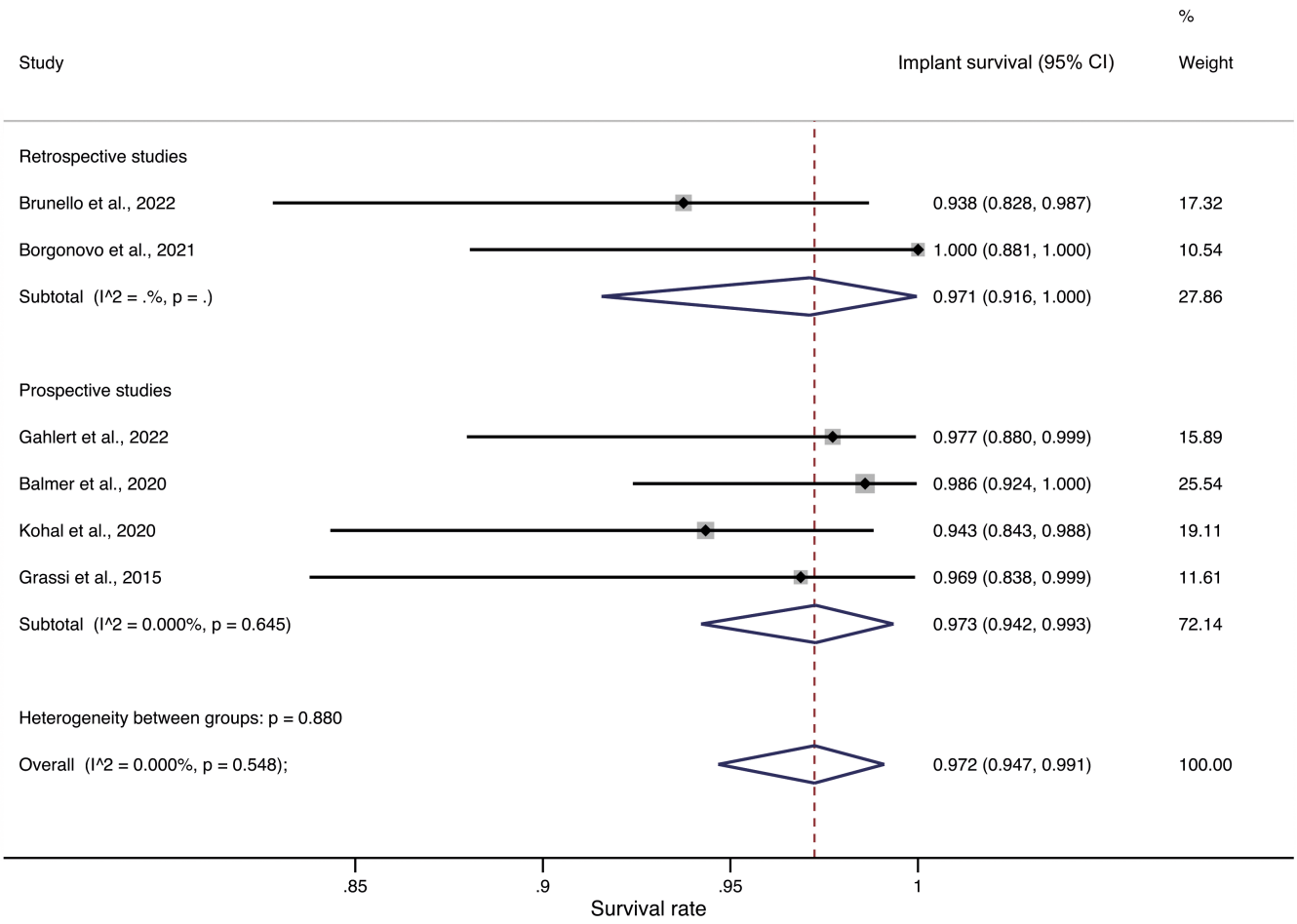


FIGURE 2 Forest plot of 5-year survival rate of implants. ATZ, alumina-toughened zirconia; CI, confidence intervals; YTZP, yttria-stabilized zirconia. Calculations were performed according to the data presented in Table 3.

At the beginning of 2004, the first zirconia implants were established on the market. Consequently, only studies published after 2000 were selected for data extraction in the present review.

Based on many further developments in implant designs and manufacturing processes within the last 2 decades, it has become difficult to interpret published data on zirconia implants and to evaluate the clinical relevance of the investigated implant type and the reported results. This fact must be considered since even the most recently published clinical studies investigate zirconia implants that have been removed from the market many years ago (Cionca et al., 2021; Koller et al., 2020; Lorenz et al., 2019). From a scientific point of view, the reported data are important and well presented; however, the clinical relevance is rather controversial. A meta-analysis has confirmed that physical properties and ongoing market availability significantly influenced the reported zirconia implant survival rates. In a systematic review, clinical studies investigating zirconia implants that were published between 2004 and 2017 were evaluated. The reported 1-year mean survival rates for commercially available zirconia implants (98.3%) were significantly higher compared with zirconia implants that are not any longer commercially available on the market (91.2%). In addition, a mean 2-year survival rate for commercially available zirconia implants of 97.2% was evaluated. This analysis has clearly shown that zirconia implant survival rates have significantly increased between 2004 and 2017 and that the fracture incidence of zirconia oral implants was significantly reduced from 3.4% to 0.2% (Roehling et al., 2018). Consequently, the ongoing market clinical availability of the investigated zirconia implants was considered an important inclusion criterion for the present review.

For example, Cionca and coworkers investigated 39 2-piece zirconia implants after a follow-up period of 6 years. However, the evaluated implant type was removed from the market already in 2013 and has been replaced by a further developed generation of implant type in the meantime (Cionca et al., 2021). Thus, this investigation was not considered for data extraction and further analysis.

Since previously published systematic reviews investigating the clinical performance of zirconia implants already estimated mean survival rates and marginal bone level changes up to 2.75 years (Afrashtehfar & Del Fabbro, 2020; Borges et al., 2020; Elnayef et al., 2017; Haro Adánez et al., 2018; Hashim et al., 2016; Pieralli et al., 2017; Roehling et al., 2018), only clinical studies investigating zirconia implants for a minimum of 5 years were included in the present review.

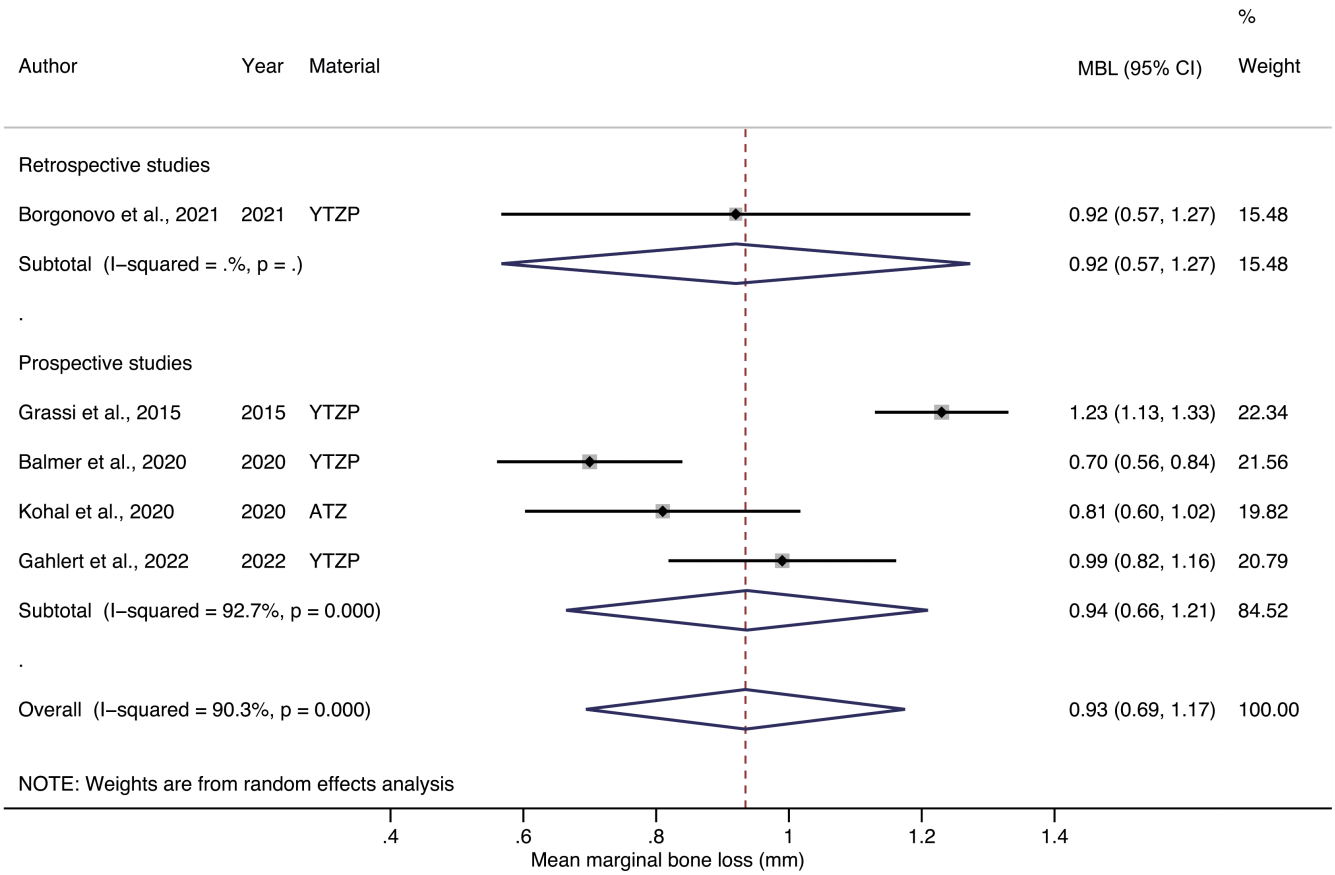


FIGURE 3 Forest plot of 5-year marginal bone loss of implants. ATZ, alumina-toughened zirconia; CI, confidence intervals; MBL, marginal bone loss; YTZP, yttria-stabilized zirconia. Calculations were performed according to the data presented in Table 3.

Implant survival was evaluated as the primary outcome. The meta-analysis has estimated a mean survival rate after 5 years of 97.2% (CI 94.7–99.1). This value is similar to previously published systematic reviews investigating titanium implants after 5 years of functional loading. The authors evaluated mean survival rates between 95.6% and 97.2%, early failure rates between 1.3% and 2.4% and late failure rates between 1.5% and 2.7% for SCs and FDPs (Jung et al., 2012; Jung, Pjetursson, et al., 2008; Pjetursson et al., 2012).

MBL and PD as secondary outcomes were also evaluated using meta-analyzes. Regarding MBL, the estimated mean MBL after 5 years was 1.1 mm (CI 0.9–1.3). The evaluated data are in accordance with previously published data for zirconia implants after 1 and 2 years of investigation (Borges et al., 2020; Roehling et al., 2018) and similar to data investigating titanium implants after 5 years of follow-up (Aglietta et al., 2009; Karl & Albrektsson, 2017).

Regarding PD, a mean value of 3.0 mm (CI 2.5–3.4) was estimated. Again, the values are similar to previous data investigating titanium implants after follow-up periods of 5 years (range between 2.7 and 3.6 mm [Hosseini et al., 2022; Zembic et al., 2013]).

Considering technical complications, only 1 study provided information regarding 2-piece zirconia implants with cement-retained abutments and SCs and 1 investigation reported on technical complications of SCs cemented on 1-piece zirconia implants (Brunello et al., 2022). In addition, Spies and coworkers investigated the same patient population as Balmer and coworkers and reported data on technical complications regarding the prosthetic suprastructures after a mean follow-up period of 61 (±1.4) months. However, of the 71 placed implants (49 SCs and 22 FDPs), only information was provided regarding 44 SCs placed in molar areas. The authors reported that chipping of the cemented crowns could be observed in 19 patients. Consequently, the authors questioned the concept of bi-layered zirconia-based reconstructions and concluded '...monolithic approaches might be preferable to overcome this issue...' (Balmer et al., 2020; Spies et al., 2019). Moreover, the posterior location of the implants and crowns might also have influenced the high-chipping incidence, since in clinical studies, it has been shown that a single crown location had a significant impact on the occurrence of veneer fractures in favor of reconstructions located in the anterior region (Rabel et al., 2018).

The evaluated incidence of soft tissue complications and bone loss of more than 2 mm were 5.5% and 1.7% at the time point of the last follow-up investigation. The values for soft tissue complications are inferior to data on titanium implants reporting values between 7.1% and 8.5% for soft tissue complications and between 5.2% and 2.6% for bone loss of more than 2 mm after 5 years of investigation (Jung et al., 2012; Pjetursson et al., 2012). However, in the latter studies, more implants were evaluated. Regarding peri-implantitis, a low incidence of 0.4% for investigation periods

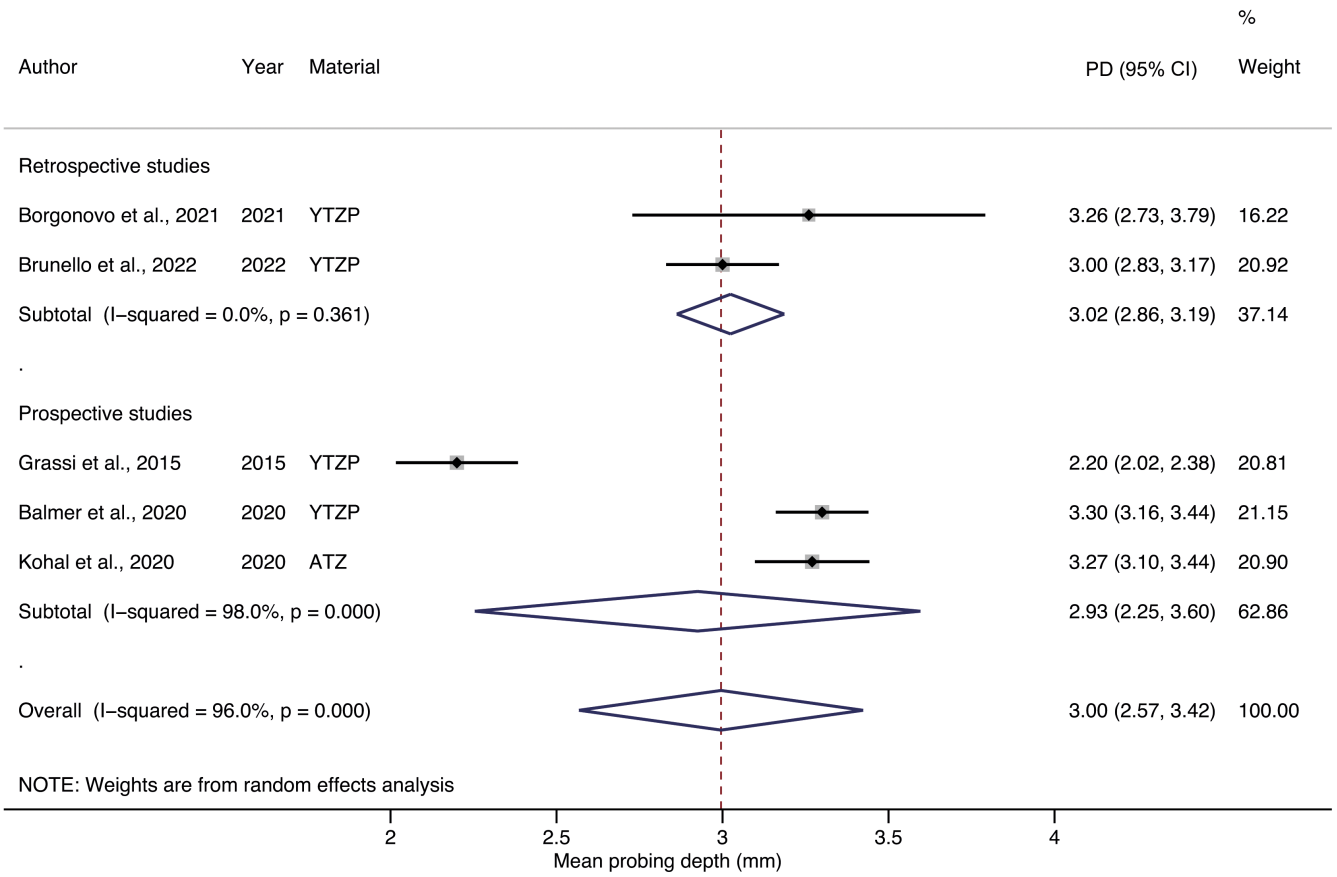


FIGURE 4 Forest plot of probing depth values for implants after 5 years. ATZ, alumina-toughened zirconia; CI, confidence intervals; PD, probing depths; YTZP, yttria-stabilized zirconia. Calculations were performed according to the data presented in Table 3.

between 60 and 120 months was evaluated. For titanium implants, incidences of 43% and 22% were evaluated for peri-implant mucositis and peri-implantitis, respectively, whereas a statistically significant positive relationship between the prevalence of peri-implantitis and mean function time were reported (Derks & Tomasi, 2015). In another study, 4591 titanium implants were investigated. The authors reported that the prevalence of peri-implantitis was between 3.6% and 4.7% after 6 to 7 years of follow-up (French et al., 2019). The presently evaluated peri-implantitis incidence for zirconia implants is inferior compared with the data reported in the latter studies. However, it must be considered that in the present review only information for 235 implants was available.

A limitation of the present review is the low number of zirconia implants ($n = 277$) that were evaluated in the meta-analysis for implant survival. In contrast, systematic reviews investigating titanium implants after 5 years of loading included more than 3223 implants (Jung et al., 2012; Pjetursson et al., 2012). Moreover, only observational studies and no randomized clinical trials were considered in the present review. However, based on the current literature search, 6 RCTs are available, comparing titanium and zirconia implants (Koller et al., 2020; Osman et al., 2014; Payer et al., 2015; Ruiz Henao et al., 2021), immediately and conventionally loaded zirconia implants (Cannizzaro et al., 2010) or porcelain-fused-to-metal and indirect-composite-resin fixed dental prosthetics on zirconia implants (Aldebes et al., 2022). However, 4 studies investigated zirconia implants that are not commercially available, respectively, were removed from the market (Cannizzaro et al., 2010; Koller et al., 2020; Osman et al., 2014; Payer et al., 2015), investigated the same patient population (Koller et al., 2020; Payer et al., 2015) and/or used a novel, unestablished surgical protocol combining alveolar and palatal implants in the maxilla (Osman et al., 2014) or evaluated individually designed, custom-made zirconia implants (Aldebes et al., 2022). Only 1 RCT investigated 16 currently marked available zirconia implants in comparison to 14 titanium implants. After a follow-up period of 12 months, survival rates of 100% for both types of implants and a mean MBL of 2.08 mm (±0.55) and 1.96 mm (±0.48) for zirconia and titanium implants, respectively, were reported (Ruiz Henao et al., 2021).

Based on the low number of included studies, it was not reasonable to perform further statistical methods like meta-regressions to analyze associations between implant survival, MBL as well as PD and study characteristics like type of implant placement, immediate loading, prosthetics, zirconia implant material, and implant design (1-piece compared with 2-piece). In addition, the included studies did not provide detailed data to evaluate the impact of implant location (anterior or posterior) or implant diameter on the reported primary and secondary outcomes. Previously, it has been reported that

implant diameter and implant location influenced technical complications like zirconia implant fractures. The authors of the latter study investigated 170 zirconia implants with an average in situ period of 36.8 ± 5.3 months. They reported 13 implant fractures, whereas all implants were placed in anterior sites and 12 implants had a reduced diameter of 3.25 mm. The authors related the high-fracture rate to notches and scratches created by an uncontrolled manufacture process. However, it must be noted that the investigated fractured zirconia implants have been removed from the market already in 2006 (Gahlert et al., 2012).

5 | CONCLUSIONS

Regarding zirconia implants, the present meta-analyses estimated 5-year mean values of 97.2% (95% CI: 94.7–99.1%), 1.1 mm (95% CI: 0.9–1.3 mm), and 3.0 mm (95% CI: 2.5–3.4 mm) for implant survival, peri-implant MBL and PDs, respectively. Thus, commercially available zirconia implants are a reliable treatment option for follow-up period up to 5 years. Further prospectively designed clinical long-term studies and randomized clinical trials investigating titanium and zirconia implants are needed to confirm the presently evaluated promising outcomes.

AUTHOR CONTRIBUTIONS

S. Roehling: Data curation; Writing – original draft; Writing – review & editing. M. Gahlert: Supervision; Writing – review & editing. M. Bacevic: Conceptualization. H. Woelfler: Statistical Analysis; Visualization. I. Laleman: Data curation; Writing – original draft; Writing – review & editing.

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CONFLICT OF INTEREST STATEMENT

The authors report no conflicts of interest.

DATA AVAILABILITY STATEMENT

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

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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REVIEW ARTICLE

CLINICAL ORAL IMPLANTS RESEARCH WILEY

The effect of different abutment materials on peri-implant tissues—A systematic review and meta-analysis

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Abstract

Objectives: In patients with dental implants, what is the effect of transmucosal components made of materials other than titanium (alloys) compared to titanium (alloys) on the surrounding peri-implant tissues after at least 1 year?

Materials and Methods: This systematic review included eligible randomized controlled trials identified through an electronic search (Medline, Embase and Web of Science) comparing alternative abutment materials versus titanium (alloy) abutments with a minimum follow-up of 1 year and including at least 10 patients/group. Primary outcomes were peri-implant marginal bone level (MBL) and probing depth (PD), these were evaluated based on meta-analyses. Abutment survival, biological and technical complications and aesthetic outcomes were the secondary outcomes. The risk of bias was assessed with the RoB2-tool. This review is registered in PROSPERO with the number (CRD42022376487).

Results: From 5129 titles, 580 abstracts were selected, and 111 full-text articles were screened. Finally, 12 articles could be included. Concerning the primary outcomes (MBL and PD), no differences could be seen between titanium abutment and zirconia or alumina abutments, not after 1 year (MBL: zirconia: MD = −0.24, 95% CI: −0.65 to 0.16, alumina: MD = −0.06, 95% CI: −0.29 to 0.17) (PD: zirconia: MD = −0.06, 95% CI: −0.41 to 0.30, alumina: MD = −0.29, 95% CI: −0.96 to 0.38), nor after 5 years. Additionally, no differences were found concerning the biological complications and aesthetic outcomes. The most important technical finding was abutment fracture in the ceramic group and chipping of the veneering material.

Conclusions: Biologically, titanium and zirconia abutments seem to function equally up to 5 years after placement.

KEYWORDS
dental abutment, implant abutment, marginal bone level, meta-analysis, yttria stabilized tetragonal zirconia, zirconium oxide

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1 | INTRODUCTION

Successful integration of an implant into the surrounding peri-implant tissues is situated on two levels: osteo-integration and muco-integration. Although the first is largely dependent on the characteristics of the implant, the latter is mainly affected by the transmucosal component/abutment and its characteristics. The implant-abutment connection, the number of abutment disconnections, the height of the abutment, its emergence angle and its material all influence the surrounding soft tissues (Laleman & Lambert, 2023).

Currently, a plethora of materials are available to fabricate implants and abutments, such as metals, ceramics and composites (Linkevicius & Vaitelis, 2015). Each of these materials has its benefits and shortcomings regarding biocompatibility, long-term stability and aesthetics.

For decades, titanium was the preferred implant and abutment material, based on its many advantages such as excellent biocompatibility, material strength and resistance to distortion (Linkevicius & Vaitelis, 2015). Its most important disadvantage is that its color may show through the gingiva, causing an unaesthetic grayish discoloration (Jung et al., 2007).

Based on their tooth-like color, ceramics like alumina or zirconia seem interesting alternatives to titanium from an aesthetic point of view (Glauser et al., 2004; Jung et al., 2008). Additionally, they show similar properties as titanium regarding biocompatibility and less plaque-accumulation (de Avila et al., 2016; Rimondini et al., 2002). But, they are brittle and prone to fatigue and thus less resistant to fractures (Apicella et al., 2011; Belser et al., 2004).

The available systematic reviews regarding implant/abutment materials focus mainly on survival and technical complications (Fiorillo et al., 2022; Hu et al., 2019; Pjetursson et al., 2018; Roehling et al., 2018; Sailer et al., 2018) or on aesthetic outcomes (de Moura Costa et al., 2021). Less information is available about the biological impact of different materials (Sanz-Martín et al., 2018). The envisaged focused question for this invited review for the 2023 ITI consensus meeting was, therefore: "In clinical studies, what other materials compared to commercially pure titanium, or a specific titanium alloy allow peri-implant soft and hard tissue integration?" However, the available studies on this subject were too heterogeneous making it impossible to combine information regarding implants and abutments. The main limiting factor is that there are several randomized controlled clinical trials available about the abutment materials, while this is not the case for the implant materials.

This focused question was thus answered in two separate systematic reviews. One focused on the effect of implant materials on the peri-implant tissues in clinical trials (here, we want to cite the other systematic review about implants: Roehling S. et al., 2023). The current systematic review examined the effect of different abutment materials, directly compared to commercially pure titanium or a specific titanium alloy on peri-implant tissues based on randomized controlled trials.

2 | MATERIALS AND METHODS

This systematic review was conducted according to the Preferred Reporting Items for Systematic review and Meta-Analysis Protocols (PRISMA-P) (Page et al., 2021) statement using the Population, Intervention, Comparison and Outcome (PICO) method (Schardt et al., 2007). The protocol for this systematic review was registered on PROSPERO with the number (CRD42022376487).

2.1 | Focused question

The focused question of this systematic review was: "In patients with dental implants, what is the effect of transmucosal components made of materials other than titanium(alloys) compared to titanium(alloys) on marginal bone level, pocket depth, abutment survival, technical and biological complications and esthetic outcomes after at least 1 year?"

This led to the following PICOT-question:

- Patients: patients with dental implants.
- Intervention: abutments in materials different from titanium (alloys).
- Comparison: titanium(alloy) abutments.
- Outcome: marginal bone level, pocket probing depth, abutment survival, biological and technical complications and esthetic outcomes.
- Time: at least 1-year follow-up.

2.2 | Search strategy

An electronic, systematic search of Medline via Pubmed, Embase via Elsevier and Web of Science via Clarivate databases was performed in July 2022. The specific search terms can be found in Appendix S1.

Additional hand searches were performed and included the following: (1) bibliographies of previous reviews on the subject and (2) bibliographies of all included full-text articles.

2.3 | Eligibility criteria

The following inclusion criteria were defined:

- Human studies published after January 2000.
- Randomized clinical trials.
- At least 10 patients/group at follow-up.
- Control: abutments consisting of titanium (alloy).
- Intervention: abutments made of 1 material alternative to titanium (alloy).
- Follow up for at least 12 months after implant placement.
- Outcomes reporting details about peri-implant marginal bone level and/or pocket probing depth.
- Language: English.

The following exclusion criteria were defined:

- Transmucosal components for which we can assume with high certainty that different materials are in contact with the surrounding soft tissues.
- Different macroscopic designs between control and intervention group.
- Studies focusing on the effect of different implant-abutment connections, different surgical approaches, different loading protocol, etc.
- Studies in other languages than English (due to the time limitations of this invited review).

2.4 | Selection of studies

After elimination of duplicates, the reviewers (SR, IL) independently screened titles, abstracts and full texts. For the screening of titles and abstracts, the free web and mobile app Rayyan (http://rayyan.qcri.org) was used (Ouzzani et al., 2016). If the decision was unclear after title screening, these articles were included in the abstract screening. If titles or abstracts did not provide sufficient information for selection, full texts were obtained. Any disagreement regarding inclusion and exclusion was resolved by discussion between the reviewers. To evaluate the agreement between the reviewers, Cohen's kappa coefficient (κ) was calculated for title and abstract selection (Landis & Koch, 1977).

2.5 | Data extraction and outcome measures

Peri-implant marginal bone level (MBL) and probing depth (PD) were the primary outcome. Secondary outcomes included abutment survival, technical and biological complications and esthetic outcomes.

Marginal bone level is the distance from the implant-abutment interface to the marginal bone.

Abutment survival was defined as the original abutment (with or without modifications) still in place for the observation period.

The **biological complications** included bone loss of more than 2 mm over the observation periods, soft tissue complications (swelling, suppuration, fistulas, mucositis, etc.) and peri-implantitis. Also, peri-implant PD were extracted.

Technical complications were classified based on the framework proposed by Lang et al. (2012) (Lang et al., 2012). They were classified as major complications if replacement of the restoration was needed due to implant fracture or loss of the supra-structures. Abutment fracture, veneer or framework fracture, phonetic complications were seen as medium complications. And minor complications were defined as complications that could be corrected with small efforts, such as abutment and screw loosening, loss of retention, debonding, loss of screw hole sealing, veneer chipping (to be polished) and occlusal adjustment.

All **aesthetic outcomes** reported in the included articles were extracted. On one hand those based on standardized indices/measurement methods and/or devices by the examiners, and on the other hand patient-reported aesthetic outcomes.

Data extraction by the reviewers was independently performed for all included studies (SR, IL) using data extraction tables. Disagreement regarding data extraction was resolved by discussion.

From the included clinical full-text articles, the following data were extracted: author(s), year of publication, study design (parallel versus split-mouth), setting (university versus private practice), follow-up period, abutment materials, number of included patients and abutments, number of dropouts, type of prosthetic restoration (single crown (SC)/fixed dental partials (FDP)) and retention modes of the crown/bridges (cement-retained (CR)/screw-retained (SR)).

2.6 | Risk of bias

Two reviewers (SR and IL) independently assessed the risk of bias of the included studies according to the RoB2 tool (Sterne et al., 2019). This was based on the outcomes for MBL.

2.7 | Statistical analysis

For rate ratios of survival rates and mean differences in MBL and probing depth between treatment and control group after 1 and 5 years, DerSimonian–Laird random-effect meta-analyses were performed using meta in Stata statistical software version 17.0 (StataCorp LLC). The amount of heterogeneity across studies was assessed with the I^2 measure. For the survival rates, exact binomial 95%-confidence intervals were calculated. As the survival rates are at 1 in some studies, we added 0.5 to all cells of studies with at least one zero cell to include such studies in the pooled estimate. Robustness checks using the Freeman-Tukey double arcsine transformation yield very similar results. For MBL and probing depth, 95%-confidence intervals for means were calculated based on the reported standard deviations.

Forest plots were used for graphic presentation of the rate ratios of survival rates and mean differences in MBL and probing depth in the treatment and control group in each study with confidence intervals along with the overall pooled prevalence. In the graphs, the weight of each study to the meta-analyses is represented by the area of a box whose center represents the size of the effect estimated from that study. The confidence interval for the effect from each study is also shown. The summary effect is shown by the middle of a diamond whose left and right extremes represent the corresponding confidence interval.

3 | RESULTS

The electronic database search resulted in 7718 publications (Pubmed: 4972; Embase: 1981; Web of Science: 1665). After removal of duplicates, 5129 titles were available and screened resulting in 580 abstracts for further evaluation. After screening

the abstracts, a total of 111 publications were selected for full-text evaluation. After analysis of the included full-text articles, a total of 12 clinical studies fulfilled the inclusion criteria and were included in the qualitative and quantitative analyses for this focused PICOT question (Figure 1).The inter-examiner agreement was $\kappa = 0.82$.

3.1 | Study characteristics

Thirteen studies comparing different abutment materials with titanium abutments were included for data extraction (Andersson et al., 2001, 2003; Baldini et al., 2016; Carrillo de Albornoz et al., 2014; Fenner et al., 2016; Ferrari et al., 2015; Hosseini et al., 2011, 2022; Sailer, Zembic, et al., 2009; Vigolo et al., 2006; Zembic et al., 2009, 2013). These reported on 10 original investigations. Sailer et al., 2009, Zembic et al., 2009 and Zembic et al., 2013 included the same patient population at different time points, just like Hosseini et al., 2022 described the 5-year follow-up of the same patient group described after 1 year in Hosseini et al., 2011. Most of the articles (9 out of 12) compared titanium abutments with zirconia abutments, 3 examined titanium versus alumina abutments and 2 titanium versus gold. All except one study examined a pair-wise comparison, Fenner et al., 2016 examined three different abutment materials. More study details are described in Table 1.

3.2 | Peri-implant marginal bone loss

Figure 2 shows the meta-analyses in terms of marginal bone loss. After 1 year the mean marginal bone loss around implants was not statistically different between implants with zirconia or titanium abutments (MD = −0.24, 95% CI: −0.65 to 0.16 based on four studies and 151 abutments). Just as no difference could be found between implants with alumina versus titanium abutments (MD = −0.06, 95% CI: −0.29 to 0.17 based on 2 studies and 101 abutments). These findings carry over to the five-year data where no differences could be examined between zirconia and titanium (MD = 0.21, 95% CI: −0.22 to 0.65 based on 2 studies and 91 abutments) and neither between alumina and titanium (MD = −0.04, 95% CI: −0.32 to 0.25 based on 2 studies and 115 abutments).

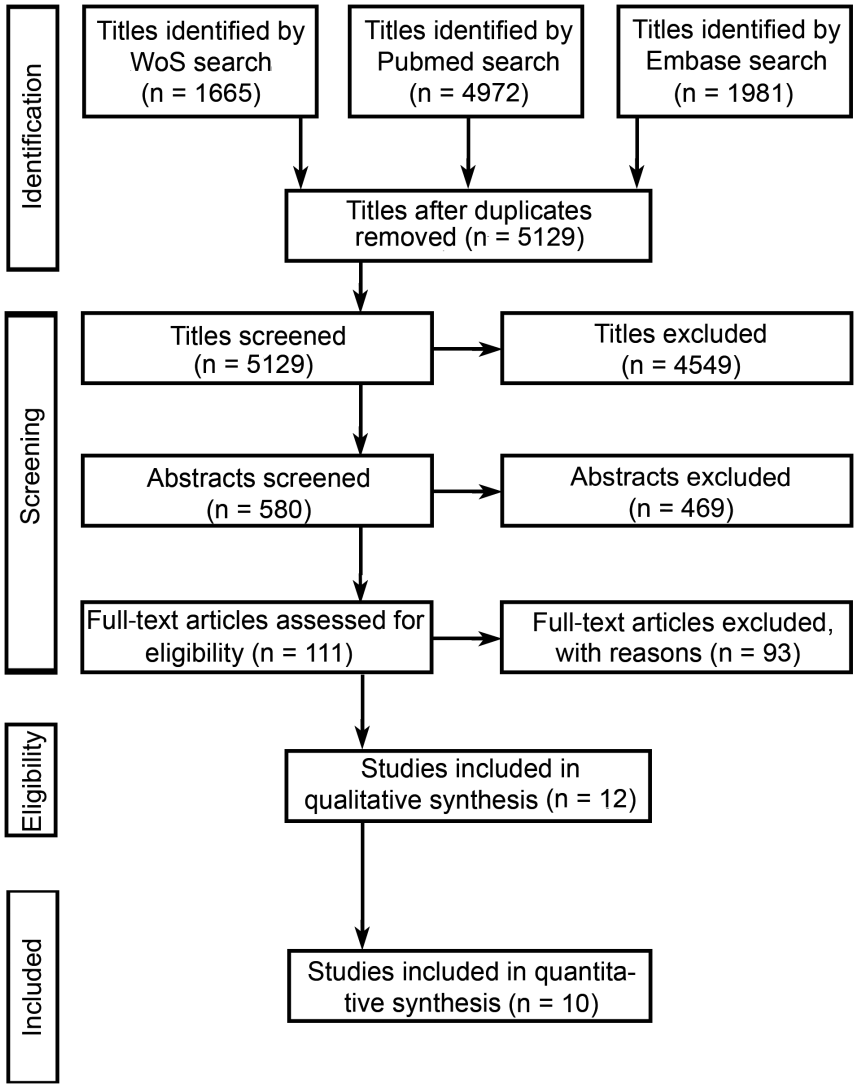


FIGURE 1 PRISMA flow diagram.

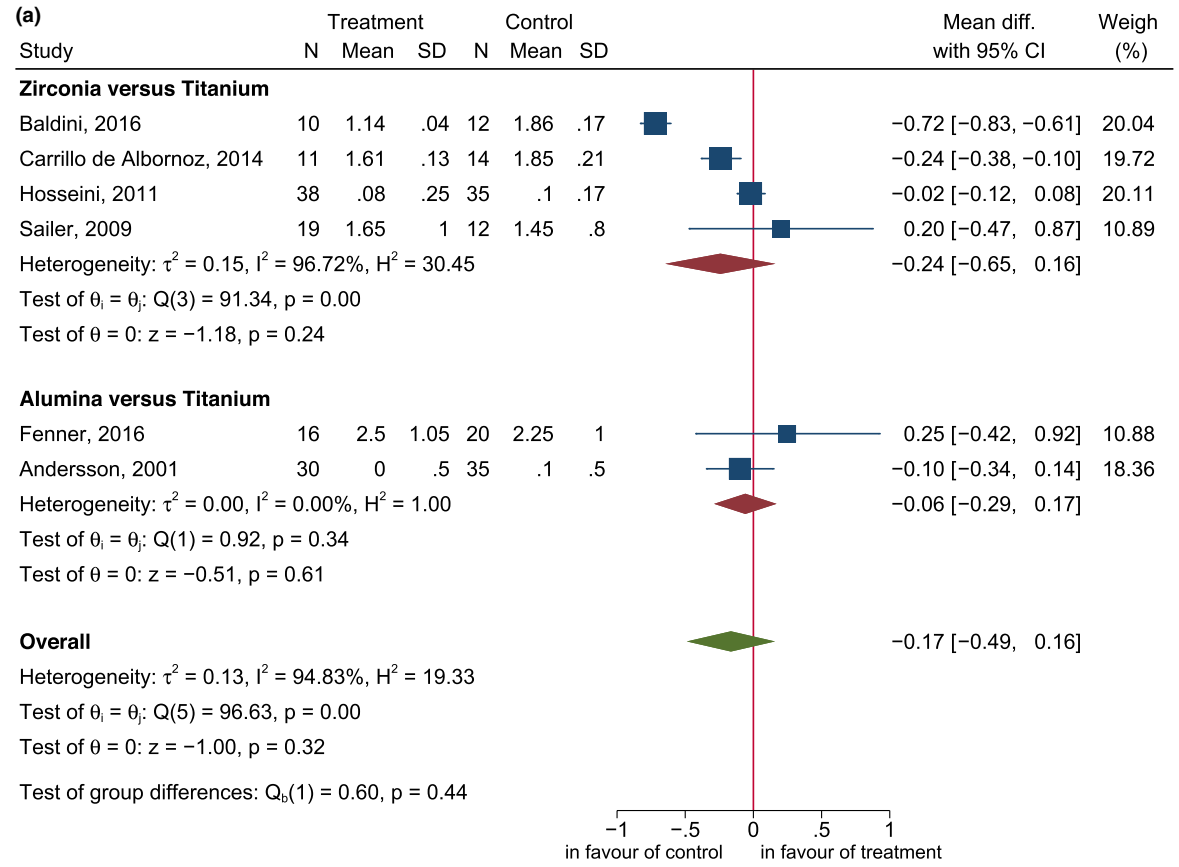
TABLE 1 Descriptive characteristics of RCTs investigating abutments.

Author/year	Study design setting	Follow up (mo)	Control abutment	Test abutment	No of patients (BL)	No of abutments c/t (BL c/t)	Prosthetics	Screw-retained versus cemented
Hosseini et al., 2022[a]	RCT, split-mouth and parallel University	60	Titanium (TiDesign, Astra Tech, Sweden)	Zirconia (ZirDesign, Astra Tech, Sweden)	30 (36)	32/31 (35/38)	SC	CR
Baldini et al., 2016	RCT, parallel University	12	Titanium (SPIEASY, Thommen)	Zirconia (SPIART, Thommen)	24	12/10 (12/12)	SC	CR
Fenner et al., 2016	RCT, split-mouth NR	60	Titanium abutments (synOcta cementable abutment, Straumann)	Aluminum oxide-based (Al_2O_3) abutments (synOcta In-Ceram blank, Straumann)	28	20/16	SC	SR/CR
Ferrari et al., 2015	RCT, parallel University	24	Titanium	Gold-hue titanium/titanium nitride OR Zirconia (Atlantis)	47	15/18/14	SC	NR
Carrillo de Albornoz et al., 2014	RCT, parallel University	12	Titanium (SPIEASY, Thommen Medical AG, Grenchen, Switzerland)	Zirconia (SPIART, Thommen Medical AG, Grenchen, Switzerland)	25 (30)	14/11 (15/15)	SC	CR
Zembic et al., 2013	RCT NR	60	Titanium (Procera, Nobel Biocare AB, Carolinsk, Sweden)	Zirconia (Procera, Nobel Biocare AB, Carolinsk, Sweden)	18 (22)	10/18 (20/20)	SC	CR (2 SR)
Hosseini et al., 2011[a]	RCT, split-mouth and parallel University	12	Titanium (TiDesign, Astra Tech, Sweden)	Zirconia (ZirDesign, Astra Tech, Sweden)	36	35/38	SC	CR
Sailer et al., 2009[b]	RCT NR	12	Titanium (Procera, Nobel Biocare AB, Carolinsk, Sweden)	Zirconia (Procera, Nobel Biocare AB, Carolinsk, Sweden)	20 (22)	12/19 (20/20)	SC	CR (2 SR)
Zembic et al., 2009[b]	RCT NR	36	Titanium (Procera, Nobel Biocare AB, Carolinsk, Sweden)	Zirconia (Procera, Nobel Biocare AB, Carolinsk, Sweden)	18 (22)	10/18 (20/20)	SC	CR (2 SR)
Vigolo et al., 2006	RCT, split-mouth University	60	Titanium (Procera, NobelBiocare, Göteburg, Sweden)	Gold-alloy (gold, machined UCLA, SGUCA1C, 3i/ Implant Innovations, Palm Beach Gardens, FL)	20	20/20	SC	CR
Andersson et al., 2003	RCT, parallel NR	48	Titanium abutment (CeraOne abutment, Nobel Biocare)	Sintered aluminum oxide abutment (CerAdept, Nobel Biocare)	30 (32)	39/40 (50/53)	Short-span FDPs	c: SR t: CR
Andersson et al., 2001	RCT, parallel NR	36	Titanium abutment (CeraOne abutment, Nobel Biocare)	Sintered aluminum oxide abutment (CerAdept, Nobel Biocare)	60	35/34 (35/30)	SC	c: CR t: CR/SR

Abbreviations: BL, baseline; c, control; CR, cemented crown; FDP, Fixed partial dentures; mo, months; NR, not reported; RCT, randomized controlled trial; SC, single crown; SR, screw retained crown; t, test.

[a]Examining the same patient population.

[b]Examining the same patient population.



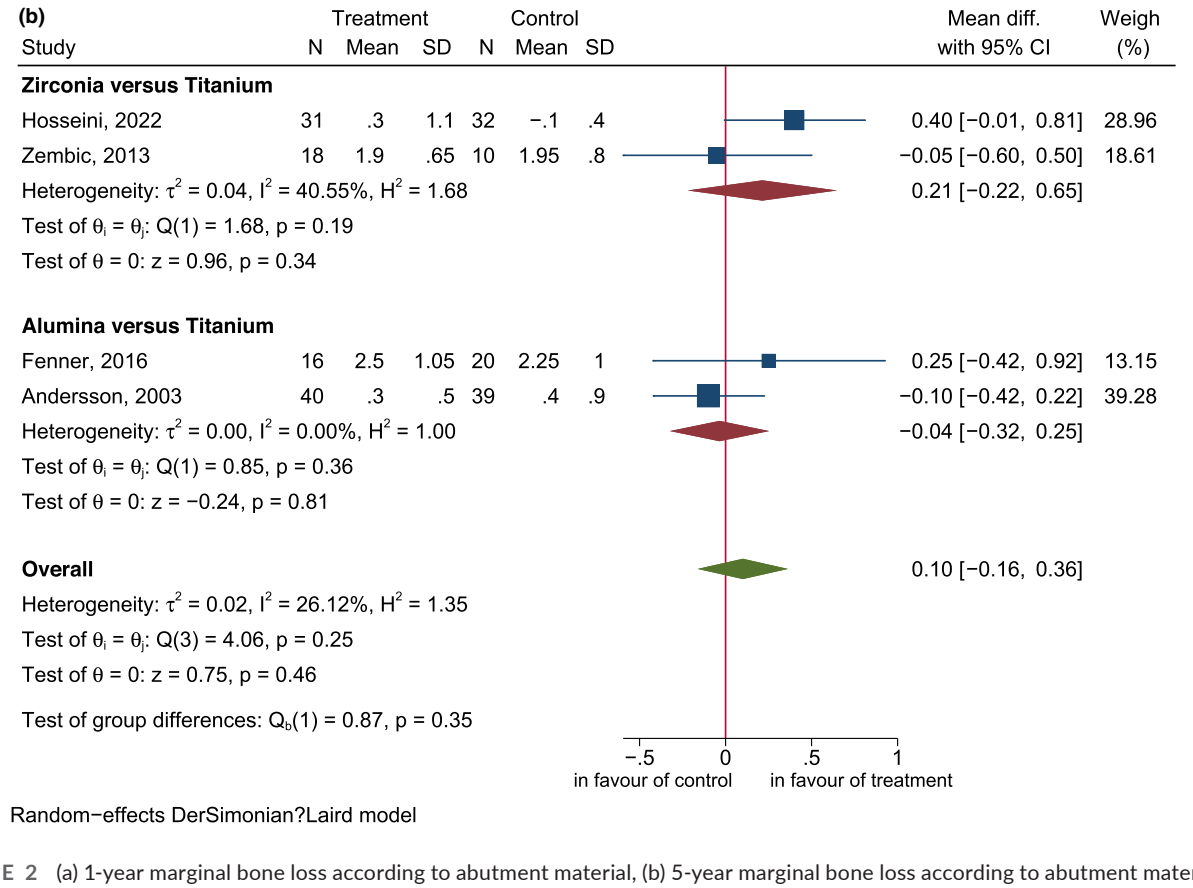


FIGURE 2 (a) 1-year marginal bone loss according to abutment material, (b) 5-year marginal bone loss according to abutment material.

3.3 | Peri-implant probing depths

The meta-analyses for pocket probing depth are shown in Figure 3. After 1 year the mean pocket probing depth around implants with zirconia abutments was not significantly different than around implants with titanium abutments (MD = −0.06, 95% CI: −0.41 to 0.30 based on 3 studies and 78 abutments). The same observations could be made for implants with alumina versus titanium abutments (MD = −0.29, 95% CI: −0.96 to 0.38 based on 1 study and 36 abutments). After 5 years, the results were comparable (respectively MD = −0.02, 95% CI: −0.38 to 0.34 based on 2 studies and 91 abutments and MD = −0.29, 95% CI: −0.96 to 0.38 based on 1 study and 36 abutments).

3.4 | Abutment survival

Figure 4 shows the forest plots for the pairwise meta-analyses in terms of survival rate of the abutment after 1- and 5-years. No differences could be found between titanium and zirconia or alumina.

3.5 | Biological complications

Table 2 summarizes all biological/clinical outcomes reported in the selected studies. In general, no differences could be found examining plaque, bleeding, pocket depth and marginal bone loss.

3.6 | Technical complications

Table 3 shows all details concerning technical complications separated in minor, medium and major complications.

The only major complication described in all the included studies was a crown fracture 2 years after loading in the study of Andersson et al., 2001 in the titanium abutment group (Andersson et al., 2001). The most common weakness seen with ceramic abutments was abutment fracture (Andersson et al., 2001, 2003; Carrillo de Albornoz et al., 2014).The most frequent (minor) complication was chipping of the veneering material (Hosseini et al., 2011, 2022; Sailer, Zembic, et al., 2009; Zembic et al., 2009, 2013).

3.7 | Esthetic outcomes

No statistical significant intergroup differences were found when between titanium and ceramic abutment materials concerning aesthetics. Not when this was measured by professionals (mostly based on the Implant Crown Aesthetic Index (Meijer et al., 2005) and Papilla index (Jemt, 1997)), nor when the patients were surveyed about their satisfaction (mostly based on VAS scales). Details are provided in Tables 4 and 5. Data about aesthetics and gold abutments were not reported.

3.8 | Risk of bias assessment

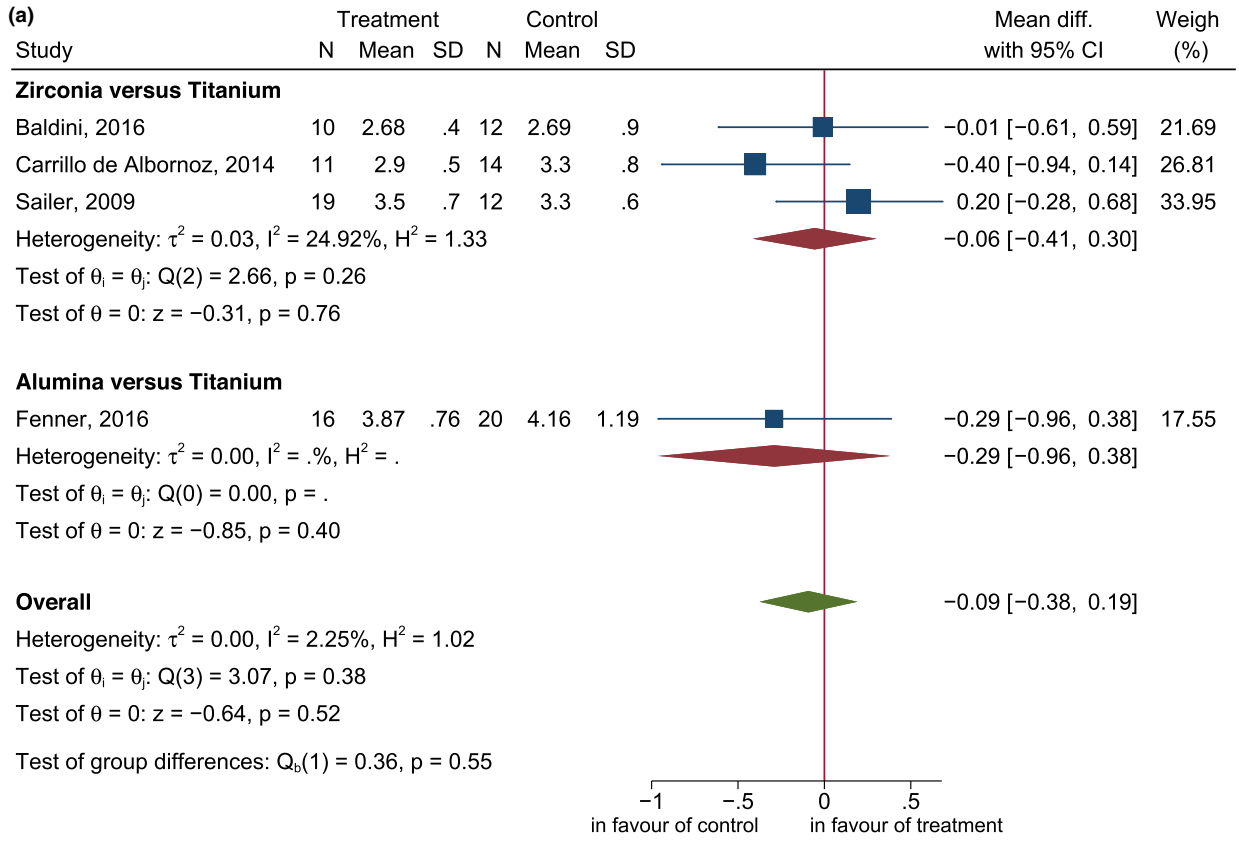
The risk of bias assessment based on the Cochrane Risk of Bias 2 tool showed some concerns of bias for all (Andersson et al., 2001, 2003; Baldini et al., 2016; Fenner et al., 2016; Hosseini et al., 2011, 2022; Sailer, Zembic, et al., 2009; Vigolo et al., 2006; Zembic et al., 2009, 2013) but two studies (Carrillo de Albornoz et al., 2014; Ferrari et al., 2015) (Table 6). This was most often based on concerns for risk of bias concerning randomization (e.g. often there was ambiguity about how the treatment allocation was concealed) and concerning missing outcome data (often it was unclear how missing outcome data impacted the final results).

4 | DISCUSSION

The present review showed a similar MBL, PD and abutment survival after 1- and 5-years of follow-up for abutments made of alternative materials compared to titanium abutments. Additionally, few biological and technical complications were reported. The included studies did not report differences concerning esthetics between titanium and ceramic abutments.

The abutment survival rates ranged from 83% (zirconia) to 100% (titanium) after 1 year. The 5-year data were even higher ranging from 93% (alumina) to 100% (zirconia). This can be due to attrition bias, since in the studies with 5-year follow-up the number of drop-outs was noticeably higher than in the studies with 1-year follow-up. Moreover, caution should be exercised in interpreting this result. It seems that in most studies, the abutment fractures that occurred at the try-in or initial placement are usually not counted for the survival rate and were just replaced (Andersson et al., 2001, 2003). This problem of not taking into considerations problems that might have occurred over time with the abutment/reconstruction has also been reported in other systematic reviews (Pjetursson et al., 2018). And it is common knowledge that survival does not equal a successful treatment (Halim et al., 2022).

The only clinical parameter that could be analyzed for abutment materials in a meta-analysis was PD. The heterogeneity of the used indexes to measure plaque and bleeding on probing/ gingival health made a meta-analysis impossible. However, all but one studied reported no differences in plaque index, nor in bleeding/gingival indices. However, it seems that in the sole study reporting slightly more plaque on titanium than on zirconia abutments (Zembic et al., 2013) the specific *p*-value supporting this is lacking in the paper. Although this is in contrast to earlier studies examining plaque accumulation on disks showing less plaque accumulation to zirconia than to titanium (Rimondini et al., 2002; Scarano et al., 2004), these findings are in line with those of previously published systematic reviews based on clinical examinations (Linkevicius & Vaitelis, 2015; Totou et al., 2021). Similarly, Sanz-Sanchez and coworkers, did find a greater increase in bleeding on probing around titanium compared to zirconia abutments; however, this was based on a meta-analysis of solely three studies (Sanz-Sánchez et al., 2018).



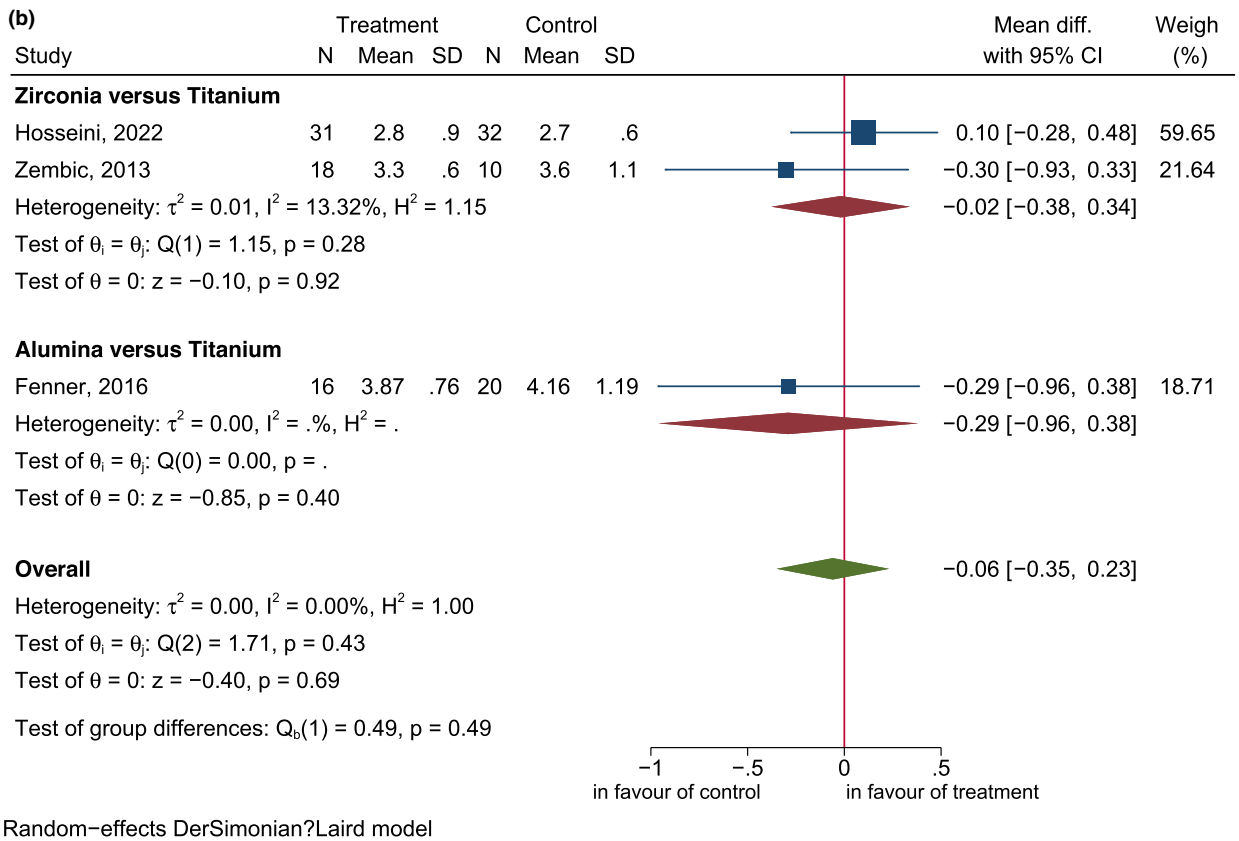
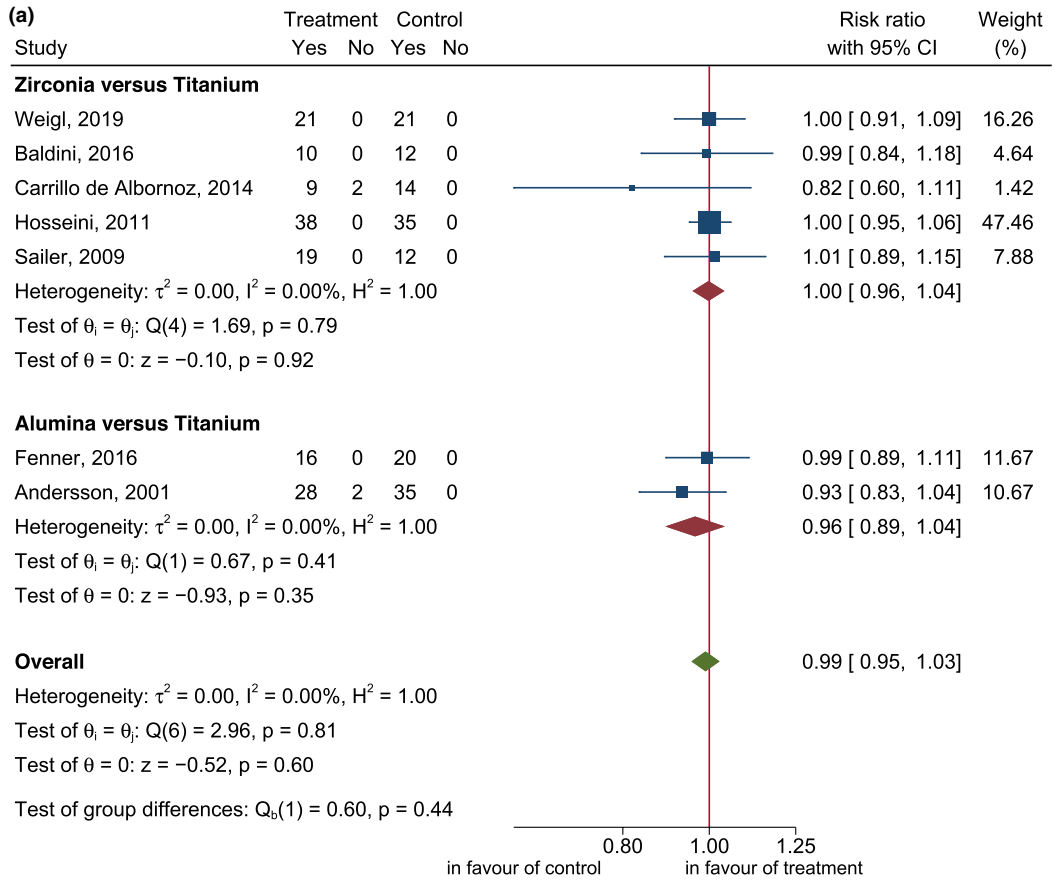


FIGURE 3 (a) Probing pockets depth (PD) values after 1 year according to abutment material, (b) Probing pockets depth (PD) values after 5 years according to abutment material.



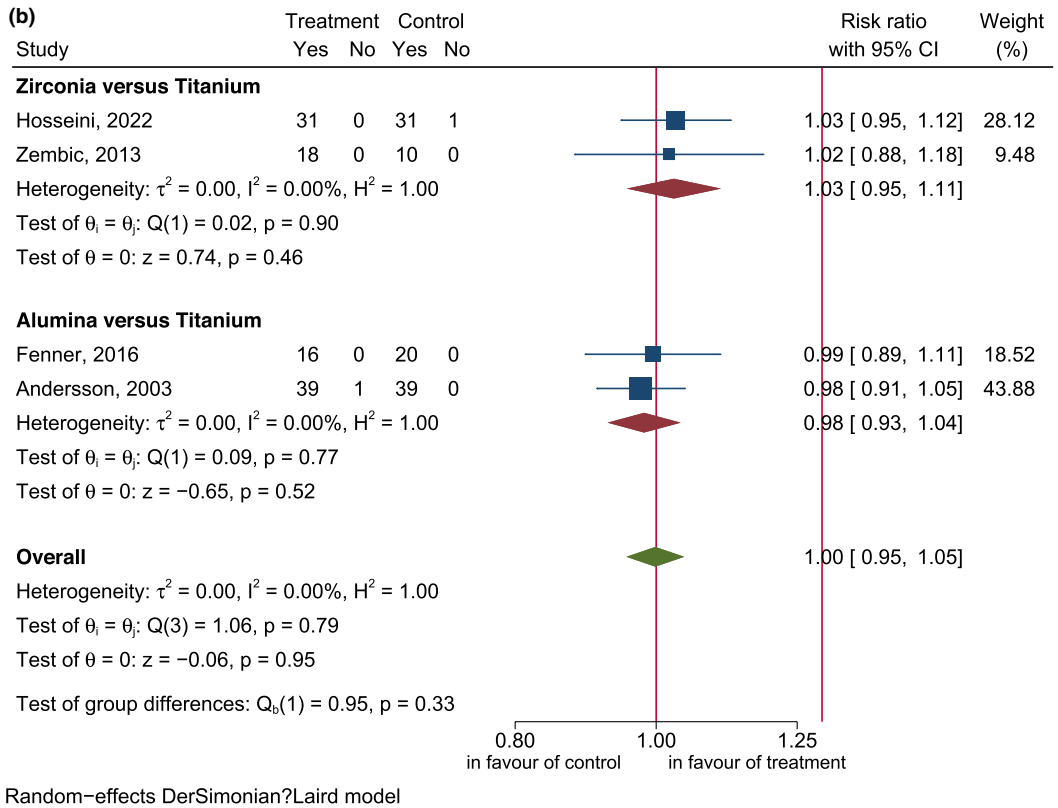


FIGURE 4 (a) 1 year survival rate of the abutments according to abutment material, (b) 5-year survival rate of the abutments according to abutment material.

TABLE 2 Biological complications of abutment studies.

Author/year	Follow up (mo)	Abutment type	Biological-clinical outcomes
Hosseini et al., 2022[a]	60	Titanium vs Zirconia	• No significant differences in mPI ($p = .360$) • No significant differences in mBI ($p = .350$) • 1 Zirconia implant with >2 mm bone loss • 1 Zirconia implant with PPD >5 mm • Peri-implant mucositis in 22.6% of the titanium restorations and 34.4% of the zirconia restorations
Baldini et al., 2016	12	Titanium vs Zirconia	• No significant differences regarding BoP ($p = .6$) • No significant differences regarding PPD ($p = .8$) • No significant differences regarding recession ($p = .8$) • MBL: mesially significantly more for titanium implants versus zirconia ($p = .02$)
Fenner et al., 2016	60	Titanium vs Aluminum oxide	• No significant differences in PI ($p = .274$) • No significant differences regarding BoP ($p = .339$) • No significant differences regarding PPD ($p = .586$) • The recession of the mucosa was statistically less significant in the aluminum oxide than in the titanium group ($p = .002$) • No significant differences in MBL
Ferrari et al., 2015	24	Titanium vs Gold-hue vs Zirconia	• MBL: significance NR
Carrillo de Albornoz et al., 2014	12	Titanium vs Zirconia	• No significant differences in FMPS (p-value NR) • No significant differences in FMBS (p-value NR) • No significant differences regarding PPD (p-value NR) • No significant differences in MBL ($p = .430$)
Zembic et al., 2013[b]	60	Titanium vs Zirconia	• Slightly more plaque on titanium than on zirconia abutments ($p = .96$) • No significant differences regarding BoP ($p = .96$) • No significant differences in mean PPD ($p = .85$) • No significant differences in MBL (MBL: $p = .95$, DBL: $p = .99$)
Hosseini et al., 2011[a]	12	Titanium vs Zirconia	• No significant differences in mPI (p-value NR) • No significant differences in mBI (p-value NR) • No significant differences in MBL ($p = .69$) • 3 implants with a titanium abutment with suppuration and PPD ≥5 mm • 1 implant with a zirconia abutment with marginal fistula • 3 implants with a zirconia abutment with suppuration upon probing • 2 implants with a zirconia abutment with PPD ≥5 mm • 1 implant with a zirconia abutment with continuous, weak pain
Sailer et al., 2009[b]	12	Titanium vs Zirconia	• No significant differences in PI (p-value NR) • No significant differences regarding BoP (p-value NR) • No significant differences regarding PPD (p-value NR)
Zembic et al., 2009[b]	36	Titanium vs Zirconia	• No significant differences in PCR (p-value NR) • No significant differences regarding BoP (p-value NR) • No significant differences regarding PPD (p-value NR) • No significant differences in MBL (p-value NR)
Vigolo et al., 2006	60	Titanium vs Gold-alloy	NR
Andersson et al., 2003	48	Titanium vs Alumina	• No significant differences for plaque ($p > .05$) • No significant differences for mucosal bleeding ($p > .05$) • 3 implants with an alumina abutment with PPD 5 mm • No significant differences in MBL ($p > .3$)
Andersson et al., 2001	36	Titanium vs Alumina	• No significant differences in presence of plaque (p-value NR) • No significant differences in mucosal/ginigival bleeding (p-value NR)

Abbreviations: BoP, bleeding on probing; FMBS, full mouth bleeding score; FMPS, full mouth plaque score; mBI, Sulcus Bleeding Index; MBL, marginal bone loss; mPI, modified Plaque Index; NR, not reported; PCR, plaque control record; PPD, probing pocket depth.

[a,b]Studies followed by the same letter were conducted on the same patient population.

TABLE 3 Technical complications of abutment studies (based on the framework proposed by Lang et al., 2012).

Author/year	Follow up (mo)	Abutment type	Abutment survival (%)	Major complications(requiring replacement of the restoration, such as, implant fracture, abutment tooth fracture, loss of supra-structures)	Medium complications (such as abutment fracture, veneer or framework fractures, phonetic complications)	Minor complications (to be corrected with small efforts; such as abutment and screw loosening, loss of retention, de-bonding, loss of screw hole sealing, veneer chipping (to be polished) and occlusal adjustment)
Hosseini et al., 2022[a]	60	Titanium	100	-	-	3 losses of retention (1 after 1 yr, 2 after 3 yrs) 1 ceramic veneering fractures
		Zirconia	100	-	-	1 ceramic veneering fractures
Baldini et al., 2016	12	Titanium	100	-	-	-
		Zirconia	100	-	-	-
Fenner et al., 2016	60	Titanium	100	-	-	-
		Aluminum oxide	100	-	-	-
Ferrari et al., 2015	24	Titanium	NR	NR	NR	NR
		Gold-hue	NR	NR	NR	NR
		Zirconia	NR	NR	NR	NR
Carrillo de Albornoz et al., 2014	12	Titanium	100	-	-	-
		Zirconia	83.3	-	2 abutments fractured when tightened at the required torque	-
Zembic et al., 2013[b]	60	Titanium	100	-	-	3 minor chippings of the veneering ceramic (at 6 and 12 mo, 5 yrs)
		Zirconia	100	-	-	-
Hosseini et al., 2011[a]	12	Titanium	100	-	-	1 loss of retention 1 chipping of veneering porcelain
		Zirconia	100	-	-	0
Sailer et al., 2009[b]	12	Titanium	100	-	-	2 minor chippings of the veneering ceramic (at 6 and 12 mo)
		Zirconia	100	-	-	-
Zembic et al., 2009[b]	36	Titanium	100	-	-	2 minor chippings of the veneering ceramic (at 6 and 12 mo)
		Zirconia	100	-	-	-
Vigolo et al., 2006	60	Titanium	100	-	-	-
		Gold-alloy	100	-	-	-
Andersson et al., 2003	60	Titanium	100	-	-	-
		Alumina	98.1	-	2 minor abutment fractures during initial prosthetic work (proshtetic treatment was continued) 1 abutment fracture	-

(Continues)

TABLE 3 (Continued)

Author/year	Follow up (mo)	Abutment type	Abutment survival (%)	Major complications(requiring replacement of the restoration, such as, implant fracture, abutment tooth fracture, loss of supra-structures)	Medium complications (such as abutment fracture, veneer or framework fractures, phonetic complications)	Minor complications (to be corrected with small efforts; such as abutment and screw loosening, loss of retention, de-bonding, loss of screw hole sealing, veneer chipping (to be polished) and occlusal adjustment)
Andersson et al., 2001	12	Titanium	100	-	-	-
		Alumina	93	-	5 abutments fractured during preparation or placement (were replaced) 2 minor chip fractures during placement 2 fractured after loading (1 and 7 mo)	-
	36	Titanium	100	Crown fracture after 2 years of loading	-	-
		Alumina	100	-	-	-

Abbreviations: Mo, months; NR, not reported; yr, year.

[a]Examining the same patient population.

[b]Examining the same patient population.

In all included studies, there were few technical complications. The ones that were reported were mainly chipping in the titanium abutment group and abutment fracture with the ceramic abutments. The latter can be explained by the inherent characteristics of ceramic materials, with lower fracture resistance as shown repeatedly in in vitro studies (Foong et al., 2013; Leutert et al., 2012; Mitsias et al., 2010). This is also affected by other abutment characteristic such as the angulation and thickness of the ceramic abutment (Park et al., 2017; Zandparsa & Albosefi, 2016) and the effect of (exorbitant) occlusal forces (Gou et al., 2019).

The esthetic outcomes seem comparable for the four examined materials. This is in contrast with animal data (Jung et al., 2007) and clinical data based on spectrophotometric data (Pitta et al., 2020; Totou et al., 2021). A sidenote has to be made that, although Pitta and co-workers found significantly better spectrophotometric data for ceramic abutments compared to the overall metal abutments, when comparing directly the data of titanium and zirconia abutments no significant differences could be found (Pitta et al., 2020). The thickness of the mucosa also plays an important role in this process (Bienz et al., 2022; Sala et al., 2017).

Although this systematic review failed to detect significant differences between the materials examined (titanium, zirconium, alumina and gold), we see that the data we were able to collect on alumina and gold are very limited and mostly at least 15 years old. Clinically, the use of these materials seems largely abandoned. The use of gold abutments has been discontinued due to the high pricing and the subpar biocompatibility compared to titanium (Abrahamsson et al., 1998; Furuhashi et al., 2021; Welander et al., 2008). The use of alumina has been replaced by the use of zirconia, since both have the same aesthetic and biological characteristics, but zirconia is a much stronger ceramic. The fracture toughness of Zirconia is 9 MPa $m^{1/2}$ (Sailer, Philipp, et al., 2009) versus 3.6 MPa $m^{1/2}$ (Guazzato et al., 2004) for alumina. Additionally, its bending strength (900 MPa) (Sailer, Philipp, et al., 2009) is double of the bending strength of alumina (440 MPa) (Guazzato et al., 2004).

There are certain shortcomings in the current literature investigating the influence of abutment materials, shortcomings that are therefore reflected in this systematic review. First, when interpreting these results, on must be aware that the meta-analyses are based on pooled data from different types of abutments. For example, this systematic review pooled implants placed in the anterior and posterior regions in the mouth.

Second, almost every included study used different indices for plaque, gingival health, bleeding, technical complications and aesthetics. This made summarizing the results very complex and made meta-analyses impossible for these parameters. In addition, it should be noted that even for the parameters for which a meta-analysis could be performed, sometimes only a limited number of articles could be included. There is thus a need for standardized reporting concerning peri-implant health and disease. Additionally, although more and more patient satisfaction/patient reported outcomes are reported, here is also a need for more standardized reporting.

TABLE 4 Aesthetic outcomes.

Author/year	Follow up (mo)	Abutment type	Index	Outcome
Hosseini et al., 2022[a]	60	Titanium vs. Zirconia	Copenhagen Index Score	The six professional-reported aesthetic scores at the 5-year examination were not significantly different between both types of restorations
Baldini et al., 2016	12	Titanium vs. Zirconia	Implant Crown Aesthetic Index	Total: 14 for Zirconia and 9 for titanium. No statistical significant intergroup differences.
			Papilla Index	An improvement was observed after 12 months in both groups, with significant intragroup differences (for the test group, $p = .008$; for the control group, $p = .001$). Intergroup difference NR.
Fenner et al., 2016	60	Titanium vs. Aluminum oxide	Papilla index	No intergroup differences
			Clinical crown length	Clinical crown length showed significantly higher values in the titanium group.
Ferrari et al., 2015	24	Titanium vs. Gold-hue vs. Zirconia	NR	NR
Carrillo de Albornoz et al., 2014	12	Titanium vs. Zirconia	Implant Crown Aesthetic Index	ICAI total: 7.6 for Zirconia and 10.6 for titanium. No statistical significant intergroup differences.
			Papilla index	Tendency to higher interdental papilla score in the test group.
Zembic et al., 2013[b]	60	Titanium vs. Zirconia	Distance from the mucosal/gingival margin to the crown margin/cemento-enamel junction	No significant differences were detected examining the mean distance of the mucosal margin to the crown margin when using zirconia versus titanium abutments.
			Papilla index	No significant difference in the mean papilla height mesial and distal of crowns supported by zirconia or titanium abutments.
Hosseini et al., 2011[a]	12	Titanium vs. Zirconia	Copenhagen Index Score	The overall professional reported aesthetic outcome was not significantly different between both types of restorations after 1 year (AC: mean 9.3, SD 1.9; MC: mean 9.1, SD 1.4; $p = .705$).
Sailer et al., 2009[b]	12	Titanium vs. Zirconia	Difference of color of the peri-implant mucosa and the gingiva of control teeth was evaluated by means of a spectrophotometer (Spectroshade).	Visible difference of the mucosal color compared with natural teeth. But the amount of discoloration was not significantly different between the titanium and the zirconia abutment-borne crowns.
			Soft tissue thickness	No intergroup comparison mentioned.
			Papilla index	No intergroup comparison mentioned.
Zembic et al., 2009[b]	36	Titanium vs. Zirconia	Difference of color of the peri-implant mucosa and the gingiva of control teeth was evaluated by means of a spectrophotometer (Spectroshade).	Visible difference of the mucosal color compared with natural teeth. But the amount of discoloration induced by zirconia and titanium abutments was not significantly different.
			Soft tissue thickness	No difference at zirconia versus titanium abutments.
			Papilla index	No intergroup differences.
Vigolo et al., 2006	60	Titanium vs. Gold-alloy	NR	NR
Andersson et al., 2003	48	Titanium vs. Alumina	NR	The clinicians rated the esthetic result as excellent or good in 92% and acceptable in 8% of the cases at FPD insertion. The results were comparable for ceramic and titanium abutments.

(Continues)

TABLE 4 (Continued)

Author/year	Follow up (mo)	Abutment type	Index	Outcome
Andersson et al., 2001	36	Titanium vs Alumina	NR	At the 1-year follow-up the clinician rated the esthetic result in 100% of the cases as excellent or good in the test group and in 97% of the cases as excellent or good in the control group (and 3% as acceptable).

Abbreviations: Mo, months; NR, not reported; yr, year.

[a]Examining the same patient population.

[b]Examining the same patient population.

TABLE 5 Patient satisfaction.

Author/year	Follow up (mo)	Abutment type	Index	Outcome
Hosseini et al., 2022[a]	60	Titanium vs. Zirconia	Patient-reported aesthetic outcome based on selected questions from the Oral Health Impact Profile questionnaire (OHIP-49)	The patients were also satisfied with both the aesthetic and functional results of the implant-supported single-tooth restorations of both materials.
Baldini et al., 2016	12	Titanium vs. Zirconia	Satisfaction questionnaire concerning items such as the esthetic-related variables	Patient feedback was positive in both test and control groups: the final opinion on esthetic outcomes demonstrated a degree of general satisfaction.
Fenner et al., 2016	60	Titanium vs. Aluminum oxide	Visual analog scale (VAS) to evaluate patient's overall satisfaction (on a scale from 0 to 10)	Patient's satisfaction revealed 9.7 on the visual analog scale.
Ferrari et al., 2015	24	Titanium vs. Gold-hue vs. Zirconia	NR	NR
Carrillo de Albornoz et al., 2014	12	Titanium vs. Zirconia	Visual analog scale (VAS) to evaluate patient's aesthetics satisfaction.	Patient satisfaction was similarly high in both groups (visual analogue scale 8.5).
			Written questionnaire evaluating satisfaction regarding the aesthetic appearance, the phonetic ability, and overall satisfaction with the treatment (six-grade ordinal scale).	The questionnaire demonstrated a good acceptance of the received treatment.
Zembic et al., 2013[b]	60	Titanium vs. Zirconia	NR	NR
Hosseini et al., 2011[a]	12	Titanium vs. Zirconia	Patient reported visual analogue scale (VAS)—a 100 mm line with the end phrases 'Very bad aesthetic' on the left (0 mm) and 'Very good aesthetic' on the right (100 mm)	The patient-reported overall aesthetic evaluations demonstrated no significant difference in the VAS scores between the AC and the MC restorations
Sailer et al., 2009[b]	12	Titanium vs. Zirconia	NR	NR
Zembic et al., 2009[b]	36	Titanium vs. Zirconia	NR	NR
Vigolo et al., 2006	60	Titanium vs. Gold-alloy	NR	NR
Andersson et al., 2003	48	Titanium vs. Alumina	NR	All patients were fully satisfied with the achieved esthetic results at both FPD insertion and the 5-year appointment.
Andersson et al., 2001	36	Titanium vs. Alumina	NR	All patients were fully satisfied with the achieved esthetic results at the 1-year follow-up.

Abbreviations: Mo, months; NR, not reported; yr, year.

[a]Examining the same patient population.

[b]Examining the same patient population.

TABLE 6 Risk of bias assessment according to the Cochrane Risk of Bias 2 tool.

Author/year	Randomization	Deviations from intended intervention	Missing outcome data	Measurement of the outcome	Selection of the reported result	Overall risk of bias
Hosseini et al., 2022[a]	🟡	🟢	🟢	🟢	🟢	🟡
Baldini et al., 2016	🟢	🟢	🟡	🟢	🟢	🟡
Fenner et al., 2016	🟢	🟢	🟡	🟢	🟢	🟡
Ferrari et al., 2015	🟢	🟢	🟢	🟢	🟢	🟢
Carrillo de Albornoz et al., 2014	🟢	🟢	🟢	🟢	🟢	🟢
Zembic et al., 2013[b]	🟡	🟢	🟡	🟢	🟢	🟡
Hosseini et al., 2011[a]	🟡	🟢	🟢	🟢	🟢	🟡
Sailer et al., 2009[b]	🟡	🟢	🟡	🟢	🟢	🟡
Zembic et al., 2009[b]	🟡	🟢	🟡	🟢	🟢	🟡
Vigolo et al., 2006	🟡	🟢	🟢	🟢	🟢	🟡
Andersson et al., 2003	🟡	🟢	🟢	🟢	🟢	🟡
Andersson et al., 2001	🟡	🟢	🟢	🟢	🟢	🟡

Note: Green: low risk of bias; yellow: some concerns for risk of bias; red: high risk of bias.

[a]Examining the same patient population.

[b]Examining the same patient population.

Finally, there is also often a lack of details about the abutment characteristics, such as the macroscopic design and surface roughness, abutment height and emergence angle, although we know that these also influence the surrounding tissues (Laleman & Lambert, 2023; Nothdurft et al., 2015; Quirynen et al., 1996; Teughels et al., 2006; van Brakel et al., 2011). Additionally, details about the implant-abutment interface (e.g. type of connection) are lacking. On the other hand, most studies mention if screw-retained or cemented restorations were used, but in several studies both types are used interchangeably, which made a subanalysis impossible.

A limit of this study is that because of time limitations the search was limited to studies published from January 2000. Due to this time limit, we will most likely not have missed any eligible articles on zirconia abutments, as they were only introduced around this time. However, we are aware that we probably did not include potentially eligible articles on alumina and gold abutments. Another limitation of this study is that transmucosal components clearly consisting of different materials were excluded. This was done because the authors deemed that it impossible to assess the effect of each material individually for transmucosal components existing of two materials. However, this ignores the clinical reality where dental implant are now frequently restored with monolithic restorations bonded on a titanium bases (TiB) of various tranmucosal heights. This type of restoration brings new challenges as, especially in case of short TiB heights, a significant part of the transmucosal tissues is in direct contact with the restorative material such as zirconia, lithium disilicate, hybrid composite, polymer infiltrated composite newtwork (PICN) or even polyetheretherketone (PEEK). Although there are some promising clinical results about abutments made of for example PEEK (Ayyadanveettil et al., 2021), in general this new generation of materials is poorly investigated clinically concerning their effect on the surrounding peri-implant tissues.

5 | CONCLUSIONS

This systematic review shows that based on randomized clinical trials no differences between abutment materials can be found on the surrounding peri-implant tissues.

AUTHOR CONTRIBUTIONS

I. Laleman: Data curation and writing–original draft/review and editing, F. Lambert: supervision and writing–review and editing, M. Gahlert: writing–review and editing, M. Bacevic: conceptualization, H. Woelfler: statistical analysis and visualization, S. Roehling: data curation and writing–original draft/review and editing.

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DATA AVAILABILITY STATEMENT

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

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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REVIEW ARTICLE

CLINICAL ORAL IMPLANTS RESEARCH WILEY

Effect of agents affecting bone homeostasis on short- and long-term implant failure

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Abstract

Objectives: To review the current evidence on the relationship between agents that affect bone homeostasis and dental implant failures.

Materials and Methods: Electronic searches for bisphosphonates, denosumab, methotrexate, corticosteroids, romosozumab, sunitinib, and bevacizumab were performed using PubMed, MEDLINE (OVID), EMBASE (OVID), Cochrane Central Register of Controlled Trials (Cochrane Library), Cochrane Oral Health Group Trials Register (Cochrane Library) and Web of Science (Thomson Reuters). Manual searches were also conducted to complement the digital searches for recent issues.

Results: Previous publications suggested that bisphosphonates do not compromise the survival of dental implants. However, one study documented an increased risk of implant failure in patients who had received high-dose of intravenous bisphosphonate therapy after implant rehabilitation. There has been an issue of MRONJ around implants in patients who have successfully received implant therapy before and after antiresorptive therapy, leading to late implant failure. Despite evidence on the detrimental effects of denosumab, methotrexate and corticosteroids on bone metabolism, their role in implant survival is not conclusive.

Conclusions: At present, there is insufficient evidence to establish a potential connection between agents that affects bone homeostasis and implant failure. However, some studies have reported negative results for implant therapy. In addition, implant-related sequestration in patients who received anti-resorptive therapy, despite of successful osseointegration, is also noticeable. Although limited studies are available at present, clinicians should still carefully consider the potential hazards and take appropriate precautions to minimize the risks associated with the medications and implant therapy.

KEYWORDS
bisphosphonate, corticosteroids, denosumab, dental implant, endosseous implant, implant failure, methotrexate, MRONJ

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1 | INTRODUCTION

With the increase in the aging population across several countries, the demand for implant-supported rehabilitation is on the rise. Moreover, aging populations suffering bone metabolic diseases are becoming increasingly common, and the use of medications altering bone metabolism is accordingly on the increase for the management of various bone diseases, including osteoporosis, rheumatic disease, and bone malignancies. Therefore, the longevity and survival of dental implants in patients taking such medications must be of interest to dental clinicians. Although dental implantation is certainly a highly successful prosthetic option for replacing missing teeth, any medication that modifies bone metabolism may jeopardize the homeostasis of the bone tissue (Abtahi et al., 2013; Baron et al., 2011; He et al., 2020; Kanagawa et al., 2016; Kondo & Yoda, 2011; Teitelbaum, 2015).

Remodeling of the bone tissue around the implant fixture continues to occur during and after osseointegration of dental implants (Guglielmotti et al., 2019). After insertion of the implant fixture, the dynamic action of osteoclasts and osteoblasts allows a direct structural and functional connection between the bone and implant surface, and the peri-implant bone is subsequently adapted and remodeled as a response to mechanical load (Isidor, 2006). Therefore, it is important to understand how medications that regulate osteoclast or osteoblast activity affect the prognosis of dental implants.

Bisphosphonates (BPs) and denosumab are currently the most widely prescribed anti-resorptive medications for metabolic bone diseases, bone malignancies, and bone metastases to reduce skeletal-related events (Body, 2012; Drake et al., 2008; Gul et al., 2016; Hernlund et al., 2013). Methotrexate (MTX) and corticosteroids (CS) are also known to alter bone metabolism and reported to contribute to the development of medication-related osteonecrosis of the jaw (MRONJ) (Henien et al., 2017; Milosavljevic et al., 2022; Weinstein, 2012). This review aimed to explore the relationship between dental implant failure and the intake of medications that affect bone metabolism. Furthermore, previous reports on MRONJ developed around dental implant and late implant failure, referred to as implant presence-related osteonecrosis or peri-implantitis like MRONJ, is reviewed and discussed.

2 | SEARCH STRATEGY

The focus questions were as follows: In patients who had taken medications known to alter bone metabolism (BPs, denosumab, MTX, and CS) before or after implant installation, if implant failure occurred more frequently than in those who had not taken the medications, and if biological complications (peri-implant marginal bone level, soft tissue reaction) and comorbidities (type of medication, therapy length, and other medications) (secondary outcomes) were associated with implant failure in such patients.

Electronic databases including PubMed, MEDLINE (OVID), EMBASE (OVID), Cochrane Central Register of Controlled Trials (Cochrane Library), Cochrane Oral Health Group Trials Register (Cochrane Library) and Web of Science (Thomson Reuters) were electronically searched for articles published up to July 31, 2022. The searches were limited to the English language. The search strategy in the electronic databases were as follows: (bisphosphonate* OR "diphosphonates" [Mesh term] OR "denosumab" [Mesh term] OR Xgeva OR AMG 162 OR Prolia OR "Methotrexate" [Mesh term] OR Amethopterin OR Methotrexate OR Mexate OR Methotrexate Sodium OR "Arthritis, Rheumatoid" [Mesh term] OR Rheumatoid Arthritis OR "Bone Density Conservation Agents" [Mesh term] OR Anti-resorptive Agent* OR Bone Resorption Inhibitor* OR Antiresorptive Drug* OR "Steroids" [Mesh term] OR Steroid* OR Corticosteroid*) AND ("Dental Implants" [Mesh term] OR Dental Implant* OR dental implant failure* OR dental implant survival* OR (Dental AND Implant*)).

Manual searches were also conducted to complement the digital searches on recent issues in the following scientific journals: Clinical Implant Dentistry and Related Research, Clinical Oral Implants Research, European Journal of Implantology, Implant Dentistry, International Journal of Oral Maxillofacial Implants, International Journal of Oral Maxillofacial Surgery, International Journal of Periodontics and Restorative Dentistry, International Journal of Prosthodontics, Journal of Clinical Periodontology, Journal of Dental Research, Journal of Oral Implantology, Journal of Oral and Maxillofacial Surgery, Journal of Oral Rehabilitation, and Journal of Periodontology.

In addition, grey literature was perused for potential candidates to be included in the New York Academy of Medicine grey literature report (http://greylit.org) and the registry of clinical studies hosted by the US National Institutes of Health (www.clinicaltrials.gov). The reference lists of relevant full-text articles were cross-checked and screened for assessment.

3 | LITERATURE SELECTION AND DATA EXTRACTION

Clinical studies, including prospective or retrospective cohort, case–control, cross-sectional, or randomized controlled trials investigating the influence of relevant medications on implant survival or failure, were considered for inclusion by two independent examiners (JJ and GJS). The selected data were subsequently extracted and presented in Table 1. Publications that did not meet the inclusion criteria but contained significant clinical and pre-clinical data at all levels of evidence were presented in Tables 2–5. Studies on the local application of the medications were excluded. The overall findings for each medication are summarized and discussed in a narrative manner.

4 | ANTI-RESORPTIVE DRUGS AND THEIR POTENTIAL EFFECT ON HEALING AROUND DENTAL IMPLANTS

4.1 | Bisphosphonates

Bisphosphonates, especially nitrogen-containing BPs, are effective anti-resorptive medications for the management of metabolic bone diseases and cancer-related conditions (Drake et al., 2008; Hernlund

et al., 2013). Owing to their high affinity for hydroxyapatite, BPs deposit and accumulate in bone tissues and serve their purpose to interfere with osteoclast functions and differentiation by suppressing the mevalonate pathway (Amin et al., 1992; Singh et al., 2015). Since osteonecrosis of the jaw was first described as an adverse effect of BPs in 2003, MRONJ has become a well-recognized complication of BP therapy (Alhussain et al., 2015; Campisi et al., 2020; Patil et al., 2020; Ruggiero et al., 2022).

The inhibitory effects of BPs on the mevalonate pathway, leading to cell apoptosis, extend beyond osteoclasts. Several in vitro studies have demonstrated that osteoblasts, vascular cells, and fibroblasts are also susceptible to apoptosis induced by BPs (Jung et al., 2018; Misso et al., 2012; Walter et al., 2011). This nonspecific action of BPs not only inhibits bone turnover but also suppresses angiogenesis and cause soft tissue toxicity (Ruggiero et al., 2022). Consequently, in the presence of inflammation and infection accompanied by tissue injury, such as those resulting from dentoalveolar surgery and tooth extraction, surgical wound healing is impaired, and it provides a conducive setting for the development of MRONJ along with suppressed bone remodeling. Accordingly, this raised the question of whether there is an association between BPs and dental implant failure. The invasive surgical procedure involved in dental implant insertion, coupled with the multiple detrimental effects of BPs, may act as a trigger for the onset of MRONJ and impede osseointegration, thereby increasing the risk of early implant failure (Ruggiero et al., 2022). In addition, the acidic environment resulting from bone and soft tissue injury, along with local inflammation, may lead to an increased release of BPs (Otto, Hafner, et al., 2010; Otto, Pautke, et al., 2010), further contributing to the pathophysiological progression of MRONJ or implant failure.

Another notable characteristic of BPs is their long elimination terminal half-life, exceeding 10 years due to their skeletal retention (Khan et al., 1997). Consequently, the long-term administration of BPs becomes a risk factor for developing MRONJ, especially when a high dose is administered (Ruggiero et al., 2022). In a systematic review, the risk of MRONJ in cancer patients exposed to zoledronate was reported to be 1.6%–4% after 2 years and 3.8%–18% after more than 2 years (Ng et al., 2021). However, in patients receiving low-dose BPs for osteoporosis management, the prevalence of MRONJ was found to be 0.05% at 2–4 years and 0.21% after 4 or more years (Lo et al., 2010). Although the risk of MRONJ associated with low-dose anti-resorptive drugs is still a topic of debate, it remains relatively low, and the risk of implant failure and related complications in patients receiving low-dose BPs might also be low, accordingly.

Meanwhile, the development of osteonecrosis related to previously osseointegrated implants has also been reported (Goss et al., 2010; Jacobsen et al., 2013; Pichardo et al., 2020). Local inflammation, such as peri-implantitis, and mechanical stress caused by occlusal force being transferred directly to the bony structure, have been suggested as potential factors associated with MRONJ and late implant failure (Allen & Burr, 2011; Hoefert et al., 2010; Pichardo et al., 2020). Moreover, since the accumulation of BPs occurs in the bone, driven by both chemical and biological factors, patients with prolonged treatment with BPs would be at an increased risk of MRONJ and dental implant failure (Allen, 2008; Granate-Marques et al., 2019).

4.2 | Denosumab

Denosumab, a human monoclonal IgG2 antibody, is also used to manage osteoporosis, metabolic bone diseases, and bone metastasis (Body, 2012; Gul et al., 2016; Polyzos et al., 2019; Reid & Billington, 2022). A market analysis for osteoporosis treatment in 2018 estimated that denosumab accounted for approximately 15.5% of the osteoporosis market, and it is expected that there will be an increase in its use as an effective anti-resorptive drug as well as for oncological patients (McClung et al., 2006). In addition to the specific inhibition of osteoclast formation and function, its convenience in medication adherence, which requires a subcutaneous injection every 6 months, is another advantage over oral osteoporotic drugs.

In contrast to BPs, the action of denosumab is highly specific to osteoclasts (Baron et al., 2011). Its target is to block the receptor activator of the nuclear factor kappa-B ligand (RANKL), and it subsequently prevents the binding of RANKL to its receptor, the receptor activator of nuclear factor kappa-B (RANK). Eventually, the development of multinucleated osteoclasts through the fusion of monocytes and macrophages is inhibited, thereby achieving the goal of denosumab treatment, which is to decrease bone resorption (Baron et al., 2011).

Although its potential to suppress bone turnover is not inferior to that of BPs (Miller et al., 2016; Reid & Billington, 2022), the specific inhibition of RANKL by denosumab raised the hope of decreasing the well-known adverse effects of BPs, MRONJ. Whereas BPs are known to induce apoptosis in various cell types (Jung et al., 2018; Misso et al., 2012; Walter et al., 2011) and have a long retention half-life in bone tissue, denosumab only targets the inhibition of osteoclasts and has a relatively short half-life (15–30 days), which is distinct from that of BPs (Chen et al., 2018; Laskowski et al., 2016). However, denosumab is used as a substitute for BPs, MRONJ in patients treated with denosumab has also begun to emerge (Aghaloo et al., 2010; Taylor et al., 2010), and it serves as a momentum to change the term BRONJ to MRONJ. Several clinical trials have reported MRONJ occurrence as an adverse effect. The incidence of MRONJ in cancer patients receiving high-dose denosumab ranged from 0.76% to 6.88%. When compared with zoledronate, the use of denosumab was associated with a statistically significant increase in the risk of MRONJ (Boquete-Castro et al., 2016). A systematic review also reported that the prevalence of MRONJ in cancer patients varies from 0.5% to 3.2% depending on the exposure time, which is significantly higher in patients receiving denosumab than in those receiving BPs (Limones et al., 2020). However, osteoporosis patients receive a relatively low dose of denosumab (60 mg/6 months), and accordingly, the incidence ranges from 0 to 30.2 per 100,000 patient-years, although data on this subject are currently very limited (Khan et al., 2015).

TABLE 1 Implant failures in patients on ARD.

Authors (year)	Study design and mean follow-up (months)	Systemic condition	Other controlled factors	Confounding factors reported (subjects; *n*) a: success b: failed	MRONJ incidence (*n*)	Medication (subjects; *n*)	Dosage (mg/mL)	Therapy length (months) (*n*)	Administration route
Prior to implant placement									
Pandey et al. (2019)	RC 84	Osteoporosis	Age, gender, steroids intake, type II DM, periodontal disease, other bone resorptive disorder	NR	NR	BPs Parathyroid hormone derivative	10 mg once daily Teriparatide 20 mcg once daily	12–36 months N	Oral Subcutaneous
French et al. (2019)	RC 32.2 ± 26.8	NR	N	Autoimmune disease, smoking	NR	BPs NSM	NR	NR	NR
Yajima et al. (2017)	RC 39.12 ± 15.6	Osteoporosis	Age, gender, steroids intake, smoking, type II DM, severe periodontal diseases, other metabolic bone disease	NR	N	BPs Selective estrogen receptor modulator (8)/ parathyroid hormone (6)	NR	12–36 months (5), >36 months (6) NR	NR
Al-Sabbagh et al. (2015)	RC NR	NR	N	Smoking (a: 39, b: 7), DM (a: 37, b: 6), osteoporosis (a: 51, b: 8)	N	BPs NSM	NR	NR	NR
Siebert et al. (2015)	PC 12	Osteoporosis ASA I-II	Age, gender, smoking, chemotherapy, radiation, steroids intake	NR	N	Zoledronate NSM	5 mg/year N	12–36 months	IV N
Memon et al. (2012)	RC NR	Osteoporosis	Age, gender, IV BPs	Smoking (3), type II DM (3), bone graft (44)	NR	Alendronate (72), risedronate (23), ibandronate (5)	NR	≤12 months (20), 13–35 months (19), ≥36 months (15), unspecified (46)	Oral
		ASA I-II		Smoking (5), type II DM (4), bone graft (44)		NSM	N	N	N

Subjects (*n*)	Age (years)	Gender (M/F)	Implants (*n*)	Failure (months)	Marginal bone loss (mm)	Implant survived (rate: %)	Implant failure (rate: %)	Biological complications	Comments
30	62.4	NR	26	NR	NR	25 (96.16%)	1 (3.84%)	NR	Retrospective radiographic study. Non-BP group had also osteoporosis with teriparatide hormone therapy. Statistical analysis methods were not clarified. Poor demographic data.
	63.1		32			31 (96.88%)	1 (3.12%)		
2060	50.58 ± 12.96	992/1138	84	N	NS	84 (100%)	0 (0%)	NR	All implant surgery was performed by one clinician as well as radiographic assessment. Poor demographic data. The regime and duration for BPs treatment were not specified. The length of marginal bone loss was not specified; however, marginal bone loss was greater in BPs.
			4507	NR		4475 (99.3%)	32 (0.7%)	22 failed before loading, 4 failed related to peri-implantitis, 6 failed due to biomechanical reason	
11	69.6 ± 5.2	NR	25	<12	NR	22 (88.9%)	3 (11.1%)	NR	Retrospective radiographic study on university setting. Poor demographic data. Patients taking BP with early implant failure had significantly higher cortical BMD. All three implants failed within 1 year. The type of BPs was not reported.
14	67.3 ± 4.2		28	NR		28 (100%)	0 (0%)		
415	59.4 ± 13.3	174/237	39	NR	NR	35 (89.7%)	4 (10.3%)	NR	Increasing age and no use of BP were associated with implant failure. Multiple surgeons involved in implant installment. MRONJ was not reported as consequence of implant therapy. The regime and duration for BPs treatment were not specified.
			376			318 (84.6%)	58 (15.4%)		
24	≥54	F	60	N	NR	60 (100%)	0 (0%)	NR	Prospective cohort study with university setting- Subjects in BP group received IV zoledronate for 2–3 years. Single implant system (3.7-mm wide and 16-mm long) was used and all implants were immediately inserted after extraction in the anterior mandibles. 1 year of follow up.
	≥54		60			60 (100%)	0 (0%)		
100	66 ± 9	F	153	Before loading	0.81 ± 1.02 mm	143 (93.5%)	10 (6.5%)	NR	Retrospective database on university and local clinic setting. Patients were excluded from the test group if a history of intravenous bisphosphonate use. No data of long-term dental implant failure, overall follow up was not specified.
100	63 ± 9		132	Before loading	0.78 ± 0.71 mm	126 (95.5%)	6 (4.5%)		

(Continues)

TABLE 1 (Continued)

Authors (year)	Study design and mean follow-up (months)	Systemic condition	Other controlled factors	Confounding factors reported (subjects; *n*) a: success b: failed	MRONJ incidence (*n*)	Medication (subjects; *n*)	Dosage (mg/mL)	Therapy length (months) (*n*)	Administration route
Zahid et al. (2011)	RC 26 (2–78) NR	Osteoporosis	Adequate oral hygiene, absence of local inflammation or diseases, pocket depths ≤3 mm	Smoking (56), osteoporosis (51), bone graft (173)	N	BPs	35 mg/week (5), 70 mg/week (12), unspecified (7), Boniva (2)	≤12 months (1), 13–35 months (7), ≥36 months (8), unspecified (10)	NR
		ASA I-II				NSM	N	N	N
Bell et al. (2011)	RC NR	NR	N	Smoking, DM, periapical lesion	NR	BPs	NR	NR	NR
						NSM	N		
Famili et al. (2011)	RC 12 NR	Osteoporosis, osteoarthritis	Age, gender, IV BPs	Smoking, DM	N	BPs	NR	<12 months (6), ≥12 months (9), ≥60 months (5), unspecified (2)	Oral
						NSM	N	N	N
Koka et al. (2010)	RC NR	Osteoporosis/osteopenia	Age, gender	Smoking (a: 2, b: 0), DM (a: 10, b: 0), osteoporotic (a: 49, b: 0), steroids (a: 5, b: 0), HRT (a: 30, b: 1)	NR	BPs	NR	<36 months (16), 36–59 months (20), ≥60 months (19)	NR
		NR		Smoking (a: 7, b: 1), DM (a: 8, b: 0), steroids (a: 5, b: 0), HRT (a: 46, b: 2)		N	N	N	N
Kasai et al. (2009)	RC 84.3 (64–146)	Osteoporosis	Age, gender, date and number of implants	NR	N	Alendronate	NR	>36 months	Oral
		NR				N	N	N	N
Grant et al. (2008)	RC NR	NR	Age, gender and number of implants	Steroids (3), DM (2), bone graft (6)	N	N	N	N	N
				Bone graft (26)					
Jeffcoat (2006)	PC 36	Osteoporosis	Age, gender, two-stage installment	Smoking (1)	N	BPs (alendronate & risedronate)	NR	3 ± 0.1 years	Oral
				Smoking (1)		N	N	N	N

Subjects (*n*)	Age (years)	Gender (M/F)	Implants (*n*)	Failure (months)	Marginal bone loss (mm)	Implant survived (rate: %)	Implant failure (rate: %)	Biological complications	Comments
26	56 (17–87)	1/25	51	<2	NR	48 (94.1%)	3 (5.9%)	NR	Retrospective database on university setting. A statistically significant association was found between implant thread exposure and use of BP ($p = .001$; odds ratio = 3.25). Cases without follow up radiographs were excluded.
274		NR	610	NR		594 (97.4%)	16 (2.6%)		
655	NR	NR	24	N	NR	24 (100%)	0 (0%)	NR	Retrospective database on private clinic setting. All implants were immediately inserted after extraction. Poor demographic data. Type of BPs, therapy length, and systemic conditions were not specified.
			898	NR		883 (98.3%)	15 (1.7%)		
22	≥50	F	75	Early	NR	74 (98.7%)	1 (1.3%)	NR	Retrospective cohort study based on university setting. Lack of long-term outcome of dental implant. 7 implants were placed in osteoporotic patients, but data on patient-level were not reported. The number of each type of BPs was not specified. Poor demographic data.
5	≥50		7	N		7 (100%)	0 (0%)		
55	71 (50–93)	F	121	NR	NR	120 (99.2%)	1 (0.8%)	NR	Retrospective review on medical chart and phone survey. As data collection relied on self-reporting, reliability and accuracy of data may be insufficient.
82	66 (50–89)		166	NR		163 (98.2%)	3 (1.8%)		
11	52–73	F	35	Early (2), 33 months (2), 11 months (1)	NR	30 (85.7%)	5 (14.3%)	NR	Retrospective database on university setting. Poor demographic data. Confounding factors are not specified.
40	>36		161	NR		154 (95.7%)	7 (4.3%)		
40	>36	F	161	NR	NR	154 (95.7%)	7 (4.3%)	NR	Retrospective review on medical chart and online survey regarding BPs. Systemic conditions were not specified. Patients who received BPs prior to implant placement were only included. Poor demographic data.
343			1450			1436 (99%)	14 (1%)		
25	NR	F	102	N	NR	102 (100%)	0 (0%)	NR	Prospective single-blind controlled study. Confounding factors are not specified. Two-stage installment and fixed screw-retained protheses were used.
25			108	NR		107 (99.2%)	1 (0.8%)		

(Continues)

TABLE 1 (Continued)

Authors (year)	Study design and mean follow-up (months)	Systemic condition	Other controlled factors	Confounding factors reported (subjects; *n*) a: success b: failed	MRONJ incidence (*n*)	Medication (subjects; *n*)	Dosage (mg/mL)	Therapy length (months) (*n*)	Administration route
After implant placement									
Kim et al. (2020)	RC 85.26 ± 36.72 83.49 ± 41.51	NS	Age, gender, extensive MRONJ, surgical resection in the jaw	Smoking (30), DM (95), alcohol (31), bone graft (80), HTN (124)	11	Denosumab (55), ibandronate risedronate alendronate and zoledronate	NR	≤12 months (87), 13–35 months (130), ≥36 months (127)	IV (71), oral (218), Subcutaneous (55)
		ASA I-II		Smoking (21), DM (82), alcohol (27), bone graft (97), HTN (111)	N	NSM	N	N	N

Note: Studies reporting on implant failure in patients exposed to ARD were only listed, and single-arm case studies were excluded.

Abbreviations: ARD, anti-resorptive drugs; ASA, American Society of Anesthesiologists; BP, bisphosphonate; DM, diabetes mellitus; F, female; HRT, hormone replacement therapy; M, male; MRONJ, medication-related osteonecrosis of the jaws; N, none; NR, not reported; NSM, no specific medications; PC, prospective cohort; RC, retrospective cohort.

Inhibited differentiation and activation of osteoclasts by denosumab, which in turn decreases bone turnover, suggests that dental implant installation may trigger the development of MRONJ. Trauma caused by drilling in bone tissue requires active bone remodeling, and peri-implant inflammation during the healing period or induced by the deposition of dental plaque may interfere with normal physiological bone metabolism at these sites. Additionally, decreased bone turnover may impair the repair of microcracks or cause microdamage to the alveolar bone around the implant fixture under load, leading to sequestration around the implant. Therefore, it may be hypothesized that denosumab contributes to the occurrence of MRONJ around the early or late stages of implant function and incidence of implant failure.

5 | IMPLANT THERAPY IN PATIENTS RECEIVING BISPHOSPHONATES

5.1 | Implant failure

Although several attempts have been made to reveal the possible association between BPs and dental implant failure, this review still noted the absence of well-designed prospective studies. Most of the studies included in this review were retrospectively designed cohort studies and only two were controlled prospective studies.

Thirteen studies on implant failure in patients exposed to BPs at the time of implant placement were found according to the inclusion criteria and listed in Table 1 (Al-Sabbagh et al., 2015; Bell et al., 2011; Famili et al., 2011; French et al., 2019; Grant et al., 2008; Jeffcoat, 2006; Kasai et al., 2009; Koka et al., 2010; Memon et al., 2012; Pandey et al., 2019; Yajima et al., 2017; Zahid et al., 2011). Altogether, 1263 dental implants were placed in individuals who had been exposed to BPs. Of them, 30 implants failed with an overall survival rate of 97.6%. Individuals not exposed to BPs received 8535 implants, of which 153 implants failed. Thus, the overall survival rate was 98.2%. Results from the literature suggest that individuals exposed to BPs may not be at a higher risk of dental implant failure than that of individuals not exposed to BPs. Nine out of 13 studies specified the timing of implant failure. Again, seven studies that had at least one implant failure reported that 20 out of 22 failed implants were early failures. These occurred less than 1 year after implant placement. In addition, none of the studies reported the incidence of MRONJ after implant placement, regardless of implant failure.

A previous consensus review study (Chappuis et al., 2018) was in accordance of this finding, which demonstrated that the effect of BPs could not be concluded (OR: 1.11). Another systematic review also reported that low-dose BP administration did not negatively affect the outcomes of dental implant therapy (Stavropoulos et al., 2018). According to a retrospective propensity-matched national cohort study, dental implant placement was not a risk factor, and patients with dental implants presented with a rather low hazard ratio, while dental extraction was confirmed as a risk factor (Ryu et al., 2021). Nonetheless, since BPs have a relatively longer retention half-life, confounding factors, including given dosages and therapy duration, must be considered as well as additional surgical procedures. Owing to the limitations of retrospective studies, these factors were reported heterogeneously among the studies, making it impossible to analyze them. These provided us with headroom for the interpretation of the presented data. It is noteworthy that the odds of oral BPs use was 2.5 times greater in patients with implant failure than those without implant failure in a case–control study, which was not listed due to the patient-level data (Yip et al., 2012).

5.2 | Late failures after loading

According to the literature reporting late failure, the timing of anti-resorptive drug (ARD) therapy in patients who have received implant therapy is not well reported (Table 2). The continuous effects

Subjects (*n*)	Age (years)	Gender (M/F)	Implants (*n*)	Failure (months)	Marginal bone loss (mm)	Implant survived (rate: %)	Implant failure (rate: %)	Biological complications	Comments
344	67.7 ± 7.2	38/340	344	NR	NR	Overall 310 (90.12%), denosumab 50 (90.91%), Oral 204 (93.58%), IV 56 (78.9%)	Overall 34 (9.88%), denosumab 5 (9.09%), Oral 14 (6.42%), IV 15 (21.1%)	NR	Retrospective cohort study with university setting. A reason for anti-resorptive treatment was not report. The length of marginal bone loss was not specified. IV administration of anti-resorptive had the highest implant failure rate.
378	67.0 ± 7.3	30/314	378			363 (96.03%)	15 (3.97%)		

of previous or current antiresorptive therapy after osseointegration of implants are unclear. Since most dentists are now aware of the possible risk of failure related to long-term ARD therapy and avoid dental surgeries as much as possible, number of late failures in patients receiving ARD therapy started before implant placement is rarely reported from the literature.

In the first report on osteonecrosis related to dental implants, the authors suggested two clinically possible subtypes based on the time elapsed from implant placement to the development of osteonecrosis (Lazarovici et al., 2010). Among the 27 patients, 77.8% had 'spontaneous' osteonecrosis and this might suggest that the successfully integrated implants might be a risk for MRONJ. However, there have been no prospective cohort studies or systematic reviews on late implant failure related to sequestration, and only a few retrospective single-arm cohort studies and case series are available (Table 2).

Regarding the nomenclature, there is no widely accepted terminology describing osteonecrosis around successfully integrated implants.

- BRONJ associated with dental implant (Lazarovici et al., 2010).
- Implant-related BRONJ (Kwon et al., 2014).
- Peri-implant MRONJ (Troeltzsch et al., 2016).
- Implant presence-triggered osteonecrosis (Escobedo et al., 2020; Giovannacci et al., 2016).
- Peri-implantitis like MRONJ (Tempesta et al., 2022).

Among the terms proposed in the above studies, "implant presence-triggered osteonecrosis" may be the most frequently used to refer to this type of failure of long-term functioning implants. This is because this term may be differentiated from implant failure due to the surgical trauma of implant surgery, referred to as "implant surgery-triggered osteonecrosis" (Escobedo et al., 2020). Nevertheless, the presence of an implant cannot establish a cause- and -effect relationship because of the lack of scientific evidence. Therefore, the term "implant presence-triggered osteonecrosis" is currently considered premature.

The common clinical feature is "en block" style failure wherein the implant is still osseointegrated in the dead bone (Kwon et al., 2014; López-Cedrún et al., 2013; Pogrel & Ruggiero, 2018). This phenomenon is distinct from traditional type of implant failure, which may result from osseointegration failure or progression of peri-implantitis. We propose the term implant-related sequestration (IRS) to refer to this type of late implant failure combined with sequestration.

Recently, Escobedo et al. (2020) claimed that a functional load of 6 months or more would be a critical point in determining whether necrosis is implant-triggered. In most studies reporting IRS, the onset time of MRONJ lesions ranged from 6 to 126 months, although some missing records were observed (Table 2). According to a review (Escobedo et al., 2020), the loading time before the onset of MRONJ was 44.4 months based on their literature review and 89.6 months in their cases.

5.2.1 | Peri-implantitis as a risk of late failure or implant- related sequestration

As mentioned above, peri-implantitis may play a role in the development of IRS (Pichardo et al., 2020; Tempesta et al., 2022; Troeltzsch et al., 2016). Troeltzsch et al. (2016) reported that 39% (46 out of 117) of implants involved in MRONJ lesions showed signs of peri-implantitis. In a small retrospective cohort study, the majority of cases (14 out of 18 cases) showed signs of peri-implantitis (Pichardo et al., 2020). Another study reported that 19 osteoporosis patients had MRONJ associated with peri-implantitis (Tempesta et al., 2022).

Although peri-implantitis is considered a possible risk factor of IRS, the pathological mechanism has not yet been fully elucidated. Large areas of bone resorption were observed at the implant-bone interface, which might suggest that peri-implantitis may contribute

to IRS (Tempesta et al., 2022). This peri-implantitis origin theory of IRS is a part of the "outside-in" process (Hansen et al., 2006) suggested for the development of MRONJ, which may start from the soft tissue breakdown due to peri-implant mucositis, and infection may spread down to the bone. The pivotal role of infections in the pathogenesis of MRONJ is generally accepted (Boff et al., 2014; Sedghizadeh et al., 2008; Wei et al., 2012; Zirk et al., 2019) and the microbial profile may be similar to that of pre-existing dental infection, such as periodontitis or any odontogenic infection (Kumar et al., 2010). Inflammatory reactions, whether it is derived from infection or not, are considered a potential risk factor for the development of MRONJ (Lesclous et al., 2009; Otto, Hafner, et al., 2010; Otto, Pautke, et al., 2010).

Local inflammation may result in acidic conditions, which may aggravate the cytotoxicity of N-BPs (Otto, Hafner, et al., 2010; Otto, Pautke, et al., 2010). It may also be assumed that increased acidity during

TABLE 2 Studies reporting on medication-related osteonecrosis of the jaw involved in dental implant.

Authors (year)	Study design	Implant surgery or implant presence	Subjects (sample size)	Timing of ARD therapy (IMP-ARD/ ARD-IMP)	Systemic condition (*n*)	Medication (*n*)/duration (months)
Tempesta et al. (2022)	Case series	Presence	19	19/0	Osteoporosis (19)	Alendronate (6)/NR Denosumab (5)/NR Risedronate (4)/NR Clodronate (2)/NR Ibandronate (2)/NR
Seki et al. (2021)	Case report	Presence	1	1/0	Hypercalcemia and Osteoporosis due to Hyperparathyroidism (Thyroid cancer)	Alendronate/NR
Escobedo et al. (2020)	Case series	Presence	7	NR	Multiple myeloma (3) Osteoporosis (2) Rheumatoid arthritis (1) Spondylitis (1)	Zoledronate IV (3)/NR Risedronate + Denosumab (1)/NR Alendronate + Denosumab (1)/NR Alendronate (2)/NR
Pichardo et al. (2020)	RC	Presence	18	14/4	Osteoporosis (11) Cancer (7)	Zoledronate IV (2)/NR Pamidronate IV (3)/NR Alendronate (8)/NR Risedronate (2)/NR Denosumab (3)/NR
Nisi et al. (2020)	Case series	Presence	15	NR	Osteoporosis (7) Metastatic breast cancer (4) Multiple myeloma (3) Metastatic prostate cancer (1)	Alendronate (6)/64.5 months Ibandronate (2)/48 months Neridronate (2)/40 months Zoledronate IV (6)/18.3 months Denosumab (1)/10 months
Pogrel and Ruggiero (2018)	Case series	Presence	11	11/0	Osteoporosis (8) Metastatic bone disease (2)	Alendronate (8) Zoledronate (1) Denosumab (2) All longer than 24 months
Zushi et al. (2017)	Case report	Presence	1	0/1	Osteoporosis	Alendronate/48 months
Giovannacci et al. (2016)	RC	Surgery	6	NR	Osteoporosis (5)	Ibandronate/60 months Ibandronate + Alendronate/108 months Alendronate/67.7 months Ibandronate + Zoledronate IV/131 months
		Presence	9		Breast cancer (5) Lung cancer (1) Multiple myeloma (3) Osteoporosis (1)	Zoledronate IV/73 months Zoledronate and/or Pamidronate IV 35. 6 months Alendronate
Troeltzsch et al. (2016)	RC	Surgery Presence	1 15	34/0	Cancer (1) Cancer (12) Osteoporosis (3)	Zoledronate IV/32.3 months Zoledronate IV/32.3 months Pamidronate IV/32.3 months Ibandronate/32.3 months Denosumab/32.3 months
Favia et al. (2015)	Case report	Presence	1	1/0	Breast cancer	Zoledronate IV/33 months

inflammatory conditions caused by periodontal pathogens may increase BP release from the alveolar bone, where BP accumulated due to long-term anti-resorptive therapy. The released BP may exert detrimental effects on various cells near dental implants, resulting in worsened local conditions via increased cytotoxicity to osteoclasts, endothelial cells, and gingival soft tissue cells (Figure 1). However, it is important to note that the possible role of acidic conditions in the development of osteonecrotic lesions remains yet an experimental theory.

5.2.2 | Mechanical stress as a risk of late failures

Long-term BP therapy may decrease the toughness of the bone and long-term mechanical stress may damage the bony structure by developing microcracks (Allen & Burr, 2011). Microdamage and microcracks are repaired by osteoblasts because of the release of local mediators from the bone by osteoclastic bone resorption (Canalis et al., 2007). The possible role of mechanical trauma begins with understanding

Location of MRONJ (*n*)	MRONJ stage	No. implant with MRONJ/No. implant placement	Time from implant to MRONJ (months)	Treatment	Outcome (*n*)	Peri-implantitis
Mn (14) Mx (6)	NR	Mn (24) Mx (13)	45	Explantation	NR	Yes
Mx.	II	2/2	126	Explantation Sequestrectomy	Resolution	Yes
Mx (1) Mn (2)	II (1) III (6)	13 (total)	NR	Sequestrectomy (6) Sequestrectomy and Osteosyntesis (1)	Favorable (5) No resolution (2)	NR
Mx (6) Mn (12)	II (9) III (9)	30/47	NR	Sequestrectomy	Resolution	NR
Mn (10)	II (3) III (12)	11/29	NR	Sequestrectomy	Resolution (86.7%)	NR
Mx (2) Mn (9)	NR	NR	NR	Explantation Sequestrectomy	Resolution	NR
Mn (1)	III	2/13	24	Sequestrectomy	Resolution	Yes
Mx (2) Mn (2) Both (2)	I–III	3/12	2–10	Sequestrectomy	Resolution	NR
Mx (1) Mn (5) Both (3)	II (5) III (2) NR (2)	5/22	18–96	NR		
NR Mx (13) Mn (2)	NR	2/117 15/117	NR 37.6	Sequestrectomy	NR	Yes
Mn (1)	NR	4/7	60	Mandibular partial resection with involved 4 implants + antibiotics	Resolution	NR

(Continues)

TABLE 2 (Continued)

Authors (year)	Study design	Implant surgery or implant presence	Subjects (sample size)	Timing of ARD therapy (IMP-ARD/ ARD-IMP)	Systemic condition (*n*)	Medication (*n*)/duration (months)
Marín-Fernández et al. (2015)	Case report	Presence	1	1/0	Breast cancer	Zoledronate IV/14 months
Junquera et al. (2014)	RC	Surgery	1	NR	Osteoporosis	Alendronate/48 months
		Presence	1		Multiple myeloma	Zoledronate IV/17 months
Holzinger et al. (2014)	RC	Surgery	13	3/10	Multiple myeloma (3) Osteoporosis (5) Breast cancer (3) Lung cancer (1) HLC (1)	Zoledronate IV (7)/NR Alendronate (3)/NR Pamidronate (2)/NR Ibandronate (1)/NR
		Presence	15		Cancer (12) Osteoporosis (3)	Zoledronate IV/32.3 months Pamidronate IV/32.3 months Ibandronate/32.3 months Denosumab/32.3 months
Kwon et al. (2014)	Case series	Surgery	3		Osteoporosis (2) Multiple myeloma (1)	Alendronate/22 months Ibandronate IV/9 months Zoledronate IV/55 months
		Presence	16	16/3	Osteoporosis (16)	Pamidronate IV/18 months Risedronate/57 months Alendronate/24 months
López-Cedrún et al. (2013)	Case series	Presence	9	NR	Osteoporosis	Alendronate/71 months Ibandronate/62 months Risedronate/48 months
Jacobsen et al. (2013)	RC	Presence	14	NR	Multiple myeloma (2) Breast cancer (5) Prostate cancer (1) Lung cancer (1) Osteoporosis (5)	Zoledronate IV (8) Pamidronage IV (2) Pamidronate + Zoledronate IV (1) Alendronate (2) Ibandronate (1)
Yuan et al. (2012)	Case report	Presence	1	1/0	Osteoporosis	Risedronate/24 months Alendronate/1 months
Lazarovici et al. (2010)	Case series	Surgery	6	NR	Osteoporosis (11) Multiple myeloma (7) Breast cancer (7) Prostatic cancer (2)	Alendronate (6)/63.5 months Zoledronate IV (1)/13 months
		Presence	21	4/17		Alendronate (5)/72.4 months Zoledronate IV (6)/57 months Pamidronate IV (5)/50.2 months Pamidronate + Zoledronate IV (4)/53 months
Goss et al. (2010)	Case series	Surgery	3		Osteoporosis	Alendronate (1)/60 months Risedronate (2)/68 months
		Presence	4	4/0		Alendronate (4)/58.5 months Risedronate (1)/10.5 months
Shirota et al. (2009)	Case report	Presence	1	1/0	Breast cancer (1)	Pamidronate + Zoledronate IV/17 months

Abbreviations: ARD, antiresorptive drug; ARD-IMP, ARD therapy before implant therapy; IMP-ARD, the implants before ARD therapy; Mn, mandible; MRONJ, medication-related osteonecrosis of the jaws; Mx, Maxilla; NR, not reported; RS, retrospective single-arm study.

the action of osteocytes in monitoring trauma and transmitting injury signals. Since an empty lacuna is a typical histological hallmark of MRONJ, mechanotransduction factors may be considered as a possible etiological factor of MRONJ (George et al., 2018, 2019). According to traditional biomechanical theory, excessive strain (>3000 με) would cause pathologic mechanical bone failure (Stanford & Brand, 1999), and such a strain may be observed in the peri-implant bone under an oblique load of 100 N (Chou et al., 2010).

Some studies have investigated the possible relationship between microcracks and MRONJ. In a scanning electro-microscopic study of human histopathological specimen, microcracks were significantly more frequent in MRONJ samples (82%) than in ordinary osteomyelitis of the jaw or osteoradionecrosis which is another type of avascular necrosis (Hoefert et al., 2010). In this study, no microcracks were observed in OM or RA. This finding was confirmed by an animal study that showed that unrepaired microcracks may be associated with the development of MRONJ (Kim et al., 2016).

Long-term occlusal stress demands increased bone remodeling, and as the BP-accumulated bone cannot meet the upregulated

Location of MRONJ (*n*)	MRONJ stage	No. implant with MRONJ/No. implant placement	Time from implant to MRONJ (months)	Treatment	Outcome (*n*)	Peri-implantitis
Mx (1)	III	1/3	60	Subtotal maxillectomy	Resolution	Yes
Mn (1) Mx (1)	III II	1/2 2/2	5 18	Sequestrectomy	Resolution	NR
Mx (1) Mn (12)	NR	10/47	4	NR	Resolution	NR
Mx (13) Mn (2)		20/47	50.8	Sequestrectomy		
Mx (3)	II, III	2 (total)	4	Sequestrectomy (1)	NR	NR
Mx (7) Mn (8) Both (1)	III (14) II (2)	19 (total)	30.18	Sequestrectomy (14)		
Mx (3) Mn (11)	NR	12/57	34	Sequestrectomy	Resolution (7) No resolution (2)	NR
Mx (4) Mn (8)	NR	12/23	20.9 months (Malignant disease: 17 months Osteoporosis: 25.6 months)	Sequestrectomy (10)	Resolution (9) - one patient died due to underlying disease	Yes
Mn.	NR	2/2	120	Sequestrectomy Explantation	Resolution	Yes
Mx (7) Mn (20)	NR	NR	1.8 23.8	Antibiotics Explantation	Resolution (12) No resolution (15)	NR
NR	NR	3/7 6/12	3 NR	NR	Resolution	NR
Mx (1)	NR	2/2	NR	Sequestrectomy	Resolution	NR

remodeling, this may lead to sequestration of the microdamaged area due to failure of the bone repair mechanism (Mine et al., 2022). Because MRONJ may be primarily an aseptic process (Lesclous et al., 2009), long-term occlusal trauma would cause inflammation in the bone, and this may initiate osteonecrosis underneath the soft tissue. However, there are no clinical data on IRS due to mechanical stress, and only experimental data are available. The pathophysiology of MRONJ and IRS is multifactorial. Therefore, it does not sufficiently account for the relationship between mechanical overload and IRS.

5.3 | Implant failures related to other factors

Among the 13 studies that reported implant failure in patients previously exposed to BPs before implant placement, 9 studies specified the therapeutic indication for BPs treatment. All these studies demonstrated that BPs were administered to osteoporosis patients, and this implied that low-dose regimens were used. A total of 648 implants in the studies were placed and 24 implants failed, with a survival rate of 96.3%, which was comparable to the overall survival rate of 97.6%. There was only one prospective study that investigated

TABLE 3 Adverse events of denosumab related to dental implant and/or osteonecrosis of the jaw.

Authors (year)	Study design	Subjects (sample size)	Follow up (months)	Systemic condition	Dosage (mg/mL)	Therapy duration (months)	Outcome parameter	Implant related events	ONJ incidence	Drug therapy at time of implant
Andersen et al. (2022)	PS	7 (15 implants)	5	Malignancy	Various	25	Implant failure	0	0	Drug holiday at least 2 months
Kim et al. (2020)	RC	55	85.26±36.72	NS	NS	NS	Implant failure	5 out of 55 implants failed	0	Implants inserted before medication
Watts et al. (2019)	RCT	4550	≤120	Osteoporosis (female)	60 mg/6 months	120	Adverse effect	1 out of 212 patients developed ONJ around implant	13	Yes
Raje et al. (2018)	RCT	850	24	Malignancy	120 mg/4 weeks	15.8	Adverse effect	NR	35	NR
Stopeck et al. (2016)	RCT	465	34–41	Malignancy	120 mg/4 weeks	10.2–18.4	Adverse effect	NR	32	NR
Henry et al. (2014)	RCT	792	24–30	Malignancy	120 mg/4 weeks	6.7	Adverse effect	NR	6	NR
Chawla et al. (2013)	RCT	281	24	Malignancy	120 mg/6 months	7–20	Adverse effect	NR	3	NR
Scagliotti et al. (2012)	RCT	395	NR	Malignancy	120 mg/4 weeks	NR	Adverse effect	NR	3	NR
Lipton et al. (2012)	RCT	2841	8.2	Malignancy	120 mg/4 weeks	NR	Adverse effect	NR	52	NR
Smith et al. (2012)	RCT	676	36	Malignancy	120 mg/6 months	20.2	Adverse effect	NR	33	NR
Henry et al. (2011)	RCT	878	27	Malignancy	120 mg/4 weeks	7	Adverse effect	NR	10	NR
Fizazi et al. (2011)	RCT	943	41	Malignancy	120 mg/4 weeks	12.2	Adverse effect	NR	22	NR
Stopeck et al. (2010)	RCT	1020	34	Malignancy	120 mg/4 weeks	8	Adverse effect	NR	20	NR

Note: The studies from Kim et al. (2020) and Andersen et al. (2022) consisted of patients taken various anti-resorptive drugs such as bisphosphonate and denosumab, and the data related to denosumab were only extracted, accordingly.

Abbreviations: N, none; NR, not reported; NS, not specified; ONJ, osteonecrosis of the jaws; PS, prospective case series; RC, retrospective cohort; RCT, randomized controlled trial.

TABLE 4 Methotrexate and dental implant.

Authors (year)	Study design	Subjects (sample size)	Follow up (months)	Systemic condition	Medication & dosage (mg/mL)	Therapy duration (months)	Outcome parameter	Implant related outcome	ONJ incidence	Drug therapy at time of implant
Weinlander et al. (2010)	Case series	22 (89 implants)	36	RA, CTD	CS, MTX	14–91	Implant failure	3 of 89 implants failed	NR	Yes
Eder and Watzek (1999)	Case report	1 (6 implants)	60	Osteoporosis, Polyarthritis	7.5 mg/week MTX	72	Implant failure	None failed	0	Yes
Tavakoli et al. (2018)	Animal study	8 (48 implants)	1	N	2.5 mg/week MTX	1	Osseointegration	Lesser BIC in MTX group	0	Yes
Carvas et al. (2011)	Animal study	24–32 (24–34 implants)	4	N	3 mg/kg/week MTX	1.5	Osseointegration	Not significant reductions of cortical thickness, total bone area and BIC	0	Yes

Abbreviations: BIC, bone to implant contact; MTX, methotrexate; N, none; NR, not reported.

implant failure in patients who were exposed intravenous (IV) BPs for 2–3 years before implant therapy (Siebert et al., 2015). This demonstrated that the failure did not occur in all groups. In this study, although BPs were administered intravenously, a low-dose regimen was used for osteoporosis patients, and these results may be different from that in patients with malignancy receiving high-dose BPs. A limitation of this study was the follow-up period. Although the study was prospectively designed, data were only collected 1 year after functional loading. Since the prolonged effect of BPs is not negligible, studies on the long-term survival of these implants are crucial.

It is generally accepted that the dose regimen of ARD is much more influential than its route of administration is. However, there is a possibility that IV BPs may be riskier than oral BPs because of the low availability of oral BPs, which is reported to be approximately 0.6% (Gertz et al., 1995). When BPs were orally administered, the proportion of BPs bound to bone tissue is relatively low compared to the total dose administered. A daily or weekly low-dose regime of oral BPs also requires a relatively long time to significantly impact the implant and bone metabolism compared to the effect of a high-dose regime of IV BPs with a low frequency. However, it is inappropriate to focus only on the administration route, and the medication regimen and potency should be considered first.

Current data are insufficient to analyze the long-term survival of implants in patients exposed to BPs. Four studies had a mean follow-up duration of >3 years. The survival rate was 95.2% (179/188) in osteoporosis patients on BPs, while it was 97.3% (320/329) in those not on BPs. However, owing to insufficient sample size and heterogeneous study designs, the longevity of implants in patients receiving BPs remains unclear. The duration and dosage of ARD therapy are also crucial factors for the survival of implants, although the risk could not be estimated, because each study included varying durations of ARD therapy. Considering that BPs have a relatively longer retention half-life, periodic check-ups and maintenance periodontal therapy are recommended to ensure optimal and safe outcomes.

Despite the heterogeneity of the study design and confounding factors, these results suggest that dental implants are viable option for patients receiving BP therapy. However, it would be wise to exercise caution when treating patients with dental implants who are receiving or have received high-dose BPs, particularly in cases where there has been prolonged exposure to them. The major limitation of this review is the absence of well-designed prospective controlled clinical trials. Owing to the potential hazards and medical importance of medications that affect bones, it may be challenging to randomly assign participants. However, a prospective study that controls for other confounding factors, such as the type of medication, therapy duration, follow-up time, and local and systemic conditions must be possible, which is necessary to gain a better understanding of the impact of these medications on implant failure. Additionally, information on peri-implant health was not included in the available studies. Standardized measurement and reporting of these factors would help reveal how peri-implant tissues respond to these medications and potentially lead to implant failure.

TABLE 5 Corticosteroids and dental implant.

Authors (year)	Study design	Subjects (sample size)	Follow up (months)	Systemic condition	Medication & dosage (mg/mL)	Therapy duration (months)	Outcome parameter	Implant related outcome	ONJ incidence	Drug therapy at time of implant
Carr et al. (2019)	RC	6358	70	Various	Various	NR	Implant failure (patient level data)	HR 0.72 (0.60–0.86)	NR	Yes
Krennmair et al. (2010)	Case series	34 (126 implants)	47.6	RA, CTD	CS, NSAID	NR	Implant failure	7 of 126 implants failed	NR	Yes
Weinlander et al. (2010)	Case series	22 (89 implants)	36	RA, CTD	CS, MTX	14–91	Implant failure	3 of 89 implants failed	NR	Yes
Carvas et al. (2010)	Animal study	18 (18 implants)	4.5	N	0.35 mg/kg CS	4.5	Osseointegration	Statistically significant decreases of osseointegration and BMD	0	Yes
Keller et al. (2004)	Animal study	40 (40 implants)	2	N	7.5 mg/kg CS	1	Osseointegration	Statistically significant decrease of BIC	0	Yes
Fujimoto et al. (1998)	Animal study	12 (48 implants)	3	N	10 mg/kg CS	2	Osseointegration	No significant difference in removal torque	0	No

Abbreviations: BIC, bone to implant contact; BMD, bone mineral density; CS, corticosteroid; CTD, connective tissue diseases; HR, hazard ratio; MTX, methotrexate; N, none; NR, not reported; RA, rheumatoid arthritis; RC, retrospective cohort study.

6 | EFFECT OF BISPHOSPHONATE ADMINISTERED AFTER SUCCESSFUL OSSEO INTEGRATION OF IMPLANTS

6.1 | Late failures in functioning implants

The available studies do not provide sufficient information regarding the timing of ARD therapy initiation with the presence of functioning implants. However, some studies have distinguished the timing of ARD therapy based on the presence of functional implants (Table 2). In most cases, implant therapy preceded ARD therapy, which addresses the timing issue. This finding implies that long-term ARD therapy may pose a risk for late failure or IRS. Some studies have included only late failures in patients who received ARD therapy after implant placement (Kim et al., 2020; Pogrel & Ruggiero, 2018; Tempesta et al., 2022; Troeltzsch et al., 2016).

Among them, only one cohort study has investigated the effect of BP treatment in patients with previously osseointegrated implants (Kim et al., 2020). The reported survival rate of implants was 90.0% (260/289). These rates were lower than the overall survival rates reported for patients receiving BP therapy before implant placement mentioned earlier, although statistical comparisons with control groups were not conducted. The mean follow-up period beyond 7 years was longer than that in most other studies, which might explain the difference in results other than dose regime. Besides, delayed exposure to BPs after implant surgery could be a contributing factor, or it is possible that both a longer follow-up period and delayed BP exposure were responsible for the lower implant survival rates observed in this study. However, the specific pathophysiological mechanisms that determine whether delayed BP exposure is more detrimental or not have not been be currently elucidated, and further studies are required to verify them.

Interestingly, 11 of the 34 failed implants were associated with the presence of sequestration, which may be classified as an IRS. The action of BPs may also contribute to detrimental environments even around successfully integrated dental implants. Peri-implantitis, characterized by local inflammation and infection, can exacerbate the cytotoxic effects of N-BPs (Otto, Hafner, et al., 2010; Otto, Pautke, et al., 2010). Additionally, a decreased bone toughness and a long-term occlusal stress causing microcracks around implants may require upregulated bone remodeling, leading to late implant failure and IRS. It is reasonable to think that the same pathophysiology as in the development of IRS and late failure in patients receiving ARD therapy before implant placement could be applied, although it has yet been a hypothetical theory based on retrospective single-arm case studies and experimental models (George et al., 2018, 2019; Mine et al., 2022; Pichardo et al., 2020; Tempesta et al., 2022; Troeltzsch et al., 2016).

6.2 | Implant failures related to other factors

In a cohort study that investigated the effect of BPs treatment in patients who had previously osseointegrated implants (Kim et al., 2020), the survival rates were 93.58% (204/218) for patients treated with

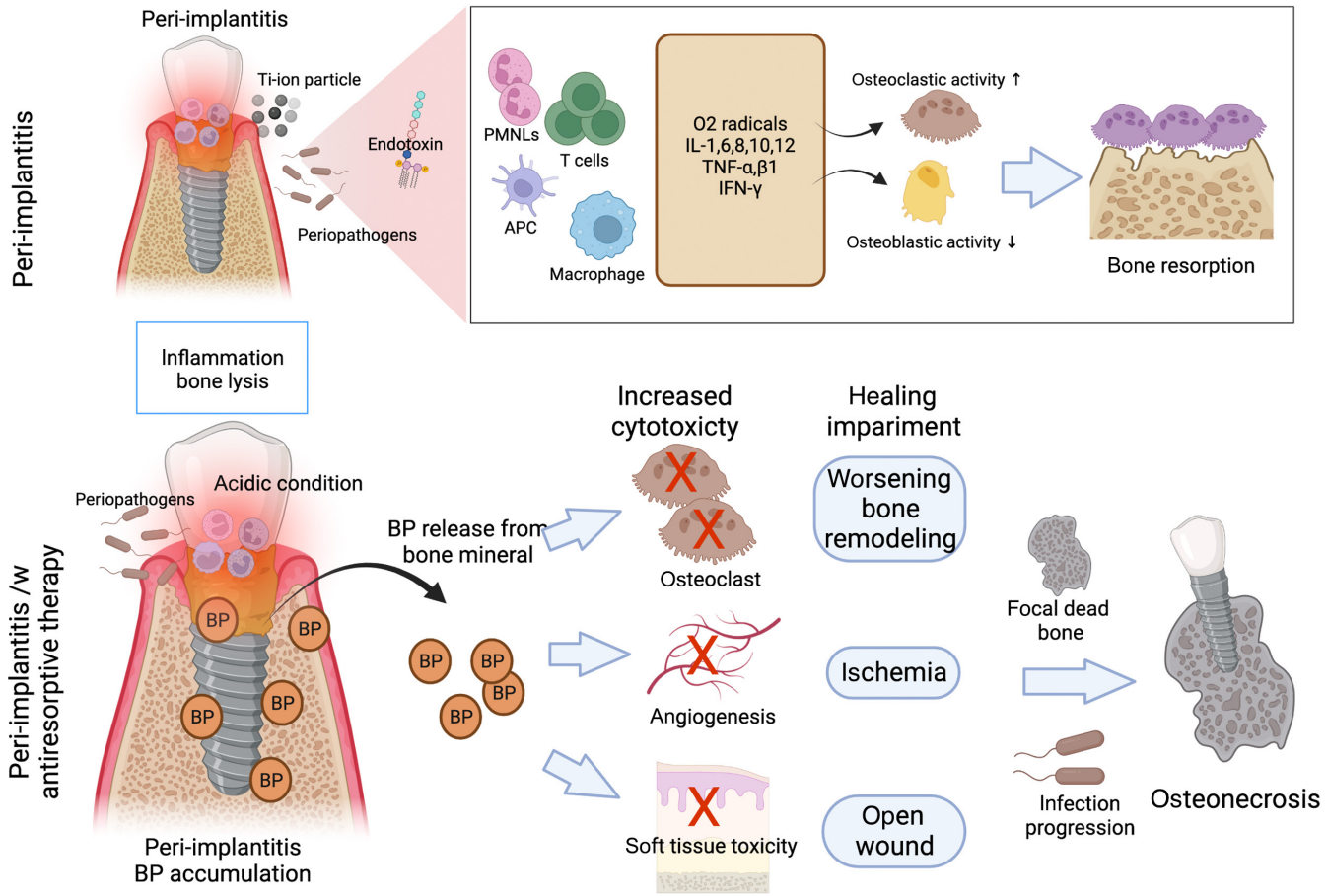


FIGURE 1 Pathophysiology of implant-related sequestration.

oral BPs and 78.9% (56/71) for those treated with IV BPs. The therapeutic indication for IV BPs was not specified in the study; however, considering that IV BPs have usually been prescribed for oncology patients who require high doses at frequent intervals, whereas oral BPs have been administered in low doses for osteoporosis patients (Ensrud, 2021; Khan et al., 2015; Lipton, 2003), it is assumed that a high dose regimen might have been used in majority of patients. Additionally, as mentioned above, the route of administration might also have had an influence on implants failure.

When the cumulative dose reaches a level that may disrupt bone metabolism around functioning implants, the increased metabolic demand caused by peri-implantitis may initiate IRS, as elaborated above (Pichardo et al., 2020). In cases where ARD therapy begins after the successful osseointegration of implants, it may take a considerable amount of time to reach the cumulative dose. Consequently, the development of IRS may be slower compared to patients receiving ARD therapy before implant placement (Pichardo et al., 2020). According to a nationwide study in Japan, the cumulative incidence of MRONJ has increased in a time-dependent manner (Ishimaru et al., 2022). Therefore, the cumulative dose or sustained effect of ARD therapy could be a crucial factor in the late failure or IRS, regardless of the timing difference between ARD and implant therapies.

Regarding the severity of the lesions, staging information was available for 67 patients of the 168 patients who were diagnosed with IRS. Altogether, 46 out of 67 patients (69%) presented with stage 3 lesions. This suggests that when an IRS is detected, it may already be at an advanced stage. No cases of stage 1 disease have been reported in the literature, indicating that early detection of IRS may be challenging. Fortunately, many studies have reported favorable treatment outcomes consistent with the surgical outcomes of MRONJ, as described in Table 2.

Researches investigating the influence of BP duration and dosage on osseointegrated implants are extremely limited. Furthermore, relying solely on one cohort study and case series is insufficient to draw any definitive conclusions on this topic. Given the characteristics of BPs, which accumulate in bone tissue and exert a prolonged suppressive effect on bone remodeling, we can only speculate based on the pathophysiology of MRONJ, and IRS and late failures might also be influenced by the duration and dosage of BP treatment. It is imperative to conduct further research in order to determine the effects of BPs on successfully osseointegrated implants, as the existing literature on this topic is currently very limited.

7 | DENOSUMAB AS A RISK FACTOR FOR DENTAL IMPLANTS

Despite a thorough search, only one retrospective cohort study was found, which investigated the implant failure rate in patients

receiving denosumab or BPs along with non-ARD users (Kim et al., 2020) (Table 3). It demonstrated that the implant survival rates were 96.03% in non-ARD (363/378) and 90.91% (50/55) in denosumab users. However, this study investigated the effect of denosumab in patients who treated with dental implants before ARD therapy, and statistical analysis between the two groups was not performed. Instead, the overall implant survival rate in ARD users was reported to be 90.12%, with a statistically significant difference ($p < .003$) compared to that in non-users. The major limitations of this study include the absence of a comparison of the survival rate of denosumab users with that of controls. In addition, the duration of treatment and dose regimen of denosumab was not demonstrated. Therefore, the results should be interpreted with caution.

Two other studies have mentioned the influence of denosumab on dental implants (Andersen et al., 2022; Watts et al., 2019) (Table 3). However, these were single-arm observational studies in terms of denosumab usage. The overall design of the Phase III clinical trial was a randomized controlled study (Watts et al., 2019); however, of the 212 patients treated with dental implants over the 7 years of data collection, both control and experimental groups received denosumab injections when dental implants were installed (Watts et al., 2019). In this study, only one case of implant-related MRONJ was reported in 212 patients treated with dental implants and it was successfully treated without fixture removal. Another prospective single-arm study demonstrated that there were no early implant failures after 15 implant insertions in seven patients, despite a relatively higher dose regimen for malignancy (Andersen et al., 2022). In addition to the study design and small sample size, the major weakness of this study was that follow-up was not conducted after the implant prosthesis.

Unlike BPs, denosumab does not have an affinity for bone minerals. Based on its pharmacokinetic properties, the effect of denosumab is expected to be eliminated approximately 6 months after injection. Despite the completely different modes of action of BPs and denosumab, some cases of IRS associated with denosumab have also been reported (Pichardo et al., 2020; Pogrel & Ruggiero, 2018; Tempesta et al., 2022; Troeltzsch et al., 2016). In contrast to the release of accumulated drugs such as BPs near dental implants, this does not occur in cases of local infections such as peri-implantitis. However, it is plausible that suppressed bone remodeling and subsequent impaired response to mechanical stress and inflammation could similarly contribute to IRS for both BPs and denosumab.

Due to insufficient data and uncontrolled study design, the impact of denosumab on implant survival is inconclusive, despite the well-documented detrimental effect of denosumab on bone metabolism. Furthermore, drug holidays or therapeutic window periods before implant placement were not included in these studies. Accordingly, whether a drug holiday plays a critical role in implant therapy and how long the drug-free status should be maintained, remain questionable. Owing to the rarity and inconsistency of these outcomes, further studies should be encouraged to thoroughly analyze the topic. Nevertheless, considering the higher prevalence of MRONJ in patients with malignancies, implant rehabilitation should be approached cautiously when high-dose denosumab is administered or is expected.

8 | METHOTREXATE AND CORTICOSTEROIDS AS RISK FACTORS FOR DENTAL IMPLANTS

8.1 | Methotrexate

Rheumatoid arthritis (RA) is a systemic inflammatory autoimmune disorder characterized by progressive joint destruction and various systemic manifestations such as skin, ocular, oral, gastrointestinal, pulmonary, neurological, cardiovascular, and hematological events (Cojocaru et al., 2010; Friberg, 1994; Radu & Bungau, 2021). High levels of proinflammatory cytokines and inflammatory cells have been found in RA patients. The key drugs employed in RA treatment include CS and disease-modifying anti-rheumatic drugs (DMARDs). MTX has long been considered the most effective DMARD and a safe treatment for RA. Initially, high doses of MTX were prescribed as anti-neoplastic agents, but low-dose MTX is now widely administered to patients with RA. However, hindered osseointegration has been suggested because of suppressed osteoclast activation by decreasing RANKL-induced calcium influx into osteoclast progenitors (Cranney et al., 2001; El Miedany et al., 1998; Kanagawa et al., 2016; May et al., 1994; Suematsu et al., 2007).

Administration of MTX may impair osteoblast proliferation. An in vitro study assessed the effects of short-term administration of low-dose MTX in bovine osteoblasts by incubating them for 14 days. Osteoblast proliferation and mitochondrial metabolism were significantly reduced, suggesting that MTX may inhibit bone healing and osseointegration of implants (Annussek et al., 2012). Following these results, animal studies have reported a negative effect on dental implants. In a study using a canine model, a low-dose MTX reduced bone-to-implant contact (BIC), although osseointegration of inserted implant was acceptable (Tavakoli et al., 2018). On the other hand, another study demonstrated that cortical thickness, total bone area and BIC were not significantly different between the control and MTX groups in a rabbit model (Carvas et al., 2011). In a retrospective case series analyzing implant treatment in patients with RA and connective tissue disease (CTD), 13 implants were inserted in patients receiving MTX, and they all survived (Weinlander et al., 2010) (Table 4). A case report also showed that implant failure and peri-implantitis did not occur, despite old age, severe osteoporosis, chronic polyarthritis, and long-term MTX administration during a 4-year observation period (Eder & Watzek, 1999). Although MRONJ has been reported in association with MTX (Furukawa et al., 2018; Henien et al., 2017), only case reports have been found, and additional research is required to determine the relationship between MTX and MRONJ.

Studies on MTX and dental implants are scarce, and contradictory results highlight the need for further studies to determine the effect of MTX on the osseointegration of dental implants and their long-term prognosis.

8.2 | Corticosteroids

Anti-inflammatory, immunomodulatory, and antineoplastic properties of CS are known to be useful in numerous conditions, such as allergic reactions, asthma exacerbations, chronic obstructive pulmonary disease, and autoimmune conditions (Morand, 2007; Wan et al., 2012). However, several studies have indicated that long-term use of CS may lead to osteoporosis in humans as it initially enhances bone resorption and subsequently reduces bone formation and bone turnover (Woolf, 2007). The use of CS induces osteoblast apoptosis, reduces the number of pre-osteoblasts and promotes the differentiation of bone marrow stromal cells into adipocyte-lineage cells (Pereira et al., 2002; Smith et al., 2002; Weinstein, 2001). This results in an imbalance between the osteoclasts and osteoblasts in the bone microenvironment. The effects of CS on bone metabolism, apoptosis, lipid metabolism, and inflammatory pathways have been found to play a role in steroid-induced osteonecrosis (Chang et al., 2020). Likewise, it may be applied to the jaws, which, in turn, increases the risk of MRONJ (Saad et al., 2012). Several studies have discussed CS as a risk factor for the development of MRONJ (Aghaloo & Tetradis, 2017; McGowan et al., 2018; Tsao et al., 2013).

Several have investigated whether CS negatively affects bone healing, bone remodeling, and implant osseointegration (Table 5). In an in vitro study, the cellular attachment to the implant surface was significantly lower in dexamethasone-treated osteoblasts than in the controls (Cho et al., 2006). The CS group also showed a significant reduction in lumbar spine and tibia bone mineral density, BIC, and peri-implant bone area, which were considered osseointegration measurements in a preclinical study (Carvas et al., 2010). Another study reported cortical thinning, irregular trabecular patterns, and impaired extracellular matrix formation, and mineralization were observed as well as decreased BIC after CS administration (Keller et al., 2004). However, the removal torque of implants in the mandible was not significantly different between the CS and non-CS groups in an animal study (Fujimoto et al., 1998).

Only a few clinical studies have reported an association between CS administration and the prognosis of dental implants (Table 5). A retrospective cohort study evaluated the clinical outcomes of dental implants and biological complications in patients with RA with or without CTD. In both groups, marginal bone resorption and bleeding index were slightly higher in patients receiving CS, although the implant survival rate was 100% (Krennmair et al., 2010). Another study also reported a 100% implant survival rate for 46 implants placed in patients receiving CS (Weinlander et al., 2010). Interestingly, a reduced risk of implant failure was reported in a retrospective cohort study wherein CS was used at the time of placement (Carr et al., 2019).

In contrast to preclinical studies reporting decreased BIC, the survival of dental implant may not be influenced by CS treatment, although the evidence is very weak. Well-designed clinical studies regarding the use of CS and dental implants are necessary to determine whether the medication is influential in practice.

9 | OTHER MEDICATIONS AFFECTING BONE METABOLISM

9.1 | Romosozumab

Romosozumab, a monoclonal antibody against sclerotin, has recently been introduced in osteoporosis patients in several countries (AMGEN, 2019; European Medicines Agency, 2019). Unlike anti-resorptive agents that targets the attenuation of osteoclastic function and differentiation, romosozumab targets sclerotin (Baron et al., 2011), an osteocyte-secreted glycoprotein that inhibits osteoblastic activity and differentiation through Wnt/β-catenin signaling, leading to an anabolic effect (Lewiecki, 2014). However, as bone formation increases, a reduction in bone resorption markers has been observed in clinical trials which may lead to the development of MRONJ (McClung & Grauer, 2014; Padhi et al., 2011; Saag et al., 2017). Two events consistent with the definition of MRONJ occurred in a study of 3576 patients during a 24-month trial (Cosman et al., 2016); however, they were not associated with dental implants but with ill-fitting dentures and tooth extraction. Another study reported one case of MRONJ in 230 patients treated with romosozumab for 12 months. In contrast, an animal study using a rat model of MRONJ did not show any suspected osteonecrotic lesions, such as epithelial discontinuity or bone exposure (Hadaya et al., 2019). The number of empty osteocyte lacunae and osteoclasts in the study did not differ from those in the control group. Increased bone mass following romosozumab treatment may help consolidate implant therapy, whereas it may be related to the development of MRONJ and late implant failure. Studies exploring the association among romosozumab and MRONJ are scarce, not to mention dental implant. Further investigations are required to understand how romosozumab affects oral health and rehabilitation.

9.2 | Sunitinib

Sunitinib is an anti-angiogenic agent that inhibits different groups of tyrosine kinase receptors, including receptors for platelet-derived growth factor, vascular endothelial growth factor (VEGF), and stem cell factor (Hoefert & Eufinger, 2010; Mendel et al., 2003; Ramírez et al., 2015). Since angiogenesis plays a significant role in bone healing and remodeling, it has been suggested that sunitinib may alter bone metabolism in alveolar bone, and eventually affect the osseointegration of dental implants (Baldazzi et al., 2012; Paragliola et al., 2023). In addition, the suppression of growth factors may negatively affect biological complications in peri-implant

tissues and osseointegration. In an animal study, the ratio of bone volume to total volume and BIC were significantly lower in the sunitinib-treated group than in the control group (Al-Jandan et al., 2018). Although a clinical study regarding dental implants is yet to be conducted, several case reports and reviews of sunitinib-related osteonecrosis of the jaw have demonstrated abnormal bone healing and remodeling after sunitinib treatment (Abel Mahedi Mohamed et al., 2018; Vallina et al., 2019). Therefore, caution should be exercised when planning dental implants in patients receiving sunitinib until further research identifies the influence of this medication.

9.3 | Bevacizumab

Bevacizumab is a monoclonal antibody used for the treatment of solid, advanced cancers (Ferrara et al., 2004). Bevacizumab induces regression of the immature tumor vasculature and inhibits angiogenesis by preventing the interaction of vascular endothelial growth factor-A with its receptors and subsequent activation (Eguchi et al., 2022). Since angiogenesis is a biologically crucial step in new bone formation and osseointegration of dental implants, anti-angiogenic activity, such as inhibition of the VEGF signaling pathway, may negatively affect the integration of dental implants in the jaw (Raines et al., 2010). In an animal study, osseointegration measured using BIC was significantly lower in the bevacizumab group than in the control group (Al-Jandan, 2019). These findings suggest that impairment of angiogenesis by bevacizumab may have a negative impact on the osseointegration of titanium implants. Although there are no human studies on the relationship between bevacizumab and dental implant failure, some case reports have shown bevacizumab-related osteonecrosis of the jaw around the dental implant (Abel Mahedi Mohamed et al., 2018; Maluf et al., 2019; Ueda et al., 2022).

10 | CONCLUSION

In conclusion, this review highlights the complex relationship between dental implant rehabilitation and medications that alter bone metabolism. While previous publications have generally suggested that BPs do not compromise the survival of dental implants, there has been a report of increased failure of functioning implants after intravenous administration, which is speculated to be a high dose in oncological patients. Furthermore, there is an issue of implant-related sequestration, contributing to late implant failure in patients who had successfully undergone implant therapy before and after antiresorptive therapy. Although evidence is still lacking, peri-implantitis causing local inflammation and accumulation of micro-damage on peri-implant alveolar bone due to impaired bone repair might be associated; however, clinical data are too scarce to conclude the specific mechanisms behind the events. While the impact of denosumab, MTX, and CS on implant survival remains unclear due to insufficient data, their well-documented detrimental effects on bone metabolism underscores the importance of exercising caution when performing implant therapy.

To minimize the risks associated with medications that affect bone homeostasis and implant therapy, clinicians should carefully consider the potential hazards and take appropriate precautions. Additionally, well-designed prospective studies are needed to better understand the mechanisms underlying implant failure and inform clinical practice.

AUTHOR CONTRIBUTIONS

Junho Jung: Methodology; data curation; formal analysis; validation; visualization; writing – original draft; writing – review and editing; investigation. **Jae-In Ryu:** Validation; formal analysis; writing – original draft. **Gyu-Jo Shim:** Data curation; investigation; writing – original draft. **Yong-Dae Kwon:** Conceptualization; methodology; validation; project administration; writing – original draft; writing – review and editing; supervision.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

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

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CONSENSUS REPORT

CLINICAL ORAL IMPLANTS RESEARCH WILEY

Group 3 ITI Consensus Report: Materials and antiresorptive drug-associated outcomes in implant dentistry

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Abstract

Objectives: The aim of Working Group 3 was to address the influence of both material- and anti-resorptive drug- related factors on clinical and biological outcomes and complications in implant dentistry. Focused questions were addressed on (a) implant materials other than titanium (alloy)s, (b) transmucosal abutment materials and (c) medications affecting bone metabolism were addressed.

Materials and Methods: Three systematic reviews formed the basis for discussion in Group 3. Consensus statements and clinical recommendations were formulated by group consensus based on the findings of the systematic reviews. Patient perspectives and recommendations for future research were also conveyed. These were then presented and accepted following further discussion and modifications as required by the plenary.

Bilal Al-Nawas and France Lambert contributed equally to this work and share primary authorship.

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Results: Zirconia is a valid alternative to titanium as material for implant and transmucosal components, allowing soft and hard tissue integration with clinical outcomes—identified by implant survival, marginal bone loss and peri-implant probing depths—up to 5-years comparable to titatnium. However, most of the evidence for zirconia implants is based on 1-piece implants limiting the indication range. Furthermore, based on expert opinion, zirconia transmucosal components might be preferred in the esthetic zone. In patients receiving low-dose bisphosphonate therapy, the rate of early implant failure is not increased, while the long-term effects remain poorly studied. Although it has not been sufficiently addressed, similar outcomes can be expected with low-dose denosumab. A drug holiday is not recommended when considering implant placement in patients treated with low-dose ARD. However, the specific therapeutic window, the cumulative dose and the administration time should be considered. Access to peri-implant supportive care is mandatory to prevent peri-implantitis-related medication-related osteonecrosis of the jaw (MRONJ) or implant-related sequestra (IRS). In patients receiving low-dose anti-resorptive drugs (ARD) therapy, the risk of complications related to implant placement is high, and implant procedures in this specific population should be strictly treated in a comprehensive multidisciplinary center. Finally, healthy dental implants should not be removed before low or high-dose ARD.

Conclusions: Zirconia implants can be an alternative to titanium implants in selected indications. However, the current state of evidence remains limited, especially for 2-piece implant designs. Administration of low-dose ARD did not show any negative impact on early implant outcomes, but careful follow-up and supportive care is recommended in order to prevent peri-implant MRONJ and IRS. Implant placement in high-dose patients must be strictly considered in a comprehensive multidisciplinary center.

KEYWORDS
anti-resorptive drugs, biomaterials, drug delivery, peri-implant tissue integration, pharmacology, structural biology, tissue implant interactions, tissue physiology, wound healing

1 | INTRODUCTION

The objectives of Group 3 of the 7th ITI Consensus Conference were to provide statements and recommendations for clinicians and researchers relating to the **material- and antiresorptive drug-associated outcomes in implant dentistry**. Additionally, considerations from a patient perspective were also addressed. Three systematic/narrative reviews formed the basis for discussion within the working group and were prepared and reviewed before the consensus conference. The reviews were discussed within the group, and consensus statements, clinical recommendations and patient considerations were formulated and then presented to the plenary for approval. The working group also prepared recommendations for future research. The three systematic reviews are listed below.

2 | SYSTEMATIC REVIEW PAPER 1

2.1 | Manuscript title

Clinical and radiographic outcomes of zirconia dental implants—a systematic review and meta-analysis.

2.2 | Preamble

Currently, zirconia is the only (commercially available) material other than titanium (alloy) used for fabricating ceramic dental implants with 1- and 2-piece designs. Evidence-based data has shown that physical properties and ongoing market availability significantly influenced the reported zirconia implant survival

rates. So far, meta-analyses investigating zirconia implants are limited to a follow-up of up to 2 years. The present review aimed to evaluate in clinical studies implant survival, marginal bone loss, probing depths and technical and biological complications of commercially available zirconia implants after at least 5 years of function.

The primary outcome of this systematic review was to investigate implant survival.

Secondary outcomes were peri-implant marginal bone loss (MBL), peri-implant probing (PD) depths, and technical and biological complications.

2.3 | Consensus statements

2.3.1 | Consensus statement 1

Based on the review, only zirconia was found to be a commercially available alternative material to titanium or titanium alloy implants.

2.3.2 | Consensus statement 2

The data after 5 years mainly applies to 1-piece zirconia implants for single crowns and 3-unit implant fixed dental prostheses (iFDP). Regarding 2-piece zirconia implants, only limited data is available.

This statement is based on six clinical cohort studies (four prospective studies, two retrospective studies). A single retrospective study investigated 2-piece implants.

2.3.3 | Consensus statement 3

Zirconia implants show a mean survival rate of 97.2%, range: 93.8%–100% at 5 years, comparable to published data for titanium-based implants.

This statement is based on a meta-analysis (95% CI: 94.7%–99.1%) of six clinical cohort studies (four prospective studies, two retrospective studies).

2.3.4 | Consensus statement 4

Over 5 years, zirconia implants show similar peri-implant tissue health compared to published data for titanium implants (mean MBL of 1.1 mm – range: 0.7–1.2 and mean PD of 3 mm – range: 2.2–3.3). Bleeding on probing could not be compared because of the heterogeneity of the used indices.

This statement is based on a meta-analysis (95% CI: 0.9–1.3 mm for MBL and 2.5–3.4 mm for PD) on five clinical cohort studies.

2.3.5 | Consensus statement 5

Over 5 years, 1- piece zirconia implants for single crowns and 3-unit implant fixed dental prostheses (iFDP) do not show higher fracture risk than titanium implants.

This statement is based on six clinical cohort studies (four prospective studies, two retrospective studies).

2.4 | Clinical recommendations

2.4.1 | Clinical recommendation 1

Can zirconia implants be recommended in daily practice?

Zirconia implants can be an alternative to titanium implants in selected indications. Based on available data for up to 5 years, 1-piece zirconia implants for single crowns and 3-unit implant fixed dental prostheses (iFDP) can be recommended as a treatment option. In clinical indications that require the positioning of the restoration margin submucosally, the cementation process has to be controlled.

It has to be considered that various types and generations of zirconia implants exist today, exhibiting differences in mechanical properties and not all have been validated in clinical studies.

2.5 | Patient perspectives

2.5.1 | Patient perspective 1

Question: Are all implants made of titanium, or are there alternatives?
Answer: In addition to titanium implants, zirconia implants have been available for 20 years (2004).

2.5.2 | Patient perspective 2

Question: What is the difference between titanium and zirconia implants?
Answer: Titanium is a metal and is gray. Zirconia is an oxide ceramic and has a tooth-like color. However, both materials integrate with bone and gums in the same way.

2.5.3 | Patient perspective 3

Question: Do zirconia implants perform as well as titanium implants?
Answer: Studies show that the performance of zirconia implants in terms of survival rate and integration with the bone and gum is the same as titanium implants for up to 5 years. These studies are, however, based on the first type of one-piece zirconia implants. Zirconia

implants have evolved to offer us more options, but there are only limited studies to date on how these newer two-piece designs perform over time. **This statement is based on six clinical cohort studies (four prospective studies, two retrospective studies). A single retrospective study investigated 2-piece implants.**

2.5.4 | Patient perspective 4

Question 5: I have an intolerance to various materials, including metals. Would you recommend that I have a ceramic rather than a titanium implant?
Answer: Intolerance to titanium is scarce. If you prefer a non-metallic material, you can choose a zirconia implant instead. If you do so, you must know that an internal metal screw is needed in some of the newer two-piece zirconia implants to connect the different components. This metal screw will not come into contact with your bone or gums. **This statement is based on six clinical cohort studies (four prospective studies, two retrospective studies). A single retrospective study investigated 2-piece implants.**

2.5.5 | Patient perspective 5

Question: I lost a titanium implant because of peri-implantitis. Is a ceramic implant a better solution to prevent these complications?
Answer: Currently, there is no clinical evidence that zirconia implants perform better than titanium implants to prevent peri-implantitis.

2.6 | Recommendations for future research

After 5 years, there is data on commercially available zirconia implants. However, the evidence is limited (low sample size, lack of RCTs comparing zirconia and titanium implants).

2.6.1 | Recommendation 1 for future research

Further prospectively designed long-term clinical studies and randomized clinical trials investigating titanium and zirconia implants are needed to confirm the presently evaluated promising outcomes.

2.6.2 | Recommendation 2 for future research

More clinical data is needed on the short and long-term clinical performance of 2-piece zirconia implant designs.

2.6.3 | Recommendation 3 for future research

Additional clinical examinations investigating zirconia implants in specific patient populations are needed (e.g., patients with a history of periodontitis and auto-immune diseases…).

3 | SYSTEMATIC REVIEW PAPER 2

3.1 | Manuscript title

The effect of different transmucosal abutment materials on peri-implant tissues – a systematic review and meta-analysis

3.2 | Preamble

In the last decades, alternative abutment materials were introduced on the market. This systematic review collected data from randomized clinical trials examining the effect of these materials—compared to titanium (alloys)—on peri-implant tissues.

The primary outcome of this systematic review and meta-analysis was marginal bone loss and probing pocket depths.

The secondary outcomes were:

- Abutment survival
- Biological complications
- Aesthetic outcomes.

Thirteen randomized clinical trials could be included. Nine examined titanium abutments versus zirconia abutments, three studies examined titanium versus alumina and two titanium versus gold. Sufficient information was provided for meta-analyses of the data on marginal bone loss, pocket probing depth and abutment survival. The other outcomes could only be described descriptively. Similar marginal bone loss, probing depth and abutment survival were found for the examined materials after 1 year and 5 years of follow-up.

3.3 | Consensus statements

3.3.1 | Consensus statement 1

Bone-level implants with zirconia and titanium transmucosal abutments demonstrate comparable peri-implant parameters (MBL and PD) after 1 and 5 years. Bleeding on probing could not be compared because of the heterogeneity of the used indices.

This statement is based on meta-analyses of six RCTs. (mean diff and 95% CI after 1-year: MBL: −0.24 mm [−0.65,0.16], PD: −0.06 [−0.41,0.30] and after 5 years: MBL: [], PD: −0.06 []).

3.3.2 | Consensus statement 2

Both zirconia and titanium transmucosal abutments are clinically comparable regarding biological complications, esthetic outcomes and patient satisfaction.

This statement is based on descriptive data from nine RCTs.

3.3.3 | Consensus statement 3

Limited data regarding peri-implant tissue parameters were found for gold and alumina transmucosal abutments. Thus, a direct comparison with titanium is not possible.

This statement is based on descriptive data of respectively two and three RCTs.

3.4 | Clinical recommendations

3.4.1 | Clinical recommendation 1

Do zirconia abutments provide additional biological esthetic or patient satisfaction benefits over titanium implants?

Based on biological peri-implant parameters and patient satisfaction, titanium and zirconia can be recommended as transmucosal abutment materials. However, even though the scientific evidence remains unclear, zirconia abutments might be preferred in the esthetic region.

3.4.2 | Clinical recommendation 2

What material allows for adequate peri-implant soft tissue integration?

Titanium (alloy) and zirconia are well-documented biocompatible restorative materials for final restorations allowing cell adhesion. If ceramic glaze or other restorative materials are considered, placing these materials submucosally as coronal as possible is recommended.

3.5 | Patient perspectives

3.5.1 | Patient perspective 1

Question 1: Are zirconia abutments more esthetic than titanium ones?

Answer: Yes. We can achieve good esthetic results with titanium abutments, but where esthetics are critical, zirconia abutments are usually preferred. This avoids the risk of the metal showing through the gums in the places that become visible when you smile. **This patient's perspective is based on expert opinions.**

3.6 | Recommendations for future research

3.6.1 | Recommendation 1 for future research

Standardization for reporting clinical, biological and technical outcomes is needed in clinical trials to facilitate data comparison and future systematic reviews and meta-analyses.

3.6.2 | Recommendation 3 for future research

Randomized clinical trials examining abutment materials should consider/avoid confounding factors that may influence the results (e.g., using screw-retained and cemented restorations).

3.6.3 | Recommendation 2 for future research

Further investigation is needed to consider newly developed restorative materials as biocompatible for peri-implant soft tissue integration (e.g., lithium disilicate, composite CAD-CAM materials, …). Both ex-vivo and clinical studies are necessary to make further clinical recommendations.

4 | SYSTEMATIC REVIEW PAPER 3

4.1 | Manuscript title

Effect of medications affecting bone metabolism on short- and long-term implant failure: a narrative review.

4.2 | Preamble

Patients on low-dose bisphosphonates (BPs) or denosumab (e.g., osteoporosis therapy) are considered low-risk for medication-related osteonecrosis of the jaw (MRONJ). Those who are on high-dose antiresorptive drugs (ARDs) due to or prevention of, skeletal related events and skeletal metastasis (e.g breast or prostate cancer) and treatment of multiple myeloma are considered high-risk groups for MRONJ. The typical dosage for high and low dose ARD are displayed in Table 1.

Influencing factors are:

- Underlying diseases
- Anti-resorptive drug
- Dose, duration and frequency
- Other medication/therapy: hormone therapy, immune or antibody therapy, chemotherapy anti-angiogenic therapy, head and neck radiotherapy
- Prior osteonecrosis of the jaw.

TABLE 1 Typical therapeutic dosage of ARDs.

Type of ARDs	Low-dose	High-dose
Alendronate	70 mg/week per os.	N/A
Risedronate	35 mg/week per os.	N/A
Ibandronate	150 mg/month, per os or 3 mg/3 months i.v.	50 mg/day, per os.
Pamidronate	30 mg/3 months i.v.	90 mg/3 ~ 4 weeks i.v.
Zoledronate	5 mg/year i.v.	4 mg/3 ~ 4 weeks i.v.
Denosumab	60 mg/6 months s.c.	120 mg/3 ~ 4 weeks s.c.

4.3 | Consensus statements

4.3.1 | Consensus statement 1

In patients receiving low-dose BP therapy (e.g. for osteoporosis therapy), the rate of early implant failure after implant placement is not increased compared to patients without BP therapy. Nevertheless, the history of BP administration (cumulative dose) is not sufficiently investigated.

This statement is based on 12 cohort studies. (22 implant failures out of 1202 implants).

4.3.2 | Consensus statement 2

The influence of low-dose BP therapy on long-term implant survival has not been sufficiently documented to allow conclusions. **This statement is based on expert opinions.**

4.3.3 | Consensus statement 3

The influence of low-dose denosumab therapy on failure after implant placement and failure of existing implant has not been sufficiently reported to allow conclusions.

4.3.4 | Consensus statement 4

In patients receiving low- or high-dose ARD, prognosis and complications of augmentation procedures are not sufficiently reported to allow conclusions.

4.3.5 | Consensus statement 5

In patients receiving high-dose ARD, the early and late implant failure rate is not sufficiently documented to allow conclusions.

This statement is based on a case series (no early failures, 49 implants in 27 patients).

4.3.6 | Consensus statement 6

In patients receiving low-or high-dose ARD, implant-related sequestration (IRS)/MRONJ is reported. The incidence of IRS/MRONJ after implant insertion or around an existing implant is unknown.

This statement is based on retrospective case series. (168 patients from 20 case series).

4.3.7 | Consensus statement 7

Implant supported-rehabilitation after resective treatment and healing of MRONJ is not sufficiently reported to allow conclusion.

4.3.8 | Consensus statement 8

The influence of other drugs affecting bone metabolism (e.g. methotrexate (MTX), corticosteroid (CS), anti-angiogenic agents, or romosozumab) on failure after implant placement or failure of existing implants has not been sufficiently addressed to allow conclusions.

4.3.9 | Consensus statement 9

The potential effect of temporary withholding of ARD (drug holiday) on implant failure or MRONJ development after implant insertion has not been sufficiently documented to allow conclusions.

4.4 | Clinical recommendations

All clinical recommendations are based on expert opinions.

4.4.1 | Clinical recommendation 1

What has to be considered by the dentist before ARD Therapy?

A dentist should be involved when ARD therapy is planned.

Present and potential intraoral infections should be resolved to prevent MRONJ.

Existing dental implants without peri-implant pathology should not be removed.

Pressure sores should be avoided to reduce the risk of MRONJ.

4.4.2 | Clinical recommendation 2

Is it safe to perform dental implant therapy *during or after ARD* therapy?

Proceed with caution in specialized comprehensive centers.

In patients treated with *low-dose ARDs*, dental implant therapy is relatively safe. However, cumulative dose and administration time should be considered. Straightforward Direct implant placement in native bone and alternatives to bone augmentation procedures should be preferred.

4.4.3 | Clinical recommendation 3

In patients treated with *high-dose ARD* or *after resection of MRONJ lesion*, straightforward implant placement in the native bone can be considered only under rigorous risk evaluation.

- Strength of indication (no alternative to implant therapy, including no treatment)
- Specialized comprehensive center
- Patients' motivation
- Periodontal maintenance
- Patient awareness of specific risks (implant-related sequestration, MRONJ)
- Cooperation with ARD prescribing physicians (e.g. oncologists)
- Careful evaluation of co-morbidities, additional risk factors, and other medications.

4.4.4 | Clinical recommendation 4

How can the risk for complications around existing or newly inserted implants in patients receiving ARD be reduced?

Supportive periodontal therapy is highly recommended in patients receiving ARD to avoid peri-implantitis-related MRONJ/IRS.

4.4.5 | Clinical recommendation 5

Is a "drug holiday" recommended for implant placement in patients receiving ARD?

Withholding ARD (drug holiday) for implant placement is not recommended. Based on the general effects and pharmacokinetics of ARDs, surgery should be scheduled according to the specific therapeutic windows of the last administration.

4.4.6 | Clinical recommendation 6

Are there other relevant medications with a possible impact on implant success?

Clinicians should be aware of medications affecting bone metabolism, including methotrexate (MTX), corticosteroid (CS), anti-angiogenic agents, or romosozumab, which might impair wound healing leading to complications.

4.5 | Patent perspectives

All clinical patient perspectives are based on expert opinions.

4.5.1 | Patient perspective 1

Question: What can I do to avoid complications if I take medication that affects my bones?
Answer: Regularly check with your dentist even if you have no teeth, and tell them about your bone-modifying medication. Resolving oral infections is crucial for you because infections may lead to severe bone healing problems and even the death of bone tissue. Therefore careful daily oral hygiene and regular professional maintenance are strongly recommended. It is also essential to look out for and seek to prevent pressure sores under dentures.

4.5.2 | Patient perspective 2

Question 2: Does anti-resorptive treatment affect my existing implants?
Answer: Regular dental care during anti-resorptive drug treatment is essential to spot existing or potential infections around your implants. The goal is to avoid problems around implants that could lead to necrosis of the jaw bone (dead bone). Equally, if your existing implants are healthy, they pose no risk of necrosis, and there is no reason to remove them.

4.5.3 | Patient perspective 3

Question: Is it too risky to have implants if I am taking anti-resorptive drugs for osteoporosis?
Answer: Treatment for osteoporosis usually involves a low dose of antiresorptive drugs, and we know this carries only a low risk for bone necrosis. In this situation, dental implant therapy is possible. However, we should consider how long you have been taking the

medication because we also know that the risk of problems with bone healing and necrosis increases when the drugs are taken over the years.

4.5.4 | Patient perspective 4

Question: Is it too risky to have implants if I am taking anti-resorptive drugs as part of cancer therapy?
Answer: In cancer treatment where you receive a high drug dose, for example, in cases of bone metastases or multiple myeloma, there is an increased risk of bone necrosis. In this situation, dental implant therapy can only be performed after a thorough risk evaluation by a specialized multidisciplinary team. If you proceed with the implants, you need an ongoing regular dental follow-up to reduce the risk of bone necrosis.

4.6 | Recommendations for future research

4.6.1 | Recommendation 1 for future research

Prospective comparative studies to investigate the outcome of dental implants in patients on low and high dose denosumab.

4.6.2 | Recommendation 2 for future research

Prospective clinical studies to investigate the cause-effect relationship between some medications affecting bone metabolism and the outcome of implant therapy.

4.6.3 | Recommendation 3 for future research

Large-scale cohort studies to evaluate the effect of confounders, such as cancer and osteoporosis, co-morbidities, and multiple medications that may alter tissue metabolism, on the outcome of implant therapy.

4.6.4 | Recommendation 4 for future research

Although peri-implantitis and impairment of bone remodelling seemed to be risks of IRS, well-designed studies are required to confirm this.

AUTHOR CONTRIBUTIONS

Bilal Al-Nawas: Conceptualization; Methodology; Supervision; Project administration; Writing - original draft; Writing - review & editing; Validation. France Lambert: Conceptualization; Methodology; Supervision; Project administration; Writing - original draft; Writing - review & editing; Validation. Sanne Werner Møller Andersen: Writing - review & editing. Michael Bornstein : Supervision ; Writing - review & editing. Michael Gallert: Investigations; Writing - review & editing. Asbjorn Jokstad : Writing - review & editing. Junho Jung: Investigations; Writing - review & editing. Yong-Dae Kwon : Investigations; Writing - review & editing. Isabelle Laleman: Investigations; Writing - review & editing. Giacomo Oteri: Writing - review & editing. Stefan Roehling: Investigations ; Writing - review & editing. Eik Schiegnitz: Writing - review & editing. Yukihiro Takeda: Writing - review & editing. Hendrik Terheyden: Writing - review & editing.

CONFLICT OF INTEREST STATEMENT

The authors reported all conflits of interest at the ITI Consensus Meeting.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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REVIEW ARTICLE

CLINICAL ORAL IMPLANTS RESEARCH WILEY

Treatment effect of implant-supported fixed complete dentures and implant overdentures on patient-reported outcomes: A systematic review and meta-analysis

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Abstract

Objectives: To analyze the effect of implant treatment in edentulous patients rehabilitated with implant-supported fixed complete dentures (IFCDs) or implant overdentures (IODs) on dental patient-reported outcomes (dPROs).

Materials and Methods: In January 2022, Medline, Embase, CINAHL, Cochrane Library, PubMed Central, Web of Science, and ClinicalTrials.gov were screened for prospective clinical studies on completely edentulous patients treated with IFCDs and/or IODs, reporting pre-treatment and follow-up dPROs. Hedges' g effect sizes (ES) with corresponding 95% confidence intervals (CI) were calculated. Afterward, meta-analyses were conducted using random effect models.

Results: A total number of 1608 records was initially identified. Of those, 28 studies reporting dPROs from 1457 patients were finally included. The applied dental patient-reported outcome measures (dPROMs) included several versions of the Oral Health Impact Profile (OHIP) or specific items assessing satisfaction with Visual Analogue Scales (VAS). The overall ES was large for rehabilitation with IFCDs (1.68 [CI: 1.15, 2.20]) and IODs (1.26 [CI: 0.99, 1.52]) with no significant difference ($p = .165$) between the two. Denture stability was the only factor rated significantly higher for IFCDs (ES difference: 2.37 [CI: 0.21, 4.54]; $p = .032$). Subgroup analyses revealed moderately higher ES for IODs on two implants relative to one implant (ES difference: 0.73 [CI: 0.34, 1.12]; $p < .001$).

Conclusions: There is a strong positive effect of implant treatment in edentulous patients, independent of the type of prosthetic rehabilitation. In patients seeking high stability, IFCDs may be preferable. In mandibular IODs on a single implant, there was a significantly positive effect of an additional implant on dPROs.

KEYWORDS
complete denture, edentulous, meta-analysis, patient-reported outcome measures, patient-reported outcomes, PROMs, PROs, systematic review

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1 | INTRODUCTION

Despite a decreasing prevalence of edentulism—expected to continue—over the past several decades in many countries, many individuals worldwide have still lost all teeth in at least one jaw (Peres et al., 2019). In 2015, an estimated 4.1% of the world's population was reported to be edentulous (Kassebaum et al., 2017). Furthermore, another recent study in older adults (65–74 years) in Germany showed a prevalence of edentulism of 12.4% (Schwendicke et al., 2020). This highlights the fact that edentulism remains an important public health concern especially in older adults, with a potentially great impact on patients' daily life (Polzer et al., 2010; Rodrigues et al., 2012). Obviously, without teeth the masticatory function is compromised. Furthermore, a reduction of the perceived esthetics and, subsequently, patient self-esteem and social life can be expected. Such compromises are highly relevant to patients, and therefore negatively affect their oral health-related quality of life (OHRQoL). (John, 2018; Reissmann, 2019). Since edentulism affects the entire oral cavity and masticatory system, it is not surprising that edentulism affects all four dimensions of OHRQoL, namely *Oral Function*, *Orofacial Esthetics*, *Orofacial Pain*, and *Psychosocial Impact* (John et al., 2014, 2016). However, it is not only the direct impact of tooth loss on the patient perceptions: Edentulism also appears to be related to general health conditions such as dementia, mainly due to its impact on diet as a result of reduced masticatory function (Emami et al., 2013; Joshipura et al., 1996).

Edentulous patients can be rehabilitated with complete dentures, but this is frequently associated with various problems, mainly related to low denture stability. One solution to alleviate the shortcomings of complete dentures, such as low masticatory performance, and to substantially increase dPROs, is the provision of dental implants to either support or retain an implant-removable overdenture (IOD) or an implant-fixed complete denture (IFCD; Reissmann et al., 2017; Schierz & Reissmann, 2021). The type of prosthodontic reconstruction to be provided determines the number of implants. For IFCDs, a minimum of four implants are required in both the maxilla and the mandible according to modern implant concepts (Soto-Peñaloza et al., 2017). In contrast, a single implant in the midline of the edentulous mandible can be used for an IOD; this also results in increased dPROs relative to conventional complete dentures (Cordioli et al., 1997; Schwindling et al., 2018). However, current guidelines recommend at least two implants to retain an IOD in the mandible (Feine et al., 2002). Various attachment types can be selected for IODs, ranging from single attachments (e.g., balls) to bars for primary splinting of the implants (Al-Zubeidi et al., 2012; Bressan et al., 2012; Messias et al., 2021).

The most important decision for a patient when choosing an implant-supported denture is whether the denture should be fixed or removable. Obviously, an IFCD produces the sensation of having physiological dentition. In contrast, an IOD must be removed for cleaning and might suggest the perception of being old and not as vital as in the past. However, with an IFCD, not all lost hard and soft tissue can be replaced without preventing access to the implant and surrounding soft tissue. Given these considerations, it is not surprising that the evidence is still inconclusive whether IFCDs or IODs are preferable for patients in terms of dPROs, and which factors affect the outcomes. Therefore, the present study was designed to evaluate and compare the treatment effects of IFCDs and IODs on pre- and post-treatment dPROs and to identify potential influencing factors.

2 | MATERIALS AND METHODS

2.1 | Study protocol

The study protocol was registered in the international prospective register of systematic reviews (PROSPERO; registration number: CRD42022269277, Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022269277), and followed the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines (Moher, et al., 2009). No ethical approval was required because the present study is a systematic review. The research question was based on the P.I.C.O model as follows:

Population: Fully edentulous patients.
Intervention: Rehabilitation with implant-supported fixed complete dentures (IFCDs).
Comparison: Rehabilitation with implant overdentures (IODs).
Outcome: Patient-reported outcomes, including pre- and post-treatment evaluations.

The resulting P.I.C.O. question was: 'In edentulous patients, what is the effect on patient-reported outcomes of implant treatments using IFCDs relative to IODs?' Furthermore, the effects of attachment type, follow-up time, and implant number per reconstruction were to be evaluated.

2.2 | Search strategy

Systematic literature searches were adapted to multiple electronic databases and executed by an information specialist in medicine (H.J.) to identify potentially relevant documents:

- Medline (Ovid) (incl. Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Medline Daily and Ovid Medline Versions) (1946 – January 11, 2022).
- Embase (Ovid) (1974 – January 11, 2022).
- CINAHL (EBSCOhost) (1937 – January 11, 2022).
- Cochrane Library (Wiley) (1996 – January 11, 2022).
- PubMed Central (1946 – January 11, 2022).
- Web of Science (all editions) (1900 – January 11, 2022).
- ClinicalTrials.gov (NLM).

Candidate search terms were selected based on subject headings, titles, abstracts, and author keywords from a list of core references

of a previous systematic review (Yao et al., 2018). Thereafter, a draft search strategy was developed, adding further relevant vocabulary from various database thesauri. Search terms were also identified using the Yale MeSH Analyzer and the word frequency analysis tool of the PubReMiner. The initial search strategy in Medline (Ovid) was tested against a list of core references from the aforementioned review (Yao et al., 2018) to see whether they were included in the search results. After refinement and consultations with the research team of this systematic review, search strategies were created for each information source as a combination of database-specific controlled vocabulary (subject headings) and textwords. Synonyms and similar terms were included in the textword search. Animal studies were formally excluded from the search results. No limits were applied in the database searches considering study types, languages, publication years, or other criteria. The full search strategies are presented in the Appendix S1. Duplicate references were removed using EndNote's (EndNote; Thomson Reuters) duplicate identification strategy, followed by manual curation.

2.3 | Eligibility criteria

Inclusion and exclusion criteria were as follows:

2.3.1 | Inclusion

- Prospective clinical investigations.
- Reports of dPROs prior to implant placement and after prosthetic rehabilitation using validated dPROMs.
- Completely edentulous participants.
- Treatment with IOD or IFCD in at least one jaw.
- Minimum sample size per relevant study arm or cohort ≥10 patients.
- Mean follow-up period ≥1 year from delivery of the final restoration-supported or -retained reconstruction.
- Articles written in English.

2.3.2 | Exclusion

- In vitro or animal studies, retrospective clinical investigations, unpublished data, conference abstracts.
- Partially dentate participants, or unclear dental status.
- Insufficient documentation regarding dPROs or dPROMs.
- Non-validated or self-designed dPROMs.
- Use of categorical scales /questionnaires (e.g., yes/no responses).

2.4 | Data selection and extraction process

After automatic elimination of duplicates, the search results were imported into a software application (Rayyan; available at: www.rayyan.ai) dedicated to literature screening in systematic reviews, and two reviewers (M.F. & S.P.) performed, independently, the data screening based on the eligibility criteria. Included articles were screened based on their title, followed by the abstract, and, when meeting the inclusion criteria, the full text. After each step, the reviewers compared the in- and excluded studies and a Cohen's kappa score was calculated to assess the degree of agreement. In case of disagreement, a third reviewer (S.A.-A.) was consulted.

Data extraction from the included studies was performed by each reviewer individually. For this purpose, a data extraction sheet was designed. If multiple dPROMs were used in one study, data from all dPROMs were extracted separately. When dPROs from the same cohort were reported at multiple follow-up time points within a study or in consecutive studies, only the data from the longest follow-up period was extracted. If multiple items with VAS were used, only the data from the most frequently used items were extracted. After screening all articles, the most frequently evaluated items included the overall evaluation of the treatment, comfort, stability, chewing, speaking, esthetics, pain, and cleaning. For VAS, it was ensured that 0 represents the worst possible outcome (e.g., lowest satisfaction or lowest comfort). If this was not the case, the scales were transposed accordingly for comparison. For the different versions of the OHIP questionnaire, only the OHIP summary scores were extracted since reporting of the domain scores was inconsistent over the studies. If data could not be extracted, studies were excluded from further evaluation, and the reason for exclusion was noted. In case of doubt, the corresponding authors of the articles of interest were contacted to obtain additional information ($n = 17$; Appendix S2).

The risk of bias of the included studies was assessed, independently, by M.F. and S.P. using the Cochrane Risk of Bias tool (RoB 2.0) for randomized trials (Higgins et al., 2011) and the Risk of Bias in Non-Randomized Studies tool (ROBINS-I) in the case of non-randomized trials (Sterne et al., 2016). A third reviewer (S. A.-A.) was consulted in case of disagreement. The risk of bias visualization tool (ROBVIS) was used for graphical representation of the results. Evaluating the certainty of the evidence of included studies, the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) system was used (Mustafa et al., 2013). Accordingly, the certainty of each meta-analysis was rated as high, moderate, low, or very low.

2.5 | Statistical analysis

Data from studies were only included in the meta-analyses if either (1) mean and standard deviation (SD) could be obtained directly from the studies, (2) mean could be obtained directly from the study and standard deviation could be calculated from the 95% confidence interval of the mean, or (3) mean and standard deviation could be estimated from the median and interquartile range (Wan et al., 2014). Based on baseline and follow-up data, Hedges' g effect sizes (ES) were subsequently calculated for each dPROM (Goulet-Pelletier & Cousineau, 2018). Since cross-measurement correlations between

study baseline and follow-up data were not known for all studies and the number of patients at follow-up and baseline was not identical for all studies, Hedges' *g* was calculated assuming independent data. ES values of 0.20, 0.50, and 0.80 Hedges' *g* are commonly considered to be indicative for small, medium, and large effects, respectively (Cohen, 1992). Random effects models (REMLs) were used to estimate overall ES with a 95% confidence interval (CI). ES of subgroups were compared using a random-effects (more than one study in at least one of the subgroups) or fixed-effects (one study per subgroup) meta-regression. Any potential bias of including all studies regardless of unequal or equal number of patients at baseline and follow-up was ascertained by comparing the ES of the OHIP data of studies with unequal ($n=12$) and equal ($n=7$) patient counts at baseline and follow-up. The estimated difference (equal vs. unequal) in ES was 0.27 (CI: −0.12, 0.66; $p=.179$), indicating no substantial or statistically significant difference between the two types of analysis.

3 | RESULTS

Initially, 1608 records were identified during the systematic literature search, of which 1019 remained for title screening after duplicate elimination. After a consensus was reached for the title screening, 599 abstracts were screened. After further consensus, 191 full-texts were analyzed, of which 59 were included for data extraction (Figure 1). The kappa scores were 0.78 for the title screening, 0.86 for the abstract screening, and 0.91 for the full-text screening. Data could finally be extracted from 28 studies. The reasons for study exclusion at the data-extraction stage are provided in Appendix S3.

3.1 | Description of included studies

Among the 28 included studies were 15 RCTs (Abou-Ayash et al., 2020; Al-Zubeidi et al., 2012; Bryant et al., 2015; De Kok et al., 2011; de Resende et al., 2021; De Souza et al., 2015; Gaballa et al., 2021; Hartmann, Bandeira, et al., 2020; MacEntee et al., 2005; Meijer et al., 2003; Michaud et al., 2012; Montero et al., 2021; Park et al., 2019; Raghoebar et al., 2003; Slot et al., 2016) and 13 prospective studies (Ala et al., 2022; Alfadda et al., 2009; Attard et al., 2006; Berretin-Felix et al., 2008; Compagnoni et al., 2014; Coutinho et al., 2021; Emami et al., 2015; Guljé et al., 2012; Jabbour et al., 2012; Matthys et al., 2018, 2019; Reissmann et al., 2018; Tomasi et al., 2013). Among the RCTs, only 2 compared IFCDs and IODs directly (De Kok et al., 2011; Hartmann, Bandeira, et al., 2020). The other RCTs were randomized on the basis of loading protocol ($n=3$), attachment type ($n=3$), implant number ($n=3$), implant type ($n=2$), or comparison to removable complete dentures ($n=2$). The studies on IODs included dPROMs reported by 1407 patients, and the studies on IFCDs by 50 patients. The number of patients refers to the follow-up, which was 1 to 10 years in the IOD group and 1–1.5 years in the IFCD group (Table 1). Two main categories of dPROMs were used: multi-item instruments such as the OHIP, and single items obtained by VAS. Several variants of the OHIP questionnaire, including OHIP-49 ($n=3$), OHIP-14 ($n=4$), and the OHIP-EDENT questionnaire ($n=12$) were used. Various VAS were used for the evaluation of overall treatment ($n=19$), comfort ($n=6$), denture stability ($n=7$), chewing ability ($n=11$), speaking ability ($n=9$), esthetic outcomes ($n=10$), pain while wearing the denture ($n=3$), and denture cleaning ability ($n=3$). Less frequently used dPROMs included several types of multi-item instruments: the Short Form-36 questionnaire (SF-36; $n=2$) measuring general health-related quality of life, the Oral Impact on Daily Performance questionnaire (OIDP; $n=1$), a patient satisfaction score ($n=1$), and the Denture Satisfaction Score (DSS; $n=2$). The ES of included studies ranged from −0.23 to 6.45 (Table 2). The infrequently used questionnaires were applied only to IOD cohorts, whereas OHIP and VAS-based items were used for cohorts with IODs and IFCDs alike. The higher number of dPROMs than the number of studies included in this meta-analysis is due to the fact that some studies applied multiple dPROMs.

The risk of bias analyses showed a low risk of bias in the majority of included RCTs, and in all but one prospective study (Figure 2a,b). The most common reasons why studies were rated as having "some concerns" or a "high risk of bias" were substantial drop-out rates or unclear descriptions of the randomization process.

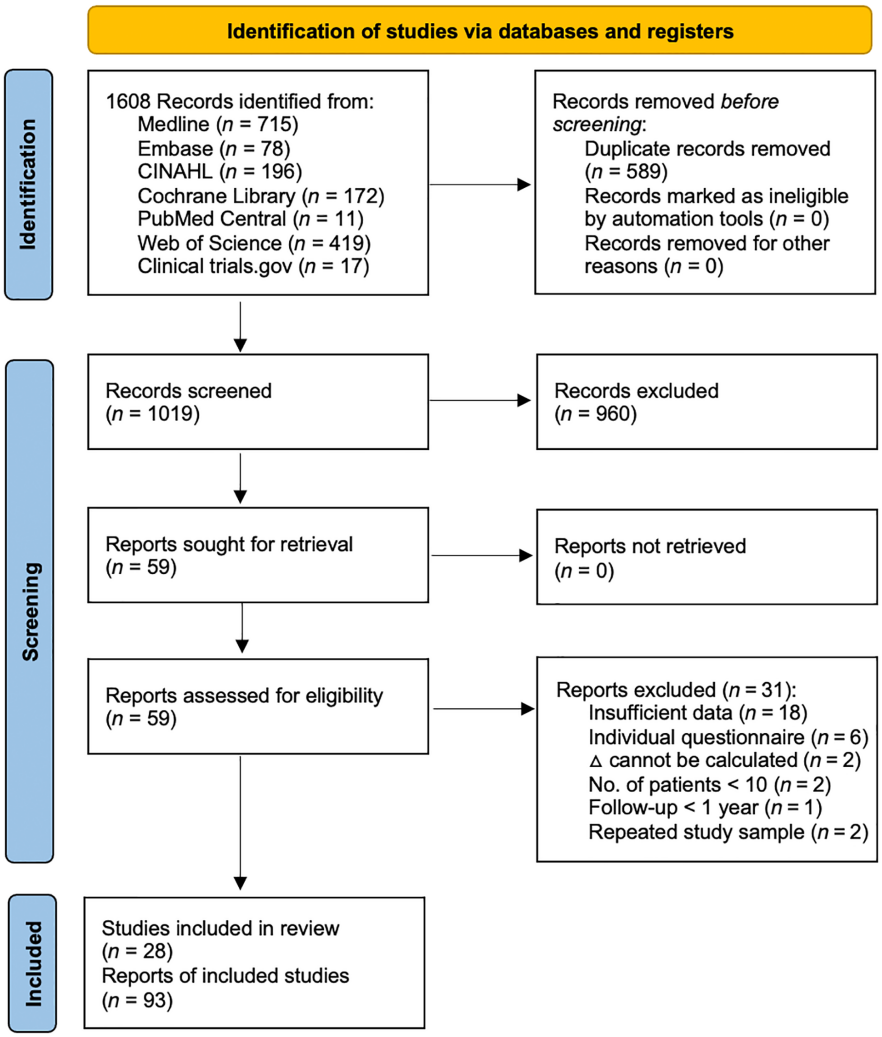
3.2 | Meta analyses

3.2.1 | Fixed complete dentures versus implant overdentures

For the comparison between IFCDs and IODs, only study cohorts with a follow-up period of 1–1.5 years were considered for IODs, as this corresponded to the maximum follow-up period of any IFCD study cohort. Studies ($n=3$) for which no standard deviations were described or could be calculated from the reported data were excluded from the meta-analyses (Compagnoni et al., 2014; de Resende et al., 2021; MacEntee et al., 2005). In the global comparison, results from 52 dPROMs in the IOD group were compared to 12 dPROMs in the IFCD group. There was a high level of heterogeneity among the included studies on IODs ($I^2=86.7\%$) and IFCDs ($I^2=65.9\%$).

Generally, all ES were greater than 0.8, indicating a large effect of implant treatment on dPROs in edentulous patients, independent of the type of restoration. The individual ES from each dPROM are shown in Figure 3. The ES was not significantly different between the IFCD and the IOD groups (ES difference: 0.45 [CI: −0.19, 1.09]; $p=.165$; Table 3). Since only dPROs from OHIP versions and individual items with VAS were included in the cohorts with IFCDs, the data were analyzed separately with respect to these dPROMs. When comparing ES of OHIP data from IOD ($n=10$) and IFCD cohorts ($n=3$), we observed no significant difference (ES difference: −0.03 [CI: −0.58, 0.52]; $p=.920$; Table 3). Within the ES of individual VAS items, only the effect on denture stability was rated higher for the IFCD group than for the IOD group ($p=.032$). No significant differences were detected among

FIGURE 1 PRISMA flow-diagram.



the other individual VAS items, although ES differences were greater than 0.8 in the VASs on comfort, stability, chewing, speaking, and esthetics, in favor of the IFCDs. Based on the GRADE analysis, the certainty of the evidence was rated as moderate or low for all meta-analyses (Table 4).

3.2.2 | Subgroup analyses in implant overdenture groups

Subgroup analyses were conducted for IODs only, as data on IFCDs was insufficient. For the analysis of the influence of the attachment type, only studies with 2–4 implants were considered. Studies with a single implant were excluded because at least 2 implants are required for a bar. For more than 4 implants, there was only one cohort from one study (Slot et al., 2016) with IODs on bars, which was excluded from this analysis due to the lack of comparison with single attachment retained IODs on the same number of implants. Consequently, 20 studies were included for the analysis (Alfadda et al., 2009; Al-Zubeidi et al., 2012; Attard et al., 2006; Bryant et al., 2015; De Kok et al., 2011; De Souza et al., 2015; Emami et al., 2015; Gaballa et al., 2021; Guljé et al., 2012; Hartmann, Bandeira, et al., 2020; Matthys et al., 2018, 2019; Meijer et al., 2003; Michaud et al., 2012; Montero et al., 2021; Park et al., 2019; Raghoebar et al., 2003; Reissmann et al., 2018; Slot et al., 2016; Tomasi et al., 2013). There was no significant difference between bars and single attachments (ES difference: −0.08 [−0.72, 0.56]; Table 5). No ES difference for the OHIP scores could be calculated since OHIP data was only available for single attachment-retained IODs.

There was no significant effect of the mean follow-up period or the number of implants per implant IODs on ES in general (Table 5). However, the ES difference for the direct comparison of single implant- and two implant-retained IODs was significant (0.72 [0.38, 1.06]; $p < .001$), indicating a medium to large difference, based on included studies (Abou-Ayash et al., 2020; Ala et al., 2022; Al-Zubeidi et al., 2012; Bryant et al., 2015; Coutinho et al., 2021; De Kok et al., 2011; De Souza et al., 2015; Gaballa et al., 2021; Hartmann, Bandeira, et al., 2020; Jabbour et al., 2012; Matthys et al., 2018, 2019; Michaud et al., 2012; Montero et al., 2021). The certainty of evidence for all meta-analyses was rated as low, based on the GRADE analysis (Table 6).

TABLE 1 Characteristics of included studies, seperated for each cohort.

Author (year)	Study design|fixed, removable|jaw|retention|antagonist|impl/recon[a]	Mean follow-up [years]	No of pat/recons/impl		Available data
			Baseline	Follow-up	
Abou-Ayash et al. (2020)	RCT|Rem|Mandible|Single|CD|1	2	158|158|158	131|131|131	Mean, SD (BL, FU)
Ala et al. (2022)	Pros|Rem|Mandible|Single|CD|1	1	18|18|18	18|18|18	Mean, SD (BL, FU)
Alfadda et al. (2009)	Pros|Rem|Mandible|Bar|CD|-	5	77|77|234	73|73|-	Mean, SD (BL, FU)
Al-Zubeidi et al. (2012)	RCT|Rem|Mandible|Single|CD|2	5	106|106|212	96|96|192	Mean, SD (BL, FU)
Attard et al. (2006)	Pros|Rem|Mandible|Bar|CD|-	1	35|35|-	35|35|-	Mean, SD (BL, FU)
Berretin-Felix et al. (2008)	Pros|Fixed|Mandible|Screw|CD|5	1.5	15|15|75	15|15|75	Mean, SD (BL, FU)
Bryant et al. (2015)	RCT|Rem|Mandible|Single|CD|1	5	42|42|42	29|29|29	Mean, SD (BL, FU)
Bryant et al. (2015)	RCT|Rem|Mandible|Single|CD|2	5	44|44|88	33|33|66	Mean, SD (BL, FU)
Compagnoni et al. (2014)	Pros|Fixed|Mandible|Screw|CD|4	1	16|16|64	12|12|48	Mean BL, FU
Coutinho et al. (2021)	Pros|Rem|Mandible|Single|CD|1	5	45|45|45	30|30|30	Mean, SD (BL, FU)
de Souza et al. (2015)	RCT|Rem|Mandible|Single|CD|4	1	38|38|152	35|35|133	Mean, SD (BL, FU)
de Souza et al. (2015)	RCT|Rem|Mandible|Single|CD|2	1	42|42|84	36|36|72	Mean, SD (BL, FU)
de Souza et al. (2015)	RCT|Rem|Mandible|Single|CD|2	1	40|40|80	35|35|70	Mean, SD (BL, FU)
de Resende et al. (2021)	RCT|Rem|Mandible|Single|CD|1	1	23|23|23	22|22|22	Mean BL, FU
de Resende et al. (2021)	RCT|Rem|Mandible|Single|CD|2	1	24|24|48	24|24|48	Mean BL, FU
Gaballa et al. (2021)	RCT|Rem|Mandible|Single|CD|2	1	18|18|36	18|18|36	Mean, SD (BL, FU)
Gaballa et al. (2021)	RCT|Rem|Mandible|Single|CD|2	1	18|18|36	18|18|36	Mean, SD (BL, FU)
Emami et al. (2015)	Pros|Rem|Mandible|Single|CD|3	1	135|135|405	135|135|405	Mean, SD (BL, FU)
De Kok et al. (2011)	RCT|Fixed|Mandible|Screw|CD|3	1	20|10|30	10|10|30	Mean, SD (BL, FU)
De Kok et al. (2011)	RCT|Rem|Mandible|Single|CD|2	1	20|10|20	10|10|20	Mean, SD (BL, FU)
Guljé et al. (2012)	Pros|Rem|Mandible|Bar|CD|3	1	12|12|36	12|12|34	Mean, SD (BL, FU)
Hartmann, de Menezes Bandeira, et al. (2020)	RCT|Rem|Mandible|Single|CD|1	1	14|14|14	11|11|11	Mean, SD (BL, FU)
Hartmann, de Menezes Bandeira, et al. (2020)	RCT|Rem|Mandible|Single|CD|2	1	17|17|34	13|13|26	Mean, SD (BL, FU)
Hartmann, de Menezes Bandeira, et al. (2020)	RCT|Fixed|Mandible|Screw|CD|4	1	15|15|52	13|13|52	Mean, SD (BL, FU)
Jabbour et al. (2012)	Pros|Rem|Mandible|Single|CD|1	2	95|95|190	85|85|170	Mean, SD (BL, FU)
MacEntee et al. (2005)	RCT|Rem|Mandible|Bar|CD|2	2	34|34|68	34|34|68	Median (BL, FU)
MacEntee et al. (2005)	RCT|Rem|Mandible|Single|CD|2	2	34|34|68	34|34|68	Median (BL, FU)
Matthys et al. (2019)	Pros|Rem|Mandible|Single|CD|2	5	37|37|74	34|34|68	Mean, SD (BL, FU)
Matthys et al. (2019)	Pros|Rem|Mandible|Single|CD|2	5	69|69|138	56|56|112	Mean, SD (BL, FU)

TABLE 1 (Continued)

Author (year)	Study design|fixed, removable|jaw|retention| antagonist|impl/recon[a]	Mean follow-up [years]	No of pat/recons/impl		Available data
			Baseline	Follow-up	
Matthys et al. (2018)	Pros|Rem|Mandible|Single|CD|2	1.3	25|25|50	25|23|50	Mean, SD (BL, FU)
Meijer et al. (2003)	RCT|Rem|Mandible|Bar|CD|2	10	61|61|122	53|53|106	Mean, SD (BL, FU)
Michaud et al. (2012)	RCT|Rem|Mandible|Single|CD|2	1	116|116|232	110|110|220	Mean, SD (BL, FU)
Montero et al. (2021)	RCT|Rem|Mandible|Single|CD|2	1	20|20|40	20|20|40	Mean, SD (BL, FU)
Park et al. (2019)	RCT|Rem|Maxilla|Single|-|4	1	20|20|-	16|16|-	Mean, SD (BL, FU)
Park et al. (2019)	RCT|Rem|Maxilla|Bar|-|4	1	20|20|-	16|16|-	Mean, SD (BL, FU)
Raghoebar et al. (2003)	RCT|Rem|Mandible|Bar|CD|2	10	32|32|64	28|28|56	Mean, SD (BL, FU)
Reissmann et al. (2018)	Pros|Rem|Mandible|Single|CD|4	1	18|18|72	17|17|-	Mean, SD (BL, FU)
Slot et al. (2016)	RCT|Rem|Maxilla|Bar|-|6	5	25|25|150	22|22|131	Mean, SD (BL, FU)
Slot et al. (2016)	RCT|Rem|Maxilla|Bar|-|4	5	25|25|100	24|24|96	Mean, SD (BL, FU)
Tomasi et al. (2013)	Pros|Rem|Both|Single|Mixed|-	1	21|21|80	19|19|72	Mean, SD (BL, FU)

Abbreviations: antagonist: CD, complete denture; Mixed, overdentures and complete dentures; BL, baseline; FU, follow-up; Fixed, removable: Rem, removable; Pros, Prospective Study; RCT, Randomized Controlled Trial; retention: Single, Single attachment (e.g. ball).

[a]No of implants per reconstruction.

4 | DISCUSSION

The present study systematically analyzed and compared dPROs after IFCD and IOD treatments. Although there was no substantial difference in the comprehensive analyses between the two treatment options in terms of dPROs, stability with IFCDs was perceived by patients as better than with IODs when only this single aspect was considered. In the subgroup analyses of the IOD group, bars showed moderately higher ES than single attachments, although this effect was not statistically significant. IODs retained on two implants were perceived more positively than IODs on one implant only.

The strong positive effect of implant treatment on dPROs, regardless of whether the prosthetic restoration was an IFCD or an IOD, seems to reflect the observed improvements in several objective criteria, such as masticatory efficiency, as described in the literature (ELsyad et al., 2022). Our findings are also concordant with previous literature. Particularly worth mentioning are the two RCTs included here that directly compared IFCD to IOD treatments (De Kok et al., 2011; Hartmann, Bandeira, et al., 2020). The result of the subgroup analysis of the IOD studies in terms of the attachment type suggests that there is no difference between bar- or single attachment-retained/supported IODs. The evidence regarding the effect of the attachment type on dPROs had not been clearly established (Kuoppala et al., 2013; Nejatidanesh et al., 2022). In general, studies have shown that patients are least satisfied with magnet-retained IODs, but no general superiority of bars over single attachments has yet been demonstrated (Cune et al., 2005; Kim et al., 2012), supporting the result of the present study. The ES difference between one and two implants retaining an IOD showed a medium effect of the additional implant, and significantly higher dPROs for two-implant retained IODs. Various studies have shown that even a single implant, increasing the retention of mandibular IODs, has a positive effect on dPROs (Hartmann, Bandeira, et al., 2020; Policastro et al., 2019; Schwindling et al., 2018). However, the result of the present study and also of RCTs that directly compared IODs on one and two implants show that patients' perception is slightly more positive with two implants (Hartmann, Bandeira, et al., 2020; Policastro et al., 2019).

4.1 | Discussion of the methods

While a previous review on dPROs comparing IODs and IFCDs concluded that reporting was inconsistent and prospective high-quality studies were lacking (Yao et al., 2018), the present study showed that the demand for further clinical trials focused on dPROs in edentulous patients was met: 16 of the 28 included studies were from 2015 or later. The analysis of dPROs in edentulous patients is not new, and has been the subject of various systematic reviews (De Bruyn et al., 2015; Yao et al., 2018). However, most of them lacked clear standardization of dPROs and dPROMs. In the present study, dPROs collected with non-identical dPROMs were evaluated by calculating effect sizes (ES) to ensure comparability. The calculation

TABLE 2 Overview of the dPROMS used in each study cohort, including the effect size of the treatment on dPROs.

	Baseline			Follow-up			Effect size
Author (year)	Patients	Mean	SD	Patients	Mean	SD	Hedges g (SE)
Oral Health Impact Profile-49 (OHIP-49)							
De Kok et al. (2011)	20	99.1	69.3	10	18.9	20.5	1.34 (0.45)
De Kok et al. (2011)	20	110.0	41.0	10	20.2	13.6	2.52 (0.54)
Reissmann et al. (2018)	18	39.9	31.7	17	26.5	28.4	0.43 (0.35)
Oral Health Impact Profile-14 (OHIP-14)							
Berretin-Felix et al. (2008)	15	18.0	16.4	15	3.0	12.3	1.01 (0.41)
Matthys et al. (2018)	25	15.6	12.3	25	3.5	4.6	1.28 (0.32)
Matthys et al. (2019)	37	15.0	12.0	34	1.9	3.7	1.43 (0.27)
Matthys et al. (2019)	69	20.2	12.5	56	3.2	5.6	1.69 (0.21)
Oral Health Impact Profile for edentulous patients (OHIP EDENT)							
Ala et al. (2022)	18	12.0	12.9	18	2.5	5.8	0.93 (0.36)
Coutinho et al. (2021)	45	9.7	8.0	30	4.3	5.2	0.77 (0.25)
de Souza et al. (2015)	38	15.2	9.1	35	4.6	4.7	1.43 (0.27)
de Souza et al. (2015)	42	13.9	7.8	36	5.1	5.3	1.29 (0.25)
de Souza et al. (2015)	40	17.6	9.4	35	8.9	7.3	1.02 (0.25)
Emami et al. (2015)	135	56.6	19.3	135	31.1	15.2	1.46 (0.14)
Hartmann, de Menezes Bandeira, et al. (2020)	14	9.0	9.9	11	0.0	9.3	0.90 (0.45)
Hartmann, de Menezes Bandeira, et al. (2020)	17	9.0	8.9	13	2.0	2.9	0.97 (0.41)
Hartmann, de Menezes Bandeira, et al. (2020)	15	7.0	6.5	13	2.0	1.7	0.98 (0.42)
Jabbour et al. (2012)	95	54.9	21.0	85	27.9	9.8	1.61 (0.17)
Michaud et al. (2012)	116	55.0	20.0	110	35.0	17.0	1.07 (0.14)
Montero et al. (2021)	20	13.7	5.1	20	3.2	4.1	2.22 (0.42)
Overall treatment outcome (VAS)							
Ala et al. (2022)	18	60.0	56.3	18	90.0	18.5	0.70 (0.36)
Gaballa et al. (2021)	18	82.2	5.7	18	86.1	5.0	0.71 (0.36)
Gaballa et al. (2021)	18	69.0	3.5	18	76.3	5.8	1.49 (0.39)
Guljé et al. (2012)	12	58.0	14.0	12	90.0	90.0	0.48 (0.44)
Montero et al. (2021)	20	41.0	32.0	20	85.0	14.0	1.75 (0.39)
Al-Zubeidi et al. (2012)	106	30.4	26.5	96	77.9	16.5	2.12 (0.18)
Bryant et al. (2015)	42	38.1	34.8	29	68.8	33.9	0.88 (0.26)
Bryant et al. (2015)	44	48.8	35.6	33	76.8	27.8	0.85 (0.24)
Coutinho et al. (2021)	45	64.7	36.3	30	81.3	28.6	0.49 (0.24)
De Kok et al. (2011)	20	36.8	28.8	10	95.1	7.0	2.36 (0.52)
De Kok et al. (2011)	20	29.2	14.3	10	93.6	8.4	4.93 (0.81)
Hartmann, de Menezes Bandeira, et al. (2020)	14	76.7	57.7	11	96.7	15.5	0.43 (0.43)
Hartmann, de Menezes Bandeira, et al. (2020)	17	63.3	57.2	13	98.3	12.5	0.77 (0.40)
Hartmann, de Menezes Bandeira, et al. (2020)	15	81.7	27.2	13	100.0	0.0	0.89 (0.42)
Meijer et al. (2003)	61	48.0	7.0	53	77.0	9.0	3.60 (0.31)
Park et al. (2019)	20	94.0	10.0	16	94.0	10.0	0.00 (0.35)

TABLE 2 (Continued)

	Baseline			Follow-up			Effect size
Author (year)	Patients	Mean	SD	Patients	Mean	SD	Hedges g (SE)
Park et al. (2019)	20	91.0	11.0	16	93.0	16.0	0.15 (0.35)
Raghoebar et al. (2003)	32	47.0	12.0	28	77.0	9.0	2.77 (0.37)
Tomasi et al. (2013)	21	36.3	31.8	19	93.3	8.0	2.36 (0.43)
Comfort (VAS)							
Ala et al. (2022)	18	45.0	50.7	18	95.0	16.1	1.30 (0.38)
Al-Zubeidi et al. (2012)	106	33.3	27.7	96	77.2	18.0	1.85 (0.17)
Coutinho et al. (2021)	45	65.0	33.3	30	81.0	28.4	0.50 (0.24)
De Kok et al. (2011)	20	21.1	30.7	10	97.5	3.7	2.93 (0.58)
De Kok et al. (2011)	20	29.1	31.1	10	95.0	5.5	2.48 (0.54)
Tomasi et al. (2013)	21	51.0	43.7	19	96.3	8.8	1.38 (0.37)
Stability (VAS)							
Ala et al. (2022)	18	40.0	42.6	18	95.0	26.5	1.51 (0.39)
Gaballa et al. (2021)	18	81.3	6.4	18	85.7	2.4	0.90 (0.36)
Gaballa et al. (2021)	18	80.3	4.7	18	83.7	4.7	0.70 (0.36)
Al-Zubeidi et al. (2012)	106	29.3	29.0	96	76.6	13.1	2.06 (0.18)
Coutinho et al. (2021)	45	59.3	37.6	30	82.7	27.2	0.68 (0.25)
De Kok et al. (2011)	20	17.1	28.8	10	96.4	4.1	3.24 (0.61)
De Kok et al. (2011)	20	24.9	32.5	10	93.7	7.5	2.47 (0.54)
Chewing (VAS)							
Ala et al. (2022)	18	45.0	58.7	18	100.0	16.1	1.25 (0.38)
Gaballa et al. (2021)	18	80.9	3.8	18	85.8	4.3	1.19 (0.38)
Gaballa et al. (2021)	18	79.8	6.1	18	84.8	4.1	0.94 (0.36)
Montero et al. (2021)	20	34.0	27.0	20	80.0	19.0	1.93 (0.40)
Al-Zubeidi et al. (2012)	106	32.4	26.1	96	75.2	18.3	1.88 (0.17)
Coutinho et al. (2021)	45	59.3	37.8	30	83.3	28.1	0.69 (0.25)
De Kok et al. (2011)	20	32.2	30.1	10	94.3	9.2	2.38 (0.53)
De Kok et al. (2011)	20	34.0	27.6	10	91.7	12.9	2.35 (0.52)
Park et al. (2019)	20	87.0	19.0	16	93.0	14.0	0.35 (0.35)
Raghoebar et al. (2003)	32	85.0	22.0	28	94.0	10.0	0.51 (0.27)
Tomasi et al. (2013)	21	37.3	24.6	19	93.0	8.8	2.89 (0.48)
Speaking (VAS)							
Ala et al. (2022)	18	65.0	42.6	18	100.0	16.1	1.06 (0.37)
Gaballa et al. (2021)	18	79.9	3.2	18	81.8	2.6	0.64 (0.35)
Gaballa et al. (2021)	18	78.2	4.3	18	80.7	2.9	0.67 (0.35)
Coutinho et al. (2021)	45	76.3	31.0	30	85.3	24.6	0.31 (0.24)
De Kok et al. (2011)	20	42.0	31.4	10	88.9	9.7	1.73 (0.47)
De Kok et al. (2011)	20	46.8	22.2	10	91.4	8.4	2.30 (0.52)
Park et al. (2019)	20	82.0	21.0	16	90.0	14.0	0.43 (0.35)
Raghoebar et al. (2003)	32	85.0	15.0	28	94.0	9.0	0.71 (0.27)
Tomasi et al. (2013)	21	50.7	47.7	19	94.0	8.8	1.21 (0.36)
Esthetics (VAS)							
Ala et al. (2022)	18	85.0	40.2	18	100.0	10.5	0.50 (0.35)
Gaballa et al. (2021)	18	78.7	1.2	18	79.1	3.0	0.17 (0.34)
Gaballa et al. (2021)	18	78.3	2.9	18	77.8	3.2	−0.16 (0.34)

(Continues)

TABLE 2 (Continued)

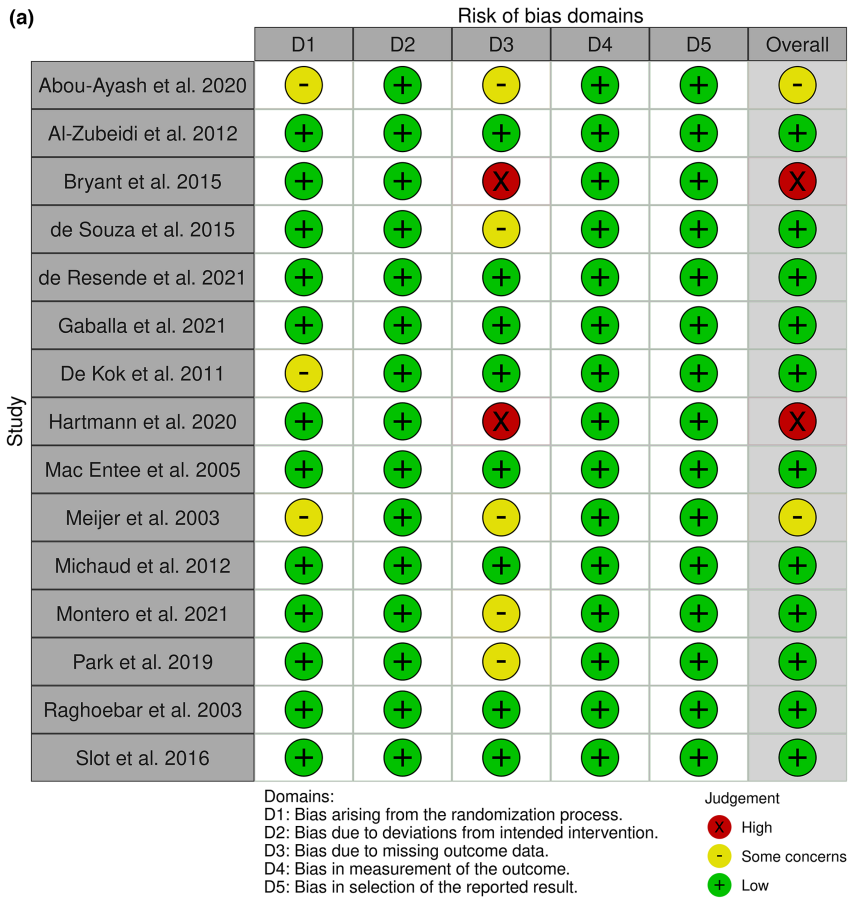
	Baseline			Follow-up			Effect size
Author (year)	Patients	Mean	SD	Patients	Mean	SD	Hedges g (SE)
Montero et al. (2021)	20	51.0	28.0	20	90.0	11.0	1.80 (0.39)
Al-Zubeidi et al. (2012)	106	51.1	29.7	96	77.2	17.9	1.05 (0.15)
Coutinho et al. (2021)	45	89.7	20.0	30	90.3	15.0	0.04 (0.24)
De Kok et al. (2011)	20	48.5	35.6	10	97.5	3.6	1.62 (0.46)
De Kok et al. (2011)	20	37.1	39.2	10	94.9	9.9	1.72 (0.47)
Park et al. (2019)	20	94.0	10.0	16	96.0	11.0	0.19 (0.35)
Raghoebar et al. (2003)	32	92.0	12.0	28	95.0	6.0	0.31 (0.26)
Pain (VAS)							
Al-Zubeidi et al. (2012)	106	40.4	31.5	96	82.1	13.2	1.69 (0.17)
Park et al. (2019)	20	91.0	13.0	16	92.0	18.0	0.06 (0.35)
Raghoebar et al. (2003)	32	75.0	28.0	28	96.0	9.0	0.97 (0.28)
Cleaning (VAS)							
Al-Zubeidi et al. (2012)	106	66.0	24.3	96	80.2	11.5	0.73 (0.15)
De Kok et al. (2011)	20	61.3	36.6	10	89.4	8.8	0.89 (0.42)
De Kok et al. (2011)	20	72.1	21.4	10	96.8	6.2	1.34 (0.45)
Short-Form 36 PCS							
Abou-Ayash et al. (2020)	158	48.1	10.5	131	45.2	14.2	−0.23 (0.12)
Short-Form 36 MCS							
Abou-Ayash et al. (2020)	158	55.7	6.1	131	54.8	7.3	−0.13 (0.12)
Denture satisfaction score (DSS)							
Attard et al. (2006)	35	21.0	2.7	35	6.6	2.1	5.89 (0.57)
Alfadda et al. (2009)	77	21.0	2.7	73	5.8	1.9	6.45 (0.41)
Oral impact on daily performance (OIDP)							
Berretin-Felix et al. (2008)	15	20.0	39.3	15	0.0	14.1	0.66 (0.39)
Patient satisfaction score							
Slot et al. (2016)	25	4.1	1.6	22	9.0	0.7	3.82 (0.52)
Slot et al. (2016)	25	4.3	1.9	24	8.8	1.3	2.71 (0.41)

Abbreviations: MCS, Mental Component Score; PCS, Physical Component Score; SD, standard deviation; SE, standard error.

of ES has been described as a valid tool to compare dPROs across studies (Reissmann, 2021). The consequence of such an approach is that in the respective "overall" effect sizes, summary scores from validated questionnaires containing several items (e.g., OHIP) are treated as equivalent to the results of individual questions (e.g., single items with VAS). At first glance, this approach is at least questionable due to the varying psychometric quality of the dPROMs and the variety of dPRO concepts included in the meta-analyses. This might partially explain the high heterogeneity among the included studies. However, considering the aim of the present study—to analyze the effect of treatment on dPROs in general—and the limited amount of available data, this approach seems to be the best way to generate an initial comparison of the respective treatment effects. Given the questionability of this "overall" approach, also including varying numbers of implants in edentulous maxillae and mandibles, further analyses were performed in the present review to compare individual dimensions of dPROs.

4.2 | Strengths and weaknesses

The major strength of the present systematic review and meta-analysis is the high number of studies that could be included, thanks of the approach of using ES for the analyses. However, the limitation of the small number of studies directly comparing IFCD and IOD treatments remains, as only two RCTs with this direct comparison could be included. While most of the included studies described the effects of implant-based rehabilitation in one jaw with a conventional complete denture as the antagonist, three studies did not include clear information about the opposing dentition (Park et al., 2019; Slot et al., 2016; Tomasi et al., 2013). Since all included studies focused on completely edentulous patients, the antagonists may include conventional complete dentures, IODs, or IFCDs. However, having an IFCD or an IOD as an antagonist is likely to result in different patient ratings, compared to situations with conventional complete dentures, and therefore represents a source of



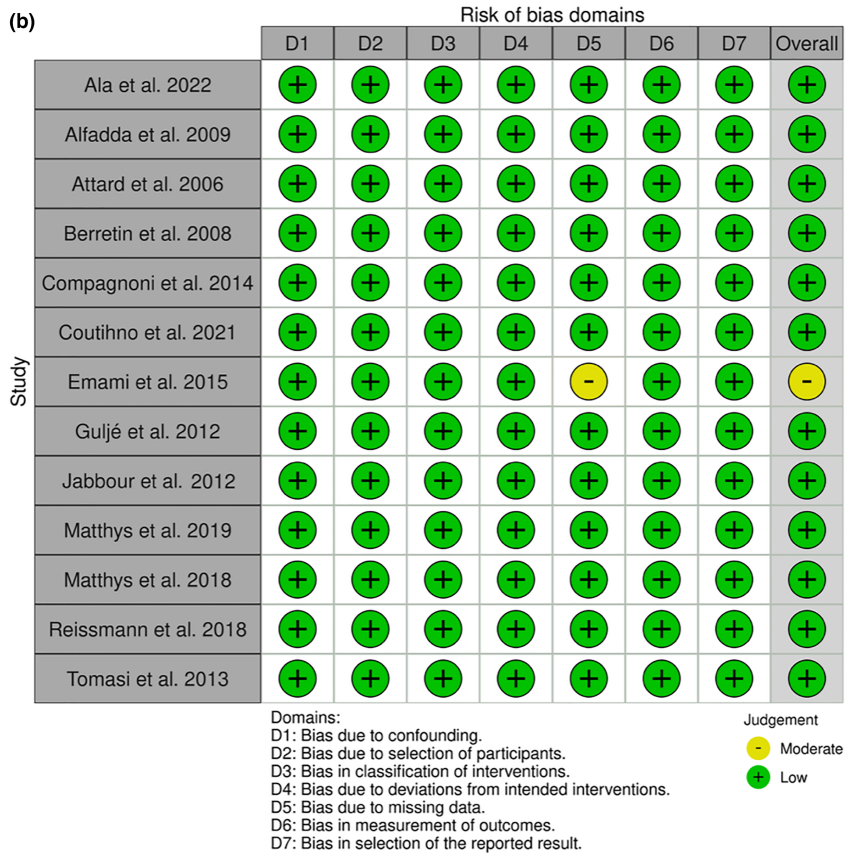


FIGURE 2 (a) Risk of bias analysis of included randomized controlled clinical studies. (b) Risk of bias analysis of included prospective studies.

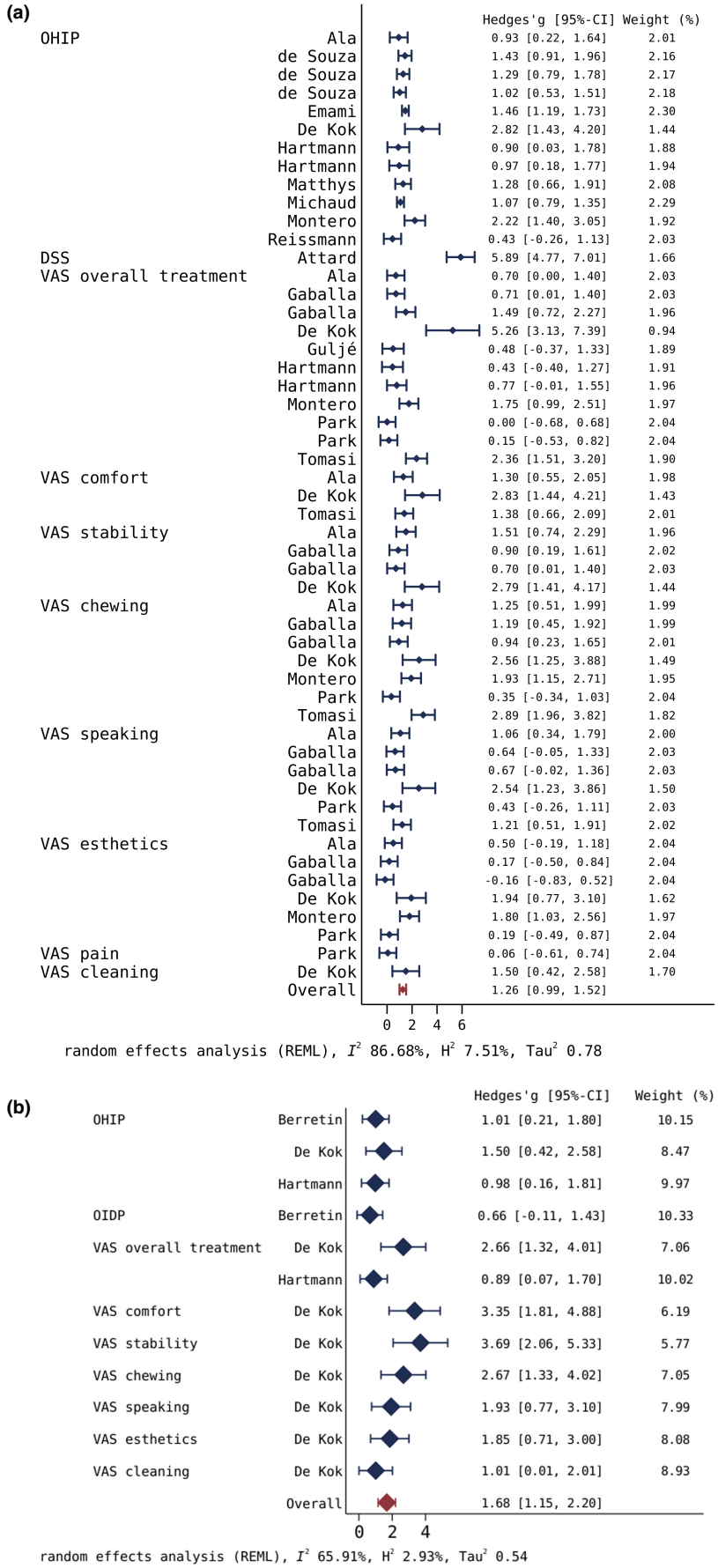


FIGURE 3 (a) Forrest plot of dental patient-reported outcomes from implant-overdenture wearers. (b) Forrest plot of dental patient-reported outcomes from implant-supported fixed complete denture wearers. Abbreviations: DSS, Denture Satisfaction Score; OHIP, Oral Health Impact Profile; OIDP, Oral Impact on Daily Performance; VAS, Visual Analogue Scale.

TABLE 3 Comparison between implant-supported fixed complete dentures (IFCDs) and implant overdentures (IODs); (follow-up: 1–1.5 years).

Outcome	No. of PROMs	Pat. BL	Pat. FU	ES (95% CI)	*p*-Value
All dPROMS					
IODs	52	500	481	1.26 [0.99, 1.52]	0.165
IFCDs	12	40	38	1.68 [1.15, 2.20]	
IFCD vs. IOS (RE)[a]				0.45 [−0.19, 1.09]	
OHIP					
IODs	9	123	116	1.14 [0.91, 1.36]	0.920
IFCDs	3	40	38	1.11 [0.60, 1.61]	
IFCD vs. IOS (RE)[a]				−0.03 [−0.58, 0.52]	
Overall treatment outcome (VAS)					
IODs	11	133	124	1.08 [0.47, 1.70]	0.491
IFCDs	2	25	23	1.69 [−0.04, 3.42]	
IFCD vs. IOS (RE)[a]				0.58 [−1.08, 2.24]	
Comfort (VAS)					
IODs	3	49	47	1.60 [0.95, 2.26]	0.059
IFCDs	1	10	10	3.35 [1.81, 4.88]	
IFCD vs. IOS (RE)[a]				1.74 [−0.07, 3.56]	
Stability (VAS)					
IODs	4	46	46	1.32 [0.58, 2.06]	0.032
IFCDs	1	10	10	3.69 [2.06, 5.33]	
IFCD vs. IOS (RE)[a]				2.37 [0.21, 4.54]	
Chewing (VAS)					
IODs	7	107	101	1.52 [0.86, 2.17]	0.287
IFCDs	1	10	10	2.67 [1.33, 4.02]	
IFCD vs. IOS (RE)[a]				1.16 [−0.97, 3.29]	
Speaking (VAS)					
IODs	6	87	81	0.92 [0.54, 1.30]	0.139
IFCDs	1	10	10	1.93 [0.77, 3.10]	
IFCD vs. IOS (RE)[a]				1.01 [−0.33, 2.35]	
Esthetics (VAS)					
IODs	6	86	82	0.68 [−0.00, 1.36]	0.246
IFCDs	1	10	10	1.85 [0.71, 3.00]	
IFCD vs. IOS (RE)[a]				1.18 [−0.81, 3.17]	
Cleaning (VAS)					
IODs	1	10	10	1.50 [0.42, 2.58]	0.514
IFCDs	1	10	10	1.01 [0.01, 2.01]	
IFCD vs. IOS (FE)[a]				−0.49 [−1.96, 0.98]	

Abbreviations: BL, baseline; dPROMs, dental patient-reported outcome measures; ES, effect size; FU, follow-up; OHIP, Oral Health Impact Profile; VAS, Visual Analogue Scale.

[a]Meta-regression, RE: random-effects meta-regression, FE: fixed-effects meta-regression.

uncertainty. Furthermore, the number of included studies on IFCDs and IODs was not balanced. Previous reviews analyzing edentulous patients have shown that dPROs are collected less frequently in patients rehabilitated with IFCDs than patients with IODs (Messias et al., 2022). In the present systematic review, more than half of IFCD-wearer PROs were obtained from prospective studies, resulting in potential selection bias. This selection bias in combination with the indirectness of the comparison ICFD versus IOD was the main reason for rating the certainty of evidence as low, for most PROMs.

A further limitation of the present systematic review is that the certainty of evidence of each meta-analysis was rated as low or moderate. Nevertheless, the reason for the result of moderate or low certainty rather than very low certainty was mainly the relatively low risk of bias of the included studies. The main reason that the risk of bias of the individual studies in the present systematic review was relatively low is most likely related to the strict inclusion and exclusion criteria (Moons et al., 2019). In particular, the criterion of sufficient reporting baseline and follow-up data led to the exclusion of many studies in which the risk of bias was estimated to be higher.

4.3 | Clinical implications

A combination of the results from the overall analysis and the more specific analyses may be used in the future to counsel patients on the best treatment options for them. This approach may be especially useful in patients seeking improvement in specific areas (i.e., stability and comfort) where the difference between IFCDs and IODs was most obvious. Despite the non-existent differences between IFCD and IOD treatments in terms of most dPROs, patients still do not seem to make a 50:50 decision for one or the other treatment option when given the choice (Heydecke et al., 2003). Individual factors, which should be further analyzed, seem to be influential for this decision. Heydecke et al. have shown that the less complex hygiene procedures of IODs could be the reason why patients who have difficulties with cleaning are more likely to choose an IOD than an IFCD (Heydecke et al., 2003). On the other hand, the present meta-analysis showed that stability with

TABLE 4 Certainty of evidence analysis for the comparison of implant-supported fixed complete dentures (IFCDs) and implant overdentures (IODs).

Outcome	No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Certainty
All dPROMS	15	8 RCTs, 7 non-RCTs	Moderate[a]	Serious[b]	Yes	Serious[c]	Low
OHIP	10	5 RCTs, 5 non-RCTs	Moderate[a]	Serious[b]	Yes	Serious[c]	Low
Overall treatment outcome (VAS)	8	5 RCTs, 3 non-RCTs	Moderate[a]	Serious[b]	Yes	Serious[c]	Low
Comfort (VAS)	3	2 RCTs, 1 non-RCTs	Low[a]	Serious[b]	Yes	Serious[c]	Low
Stability (VAS)	3	2 RCTs, 1 non-RCT	Low[a]	Serious[b]	Yes	Serious[c]	Low
Chewing (VAS)	6	4 RCTs, 2 non-RCTs	Low[a]	Serious[b]	Yes	Serious[c]	Low
Speaking (VAS)	6	4 RCTs, 2 non-RCTs	Low[a]	Serious[b]	Yes	Serious[c]	Low
Esthetics (VAS)	6	4 RCTs, 2 non-RCTs	Low[a]	Serious[b]	Yes	Serious[c]	Low
Cleaning (VAS)	1	1 RCT	Low[a]	No	No	Serious[c]	Moderate

Abbreviations: CI, confidence interval; dPROMs, dental patient-reported outcome measures; OHIP, Oral Health Impact Profile; RCT, randomized controlled trial; VAS, Visual Analogue Scale.

[a]Bias estimation based on risk of bias analyses.

[b]Presence of substantial heterogeneity.

[c]Imprecision due to small sample size especially of IFCD group, and/ or wide confidence intervals.

IFCDs was rated higher. Although this result is based only on dPROs of one cohort of patients treated with IFCDs, it suggests that younger patients looking for stability in their prosthetic restoration would be more likely to opt for an IFCD (Kuoppala et al., 2013).

One of the most frequently asked questions regarding patient information pertains to the cost effectiveness of the treatment options. Since treatment costs vary greatly around the globe, it is difficult to draw generalized conclusions here. Nevertheless, a common approach for comparing cost-effectiveness is to calculate the cost of improvement by one unit to compare two or more treatment options (Briggs & Gray, 1998). Taking the overall results of the present study as an example, the treatment costs for an IFCD and for an IOD can be divided by the factors 1.68 and 1.26, respectively, which represent the ES on overall dPROs of each treatment option. The smaller result then represents the more cost-effective choice in terms of overall dPROs. As the ES in patients treated with ICFDs was 1.33-fold higher than that of patients with IODs, it can be inferred that if the cost of an ICFD is more than 1.33-fold greater than an IOD, treatment with an IOD is more cost-effective with respect to dPROs. Another systematic review and meta-analysis on IODs, as well as a recent RCT comparing IFCDs and IODs concluded that IODs are more cost-effective (Hartmann, de Menezes Bandeira, et al., 2020; Zhang et al., 2017).

The same methodology can be applied to calculate the most cost-effective number of implants for an IOD. Although initial investment costs for IODs on two implants are higher than for IODs on one implant, single implant IODs seem to require a high follow-up effort, especially due to the adjustment of the retention, which may offset the initially lower investment costs over a longer period of time (Hartmann, de Menezes Bandeira, et al., 2020; Kern et al., 2021). A recently published study analyzed masticatory efficiency and OHRQoL in patients restored with IODs first on one, then on two, and subsequently on three implants in the edentulous mandible (Passia et al., 2022). Masticatory efficiency improved with the loading of the second implant, while the third implant had no effect on masticatory efficiency or OHRQoL. Considering these results as well as the findings of the present study, that both showed no effect when more than two implants were used in an IOD, the recommendation of the McGill Consensus Conference to restore edentulous patients with a mandibular IOD on two implants (Feine et al., 2002) can still be supported and thus represent our first treatment option. However, IODs on one implant could be considered as the "minimum standard of care" for the edentulous mandible, as this restoration already leads to an improvement of functional parameters and dPROs (Passia et al., 2017; Policastro et al., 2019). This option could be specifically recommended to patients who have limited possibilities to afford higher one-time treatment costs. More than two implants retaining a mandibular IOD, seem to be unnecessary from a patient's point of view.

4.4 | Implications for future research

Future studies should use dPRO assessment instruments with sufficient psychometric properties and several validated language versions available to ensure high methodological quality and comparability. Such an instrument should measure all four dimensions of OHRQoL, i.e., *Oral Function*, *Orofacial Pain*, *Orofacial Appearance*, and *Psychosocial Impact* (John et al., 2014). The most often applied instrument fulfilling these requirements is the OHIP with its several versions. Even the very short version with only 5 items (OHIP-5) reflects approximately 90% of the information collected in the long (49-item) version and is recommended for most clinical and scientific

TABLE 5 Subgroup analyses in implant overdentures (IODs) focusing on retention type (single attachment vs. bar), influence of the follow-up time, and number of implants per reconstruction.

	No. of dPROMs	Pat. BL	Pat. FU	ES (95% CI)	*p*-Value	Heterogeneity (I^2)
Type of retention						
All dPROMs						
Single	41	584	546	1.38 [1.17, 1.58]		82.0%
Bar	7	105	93	1.33 [0.37, 2.29]		94.5%
Bar vs. single[a]				−0.08 [−0.72, 0.56]	0.804	
OHIP[b]						
Single	9	145	134	1.30 [1.04, 1.55]		42.4%
Mean follow-up (FU) [years]						
all dPROMs						
Mean FU ≤ 2	55	753	697	1.21 [0.94, 1.47]		90.0%
Mean FU 5	21	332	284	1.53 [0.94, 2.12]		97.5%
Mean FU 10	6	93	81	1.46 [0.38, 2.55]		95.5%
Mean FU 5 vs. ≤2[b]				0.29 [−0.28, 0.86]	0.320	
Mean FU = 10 ≤ 2[b]				0.23 [−0.73, 1.19]	0.637	
OHIP						
FU ≤ 2	13	489	466	1.28 [1.07, 1.49]		49.6%
Mean FU = 5	3	82	64	1.30 [0.76, 1.85]		74.7%
Mean FU 5 vs. ≤2[a]				0.03 [−0.46, 0.52]	0.910	
Implants per reconstruction						
all dPROMs						
Impl/Recon 1	20	372	304	0.67 [0.43, 0.91]		79.4%
Impl/Recon 2	38	435	395	1.40 [1.18, 1.62]		82.3%
Impl/Recon 3	1	135	135	1.46 [1.19, 1.73]		
Impl/Recon 4	3	76	68	0.65 [−0.21, 1.50]		81.9%
Implants per recon.[a]				0.22 [−0.03, 0.46	0.081	
OHIP						
Impl/Recon 1	4	172	144	1.11 [0.65, 1.57]		63.7%
Impl/Recon 2	9	267	248	1.37 [1.12, 1.62]		47.0%
Impl/Recon 3	1	135	135	1.46 [1.19, 1.73]		
Impl/Recon 4	2	56	52	0.96 [−0.02, 1.94]		80.3%
Implants per recon.[b]				−0.01 [−0.24, 0.21]	0.925	

Abbreviations: BL, baseline; dPROMs, dental patient-reported outcome measures; ES, effect size; FU, follow-up; Impl/Recon, number of implants per reconstruction; OHIP, oral health impact profile; pat, number of patients.

[a]Meta-regression (random-effects).

[b]No studies available for bar retention.

applications (John et al., 2021, 2022; Reissmann, 2021). Nonetheless, in some cases, it is not only necessary to assess the entire OHRQoL spectrum, but some individual aspects are also of special interest. In these cases, specific questions relevant to the treatment outcome can be used (Leles et al., 2022). To ensure comparability, questions should be chosen that were already applied in other studies on the same or similar topic. Answers to these questions should be collected on commonly accepted response scales, such as VAS, ordinal response scales, or Likert scales. However, given the widespread application of VAS for assessing satisfaction with various treatment outcomes in implant dentistry, the use of a VAS is recommended. Furthermore, since individual factors seem to be very important for decision making, future studies are needed to address these patient-related psychosocial factors. Such information is related to patient values and preferences. Finally, as the commonly accepted scientific standard, prospective studies should report not only differences between treatment groups but also individual scores for each group. That is, reporting of pre-treatment and follow-up scores (including measures for central tendency, e.g., means, and for score variability, e.g., standard deviations) should be mandatory.

TABLE 6 Certainty of evidence analysis for the subgroup analyses within implant overdenture groups (IODs).

Outcome	No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Certainty
Type of retention; all dPROMs	20	14 RCTs, 6 non-RCTs	Moderate[a]	Serious[b]	Yes	Serious[c]	Low
Mean follow-up; all dPROMs	24	15 RCTs, 9 non-RCTs	Moderate[a]	Serious[b]	Yes	Moderate[c]	Moderate
Mean follow-up OHIP	11	6 RCTs, 5 non-RCTs	Low[a]	Serious[b]	Yes	Serious[c]	Low
Implants per reconstruction; all dPROMs	24	15 RCTs, 9 non-RCTs	Moderate[a]	Serious[b]	Yes	Serious[c]	Low
Implants per reconstruction; OHIP	11	6 RCTs, 5 non-RCT	Low[a]	Serious[b]	Yes	Serious[c]	Low

Abbreviations: CI, confidence interval; dPROMs, dental patient-reported outcome measures; OHIP, Oral Health Impact Profile; RCT, randomized controlled trial; VAS, Visual Analogue Scale.

[a]Bias estimation based on risk of bias analyses.

[b]Presence of substantial heterogeneity.

[c]Imprecision due to small sample size, and/or wide confidence intervals.

5 | CONCLUSION

Although data from included dPROMs address slightly different constructs, it can be concluded that overall, implant treatment in edentulous patients generally results in a strong positive effect on dPROs, independent of the type of prosthodontic rehabilitation. IFCDs may be preferable for patients who specifically seek denture stability. Treatment with mandibular implant overdentures on two implants results in better dPROs than on one implant. On the other hand, having more than two implants in an overdenture does not increase dPROs. Due to the low to moderate certainty of evidence, the results of the present study should be interpreted cautiously. More dPRO data, especially from patients rehabilitated with IFCDs, are needed for further comparison between these two treatment options.

AUTHOR CONTRIBUTIONS

S.A-A. & D.R. conceived the idea; M.F. & S.P. performed the literature search, data extraction, and risk of bias analysis, S.A-A. interpreted the data; S.A-A. & D.R. wrote the initial draft; all authors confirmed the final version of the manuscript.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

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

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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ORIGINAL ARTICLE

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Oral function in completely edentulous patients rehabilitated with implant-supported dental prostheses: A systematic review and meta-analysis

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Abstract

Objectives: This review evaluated the effects of rehabilitation with implant-supported prostheses on the oral function of completely edentulous adults.

Materials and Methods: Systematic literature searches were performed to identify records reporting on oral function in completely edentulous adults rehabilitated with implant-supported prostheses. Meta-analyses were performed on various outcomes including bite force, masticatory performance, muscle activity, mandibular movement/chewing pattern, and salivary flow.

Results: 5507 records were identified. Thirty studies qualified for data extraction and analysis. The kappa (κ) for the search and identification strategy ranged between 0.50 and 1.00. Meta-analysis was performed grouping the studies by outcomes and split by time points of 6–12 months, 12–36 months, and >36 months after implant therapy. The meta-analyses revealed a significant improvement in oral function of completely edentulous adults after rehabilitation with implant-supported prostheses at 6–12 months ($Z = -4.895$, $p < .001$; 95% CI: −0.703, −0.301; $\tau^2 = .609$; $Q = 114.953$, df = 17, $p < .001$; $I^2 = 85.2\%$), at 12–36 months ($Z = -4.886$, $p < .001$; 95% CI: −0.580, −0.248; $\tau^2 = .908$; $Q = 280.611$, df = 35, $p < .001$; $I^2 = 87.5\%$) and at more than 36 months ($Z = -9.108$, $p < .001$; 95% CI: −1.472, −0.951; $\tau^2 = .019$; $Q = 7.918$, df = 7, $p = .340$; $I^2 = 11.6\%$). The included studies demonstrated a low to moderate risk of bias.

Conclusions: This systematic review concluded that the oral function of completely edentate adults significantly improved with implant-supported/retained prostheses, even when only one jaw received implant therapy. Therefore, implant therapy should be promoted for edentulous adults to alleviate the shortcomings of conventional complete removable dental prostheses.

KEYWORDS
bite force, complete removable dental prosthesis, implant-supported dental prostheses, masticatory performance, meta-analysis, oral function, salivary flow, systematic review

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1 | INTRODUCTION

Oral health is considered an important aspect of ageing and frailty (Castrejón-Pérez et al., 2017). Frailty is a condition that is a precursor to complex health problems; it increases the morbidity and mortality of older adults. Nutrition plays an important role in the etiology of frailty. Tooth loss is a bane that results in impaired oral functions, and is linked to problems with mobility, cognitive decline, and malnutrition. Components of oral function including chewing function, bite force, articulatory motor skills, oral tactile sensitivity, and oral diadochokinesis, decline with old age and with tooth loss (Hoeksema et al., 2017; Shwe et al., 2019; Watanabe et al., 2017). A conceptual model on orofacial health proposed that, based on an individual's biological prerequisites and resources, the orofacial functional capacity is developed throughout the entire life. The ageing process along with the medical comorbidities influence this orofacial functional capacity and may lead to a state of oral hypofunction (Schimmel et al., 2021). The absence of an efficient rehabilitation further compromises oral hypofunction and may develop into oral frailty (Matsuo et al., 2016; Minakuchi et al., 2018). Malnutrition is a frequent problem in elderly edentulous patients especially in those who have ill-fitting or poorly fabricated dentures (Altenhoevel et al., 2012). It is imperative that an efficient rehabilitation, is carried out that will restore the oral functions, in order to reestablish and maintain a healthy nutritional state.

Complete removable dental prostheses (CRDPs) have been used to treat completely edentulous patients for more than a century and are considered a "gold standard" treatment for restoring edentulous patients. However, it is important to understand that the patients' oral functions are not entirely restored when rehabilitated with conventional CRDPs (Carlsson, 1984; Fontijn-Tekamp et al., 1998; Michael et al., 1990). Studies have demonstrated that the bite forces of CRDP wearers are impaired which may be attributed to a combination of factors including retention and stability of the CRDPs, reduced muscle force, degree of jaw opening, as well as pain or frailty (Haraldson et al., 1988; Kapur & Garrett, 1984; Mericske-Stern et al., 1993; Michael et al., 1990; Slagter et al., 1993). The use of implant support for the rehabilitation of edentulous jaws is a successful treatment modality that improves mastication, patient satisfaction as well as the oral health-related quality of life (OHRQoL), and these changes are observed even in dependent older adults (Feine et al., 2002; Feine, de Grandmont, et al., 1994; Feine, Maskawi, et al., 1994; Heydecke et al., 2003; Maniewicz et al., 2019; Meijer et al., 2009; Müller et al., 2004, 2012, 2013; Nogueira et al., 2021; Payne et al., 2017; Rashid et al., 2011; Schimmel et al., 2010; Srinivasan et al., 2017; Thomason et al., 2003, 2009, 2012; van der Bilt et al., 2006; van Kampen et al., 2004; Visser et al., 2005; Wismeijer et al., 1997; 2013). There is robust evidence to support dental implant therapy as a predictable long-term treatment option, in terms of improvement of CRDP retention and stability, implant survival, clinically acceptable peri-implant marginal bone level changes, and minimal complications. However, scientific evidence evaluating the efficacy of implant therapy in improving the parameters of oral function is still scarce or missing.

Therefore, the aim of this systematic review was to examine the body of evidence, available in current literature, evaluating the effect of dental implant therapy on the parameters of oral function (bite force, masticatory performance, swallowing function, muscle activity, lip force, speech and articulation, oral tactile sensitivity, oral diadochokinesis, and salivary flow) in completely edentulous patients.

Based on our aim, the population intervention comparison outcome time (PICOT) focus question set for this systematic review was: "What are the short- to long-term benefits in completely edentulous patients rehabilitated with implant-retained/supported fixed- or removable-dental prostheses when compared to those rehabilitated with conventional complete removable dental prostheses, with regard to oral function?"

2 | MATERIALS AND METHODS

This systematic review was performed and reported adhering to the PRISMA (preferred reporting items for systematic reviews and meta-analysis) guidelines (Page, McKenzie, et al., 2021; Page, Moher, et al., 2021). The protocol of this systematic review and meta-analysis was registered with PROSPERO: International prospective register of systematic reviews (CRD42021290852).

2.1 | Eligibility criteria and information sources

The complete list of inclusion and exclusion criteria used for this systematic review along with the sources of information for identifying the relevant records are detailed in Table 1. The last search update was performed on February 28, 2022.

2.2 | Search strategy and selection process

The search terms were identified based on the PICOT (population intervention comparison outcome and time) criterion and an initial search strategy was developed by the first author (MS). The search terms were either medical subject headings (MeSH) or other relevant terms in the "all fields" category, and were combined using appropriate Boolean operators (OR, AND, NOT) to structure the initial strategy, which was discussed with all co-investigators (PK, LA, and FM) and modified to develop the final search strategy. PK ran the search in all the listed databases to check for accuracy. Errors identified were corrected and then the search strategy was appropriately modified for final implementation. The complete list of search terms and the final implemented strategy are described in Table 1.

The results of the search strategy in each of the online databases were imported into a web-based collaboration software

TABLE 1 Focus question, criteria for inclusion, sources of information, search terms, search strategy, search filters, and search dates.

Focus question	**What are the short- to long-term benefits in completely edentulous patients rehabilitated with implant-retained/supported fixed- or removable-dental prostheses when compared to those rehabilitated with conventional complete removable dental prostheses, with regard to oral function?**	
Criteria	Inclusion criteria	• Studies reporting on oral function in completely edentulous human subjects • Patients must be rehabilitated with implant-retained/supported dental prostheses (fixed or removable) • Dental implant type: micro-rough surface, root form dental implants • Patients must have been clinically examined during recall. • Minimum follow-up period: ≥ 6 months after implant loading
	Exclusion criteria	• Sample size of less than 10 cases • Animal studies • Invitro- and proof-of-concept experiments.
Information sources	Electronic databases	Medline (PubMed), Embase, the Cochrane Central Register of Controlled Trials (CENTRAL), Web of Science
	Journals	All peer reviewed journals available online in databases: Medline (PubMed), Embase, the Cochrane Central Register of Controlled Trials (CENTRAL), Web of Science
	Others	Popular online internet search engines (e.g., Google, Yahoo, Bing), Online internet research community websites (https://www.researchgate.net/), reference crosschecks, personal communications, hand-searches.
Search Terms (*PICOT*)	Population	**#1:** [MeSH]: jaw, edentulous OR mouth, edentulous **#2:** [All fields]: edentulous OR edentulous maxilla OR edentulous mandible OR completely edentulous mouth OR completely edentulous jaw
	Intervention or exposure	**#3:** [MeSH]: dental implants OR dental implantation, endosseous OR dental prosthesis, implant-supported OR denture, overlay **#4:** [All fields]: implant retained removable dental prosthesis OR implant-supported removable dental prosthesis OR overdenture OR implant overdentures OR implant retained overdentures OR implant-supported overdentures OR implant assisted overdentures OR implant-retained fixed dental prosthesis OR implant-supported fixed dental prosthesis OR implant-supported dental prosthesis
	Comparison	**#5:** [MeSH]: denture, complete OR dental prosthesis **#6:** [All fields]: conventional complete denture OR traditional complete denture OR complete removable dental prosthesis OR removable dental prosthesis
	Outcome	**#7:** [MeSH]: mastication OR chewing OR bite force OR speech OR phonetics OR salivation OR deglutition OR swallowing OR swallowing function **#8:** [All fields]: oral function OR chewing capability OR chewing efficiency OR chewing performance OR masticatory efficiency OR chewing function OR masticatory function OR masticatory performance OR eating capability OR food oral processing OR comminution OR maximum bite force OR maximum voluntary bite force OR jaw muscle activity OR masseter muscle thickness OR salivary flow rate OR stimulated salivary flow rate OR resting salivary flow rate OR tongue pressure OR tongue force OR tongue function OR lip function OR lip force OR maximum lip force OR swallowing threshold OR mandibular movement OR mandibular movement coordination OR Oral stereognosis OR oral diadochokinesis OR oral tactile sensitivity OR intra-oral sensitivity OR jaw kinematics
	Time	Minimum: 6 months post implant loading Maximum: no limit
Filters	Language	Not applied
	Species	Not applied
	Ages	Not applied
	Journal categories	Not applied
Search Builder	Search combination	(#1 OR #2) AND (#3 OR #4) AND (#5 OR #6) AND (#7 OR #8)

TABLE 1 (Continued)

Focus question	What are the short- to long-term benefits in completely edentulous patients rehabilitated with implant-retained/supported fixed- or removable-dental prostheses when compared to those rehabilitated with conventional complete removable dental prostheses, with regard to oral function?	
Search query as performed in the electronic databases	PubMed (Medline), Embase, CENTRAL, Web of Science	(jaw, edentulous OR mouth, edentulous OR edentulous OR edentulous maxilla OR edentulous mandible OR completely edentulous mouth OR completely edentulous jaw) AND (dental implants OR dental implantation, endosseous OR dental prosthesis, implant-supported OR denture, overlay OR implant retained removable dental prosthesis OR implant-supported removable dental prosthesis OR overdenture OR implant overdentures OR implant retained overdentures OR implant-supported overdentures OR implant assisted overdentures OR implant-retained fixed dental prosthesis OR implant-supported fixed dental prosthesis OR implant-supported dental prosthesis) AND (denture, complete OR dental prosthesis OR conventional complete denture OR traditional complete denture OR complete removable dental prosthesis OR removable dental prosthesis) AND (mastication OR chewing OR bite force OR speech OR phonetics OR salivation OR deglutition OR swallowing OR swallowing function OR oral function OR chewing capability OR chewing efficiency OR chewing performance OR masticatory efficiency OR chewing function OR masticatory function OR masticatory performance OR eating capability OR food oral processing OR comminution OR maximum bite force OR maximum voluntary bite force OR jaw muscle activity OR masseter muscle thickness OR salivary flow rate OR stimulated salivary flow rate OR resting salivary flow rate OR tongue pressure OR tongue force OR tongue function OR lip function OR lip force OR maximum lip force OR swallowing threshold OR mandibular movement OR mandibular movement coordination OR Oral stereognosis OR oral diadochokinesis OR oral tactile sensitivity OR intra-oral sensitivity OR jaw kinematics)
Search dates	January 1953 to 28 February 2022	A final confirmatory online search was performed on 28 February 2022. No further online searches were conducted after this date

platform that streamlines the production of systematic and other literature reviews (Covidence Systematic Review Software, Veritas Health Innovation, available at: www.covidence.org, last accessed on 22.10.2022). The software removed all the duplicate records as an initial step and then two investigators initially swept through the search results in the web-based software performing a thorough title and abstract screening. After the initial sweep, the shortlisted studies were included for a full-text analysis only after a mutual agreement between the two investigators. Disagreements, if present, were resolved by a consensus meeting with the first author. If multiple publications existed on the same cohort by the same research group, only the most recent publication was included in the review.

2.3 | Data collection process, data items, and missing data

Information relating to oral function including bite force, chewing efficiency, masticatory performance, jaw muscle activity (electromyography [EMG]), tongue function (tongue pressure and force), mandibular movement and chewing pattern, lip function (lip force), swallowing function, masseter thickness, oral stereognosis, oral diadochokinesis, oral sensitivity (tactile sensitivity), and phonetics (speech) were extracted, when present, from the identified records. The data extraction was performed by two investigators, who were reciprocally blinded to each other's data extraction. If any information was missing or not clear in the included record, the corresponding authors were contacted by email. The extracted parameters from the included studies are detailed in Tables 2–16. For any missing information from the included studies relevant to this systematic review, direct email contact was made with the corresponding author. Email reminders were sent to the authors in case of a nonresponse. Further emails were sent if the received information required further clarity. A nonresponse from the author or if the received information was not relevant, or inadequate, ultimately lead to the exclusion of the study.

2.4 | Study risk of bias assessment

The risk of bias of the included randomized controlled trials (RCTs) was assessed using the Cochrane tool for the assessment of risk of bias (Higgins et al., 2011), while the Newcastle–Ottawa tools were used for the prospectively designed cohort and case–control studies (Wells et al., 2014).

2.5 | Summary measures and synthesis of results

For each investigated parameter, mean and standard deviations along with sample sizes were extracted. A standardized

TABLE 2 Studies included in the meta-analysis reporting on bite force.

First author (year)	Study group (U/L)	Implant number (U/L)	Implant detail (U/L)	Attachment system	Follow-up period (months)	Bite force (mean ± SD in *N*)	*n*	Method	Conclusion
Bakke et al. (2002)	CD/CD					115.5 ± 73.1	12	Strain gauge transducer (Miniature Bite-Force Recorder, Kleven)	Bite forces in the IOD group improved significantly compared to the CD group.
	CD/IOD	0/2	-/Astra Tech	-/ball or bar	12	189.2 ± 72.2	12		
	CD/IOD	0/2	-/Astra Tech	-/ball or bar	60	193.4 ± 54.7	12		
da Silva et al. (2011)	CD/CD					40 ± 5 Right side	16	Digital dynamometer, model IDDK (Kratos, Cotia, São Paulo, Brazil)	Bite forces in the IOD group improved significantly compared to the CD group.
	CD/IOD	0/2	-/Neodent-Titamax, Curitiba, SC, Brazil	-/ball	3	70 ± 9 Right side	16		
	CD/IOD	0/2	-/Neodent-Titamax, Curitiba, SC, Brazil	-/ball	15	71 ± 8 Right side	16		
	CD/CD					50 ± 7 Left side	16		
	CD/IOD	0/2	-/Neodent-Titamax, Curitiba, SC, Brazil	-/ball	3	76 ± 9 Left side	16		
	CD/IOD	0/2	-/Neodent-Titamax, Curitiba, SC, Brazil	-/ball	15	77 ± 9 Left side	16		
Enkling et al. (2019)	CD/CD					58.1 ± 41.3	20	GM 10® occlusal force meter (Nagano Keiki Co. Ltd, 1-30-4 Higashimagome, Ohtra-ku, Tokyo, Japan)	Overall, bite forces in the IOD group improved significantly compared to the CD group. However, older participants showed less improvement compared to the younger cohort after the first-year post-loading
	CD/IOD	0/4	-/Mini dental implant, MDI® system 3M ESPE	-/ball	12	112.5 ± 63.3	20		
	CD/IOD	0/4	-/Mini dental implant, MDI® system 3M ESPE	-/ball	60	150.1 ± 97.1	19		

TABLE 2 (Continued)

First author (year)	Study group (U/L)	Implant number (U/L)	Implant detail (U/L)	Attachment system	Follow-up period (months)	Bite force (mean ± SD in *N*)	*n*	Method	Conclusion
Fontijn-Tekamp et al. (1998)	CD/CD					139.9 ± 42.2 Men	4	Miniature strain gauge bite-force transducer	The IOD group had significantly higher bite forces than the CD group. Women had significantly lower bite forces than men.
	CD/IOD	0/2	-/?	-/bar	28.8–62.4	235.2 ± 110 Men	5		
	CD/CD					70.6 ± 28.9 Women	13		
	CD/IOD	0/2	-/?	-/bar	28.8–62.4	148.2 ± 91.2 Women	22		
Lindquist and Carlsson (1985)	CD/CD					64.4 ± 26.94 SD was calculated from SEM	24	Steel bite fork with strain gauge transducer	Bite forces in the IFD group improved significantly compared to the CD group.
	CD/IFD	0/?	-/?	-/?	36	190.7 ± 77.89 SD was calculated from SEM	24		
Maniewicz et al. (2019)	CD/CD					48.1 ± 24.6	16	Occlusal Force-Meter GM10® (Nagano Keiki Co. Ltd., Tokyo, Japan)	The IOD group had significant higher bite forces than the CD group.
	CD/IOD	0/2	-/Straumann Standard Tissue Level Implants, Institute Straumann, Basel, Switzerland)	-/stud	3–12	111.3 ± 60.7	16		
	CD/CD					72.5 ± 45.3	16		
	CD/IOD	0/2	-/Straumann Standard Tissue Level Implants, Institute Straumann, Basel, Switzerland)	-/stud	≥24	145.9 ± 90.7	16		

(Continues)

TABLE 2 (Continued)

First author (year)	Study group (U/L)	Implant number (U/L)	Implant detail (U/L)	Attachment system	Follow-up period (months)	Bite force (mean ± SD in *N*)	*n*	Method	Conclusion
Melo et al. (2018)	CD/CD					39.23 ± 17.65 Mean and SD were calculated from kg-force to *N*	29	Digital gnathodynamometer (IDDK, Kratos, São Paulo, Brazil)	Bite forces in the IOD group improved significantly compared to the CD group after immediate post-rehabilitation and 3-to-5-year follow-up period. There was no statistically significant difference in bite forces considering facial type (brachyfacial, mesofacial, and dolichofacial).
	CD/IFD	0/5	-/Neoporos, Neodent, Curitba, Brazil	-/?	36–60	150.04 ± 89.24 Mean and SD were calculated from kg-force to *N*	24		
van der Bilt et al. (2010)	CD/CD					183 ± 110	14	Bite-force transducer	Bite forces in the IOD group improved significantly compared to the CD group.
	CD/IOD	0/2	-/Frialit-2, Friadent, Friedrichsfeld, Germany	-/ball or bar	8–14	337 ± 137	14		
	CD/IOD	0/2	-/Frialit-2, Friadent, Friedrichsfeld, Germany	-/ball or bar	120	341 ± 136	14		

Note: -, not applicable;?, not specified in the article.

Abbreviations: CD, conventional removable complete denture; IFD, implant-supported fixed dental prostheses; IOD, implant-supported removable complete overdenture; L, lower; *n*, sample size; SEM, standard error of mean; SD, standard deviation; U, upper.

TABLE 3 Studies included in the meta-analysis reporting on masticatory performance and efficiency by comminution tests (sieving methods).

First author (year)	Study group (U/L)	Implant number (U/L)	Implant detail (U/L)	Attachment system	Follow-up period (months)	Masticatory performance (mean ± SD)	*n*	Method	Conclusion
Outcome: X50 (median particle size, the less value, the better efficiency)						Standardized in mm			
Marcello-Machado et al. (2018)	CD/CD					5.29 ± 1.15	23	Chewing artificial food Optocal (17 cubes, 5.6 mm) for 40 strokes	Masticatory performance (X50) in the IOD group improved significantly compared to the CD group.
	CD/IOD	0/2	-/NeoPoros, Neodent, Curitiba, PR, Brazil	-/stud	3	4.38 ± 1.37	23		
	CD/IOD	0/2	-/NeoPoros, Neodent, Curitiba, PR, Brazil	-/stud	6	4.44 ± 1.2	23		
	CD/IOD	0/2	-/NeoPoros, Neodent, Curitiba, PR, Brazil	-/stud	12	4.31 ± 1.21	23		
van der Bilt et al. (2010)	CD/CD					4.6 ± 0.7	14	Chewing artificial food Optocal for 15 strokes	Masticatory performance (X50) in the IOD group improved significantly compared to the CD group.
	CD/IOD	0/2	-/Frialit-2, Friadent, Friedrichsfeld, Germany	-/ball or bar	8–14	3.7 ± 0.5	14		
	CD/IOD	0/2	-/Frialit-2, Friadent, Friedrichsfeld, Germany	-/ball or bar	120	3.7 ± 0.7	14		
	CD/CD					3.4 ± 0.6	14	Chewing artificial food Optocal for 30 strokes	
	CD/IOD	0/2	-/Frialit-2, Friadent, Friedrichsfeld, Germany	-/ball or bar	8–14	2.4 ± 0.4	14		
	CD/IOD	0/2	-/Frialit-2, Friadent, Friedrichsfeld, Germany	-/ball or bar	120	2.5 ± 0.7	14		
Outcome: %weight of test material that was passed through the sieve (the more value, the better efficiency)						Standardized in %weight of passed test material			
Borges Tde et al. (2011)	CD/CD					14.33 ± 14.42	16	Chewing artificial food Optocal for 40 strokes, then using 2.8-mm sieve	Masticatory performance (%weight of passed test material) in the IOD group improved significantly compared to the CD group.
	CD/IOD	0/2	-/Conexão Prosthesis System Limited, São Paulo, SP, Brazil)	-/bar	3	26.68 ± 17.85	16		
	CD/IOD	0/2	-/Conexão Prosthesis System Limited, São Paulo, SP, Brazil)	-/bar	6	27.70 ± 17.46	16		

(Continues)

TABLE 3 (Continued)

First author (year)	Study group (U/L)	Implant number (U/L)	Implant detail (U/L)	Attachment system	Follow-up period (months)	Masticatory performance (mean ± SD)	*n*	Method	Conclusion
Garrett et al. (1998)	CD/CD					39.8 ± 12.5 Peanut	28	Chewing peanuts (3 g) for 20 strokes, then using 1.7-mm sieve. Chewing carrots (3 g) for 40 strokes, then using 4.0-mm sieve	The IOD group had no significant advantage over the CD group for improving the ability to comminute food.
	CD/IOD	0/2	-/IMZ	-/bar	6	40.2 ± 14.6 Peanut	50		
	CD/CD					42 ± 11.2 Peanut	19		
	CD/IOD	0/2	-/IMZ	-/bar	24	40.5 ± 13 Peanut	30		
Pera et al. (1998)	CD/CD					8.2 ± 3.1	11	Chewing artificial food Optosil (17 cubes, 5.6 mm) for 60 strokes, then using 5.6-mm sieve	Masticatory performance (%weight of passed test material) in the IOD group improved significantly compared to the CD group.
	CD/IOD	0/2	-/?	-/ball	12	19.3 ± 5.8	12		
Sun et al. (2014)	CD/CD					47.41 ± 7.23	50	Chewing peanuts (4 g) for 20 s	Masticatory performance (%weight of passed test material) in the IOD group improved significantly compared to the CD group.
	CD/IOD	0/2	-/Strauman Company, Waldenburg, Switzerland	-/stud or magnetic	6	62.58 ± 6.64	49		
Outcome: $N_{1/2}$ (the number of chewing strokes necessary to reduce the value of X50 to half the initial particle size, the less value, the better efficiency)						Standardized in number of chewing cycles			
van der Bilt et al. (2010)	CD/CD					52 ± 25	14	Chewing artificial food Optocal for 15 and 30 strokes	Masticatory performance ($N_{1/2}$) in the IOD group improved significantly compared to the CD group.
	CD/IOD	0/2	-/Frialit-2, Friadent, Friedrichsfeld, Germany	-/ball or bar	8–14	24 ± 7	14		
	CD/IOD	0/2	-/Frialit-2, Friadent, Friedrichsfeld, Germany	-/ball or bar	120	27 ± 12	14		

TABLE 3 (Continued)

First author (year)	Study group (U/L)	Implant number (U/L)	Implant detail (U/L)	Attachment system	Follow-up period (months)	Masticatory performance (mean ± SD)	*n*	Method	Conclusion
Outcome: C_i (Chewing efficiency index (Ci, 1 = good, 5 = poor))									
Lindquist and Carlsson (1985)	CD/CD					3.5 ± 1.22 SD was calculated from SEM	24	Almonds and a sieve-system	Masticatory performance (C_i) in the IFD group improved significantly compared to the CD group.
	CD/IFD	0/?	-/?	-/?	36	2.1 ± 0.69 SD was calculated from SEM	24		

Note: -, not applicable;?, not specified in the article.

Abbreviations: CD, conventional removable complete denture; IFD, implant-supported fixed dental prostheses; IOD, implant-supported removable complete overdenture; L, lower; *n*, sample size; SEM, standard error of mean; SD, standard deviation; U, upper.

difference in means was calculated at 95% confidence intervals (95% CI). Inter-investigator reliability was assessed using Cohen's unweighted kappa (κ) (Landis & Koch, 1977). The meta-analysis was performed for prospectively designed studies reporting on and comparing cohorts rehabilitated with conventional complete removable dental prostheses (CRDPs) in both jaws (CD/CD) with cohorts rehabilitated with conventional maxillary CRDPs opposing a mandibular implant-retained/supported removable or fixed prostheses (CD/IOD or IFD) for the following outcomes: bite force, chewing efficiency or masticatory performance, muscle activity, mandibular movement and chewing pattern, and salivary flow rate. Lip force could not be included in the meta-analysis and was reported qualitatively. In this review individual subgroups in the studies were considered independent. Confidence intervals (CIs) were set to 95%, and standardized mean differences were calculated for each outcome parameter using comprehensive meta-analysis software, version 3.0 (Biostat). I-squared statistics (I^2-statistics) was used to assess the heterogeneity across the included studies, and accordingly, random-effects or fixed-effects models were used (DerSimonian & Laird, 1986).

The current review did not distinguish between: the types of implant rehabilitations (fixed or removable), or the number of implants employed for the rehabilitation, as well as the different types of attachments employed for the IODs. The meta-analyses were categorized for different time points and grouped by the outcome parameters. The different time points used in this meta-analyses were: 6–12 months, 12–36 months, and more than 36 months, after the insertion of the implant-supported prostheses.

2.6 | Publication biases and additional analyses

Descriptive analysis was performed on all studies to report their intervention groups, number of participants, number of implants, implant details, attachment systems, follow-up period, outcome parameters, methods applied for measuring outcomes, and conclusions. Publication bias was assessed across the studies with Egger's statistics, and were explored graphically with funnel plots (Sterne & Egger, 2001).

3 | RESULTS

3.1 | Study selection and study characteristics

The initial search identified 5507 records (Medline [PubMed]: *n* = 2581; Embase: *n* = 1302; CENTRAL: *n* = 187; Web of science: *n* = 1437). The automated removal of duplicates by the software resulted in 2205 records being eliminated. A total of 3302 records were screened and 30 relevant records qualified for data extraction and final analysis. The overall kappa (κ) scores for the study search, identification, and inclusion processes ranged between

TABLE 4 Studies included in the meta-analysis reporting on masticatory performance by mixing ability tests (color methods).

First author (year)	Study group (U/L)	Implant number (U/L)	Implant detail (U/L)	Attachment system	Follow-up period (months)	Masticatory performance (mean ± SD)	*n*	Method	Conclusion
Outcome: VOH (variance of hue, the less value, the better efficiency)									
de Resende et al. (2021)	CD/CD					~0.543 ± ~0.157 Mean and SD were estimated from diagram using ImageJ2 software (version 2.9.0/1.53t)	23	Chewing a two-color chewing gum (Vivident Fruitswing Karpuz/Asai Üzümü, Perfetti van Melle, Turkey) for 20 strokes. The ViewGum© software (dHAL Software, Greece, www.dhal.com) was used to measure the variance of the hue (VOH)	Masticatory performance (VOH) in the 1-IOD group improved significantly compared to the CD group after 6-month and 1-year follow-up. While masticatory performance (VOH) in the 2-IOD group improved significantly compared to the CD group after 1-year follow-up.
	CD/IOD	0/1	-/Straumann® Standard Plus SLActive®	-/ball	6	~0.512 ± ~0.114 Mean and SD were estimated from diagram using ImageJ2 software (version 2.9.0/1.53t)	23		
	CD/IOD	0/1	-/Straumann® Standard Plus SLActive®	-/ball	12	~0.402 ± ~0.104 Mean and SD were estimated from diagram using ImageJ2 software (version 2.9.0/1.53t)	22		
	CD/CD					~0.466 ± ~0.144 Mean and SD were estimated from diagram using ImageJ2 software (version 2.9.0/1.53t)	24		
	CD/IOD	0/2	-/Straumann® Standard Plus SLActive®	-/ball	6	~0.485 ± ~0.121 Mean and SD were estimated from diagram using ImageJ2 software (version 2.9.0/1.53t)	24		
	CD/IOD	0/2	-/Straumann® Standard Plus SLActive®	-/ball	12	~0.423 ± ~0.112 Mean and SD were estimated from diagram using ImageJ2 software (version 2.9.0/1.53t)	24		

TABLE 4 (Continued)

First author (year)	Study group (U/L)	Implant number (U/L)	Implant detail (U/L)	Attachment system	Follow-up period (months)	Masticatory performance (mean ± SD)	*n*	Method	Conclusion
Enkling et al. (2019)	CD/CD					0.78 ± 0.22	20	Chewing a two-color chewing gum for 20 strokes. The ViewGum© software was used to measure the variance of the hue (VOH)	The color-mixing ability revealed no difference in chewing efficiency (VOH) during the first year of function but was found to be improved at the 5-year follow-up relative to baseline and to 1 year.
	CD/IOD	0/4	-/Mini dental implant, MDI® system 3M ESPE	-/ball	12	0.86 ± 0.18	20		
	CD/IOD	0/4	-/Mini dental implant, MDI® system 3M ESPE	-/ball	60	0.66 ± 0.22	19		
Hartmann et al. (2020)	CD/CD					0.604 ± 0.14 20-stroke value	14	Chewing a two-color chewing gum (Vivident Fruitswing Karpuz/Asai Üzümü, Perfetti van Melle, Turkey) for 20 and 50 strokes. The ViewGum© software (dHAL Software, Greece, www.dhal.com) was used to measure the variance of the hue (VOH)	Masticatory performance (VOH) in the 1-IOD group, the 2-IOD group and the IFD group improved significantly compared to the CD group after 6-month and 1-year follow-up, considering both the tests for 20 and 50 cycles. There was no significant difference among the 1-IOD group, the 2-IOD group and the IFD group. It was also evident a small increase in VOH values from 6- to 12-month follow-ups, suggesting a slight declining in chewing function after 1 year for the 1-IOD group, the 2-IOD group and the IFD group.
	CD/IOD	0/1	-/Titamax TI Cortical, Neodent, Brazil	-/ball	6	0.356 ± 0.14 20-stroke value	11		
	CD/IOD	0/1	-/Titamax TI Cortical, Neodent, Brazil	-/ball	12	0.5 ± 0.16 20-stroke value	11		
	CD/CD					0.634 ± 0.09 20-stroke value	17		
	CD/IOD	0/2	-/Titamax TI Cortical, Neodent, Brazil	-/ball	6	0.388 ± 0.14 20-stroke value	13		
	CD/IOD	0/2	-/Titamax TI Cortical, Neodent, Brazil	-/ball	12	0.427 ± 0.14 20-stroke value	13		
	CD/CD					0.584 ± 0.09 20-stroke value	15		
	CD/IFD	0/4	-/Titamax TI Cortical, Neodent, Brazil	-/?	6	0.347 ± 0.11 20-stroke value	13		
	CD/IFD	0/4	-/Titamax TI Cortical, Neodent, Brazil	-/?	12	0.42 ± 0.14 20-stroke value	13		

(Continues)

TABLE 4 (Continued)

First author (year)	Study group (U/L)	Implant number (U/L)	Implant detail (U/L)	Attachment system	Follow-up period (months)	Masticatory performance (mean ± SD)	*n*	Method	Conclusion
Maniewicz et al. (2019)	CD/CD					0.83 ± 0.11	16	Chewing a two-color chewing gum (Hubba Bubba® Tape Gum, The Wrigley Company Ltd., England) for 20 strokes. The ViewGum© software was used to measure the variance of the hue (VOH)	No significant change (VOH) was observed in the IOD group compared to the CD group.
	CD/IOD	0/2	-/Straumann Standard Tissue Level Implants, Institute Straumann, Basel, Switzerland)	-/stud	3–12	0.73 ± 0.16	16		
	CD/CD					0.8 ± 0.11	16		
	CD/IOD	0/2	-/Straumann Standard Tissue Level Implants, Institute Straumann, Basel, Switzerland)	-/stud	≥24	0.66 ± 0.21	16		

TABLE 4 (Continued)

First author (year)	Study group (U/L)	Implant number (U/L)	Implant detail (U/L)	Attachment system	Follow-up period (months)	Masticatory performance (mean ± SD)	*n*	Method	Conclusion
Nogueira et al. (2019)	CD/CD				6	~0.642 ± ~0.109 20-stroke value, Mean and SD were estimated from diagram using ImageJ2 software (version 2.9.0/1.53t)	19	Chewing a two-color chewing gum (Vivident Fruitswing Karpuz/Asai Üzümü, Perfetti van Melle, Turkey) for 20 and 50 strokes. The ViewGum© software (dHAL Software, Greece, www.dhal.com) was used to measure the variance of the hue (VOH)	The masticatory performance (VOH) of edentulous patients rehabilitated with mandibular CD improved significantly after a 12-month follow- up period, irrespective of the stabilization of the mandibular denture with a single implant or not. However, the greater improvement in the mixing ability of the IOD group after 6 months suggests that the use of an implant to retain the mandibular denture may result in a different pattern of changes in masticatory performance compared to patients rehabilitated with a CD.
	CD/IOD	0/1	-/Straumann® Standard Plus SLActive®, Institut Straumann AG, Basel, Switzerland	-/ball	6	~0.567 ± ~0.088 20-stroke value, Mean and SD were estimated from diagram using ImageJ2 software (version 2.9.0/1.53t)	15		
	CD/CD				12	~0.454 ± ~0.119 20-stroke value, Mean and SD were estimated from diagram using ImageJ2 software (version 2.9.0/1.53t)	19		
	CD/IOD	0/1	-/Straumann® Standard Plus SLActive®, Institut Straumann AG, Basel, Switzerland	-/ball	12	~0.509 ± ~0.134 20-stroke value, Mean and SD were estimated from diagram using ImageJ2 software (version 2.9.0/1.53t)	15		

(Continues)

TABLE 4 (Continued)

First author (year)	Study group (U/L)	Implant number (U/L)	Implant detail (U/L)	Attachment system	Follow-up period (months)	Masticatory performance (mean ± SD)	*n*	Method	Conclusion
Outcome: mixing ability index (the more value, the better efficiency)									
Khalid et al. (2020)	CD/CD					−0.32 ± 0.69	23	Chewing a paraffin wax cube for 10 strokes. The masticated wax cubes were removed, and color mixing was analyzed on a scanner	Masticatory performance (mixing ability index) in the IOD group improved significantly compared to the CD group after 3-month and 3-year follow-up.
	CD/IOD	0/2	-/?	-/stud or telescopic	3	0.67 ± 0.48	23		
	CD/IOD	0/2	-/?	-/stud or telescopic	36	0.62 ± 0.66	22		
Yunus et al. (2014)	CD/CD					−0.2 ± 0.56	17	Chewing temperature-controlled two-color wax cubes for 10 strokes. The masticated wax cubes were scanned and analyzed by the digital image analyzer (Luzex-FS)	Masticatory performance (mixing ability index) in the IOD group improved significantly compared to the CD group after 3-month and 1-year follow-up.
	CD/IOD	0/2	-/Ankylos, Dentsply Friadent	-/telescopic	3	0.66 ± 0.44	17		
	CD/IOD	0/2	-/Ankylos, Dentsply Friadent	-/telescopic	12	0.86 ± 0.43	17		

Note: -, not applicable;?, not specified in the article.

Abbreviations: CD, conventional removable complete denture; IFD, implant-supported fixed dental prostheses; IOD, implant-supported removable complete overdenture; L, lower; *n*, sample size; SEM, standard error of mean; SD, standard deviation; U, upper.

TABLE 5 Studies included in the meta-analysis reporting on swallowing threshold.

First author (year)	Study group (U/L)	Implant number (U/L)	Implant detail (U/L)	Attachment system	Follow-up period (months)	Masticatory performance (mean ± SD)	*n*	Method	Conclusion
Outcome: number of chewing cycles required to chew test food until ready to swallow (the less value, the better efficiency)						Standardized in strokes			
Garrett et al. (1998)	CD/CD				6	46.1 ± 24.4 Carrot value	28	Chewing carrots (3 g) and peanuts (3 g) until ready to swallow	The IOD group had no significant advantage over the CD group for improving the ability to comminute food.
	CD/IOD	0/2	-/IMZ	-/bar	6	43 ± 19 Carrot value	50		
	CD/CD				24	41.8 ± 14.3 Carrot value	19		
	CD/IOD	0/2	-/IMZ	-/bar	24	36.3 ± 12.5 Carrot value	30		
	CD/CD				6	41.8 ± 19.3 Peanut value	28		
	CD/IOD	0/2	-/IMZ	-/bar	6	44.1 ± 23.1 Peanut value	50		
	CD/CD				24	44.3 ± 14.7 Peanut value	19		
	CD/IOD	0/2	-/IMZ	-/bar	24	39.7 ± 11.9 Peanut value	30		
Lindquist and Carlsson (1985)	CD/CD					56.8 ± 57.81 SD was calculated from SEM	24	Chewing 1 almond until ready to swallow	Masticatory performance (swallowing threshold stroke) in the IFD group improved significantly compared to the CD group.
	CD/IFD	0/?	-/?	-/?	36	29.7 ± 12.25 SD was calculated from SEM	24		

(Continues)

TABLE 5 (Continued)

First author (year)	Study group (U/L)	Implant number (U/L)	Implant detail (U/L)	Attachment system	Follow-up period (months)	Masticatory performance (mean ± SD)	*n*	Method	Conclusion
Marcello-Machado et al. (2018)	CD/CD					75.83 ± 54.72	23	Chewing artificial food Optocal (17 cubes, 5.6 mm) until ready to swallow	No significant change (swallowing threshold stroke) was observed in the IOD group compared to the CD group after 3-to-12-month follow-up.
	CD/IOD	0/2	-/NeoPoros, Neodent, Curitiba, PR, Brazil	-/stud	3	65.78 ± 34.97	23		
	CD/IOD	0/2	-/NeoPoros, Neodent, Curitiba, PR, Brazil	-/stud	6	67.84 ± 37.43	23		
	CD/IOD	0/2	-/NeoPoros, Neodent, Curitiba, PR, Brazil	-/stud	12	59.17 ± 24.51	23		
Outcome: time required to chew test food until ready to swallow (the less value, the better efficiency)						Standardized in seconds			
Garrett et al. (1998)	CD/CD	0/0	-/–	-/–	6	34.2 ± 23.7 Carrot value	28	Chewing carrots (3 g) and peanuts (3 g) until ready to swallow	The IOD group had no significant advantage over the CD group for improving the ability to comminute food.
	CD/IOD	0/2	-/IMZ	-/bar	6	29.9 ± 12.1 Carrot value	50		
	CD/CD				24	27.5 ± 9.9 Carrot value	19		
	CD/IOD	0/2	-/IMZ	-/bar	24	25 ± 9.9 Carrot value	30		
	CD/CD				6	30.1 ± 14.1 Peanut value	28		
	CD/IOD	0/2	-/IMZ	-/bar	6	31.1 ± 14.5 Peanut value	50		
	CD/CD				24	28.5 ± 10.6 Peanut value	19		
	CD/IOD	0/2	-/IMZ	-/bar	24	28 ± 9.3 Peanut value	30		

TABLE 5 (Continued)

First author (year)	Study group (U/L)	Implant number (U/L)	Implant detail (U/L)	Attachment system	Follow-up period (months)	Masticatory performance (mean ± SD)	*n*	Method	Conclusion
Lindquist and Carlsson (1985)	CD/CD					~48.541 ± ~22.946 Mean and SD were estimated from diagram using ImageJ2 software (version 2.9.0/1.53t)	24	Chewing 1 almond until ready to swallow	Masticatory performance (swallowing threshold time) in the IFD group improved significantly compared to the CD group.
	CD/IFD	0/?	-/?	-/?	36	~21.258 ± ~4.717 Mean and SD were estimated from diagram using ImageJ2 software (version 2.9.0/1.53t)	24		
Marcello-Machado et al. (2018)	CD/CD					75.78 ± 54.53	23	Chewing artificial food Optocal (17 cubes, 5.6 mm) until ready to swallow	No significant change (swallowing threshold time) was observed in the IOD group compared to the CD group after 3-to-12-month follow-up.
	CD/IOD	0/2	-/NeoPoros, Neodent, Curitiba, PR, Brazil	-/stud	3	57.7 ± 27.64	23		
	CD/IOD	0/2	-/NeoPoros, Neodent, Curitiba, PR, Brazil	-/stud	6	63.84 ± 36.38	23		
	CD/IOD	0/2	-/NeoPoros, Neodent, Curitiba, PR, Brazil	-/stud	12	57.8 ± 30.21	23		

Note: -, not applicable;?, not specified in the article.

Abbreviations: CD, conventional removable complete denture; IFD, implant-supported fixed dental prostheses; IOD, implant-supported removable complete overdenture; L, lower; *n*, sample size; SEM, standard error of mean; SD, standard deviation; U, upper.

TABLE 6 Studies included in the meta-analysis reporting on electromyography (EMG).

First author (year)	Study group (U/L)	Implant number (U/L)	Implant detail (U/L)	Attachment system	Follow-up period (months)	EMG (mean ± SD)	*N*	Method	Conclusion
Berretin-Felix et al. (2008)	CD/CD					30.21 ± 18.16 Masseter and chewing rubber value	15	μV RMS measured on masseter, submental muscles, and superior orbicularis by an EMG device (NeuroEducator® 3 Electromyography System, Therapeutic Alliances Inc., Fairborn, OH, USA) while chewing a 2-cm piece of natural rubber, swallowing food paste and swallowing water	Statistical analysis showed that only the masseter muscle had a significant loss in electromyographic activity, with a tendency of similar response for the submental muscles. Moreover, there was an increase in the activity of the orbicularis oris muscle during rubber chewing after treatment, yet without statistically significant difference. The IFD group revealed a decrease in electromyographic amplitude for the masseter muscles during swallowing, which may indicate adaptation to new conditions of stability provided by fixation of the complete denture in the mandibular arch.
	CD/IFD	0/5	-/?	-/?	3	30.8 ± 12.74 Masseter and chewing rubber value	15		
	CD/IFD	0/5	-/?	-/?	6	24.03 ± 13.32 Masseter and chewing rubber value	15		
	CD/IFD	0/5	-/?	-/?	18	24.41 ± 11.53 Masseter and chewing rubber value	15		

TABLE 6 (Continued)

First author (year)	Study group (U/L)	Implant number (U/L)	Implant detail (U/L)	Attachment system	Follow-up period (months)	EMG (mean ± SD)	N	Method	Conclusion
da Silva et al. (2011)	CD/CD					0.2 ± 0.05 Right masseter at rest	16	μV normalized mean measured on masseter and temporalis by an EMG device (Myosystem-Br1 apparatus, DataHominis Ltda, Uberlândia, MG, Brazil) while at rest, mandibular protrusion, right and left lateral mandibular movement	A decrease in EMG during the rest, lateral and protrusion movements after 15 months with IOD was observed.
	CD/IOD	0/2	-/Neodent-Titamax, Curitiba, SC, Brazil	-/ball	3	0.22 ± 0.04 Right masseter at rest	16		
	CD/IOD	0/2	-/Neodent-Titamax, Curitiba, SC, Brazil	-/ball	15	0.11 ± 0.01 Right masseter at rest	16		
	CD/CD					0.25 ± 0.05 Left masseter at rest	16		
	CD/IOD	0/2	-/Neodent-Titamax, Curitiba, SC, Brazil	-/ball	3	0.17 ± 0.02 Left masseter at rest	16		
	CD/IOD	0/2	-/Neodent-Titamax, Curitiba, SC, Brazil	-/ball	15	0.15 ± 0.01 Left masseter at rest	16		

Note: -, not applicable; ?, not specified in the article.

Abbreviations: CD, conventional removable complete denture; IFD, implant-supported fixed dental prostheses; IOD, implant-supported removable complete overdenture; L, lower; *n*, sample size; SEM, standard error of mean; SD, standard deviation; U, upper.

0.5 and 1.00, which can be considered as moderate to excellent agreement. The entire search and inclusion process is shown in a flow diagram (Figure 1). Of the included 30 studies, 20 studies (Tables 2–8) provided data for meta-analysis for the various investigated parameters of oral function (Bakke et al., 2002; Benzing et al., 1994; Berretin-Felix et al., 2008; Borges Tde et al., 2011; da Silva et al., 2011; de Resende et al., 2021; Enkling et al., 2019; Fontijn-Tekamp et al., 1998; Garrett et al., 1998; Hartmann et al., 2020; Khalid et al., 2020; Lindquist & Carlsson, 1985; Maniewicz et al., 2019; Marcello-Machado et al., 2018; Melo et al., 2018; Nogueira et al., 2019; Pera et al., 1998; Sun et al., 2014; van der Bilt et al., 2010; Yunus et al., 2014).

Ten studies (Tables 9–14) provided information for descriptive analysis (De Rossi et al., 2014; Geckili et al., 2011, 2012; Geertman et al., 1994; Jacobs & van Steenberghe, 1993; Manzon et al., 2021; Müller et al., 2012; Schimmel et al., 2017; Suzuki et al., 1999; Vieira et al., 2014).

In this review, studies were identified which compared the parameters of oral function in edentate subjects who were rehabilitated with conventional CRDPs in both jaws with edentate individuals rehabilitated with conventional maxillary CRDPs and mandibular implant-supported prostheses. The systematic review was unable to identify purpose-designed studies with maxillary implant-supported prostheses that satisfied the scope and inclusion criteria of the current review.

This systematic review could identify records for meta-analysis of the following listed outcomes: bite force, masticatory performance (sieve method, colorimetric method, swallowing threshold), stimulated salivary flow rate, mandibular movement, and chewing pattern (area of the chewing pattern, opening and closing velocity, masticatory cycle/second, and the vertical height) (Figure 1).

The review further identified a single record for lip force, but was not included in the meta-analysis because it was of a retrospective design (Schimmel et al., 2017).

Although this review also identified studies for evaluating the effect of implant-supported rehabilitation on the masseter muscle thickness (Amaral et al., 2019; Maniewicz et al., 2019; Müller et al., 2012; 2013), this parameter was excluded from this review since it is not oral function and will be presented in one of the other ITI consensus papers (De Souza et al., 2023).

The review further identified records for the effect of implant-supported prostheses on speech (Fonteyne et al., 2021; Jacobs et al., 2001; Meira et al., 2021) and oral tactile threshold (active and passive) (Luraschi et al., 2012), but these outcome measures were excluded either because the follow-up periods were less than 6 months, or that there were no conventional CRDP control groups or had an insufficient sample size (<10 cases).

This review, however, failed to locate records for evaluating the effect of implant-supported prostheses on the following parameters of oral function: tongue function (tongue pressure and force), swallowing function, oral stereognosis, and oral diadochokinesis.

TABLE 7 Studies included in the meta-analysis reporting on jaw kinematics (mandibular movement and chewing pattern).

First author (year)	Study group (U/L)	Implant number (U/L)	Implant detail (U/L)	Attachment system	Follow-up period (months)	Mandibular movement and chewing pattern (mean ± SD)	*n*	Method	Conclusion
Outcome: masticatory cycle per second						Standardized in cycles/s			
Benzing et al. (1994)	CD/CD					1.46 ± 0.3	15	Sirognathograph (Siemens, Bensheim, Germany) while chewing Gummy bear	No significant change (masticatory cycle per second) was observed in the IOD group compared to the CD group.
	CD/IOD	0/2	-/IMZ	-/bar	6–41	1.4 ± 0.4	15		
Outcome: opening and closing velocity						Standardized in mm/s			
Benzing et al. (1994)	CD/CD					48.71 ± 13.33 Opening velocity value	15	Sirognathograph (Siemens, Bensheim, Germany) while chewing Gummy bear	No significant change (opening and closing velocity) was observed in the IFD group compared to the CD group.
	CD/IOD	0/2	-/IMZ	-/bar	6–41	49.32 ± 12.76 Opening velocity value	15		
	CD/CD					36.91 ± 11.61 Closing velocity value	15		
	CD/IOD	0/2	-/IMZ	-/bar	6–41	37.27 ± 11.7 Closing velocity value	15		
Outcome: area of chewing pattern in the frontal plane						Standardized in mm^2			
Benzing et al. (1994)	CD/CD					138.67 ± 46.18	15	Sirognathograph (Siemens, Bensheim, Germany) while chewing Gummy bear	No significant change (area of chewing pattern in the frontal plane) was observed in the IOD group compared to the CD group.
	CD/IOD	0/2	-/IMZ	-/bar	6–41	149.42 ± 49.17	15		
Pera et al. (1998)	CD/CD					27.6 ± 14.2	12	Sirograph (Siemens Inc., Erlangen, Germany) while chewing artificial food (Optosil) during the first 10 s	Area of chewing pattern in the frontal plane in the IOD group increased significantly compared to the CD group.
	CD/IOD	0/2	-/?	-/ball	12	71.9 ± 31.7	12		

TABLE 7 (Continued)

First author (year)	Study group (U/L)	Implant number (U/L)	Implant detail (U/L)	Attachment system	Follow-up period (months)	Mandibular movement and chewing pattern (mean ± SD)	*n*	Method	Conclusion
Outcome: vertical length of chewing pattern in the frontal plane						Standardized in mm			
Benzing et al. (1994)	CD/CD					19.33 ± 5.25	15	Sirognathograph (Siemens, Bensheim, Germany) while chewing Gummy bear	No significant change (vertical length of chewing pattern in the frontal plane) was observed in the IOD group compared to the CD group.
	CD/IOD	0/2	-/IMZ	-/bar	6–41	18.49 ± 2.67	15		
Pera et al. (1998)	CD/CD					24 ± 8.7	12	Sirograph (Siemens Inc., Erlangen, Germany) while chewing artificial food (Optosil) during the first 10 s	Vertical length of chewing pattern in the frontal plane in the IOD group increased significantly compared to the CD group.
	CD/IOD	0/2	-/?	-/ball	12	32.3 ± 8.7	12		

Note: -, not applicable;?, not specified in the article.

Abbreviations: CD, conventional removable complete denture; IFD, implant-supported fixed dental prostheses; IOD, implant-supported removable complete overdenture; L, lower; *n*, sample size; SEM, standard error of mean; SD, standard deviation; U, upper.

TABLE 8 Studies included in the meta-analysis reporting on salivary flow rate.

First author (year)	Study group (U/L)	Implant number (U/L)	Implant detail (U/L)	Attachment system	Follow-up period (months)	Salivary flow rate (mean ± SD in ml/min)	*n*	Method	Conclusion
Maniewicz et al. (2019)	CD/CD					0.340 ± 0.210 Unstimulated salivary flow rate	16	Splitting and collecting for 2 min and chewing paraffin, then collecting for 2 min	No significant change (salivary flow rate) was observed in the IOD group compared to the CD group.
	CD/IOD	0/2	-/Straumann Standard Tissue Level Implants, Institute Straumann, Basel, Switzerland)	-/stud	3–12	0.395 ± 0.265 Unstimulated salivary flow rate	16		
	CD/CD					1.00 ± 0.635 Stimulated salivary flow rate	16		
	CD/IOD	0/2	-/Straumann Standard Tissue Level Implants, Institute Straumann, Basel, Switzerland)	-/stud	3–12	0.930 ± 0.610 Stimulated salivary flow rate	16		
	CD/CD					0.385 ± 0.305 Unstimulated salivary flow rate	16		
	CD/IOD	0/2	-/Straumann Standard Tissue Level Implants, Institute Straumann, Basel, Switzerland)	-/stud	≥24	0.515 ± 0.355 Unstimulated salivary flow rate	16		
	CD/CD					1.32 ± 0.725 Stimulated salivary flow rate	16		
	CD/IOD	0/2	-/Straumann Standard Tissue Level Implants, Institute Straumann, Basel, Switzerland)	-/stud	≥24	0.985 ± 0.715 Stimulated salivary flow rate	16		

Note: -, not applicable;?, not specified in the article.

Abbreviations: CD, conventional removable complete denture; IFD, implant-supported fixed dental prostheses; IOD, implant-supported removable complete overdenture; L, lower; *n*, sample size; SEM, standard error of mean; SD, standard deviation; U, upper.

TABLE 9 Descriptive analysis of studies not included in the meta-analysis reporting on masticatory performance and efficiency by comminution tests (sieving methods).

First author (year)	Study group (U/L)	Implant number (U/L)	Implant detail (U/L)	Attachment system	Follow-up period (months)	Masticatory performance (mean ± SD)	*n*	Method	Conclusion
Outcome: weight of test material that was retained on the sieve (the less value, the better efficiency)									
Vieira et al. (2014)	CD/CD					2.27 ±? Weight (g) of retained test material, 5.6-mm sieve	14	Chewing artificial food Optocal (17 cubes, 3 cm^3) for 20 and 40 strokes, then using 5.6-mm to 0.5-mm sieves	Masticatory performance (weight of retained test material) in the IOD group improved significantly compared to the CD group.
	CD/IFD	0/?	-/?	-/?	8	0.55 ±? Weight (g) of retained test material, 5.6-mm sieve	14		
Outcome: $N_{1/2}$ (the number of chewing strokes necessary to reduce the value of X50 to half the initial particle size, the less value, the better efficiency)						Standardized in number of chewing cycles			
Geertman et al. (1994)	CD/CD					68 ±?	28	Chewing artificial food Optocal (17 cubes, 5.6 mm) for 10, 20, 40 and 60 strokes	The IOD group had significantly better masticatory performance ($N_{1/2}$) than the CD group.
	CD/IOD	0/2	-/IMZ	-/bar	12	52 ±?	29		

Note: -, not applicable;?, not specified in the article.

Abbreviations: CD, conventional removable complete denture; IFD, implant-supported fixed dental prostheses; IOD, implant-supported removable complete overdenture; L, lower; *n*, sample size; SEM, standard error of mean; SD, standard deviation; U, upper.

TABLE 10 Retrospective studies included in the review reporting on bite force.

First author (year)	Study group (U/L)	Implant number (U/L)	Implant detail (U/L)	Attachment system	Follow-up period (months)	Bite force (mean ± SD in *N*)	*n*	Method	Conclusion
Geckili et al. (2011)	CD/CD					64.2 ± 64.2	23	A device with two strain gauges (Measurements Group Inc., Micro-Measurements Division, Type EA-06-125 MW-120, Raleigh, NC, USA) connected to a strain gauge measurement system (Vishay Micro-Measurements, Strain Indicator and Recorder, Model P3, Serial No: 159606, Raleigh)	Bite forces in the IOD group improved significantly compared to the CD group. The IOD-ball group showed no significant bite force compared to the IOD-bar group.
	CD/IOD	0/3	-/Osseospeed, Astra Tech	-/ball or bar	36	118.1 ± 118.1	23		
Geckili et al. (2012)	CD/CD					53.09 ± ?	50	A device with two strain gauges (Measurements Group Inc., Micro-Measurements Division, Type EA-06-125 MW-120, Raleigh, NC, USA) connected to a strain gauge measurement system (Vishay Micro-Measurements, Strain Indicator and Recorder, Model P3, Serial No: 159606, Raleigh)	The IOD group had significantly higher bite forces than the CD group.
	CD/IOD	0/2	-/Astra Tech, MˆIndal, Sweden	-/stud	48	127.23 ± ?	50		

TABLE 10 (Continued)

First author (year)	Study group (U/L)	Implant number (U/L)	Implant detail (U/L)	Attachment system	Follow-up period (months)	Bite force (mean ± SD in *N*)	*n*	Method	Conclusion
Manzon et al. (2021)	CD/CD	0/0	-/–	-/–	≥12	~74.63 ± ~29.15 Mean and SD were estimated from diagram using ImageJ2 software (version 2.9.0/1.53t)	40	Digital dynamometer (KRATOS Equipment model IDDKv4, seral number o7175142) with a bite fork	Bite forces in the IOD group improved significantly compared to the CD group. Both IOD and CD groups had significant lower bite forces compared to the Full Dentate group.
	IOD/IOD	4/4	?/?	telescopic/ telescopic	≥12	~213.59 ± ~60.16 Mean and SD were estimated from diagram using ImageJ2 software (version 2.9.0/1.53t)	40		
Müller et al. (2012)	CD/CD					61.4 ± 57.8	20	Occlusal Force-Meter GM 10 (Nagano Keiki Co. Ltd; 1-30-4 Higashimagome, Ohtaku, Tokyo, Japan)	Bite forces in CD < IOD < IFD < Full Dentate. The pairwise results were statistically significant, except between CD versus IOD and IFD versus Full Dentate.
	CD/IOD	0/2 or 4	-/Straumann implants, Basel, Switzerland	-/ball, stud or bar	≥12	88.1 ± 61.2	20		
	IFD/IFD	8–16	Nobels, Biocare, Gothenburg, Sweden or Straumann implants, Basel, Switzerland	?/?	≥12	270 ± 211.66	20		
Schimmel et al. (2017)	CD/CD					78.11 ± 5	17	Digital force gauge (Occlusal Force-Metter GM 10, Nagano Keiki, 130-4 Higashimagome)	Bite forces in CD < IOD < Kennedy Class I partially removable dental prosthesis < Full Dentate. The pairwise results were non-significant, except the Full Dentate group showed significantly higher bite forces than other groups.
	CD/IOD	0/2	-/Straumann RN	-/ball	≥6	82.4 ± 53.08	17		

(Continues)

TABLE 10 (Continued)

First author (year)	Study group (U/L)	Implant number (U/L)	Implant detail (U/L)	Attachment system	Follow-up period (months)	Bite force (mean ± SD in N)	*n*	Method	Conclusion
Suzuki et al. (1999)	CD/CD					242 ± 125.3	40	Dental Prescale films (50H R-type)	The IFD group showed significant higher bite forces than the CD group. No significant difference was seen in occlusal force balance between the left and right sides.
	CD/IFD	0/?	-/Steri-Oss OR Calcitek OR 3i	-/?	4.8–64.8	342.1 ± 163.6	40		

Note: -, not applicable;?, not specified in the article.

Abbreviations: CD, conventional removable complete denture; IFD, implant-supported fixed dental prostheses; IOD, implant-supported removable complete overdenture; L, lower; *n*, sample size; SEM, standard error of mean; SD, standard deviation; U, upper.

3.2 | Synthesis of results: Meta-analyses of the searched outcomes

The meta-analysis of the included studies revealed an overall significant improvement in the oral function for CD/IOD or IFD groups when compared with the CD/CD groups at 6–12 months (Overall: $Z = -4.895$, $p < .001$), at 12–36 months (Overall: $Z = -4.886$, $p < .001$), and for 36+ months (Overall: $Z = -9.108$, $p < .001$) after insertion of the implant-supported prostheses.

3.2.1 | Bite force

There was a significant improvement in the maximum bite force for all time points (6–12 months: $Z = -3.788$, $p < .001$, Figure 2; 12–36 months: $Z = -4.041$, $p < .001$, Figure 3; more than 36 months: $Z = -8.061$, $p < .001$, Figure 4; Table 2).

3.2.2 | Masticatory performance and efficiency

The studies reporting on the effect of implant rehabilitation on the masticatory performance assessed this outcome in a number of ways. Masticatory performance was assessed using the comminution tests by sieve methods (Table 3), mixing ability tests using the bi-color chewing gum technique (Table 4), and swallowing threshold method (Table 5). Different studies employed different techniques for the measured the sieve method which included: median particle size (X50), the number of strokes required to achieve the X50 median particle size, the percentage (%) of weight of the test material that passed through the sieves, and the chewing efficiency index. Studies using the chewing gums for the colorimetric techniques reported using the variance of hue (VoH), or the mixing ability index. The masticatory performance was also reported by measuring the number of chewing strokes required before swallowing and the time required to chew before swallowing.

The masticatory performance was significantly better at the 6–12 months timepoint for the implant-supported prosthesis group when measured with the median particle size ($Z = -4.264$, $p < .001$; Figure 2), number of strokes required for reducing the particle size to X50 mm ($Z = -3.552$, $p < .001$; Figure 2), and colorimetric methods (VoH: $Z = -2.635$, $p = .008$; Figure 2). The masticatory performance improved significantly for the implant-supported prosthesis group at 12–36 months after prosthesis delivery when measured by median particle size ($Z = -2.702$, $p = .007$; Figure 3), chewing efficiency index ($Z = -4.378$, $p < .001$; Figure 3), colorimetric methods (VoH: $Z = -2.283$, $p = .022$; mixing ability index: $Z = -4.711$, $p < .001$; Figure 3), and in swallowing threshold measuring the number of strokes required before swallowing ($Z = -2.838$, $p = .005$; Figure 3). Masticatory performance, when assessing with comminution tests, was significantly better for the implant-supported groups beyond 36 months as well (median particle size: $Z = -3.282$, $p = .001$; number of chewing strokes: $Z = -3.075$, $p = .002$, Figure 4).

TABLE 11 Retrospective studies included in the review reporting on masticatory performance by mixing ability tests (color methods).

First author (year)	Study group (U/L)	Implant number (U/L)	Implant detail (U/L)	Attachment system	Follow-up period (months)	Masticatory performance (mean ± SD)	*n*	Method	Conclusion
Outcome: VOH (variance of hue, the less value, the better efficiency)									
Schimmel et al. (2017)	CD/CD					?±?	17	Chewing a two-color chewing gum for 20 strokes. The ViewGum© software was used to measure the variance of the hue (VOH)	No significant change (VOH) was observed in the IOD group compared to the CD group. The Full Dentate group showed the best masticatory performance compared to the CD group, the IOD group and the partially removable prostheses group. The partially removable prostheses group had significantly better masticatory performance than the CD group.
	CD/IOD	0/2	-/Straumann RN	-/ball	≥6	?±?	17		

Note: -, not applicable;?, not specified in the article.

Abbreviations: CD, conventional removable complete denture; IFD, implant-supported fixed dental prostheses; IOD, implant-supported removable complete overdenture; L, lower; *n*, sample size; SEM, standard error of mean; SD, standard deviation; U, upper.

TABLE 12 Retrospective studies included in the review reporting on electromyography (EMG).

First author (year)	Study group (U/L)	Implant number (U/L)	Implant detail (U/L)	Attachment system	Follow-up period (months)	EMG (mean ± SD)	*n*	Method	Conclusion
De Rossi et al. (2014)	CD/CD					15.6 ± 2.6 Masseter at rest value	21	Percentage of Maximum Voluntary Contraction (MVC) value (μV*100/μV) on masseter and temporalis by an EMG device (Myosystem-Br1 portable electromyograph, DataHominis Tecnologia Ltda, Uberlândia, MG, Brazil) while at rest, paraffin chewing, peanut chewing, and cotton roller contraction	All groups presented symmetric muscular activity. The IFD and Full Dentate groups had a similar EMG pattern, that is, a higher EMG activity of masseter than temporalis muscles, differing from those of denture group. Not one statistical difference was found between the IFD and the Full Dentate groups.
	IFD/IFD	4/4	Nobel Biocare, Goteborg, Sweden/ Nobel Biocare, Goteborg, Sweden	?/?	≥6	25.4 ± 8.3 Masseter at rest value	21		
	CD/CD					17.2 ± 2 Masseter at rest value	21		
	IFD/IFD	4/4	Nobel Biocare, Goteborg, Sweden/ Nobel Biocare, Goteborg, Sweden	?/?	≥6	21.9 ± 3.7 Masseter at rest value	21		
Jacobs and van Steenberghe (1993)	CD/CD					0.17 ± 0.05	16	The amplitude range (AMP) and the mean power frequency (MPF) on masseter by an EMG device (Dantec Medical and Scientific Equipment, Skovlunde, Denmark) while clenching at the selected level for as long as possible until fatigue prevented them from further clenching	EMG indicated an increased myoelectrical output level for implant-supported reconstructions compared with the CD group.
	CD/IOD	0/2	-/?	-/bar	48	0.33 ± 0.21	20		
	CD/IFD or IFD/CD	0/5–6 or 5–6/0	-/? or? /0	-/? or? /–	72	0.32 ± 0.21	9		

Note: -, not applicable;?, not specified in the article.

Abbreviations: CD, conventional removable complete denture; IFD, implant-supported fixed dental prostheses; IOD, implant-supported removable complete overdenture; L, lower; *n*, sample size; SEM, standard error of mean; SD, standard deviation; U, upper.

TABLE 13 Retrospective studies included in the review reporting on lip force.

First author (year)	Study group (U/L)	Implant number (U/L)	Implant detail (U/L)	Attachment system	Follow-up period (months)	Lip force (mean ± SD)	*n*	Method	Conclusion
Schimmel et al. (2017)	CD/CD					? ±?	17	Measured as the maximum withstood pulling force with three sized (small, medium and large) of oral screens by a digital force gauge (ZP50-N, Imada)	Maximum lip force depended on the screen size and increased in the CD group, especially in challenging tasks such as restraining the smallest screen.
	CD/IOD	0/2	-/Straumann RN	-/ball	≥6	? ±?	17		

Note: -, not applicable;?, not specified in the article.

Abbreviations: CD, conventional removable complete denture; IFD, implant-supported fixed dental prostheses; IOD, implant-supported removable complete overdenture; L, lower; *n*, sample size; SEM, standard error of mean; SD, standard deviation; U, upper.

3.2.3 | Muscle activity (EMG)

There were no differences detected between the edentate individuals rehabilitated with conventional prostheses in both jaws and those rehabilitated with implant-supported protheses at the 6–12 months ($Z = 1.053$, $p = .292$; Figure 2) but significantly higher muscular activity during chewing was observed in the 12–36 months period for the conventional prosthesis group ($Z = 7.696$, $p < .001$; normalized mean; Figure 3) but no difference detected between the groups when reported with root mean square ($Z = 1.035$, $p = .301$; Figure 3; Table 6).

3.2.4 | Mandibular movements and chewing patterns

There were no differences detected between the edentate individuals rehabilitated with conventional prostheses and those rehabilitated with implant-supported protheses for the mandibular movements and chewing patterns when measuring masticatory cycles/seconds ($Z = -.464$, $p = .643$; Figure 3), opening and closing velocity ($Z = -.150$, $p = .881$; Figure 3), area of chewing pattern in the frontal plane ($Z = -1.246$, $p = .213$; Figure 3), and for vertical length of chewing pattern in the frontal plane ($Z = -1.457$, $p = .147$) (Table 7).

3.2.5 | Salivary flow rate

Rehabilitations with implant-supported prostheses did not improve the stimulated salivary flow rate when compared with rehabilitation with conventional CRDPs ($Z = -1.271$, $p = .204$; Figure 3) (Table 8).

3.3 | Synthesis of results: Descriptive analysis of the studies not included in the meta-analysis

All prospectively designed studies excluded from the meta-analyses are reported descriptively in Tables 9 and include the parameters of masticatory performance and efficiency by comminution tests. Retrospective studies that provided valuable information on bite force, masticatory performance, muscle activity (EMG), and lip force are presented in Tables 10–13. Although excluded from this review because of the predefined inclusion and exclusion criteria, studies which report on speech and articulation as well as oral tactile threshold are presented in Table 14 because these are the only studies which exist in current literature that provide valuable information on these outcomes.

3.4 | Risk of bias and quality assessment of the included studies in the meta-analysis

The quality assessments of the studies included in the meta-analysis revealed a low to moderate risk of bias and are presented in Tables 15 and 16.

TABLE 14 Descriptive analysis of studies not included in the review that report on tactile threshold, and phonetics (speech articulation).

First author (year)	Study group (U/L)	Implant number (U/L)	Implant detail (U/L)	Attachment system	Follow-up period (months)	*n*	Method	Conclusion	Reason for exclusion
Outcome: Tactile threshold									
Luraschi et al. (2012)	CD/CD					7	Three active tactile thresholds (absolute, 50% and 100%) were evaluated by means of copper foils of decreasing thickness (12 foils:700–5 μm). The passive thresholds were measured in six different sites per quadrant using a custom-made computer-supported strain gauge. MBF was evaluated electronically using the central-bearing point method	IFD/IFD are a valuable treatment option for restoring edentulous patients. Limitations concerning their physiological integration into the orofacial system are mainly related to a poor passive rather than active tactile sensitivity or maximum bite force.	Sample size of <10 cases
	IFD/IFD	6 or 8/6 or 8	-/Straumann® or Nobel Biocare®	-/?	46.8–75.6	7			
Outcome: Speech and articulation problems									
Fonteyne et al. (2021)	CD/CD					18	Assessments were taken by speech therapists and included evaluation of oromyofunctional behavior and articulation which focus on different speech sounds ex. stridens, simplex by picture naming and reading	There was no significant impact of the treatment on speech nor on the results of oromyofunction.	Follow-up period of less than 6 months
	CD/IOD	0/2	-/?	-/bar	3	19			

TABLE 14 (Continued)

First author (year)	Study group (U/L)	Implant number (U/L)	Implant detail (U/L)	Attachment system	Follow-up period (months)	*n*	Method	Conclusion	Reason for exclusion
Meira et al. (2021)	CD/CD					21	Articulation disorders were analyzed by audio and video recordings, which focuses on motor aspect ex. substitution, omission, distortion, anterior and/or lateral tongue protrusion, anterior and/or lateral lisp, exaggerated or reduced articulatory movement, anterior or lateral jaw trajectory deviation and exaggerated or reduced lip mobility	No difference in articulation disorders was found between the CD group and the IOD group.	Follow-up period of <6 months
	CD/IOD	0/1	-/Titamax-TiCortical, Neodent, São Paulo, Brazil	-/stud	2	15			

Note: -, not applicable;?, not specified in the article.

Abbreviations: CD, conventional removable complete denture; IFD, implant-supported fixed dental prostheses; IOD, implant-supported removable complete overdenture; L, lower; *n*, sample size; SEM, standard error of mean; SD, standard deviation; U, upper.

TABLE 15 Results of the quality assessment of the included RCTs using the Cochrane collaboration tool for the assessment of risk of bias.

Study	Sequence generation	Allocation concealment	Blinding	Incomplete outcome data	Selective reporting	Other bias	Summary
Garrett et al. (1998)	Low	Unclear	Unclear	Low	Low	Unclear	Medium
Maniewicz et al. (2019)	Low	Low	Low	Low	Low	Unclear	Low
Nogueira et al. (2019)	Low	Low	Low	Low	Low	Unclear	Low

3.5 | Publication biases

The analyses for the time point of 6–12 months revealed a publication bias (Egger's $p = .026$, Figure 5), but no biases were detected in other analyses (12–36 months: Egger's $p = .106$, Figure 6; +36 months: Egger's $p = .778$, Figure 7).

4 | DISCUSSION

4.1 | Principal findings

Oral function is one of the most essential criteria that needs to be re-established in completely edentulous patients. This systematic review demonstrated that completely edentulous patients rehabilitated with implant-supported dental prostheses had significantly improved oral function compared to those rehabilitated with conventional CRDPs. The effect can be acknowledged from the follow-up period of more than 6 months, which is the optimal period of denture adaptation (Müller & Barter, 2016). The oral function consists of various aspects. Hence, a single objective assessment cannot represent the overall outcome. This review included purpose-designed studies assessing outcomes of oral function through measurement of bite force, masticatory performance, muscle activity (EMG), mandibular movement and chewing pattern, salivary flow rate, and lip force. These improvements could be a reflection of an efficient implant assisted rehabilitation with good retention, stability, and support.

4.1.1 | Bite force

Bite force is an objective assessment representing the ability of force generation by masticatory muscles, which is a vital feature in food mastication. It was shown that bite force reduced dramatically after tooth loss (Müller et al., 2012; Schimmel et al., 2017); thus, dental prostheses rehabilitation helps regain this ability. This review showed that rehabilitation with implant-supported dental prostheses significantly increased the bite force in edentate patients when compared to those rehabilitated with conventional complete dentures. The effect can be recognized from 6 months after implant-supported rehabilitation and maintained until more than 36 months of the follow-up period. These findings corresponded with the majority of previous studies evaluating bite force between implant-supported dental prostheses and conventional complete dentures (Fontijn-Tekamp et al., 1998; Maniewicz et al., 2019; Melo et al., 2018; Müller et al., 2012; Schimmel et al., 2017; van der Bilt et al., 2006). Even if the follow-up period was less than 6 months after the rehabilitation, the significantly increased effect could be achieved by implant support in many studies (Amaral et al., 2019; Kashyap et al., 2021; Sharma et al., 2017; Soni et al., 2020; van Kampen et al., 2002). These findings could be implied that dental implants assisted the prostheses in gaining the ability to generate bite force since the early stage of denture adaptation. In edentulous patients with mucosa-born CRDPs, the maximum bite force is limited by pain arising from the periosteum or due to the dislodging of the CRDP. Hence CRDP wearers limit their maximum forces to avoid pain and embarrassment caused by denture loosening, in particular in a social context. CD/IODs or CD/IFDs transfer bite force and chewing load to the osseointegrated implants, thus avoiding pressure on the sensitive edentulous tissues. The implants also preclude denture dislodgement, as they mechanically retain the IOD in place and do not rely on a suction effect on the denture bearing tissues. This is a mechanical improvement, which explains the immediacy of the improvement after IOD placement.

4.1.2 | Masticatory performance

Masticatory performance is a general term representing the harmony and coordination of the masticatory organs to mix or comminute food bolus (Elgestad Stjernfeldt et al., 2017). The masticatory organs consist of teeth, tongue, salivary glands, orofacial nerves, and muscles of mastication. Masticatory performance could be objectively evaluated by various methods, such as sieving comminuted food, color-changing chewing gum, or swallowing threshold methods.

The sieving methods can be briefly performed by making patients chew brittle foods or by making artificial test-bolus by mixing condensation silicone with other materials, for an assigned number of chewing strokes (Pocztaruk Rde et al., 2008). Then the masticated foods are collected and run through a series of sieves. The food particle size, or percentage of food weight passed or retained on the sieves, can be used to represent a masticatory performance by the sieving methods. In this meta-analysis, the time frame of 6–12 months, 12–36 months, and more than 36 months was fixed; only one study could be fitted in the outcome of X50, $N_{1/2}$, and C_i

TABLE 16 Results of the Newcastle–Ottawa quality assessment scale for prospectively designed studies used in the meta-analysis

	Selection				Comparability	Outcome		
First author (Year)	Representativeness of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Outcome of interest not present at start of the study	Comparability of cohorts	Assessment of outcome	Sufficient follow-up time	Adequacy of follow-up of cohorts
Bakke et al. (2002)	*	*	*			*	*	*
Benzing et al. (1994)		*	*			*	*	*
Berretin-Felix et al. (2008)	*	*	*			*	*	*
Borges Tde et al. (2011)		*	*			*	*	*
da Silva et al. (2011)	*	*	*			*	*	*
de Resende et al. (2021)	*	*	*			*	*	*
Enkling et al. (2019)	*	*	*			*	*	*
Fontijn-Tekamp et al. (1998)	*	*	*		*	*	*	*
Hartmann et al. (2020)	*	*	*			*	*	*
Khalid et al. (2020)		*	*			*	*	*
Lindquist and Carlsson (1985)		*	*			*	*	*
Marcello-Machado et al. (2018)	*	*	*			*	*	*
Melo et al. (2018)	*	*	*			*	*	*
Pera et al. (1998)		*	*			*	*	*
Sun et al. (2014)		*	*			*	*	*
van der Bilt et al. (2010)		*	*			*	*	*
Yunus et al. (2014)		*	*			*	*	*

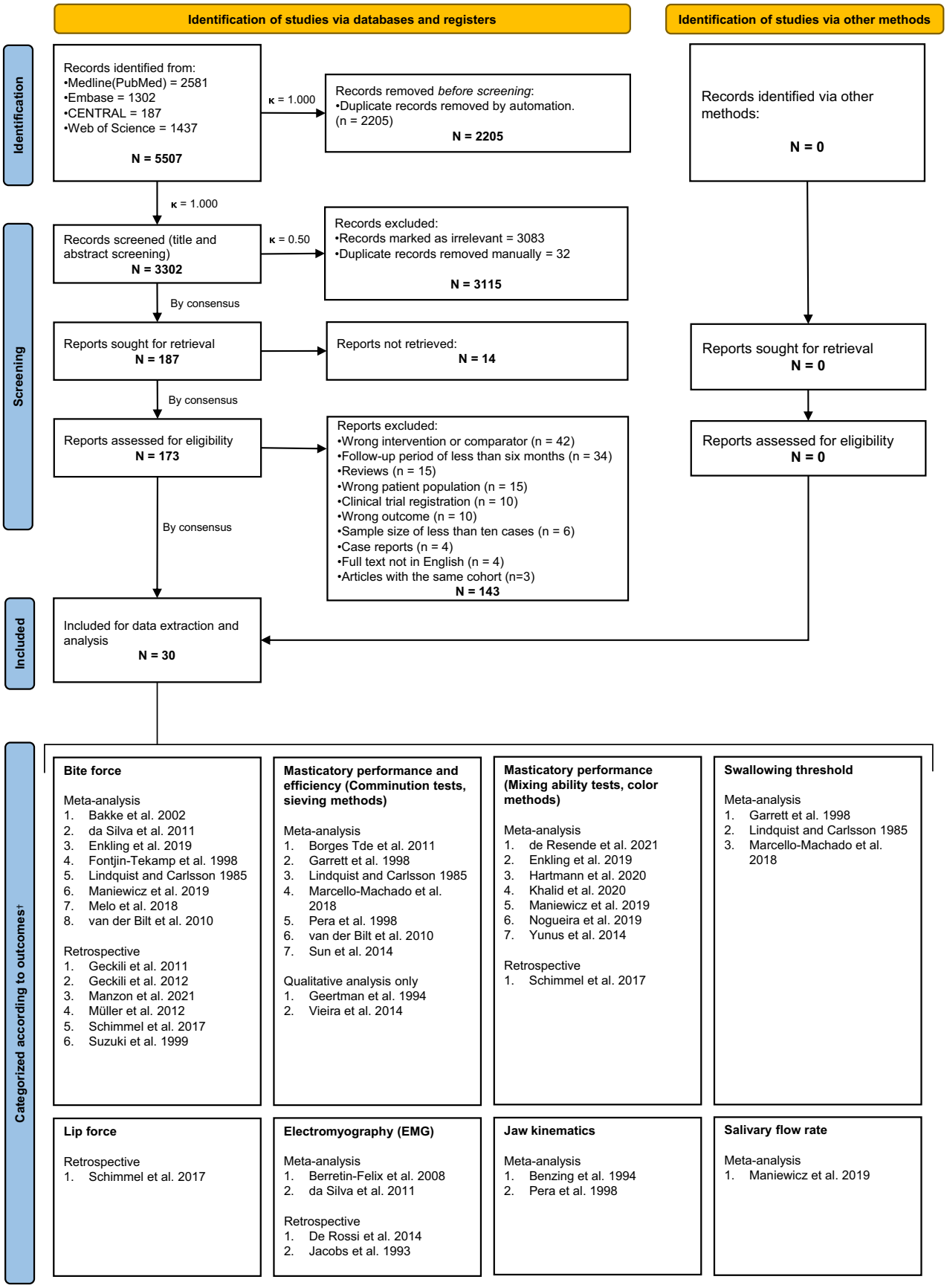


FIGURE 1 Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) flow diagram showing the entire identification, inclusion process, and studies categorized according to outcomes. *N*, number; κ, Cohen's Kappa value; †, multiple studies report on more than one outcome parameter.

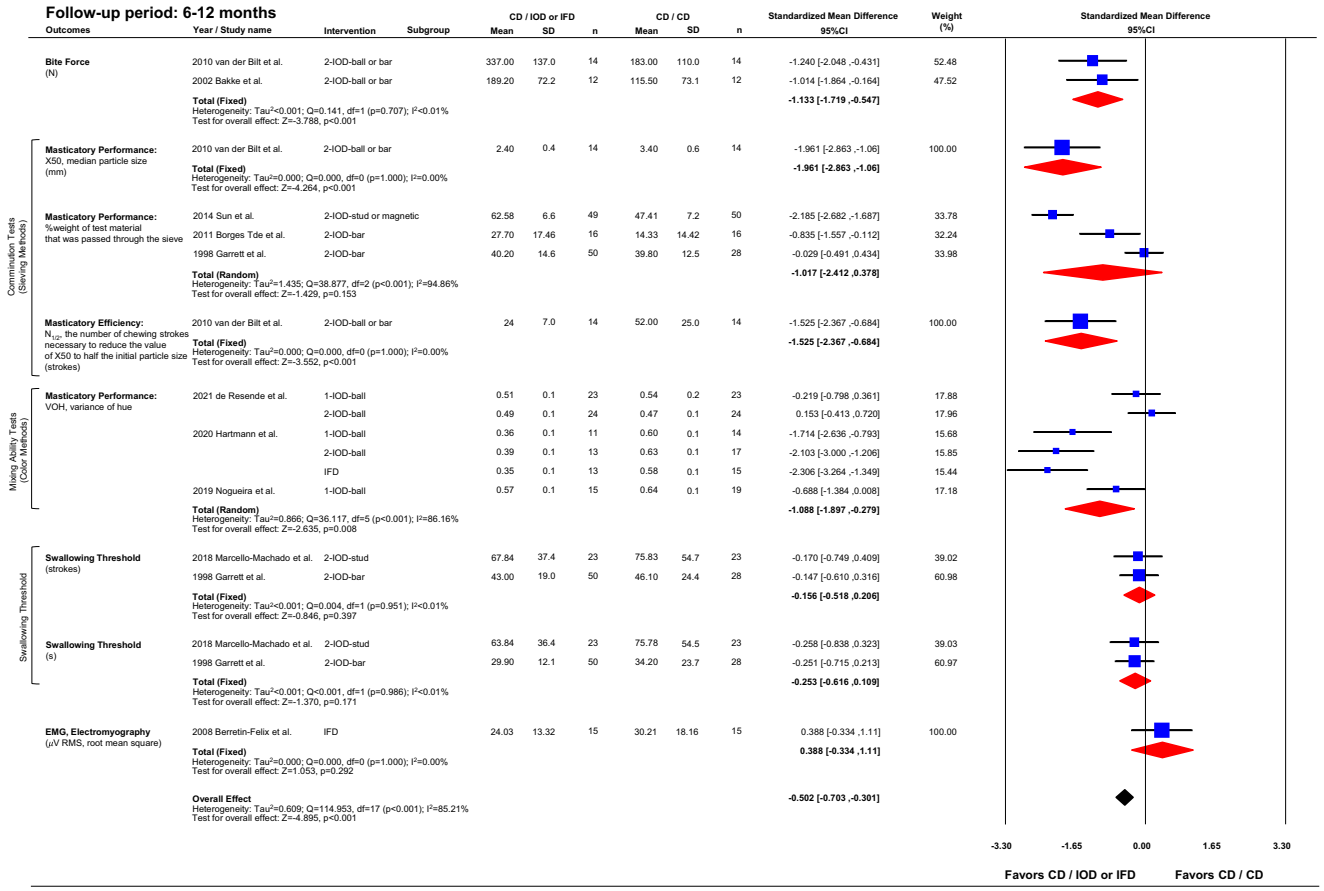


FIGURE 2 Forest plots showing outcomes of 6–12 months follow-up period. CI, confidence interval; CD, conventional removable complete denture; IFD, implant-supported fixed dental prostheses; IOD, implant-supported removable complete overdenture; *n*, sample size; SD, standard deviation.

parameters. Therefore, the meta-analysis yielded the same results of significantly improved masticatory performance when rehabilitated with implant-supported dental prostheses, as found in the original articles (Lindquist & Carlsson, 1985; Marcello-Machado et al., 2018; van der Bilt et al., 2010). However, when the percentage of food weight passed through the sieve measurement technique was used to assess the masticatory performance, the meta-analysis showed no significant effect in masticatory performance between implant-supported dental prostheses and complete dentures for the follow-up period of 6–36 months. These findings contradicted the previous studies from Borges Tde et al. (2011), Pera et al. (1998), and Sun et al. (2014), which showed significantly improved masticatory performance when rehabilitation with implant-supported dental prostheses (Borges Tde et al., 2011; Pera et al., 1998; Sun et al., 2014). The authors assumed this inconsistent trend came from the heterogeneity in the sieving methods and the different foods used in the tests (Borges Tde et al., 2011; Garrett et al., 1998).

The color methods can be briefly performed by giving patients two-color chewing gum or wax for assigned chewing strokes. Then the mixed-color gum is collected, and the variance of hue (VOH) or mixing ability index is measured as a representative parameter of masticatory performance (Khalid et al., 2020; Schimmel et al., 2017). The meta-analysis indicated a significant improvement in masticatory performance when rehabilitation with implant-supported prostheses for a follow-up period of 6–36 months. These findings corresponded with previous studies (de Resende et al., 2021; Hartmann et al., 2020; Khalid et al., 2020; Nogueira et al., 2019; Yunus et al., 2014). In contrast, Müller et al. (2013) and Maniewicz et al. (2019) demonstrated no significant change in masticatory performance by the color methods (Maniewicz et al., 2019; Müller et al., 2013). This may also be caused by a non-renewal of the occlusal surfaces in this geriatric study where existing lower CRDPs were converted to IODs without changing the denture teeth.

The swallowing threshold methods can be briefly performed by giving patients chewing foods until they desire to swallow. The time or number of chewing strokes is used to represent masticatory performance. The meta-analysis revealed no significant improvement in masticatory performance for a follow-up period of 6–12 months, which corresponded to previous studies (Garrett et al., 1998; Marcello-Machado et al., 2018). In contrast, the meta-analysis result of 12–36 months showed significant improvement in reducing strokes required to chew foods until ready to swallow, which resembled a previously published study (Lindquist & Carlsson, 1985). The swallowing threshold methods could be considered partially subjective assessments as the feeling of readiness to swallow could be varied individually.

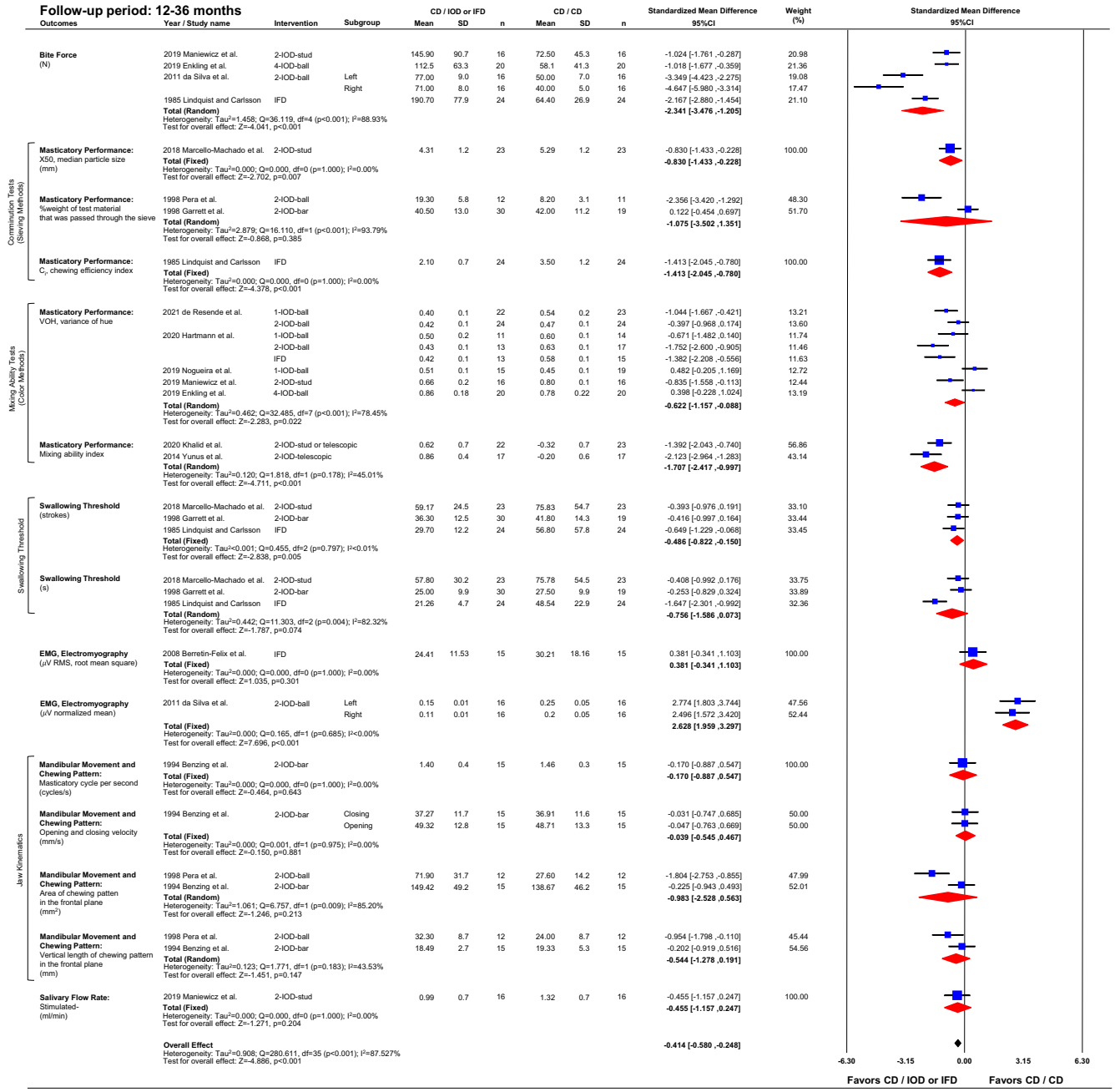


FIGURE 3 Forest plots showing outcomes of 12–36 months follow-up period. CI, confidence interval; CD, conventional removable complete denture; IFD, implant-supported fixed dental prostheses; IOD, implant-supported removable complete overdenture; *n*, sample size; SD, standard deviation.

4.1.3 | Muscle activity (EMG)

EMG is a measurement of electrical activities in various units, such as μV, μV amplitude, μV RMS, μV normalized mean, or surface under the rectified and integrated curve. For muscles of mastication, the measurements are usually taken from the masseter and temporalis muscles, during different test conditions, for instance, hard food chewing, soft food chewing, cotton-roll clenching, maximum clenching, or rest (ElSyad et al., 2019; Soni et al., 2020). Fully edentulous patients notably produced lower EMG results than dentate patients, implying less neuromuscular activities and bite force (Heckmann et al., 2009). In this meta-analysis, the time frame of follow-up periods was fixed; only one study could be suited to the parameter of μV RMS and μV normalized mean. Consequently, the meta-analysis yielded the same results of no significant change in EMG (μV RMS) results, while it showed significant decreased EMG (μV normalized mean) when rehabilitated with implant-supported dental prostheses, as found in the original articles (Berretin-Felix et al., 2008; da Silva et al., 2011). These findings are surprising, given the significant increase in maximum bite force with IODs. However, the lower muscle activity combined with a better chewing performance might be explained by a more efficient comminution of the food. Hence

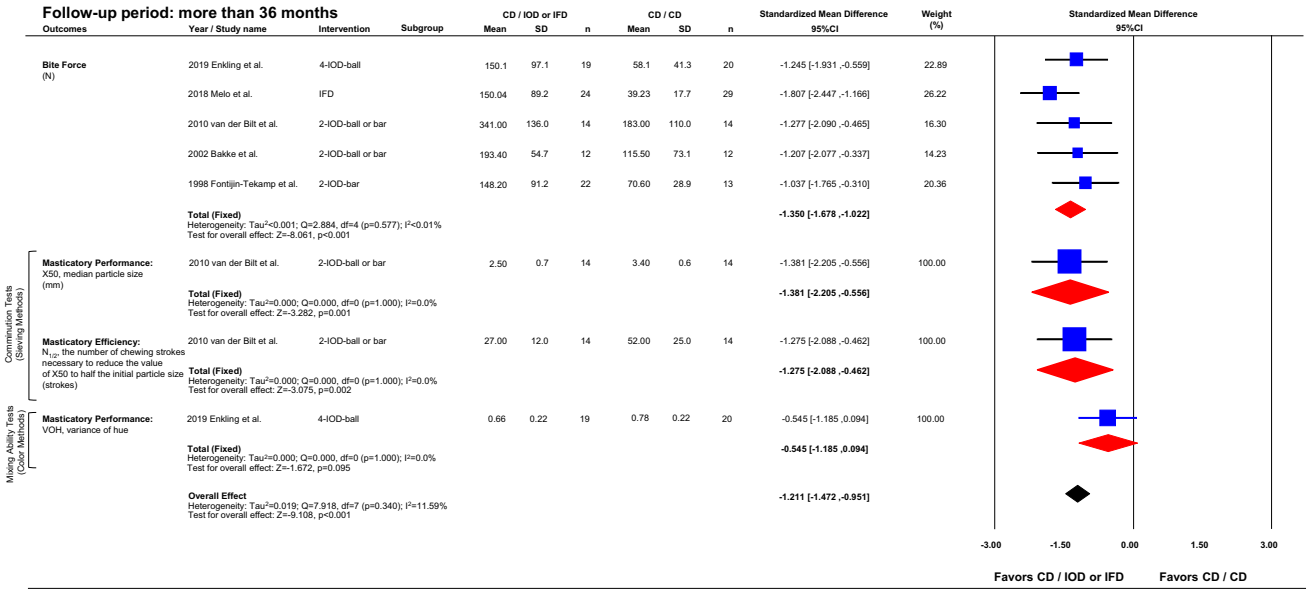


FIGURE 4 Forest plots showing outcomes of more than 36 months follow-up period. CI, confidence interval; CD, conventional removable complete denture; IFD, implant-supported fixed dental prostheses; IOD, implant-supported removable complete overdenture; *n*, sample size; SD, standard deviation.

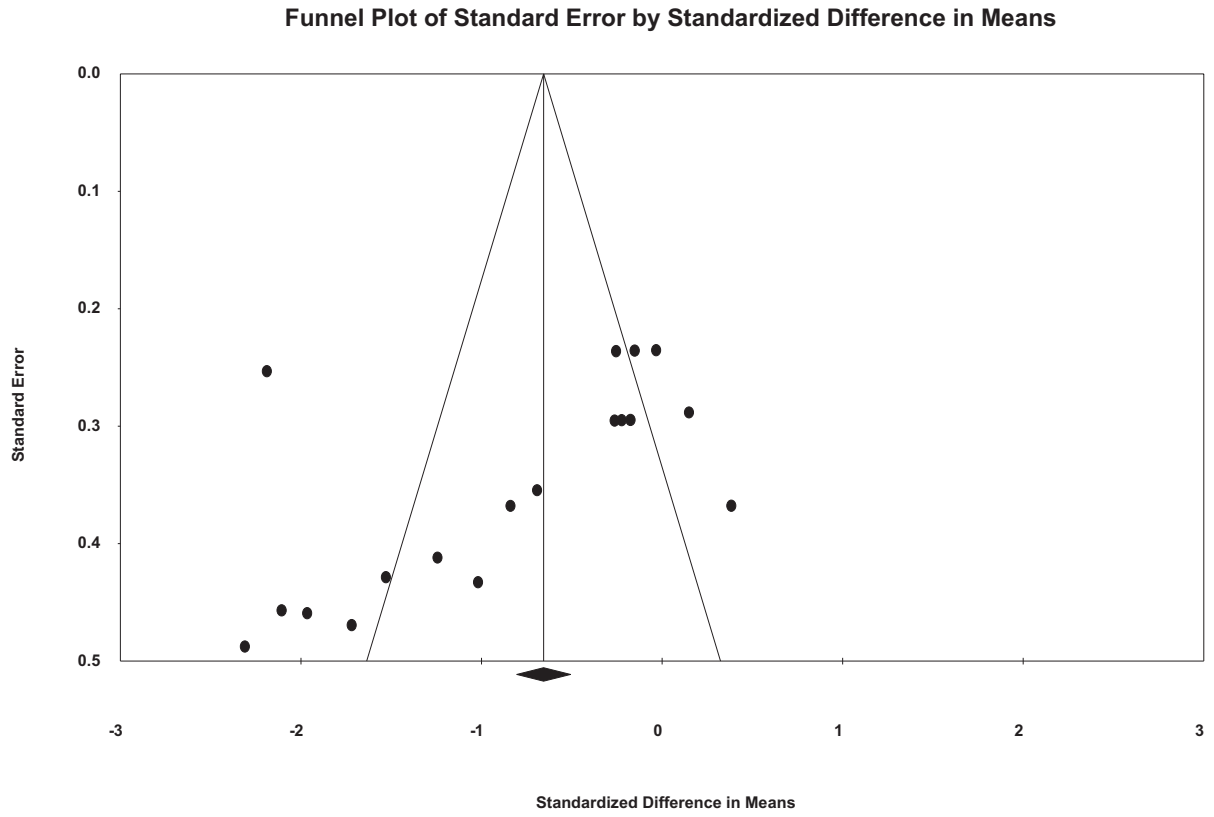


FIGURE 5 Funnel plot exploring the publication bias for the meta-analysis of the studies included for the 6–12 months timepoint (Egger's $p = .026$).

less force may be needed to achieve the same particle size with a high-performance IOD. The patients may be attempting to compensate the low chewing efficiency of conventional CRDPs by recruiting more muscle activity.

4.1.4 | Mandibular movement and chewing pattern

Mandibular movement and chewing patterns can be assessed by a jaw-tracking or video devices. Various parameters represent this

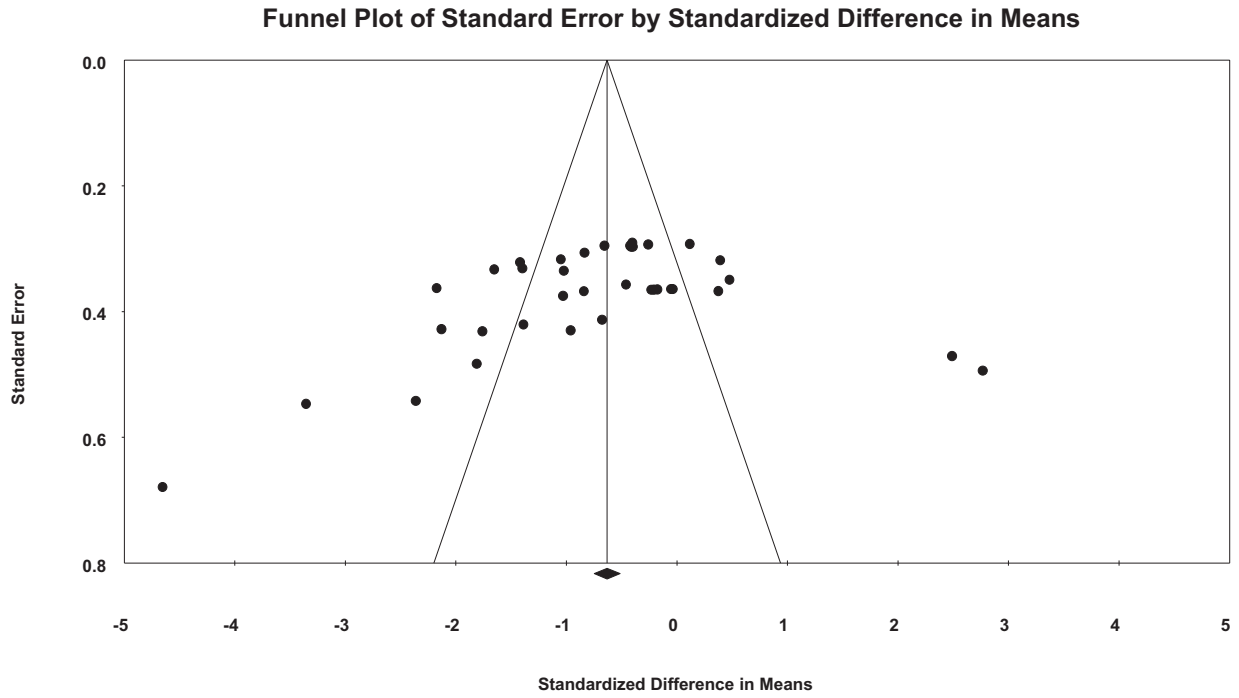


FIGURE 6 Funnel plot exploring the publication bias for the meta-analysis of the studies included for the 12–36 months timepoint (Egger's $p = .106$).

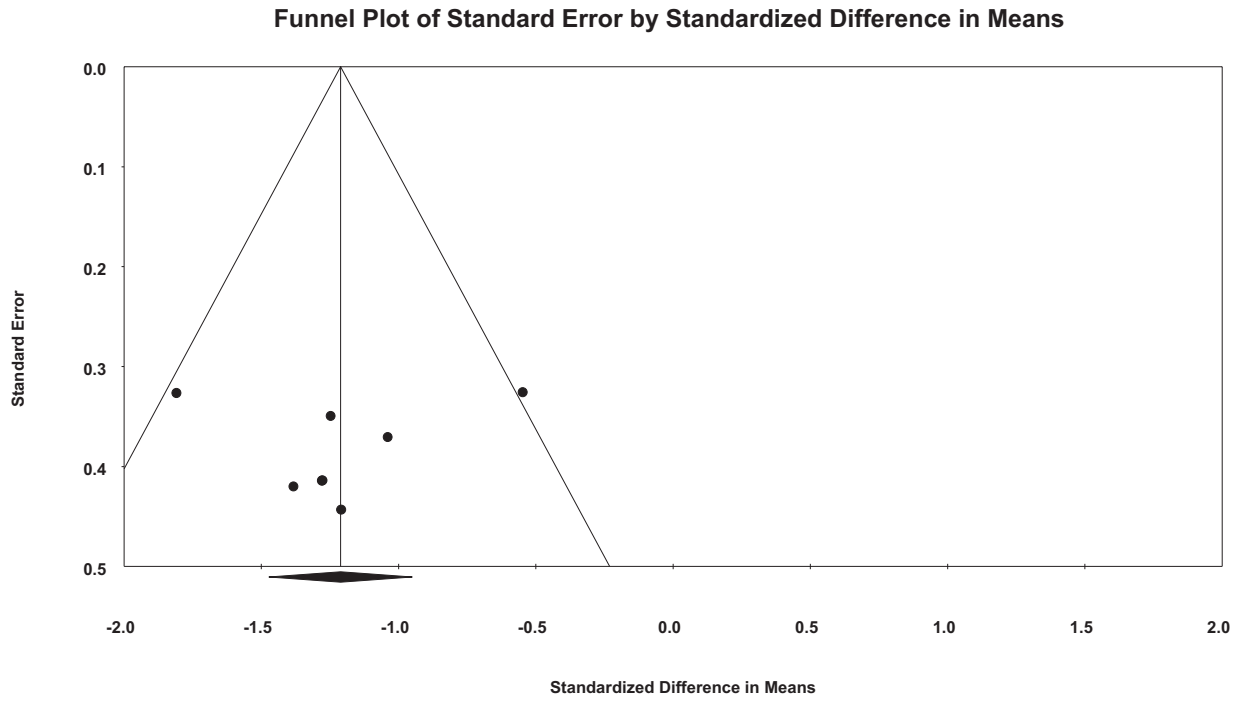


FIGURE 7 Funnel plot exploring the publication bias for the meta-analysis of the studies included for the more than 36 months timepoint (Egger's $p = .778$).

outcome; for illustration, opening and closing jaw velocity, vertical length of chewing cycles in the frontal plane, area of chewing cycles in the frontal plane, or number of masticatory cycles per second. When compared to dentate subjects, the chewing cycles of edentulous CRDP wearers show less excursion in a vertical and lateral plane, with almost unchanged movement speed (Proschel & Hofmann, 1982). An increase in these parameters would indicate an improved adaptation of the movement parameters and neuromuscular system, resulting in higher masticatory efficiency (Heckmann et al., 2009). However, this review showed no significant change in mandibular movement and

chewing pattern after rehabilitation with implant-supported dental prostheses for a follow-up period of 12–36 months. These findings corresponded with a former published study (Benzing et al., 1994). Chewing movements are programmed by a central pattern generator in the brain stem. While the chewing rhythm remains mostly consistent over a lifetime, the mandibular displacement may vary based on the food consistency and texture, as well as the type of dentition/prosthesis. The absence of increased mandibular displacement reported in the present review may be caused by methodological shortcomings, such as different test foods used. Patients might have also required some adaptation time to change their chewing habits.

4.1.5 | Salivary flow rate

Salivary function is measured in two distinctly different conditions, at rest and under stimulation (Sreebny, 2000). In this meta-analysis, only one study could be fitted in the stimulated salivary flow rate parameter; thus, the meta-analysis yielded the same results of no significant change after rehabilitation with implant-supported dental prostheses, as per evidence present in literature (Maniewicz et al., 2019; Müller et al., 2013). The salivary flow from the parotid gland is stimulated by unilateral mastication via the periodontal receptors. Increased bite force and improved masticatory efficiency would therefore suggest increased salivary flow rates. However, this very clear physiological reflex may become less visible in geriatric cohorts with substantial intake of medications and a high prevalence of hyposalivation.

4.2 | Strengths and limitations of this review

The review was successful in identifying a number of studies which assessed oral functions in edentulous patients rehabilitated with implant-supported/retained prostheses. However, not all outcome measures were suitable for meta-analyses, hence the review provides various levels of evidence relating to the effect of implant therapy for the chosen parameters of oral function. Although the systematic review was conducted with sound methodology and reported as prescribed by the PRISMA guidelines, limitations may still exist. Numerous studies were excluded for a variety of reasons due to the rigorous inclusion criteria. This may have affected the results of the review. The excluded studies along with the reasons for exclusion are presented in Appendix S1. However, some of the excluded studies, were considered to contain some valuable information and therefore for the sake of scientific interest, although excluded from the analysis, are still presented in Appendix S2, therefore, eliminating marginally the errors of inclusion bias.

4.3 | Clinical relevance of findings of this systematic review

Implant therapy can be recommended for edentulous adults to alleviate the shortcomings of conventional complete removable dental prostheses. The availability of this treatment modality should also be promoted in edentulous communities with limited access and means.

4.4 | Implication for research

The current review reveals a notable knowledge gap regarding implant therapy and certain parameters of oral function such as lip force, salivary flow, oral tactile sensitivity, and oral diadochokinesis. Moreover, this review identified that the assessment of masticatory performance was found to be the most heterogenous. Various methods with different measurement techniques exist currently for this parameter. Interpretation of the results were sometimes difficult and were not universally comparable. Therefore, a global consensus should be achieved for choosing a simplified universal technique to measure this parameter; or a technique to unify the different measurements to correspond to a single standard. Furthermore, a consensus needs to be also achieved to define standard protocols for reporting other parameters related oral functions based on the findings of this systematic review.

5 | CONCLUSIONS

This systematic review concluded that the oral function of completely edentate adults significantly improved with implant-supported/retained prostheses, even when only one jaw received implant therapy. Therefore, implant therapy should be promoted for edentulous adults to alleviate the shortcomings of conventional complete removable dental prostheses.

AUTHOR CONTRIBUTIONS

Murali Srinivasan and Frauke Müller conceived the ideas; Porawit Kamnoedboon and Lea Angst collected the data; Murali Srinivasan and Porawit Kamnoedboon analyzed the data and led the writing and the preparation of the initial draft. Murali Srinivasan, Porawit Kamnoedboon, Lea Angst, and Frauke Müller edited and approved the final manuscript.

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CONFLICT OF INTEREST STATEMENT

None.

DATA AVAILABILITY STATEMENT

Data will be made available on request.

PROSPERO REGISTRATION

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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REVIEW ARTICLE

CLINICAL ORAL IMPLANTS RESEARCH WILEY

Effect of dental implant therapy on the preservation of orofacial tissues: A systematic review and meta-analysis

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Abstract

Objective: Fundamentally, this review addresses the following question: In partially or fully edentulous patients, do implant-supported dental prostheses preserve orofacial tissues when compared to conventional prostheses or no therapy?

Materials and Methods: This study was conducted according to the 2020 PRISMA guidelines for systematic reviews. Electronic searches were conducted at PubMed and Embase databases followed by manual search. Clinical studies comparing the effect of implant-supported prostheses with conventional rehabilitation or no treatment on alveolar bone resorption, remaining teeth, and jaw muscle thickness were considered for inclusion. A qualitative synthesis was conducted with all included studies, and data from selected studies were pooled quantitatively to perform a meta-analysis.

Results: A total of 14 studies were selected for analysis. Six studies reported on the effect of implant therapy on alveolar bone resorption ($n = 453$), six on the remaining teeth ($n = 1014$), while four studies evaluated masseter muscle thickness ($n = 158$). The results of the meta-analyses assessing alveolar bone resorption in the posterior mandible and in the anterior area of the maxilla, both fixed and random effects models, yielded no benefit of rehabilitation with implant-supported prostheses when compared to conventional prostheses. For masseter bone thickness, however, a significant benefit for implant-supported prosthesis was observed.

Conclusions: This systematic review and meta-analysis were unable to unequivocally answer the focus question. There are some indicators of the benefit of implant-supported prostheses over conventional prostheses or no therapy in preserving orofacial tissues, particularly for masseter muscle thickness. However, the evidence is still insufficient to confirm such perception.

KEYWORDS
alveolar bone resorption, dental implant, implant therapy, masseter muscle thickness, orofacial tissue, tooth survival

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1 | INTRODUCTION

The effectiveness of dental implants over time has been scientifically validated for both partially and fully edentulous patients (Gallucci et al., 2014; Jemt, 2018; Papaspyridakos, 2015; Papaspyridakos et al., 2020). Published data indicate that the number of patients rehabilitated with dental implants are steadily increasing every year (Douglass & Merin, 2002). Since the 1980s, the success of the dental implant therapy has been evaluated based on implant survival and crestal bone remodeling (Albrektsson et al., 1987; Buser et al., 1990) and, as a result, implant-related biologic and mechanical complications have been under close scrutiny (Chochlidakis et al., 2020; Heitz-Mayfield et al., 2014; Zarb & Schmitt, 1990). Over the years, as implant therapy has evolved into a routine treatment modality, several different types of implants such as the pterygoid, zygoma, short, and ceramic implants have progressively been added to clinicians' armamentarium. As a result, other variables have also been receiving attention from the scientific community when assessing the success of implant-supported restorations (Papaspyridakos et al., 2012). These include the search for natural-looking esthetics, quality of peri-implant soft tissues, different prosthodontic features, as well as patient satisfaction (Furhauser et al., 2005).

With the increase in life expectancy, more patients are bound to present with missing teeth due to periodontal disease, caries, trauma, or a combination of these (Sarafidou et al., 2022). Clinicians may recommend fixed or removable conventional or implant-supported rehabilitation to treat both partially and fully edentulous spaces or even no restoration. Treatment choice must be carefully considered based on its long-term impact on function and esthetic, and to preserve remaining teeth as much as possible (Okuni et al., 2022). Fully edentulous elderly individuals have been shown to significantly benefit from rehabilitation with implant-supported overdentures (I-OD) compared to conventional removable complete dentures (RCD) due to the improved stability, retention, increased bite force, larger chewing cycles, masticatory ability, and efficiency (Awad et al., 2000). Logically, it would be expected that rehabilitation with implant-supported prostheses may also help preserving different orofacial tissues such as the alveolar bone, remaining teeth, and jaw muscles when compared to conventional treatment modalities, or no treatment, but data remains controversial.

In a recent systematic review, although overdentures supported by 4 implants presented significantly less alveolar bone resorption in the posterior edentulous mandible than RCD, such advantage, however, was not observed when overdentures were supported by 2 implants (Oh, 2020). When edentulous spaces are rehabilitated with tooth-supported removable partial dentures using adjacent teeth as abutments, biological complications such as tooth loss, caries, and crown fractures can arise (Phang et al., 2020). Conversely, implant-supported fixed dentures do not rely on the surrounding dentition for support, which may result in the preservation of remaining teeth over time (Krennmair et al., 2003). The conversion of RCD into I-OD has also been shown to significantly improve chewing efficiency and bite force (van Kampen et al., 2004). Moreover, patients rehabilitated with overdentures over two implants (Muller et al., 2013) and implant-supported removable partial prostheses (Gonçalves et al., 2013) have also demonstrated increased maximum bite force and increased masseter muscle thickness when compared with conventional rehabilitation.

The pertinent data requires pooling and proper assessment in order to better ascertain the present level of the evidence. Such information can assist clinicians in their therapeutical recommendations, and also patients when weighing the long-term benefits and limitations of each type of intervention. Therefore, the present systematic review and meta-analysis were conducted to answer the following question: In partially or fully edentulous patients, do implant-supported dental prostheses preserve orofacial tissues when compared to conventional prostheses or no therapy?

2 | METHODS

The study protocol followed the 2020 PRISMA (Preferred Reporting Items for Systematic Review and Meta-Analyses) guidelines (Page et al., 2021) and was registered at PROSPERO under the No. CRD42022354693. Considering that all the evidence was obtained from publicly accessible documents, an institutional ethical approval was not required for this systematic review.

2.1 | Eligibility criteria

2.1.1 | Inclusion criteria

- Studies including partially or fully edentulous patients rehabilitated with implant-supported prostheses in comparison with conventional rehabilitation (fixed or removable), or no treatment;
- Clinical studies, that is, cross-sectional, cohort and case–control, controlled clinical trials (CCT), and randomized clinical trials (RCT);
- Minimum 10 patients (to distinguish cohort studies from case series); and
- Studies presenting at least one of the outcomes of interest, that is, effect of implant therapy on remaining teeth, alveolar bone resorption, and/or jaw muscles thickness.

2.1.2 | Exclusion criteria

- Studies presenting insufficient information regarding the number of patients and follow-up time;
- Studies lacking information on the primary outcomes;
- Multiple publications using the same population (only the publication with the longest follow-up period was considered for inclusion); and
- Studies published in languages other than English.

2.2 | Information sources and search strategy

The search for clinical studies followed the PICO (Population, Intervention, Comparison, Outcomes) format, and was conducted electronically on the MEDLINE (PubMed) and EMBASE databases from 20 January up to 30 August 2022. The search strategy was limited to studies in English, and the descriptors used are shown in Table 1. In addition to the electronic search, a manual search was conducted in the reference lists of all articles retrieved for full-text analysis.

2.3 | Selection process

Based on the eligibility criteria, two authors (KV and FM) independently screened the titles and abstracts derived from the initial search. In case the abstracts presented insufficient information regarding the inclusion criteria, full texts were obtained for further analysis. Any disagreements at any of the stages above were resolved through discussions with a third reviewer (AS). Article screening was conducted with Rayyan software, and Endnote (Endnote X7, Thompson Reuters) was used for reference management and electronically identify and discard duplicates.

2.4 | Data items and collection process

The reviewers independently extracted the data from all included studies using data extraction tables. All extracted data were double-checked, and any questions arising at this stage were resolved through group discussions. The following information was extracted from the selected articles: authors, year of publication, study design, number of patients, mean age, jaw (maxilla or mandible), follow-up time, area in the mouth (anterior or posterior), type of edentulism (partial or full), test group (partial or full implant-supported prostheses), control group (full or partial conventional prosthesis, or no treatment), and outcomes.

2.5 | Risk of bias in individual studies

The quality of the included studies was assessed with the Cochrane Collaboration's tool for assessing risk of bias. RCTs were assessed in the following 5 domains: (D1) bias arising from the randomization process; (D2) bias due to deviations from intended interventions; (D3) bias due to missing outcome; (D4) bias in the measurement of outcomes; and (D5) bias in selection of the reported result. Observational studies were assessed in 7 different domains: (D1) bias due to confounding factors; (D2) bias in the selection of participants; (D3) bias in the classification of interventions; (D4) bias due to deviations from intended interventions; (D5) bias due to missing data; (D6) bias in the measurement of outcomes; and (D7) bias in the selection of the reported result. The selected studies were initially screened by one reviewer (A.S.), who collected the information on each individual study. A second reviewer (K.V.) crosschecked the collected information and confirmed its accuracy.

TABLE 1 Systematic review search strategy.

PICO	Search strategy
Population	#1—Partially Edentulous Patients OR Fully Edentulous Patients OR Posterior Partial Edentulous OR Dental Implant OR Implant OR Edentulous Mouth OR Edentulous Mouths OR Mouth, Toothless OR Toothless Mouth OR Jaw, Edentulous, Partially OR Edentulous Jaw OR Edentulous Jaws OR Jaws, Edentulous
Intervention or exposure	#2—Partial Implant-Supported Fixed Dental Prostheses OR Full-arch Implant-Supported Fixed Dental Prostheses OR Fixed Dental Implant Prostheses OR Dental Prosthesis, Implant-Supported OR Implant-Supported Dental Prosthesis OR Dental Prostheses, Implant-Supported OR Implant-Supported Dental Prosthesis OR Implant-Supported Dental Prostheses OR Prostheses, Implant-Supported Dental OR Prosthesis, Implant-Supported Dental OR Denture, Implant-Supported OR Denture, Implant-Supported OR Implant-Supported Denture OR Dentures, Implant-Supported OR Fixed Implant-Supported Denture OR Fixed Implant-Supported Dentures OR Prosthesis Dental, Implant-Supported OR Dental, Implant-Supported Prosthesis OR Dentals, Implant-Supported Prosthesis OR Implant-Supported Prosthesis Dental OR Implant-Supported Prosthesis Dentals OR Prosthesis Dental, Implant-Supported OR Prosthesis Dentals, Implant-Supported
Comparison	#3—Partial tooth-supported fixed dental prostheses OR full-arch tooth-supported fixed dental prostheses OR Removable Partial Denture OR Denture OR Fixed Bridge OR Bridge, Fixed OR Bridges, Fixed OR Fixed Bridges OR Fixed Partial Denture OR Denture, Fixed Partial OR Dentures, Fixed Partial OR Fixed Partial Dentures OR Partial Denture, Fixed OR Partial Dentures, Fixed OR Pontic OR Pontics OR Complete Denture OR Complete Dentures OR Dentures, Complete OR Denture, Complete, Upper OR Denture, Complete, Lower
Outcome	#4—teeth prognosis OR teeth survival OR survival of adjacent teeth OR alveolar bone loss OR alveolar bone crest OR ridge bone loss OR bone resorption OR ridge resorption OR periodontal status OR jaw muscles OR masticatory muscles OR Mucosa, Mouth OR Oral Mucosa OR Mucosa, Oral OR Buccal Mucosa OR Periodontal Atrophies OR Atrophy of Periodontium OR Periodontium Atrophies OR Periodontium Atrophy OR Gingivo-Osseous Atrophy OR Gingivo-Osseous Atrophy OR Gingivo-Osseous Atrophies OR Alveolar Processes OR Process, Alveolar OR Processes, Alveolar OR Alveolar Ridge OR Ridge, Alveolar

Any disagreements were resolved through discussions with a third reviewer (F.M.). Risk of bias was classified as being low, moderate or high.

2.6 | Study outcomes

- Effect on remaining teeth—survival rate (percentage), complication rates (caries or other types of tooth structure loss, periodontal lesions, and crown fracture);
- Alveolar bone resorption—area measurements conducted on digital panoramic radiographs in relative terms (%), or changes in the area index over time; and
- Jaw muscles thickness—measured in millimeters with real-time linear ultrasound scanner and linear array transducer.

2.7 | Synthesis methods

To facilitate the interpretation of the results found, included studies were grouped according to their main outcome (alveolar bone resorption, effect on remaining teeth, and jaw muscle thickness). A qualitative and quantitative synthesis of the studies were conducted. The data from selected studies were pooled quantitatively to perform meta-analysis using the R Software (version 4.1.2., R Foundation for Statistical Computing). Heterogeneity among studies was assessed with Cochran's Q test, and meta-analysis for the final values (i.e., weighted mean differences and 95% confidence intervals, and random-effect model to account for potential methodological differences between studies), and forest plots were also evaluated. A fixed effect model was used when no statistically significant heterogeneity was observed among studies ($p > .05$).

2.8 | Reporting bias assessment

Potential publication bias in the meta-analysis was assessed via funnel plot asymmetry using Egger's test.

3 | RESULTS

3.1 | Study selection

The identification, inclusion, and exclusion of studies is illustrated in Figure 1. A total of 2609 records were initially identified in the electronic search (PubMed = 1432; Embase = 1177). After the exclusion of 774 duplicates by automation, 1835 titles were screened, from which 1799 were considered irrelevant, resulting in 36 titles for retrieval. The manual search of references in the retrieved studies resulted in six more studies for full-text analysis. From the 42 texts analyzed, 28 were excluded for different reasons (Table S1). As a result, 14 studies fulfilled the eligibility criteria and were selected for qualitative analysis, of which seven were pooled quantitatively to perform meta-analyses.

3.2 | Study characteristics

A summary containing the data items collected from 14 studies included in the qualitative analysis can be found in Tables 2–4. Only one study was an RCT (Maniewicz et al., 2019). Of the 13 observational studies, nine were retrospective in design (Alrajhi et al., 2020; Hatta et al., 2021; Jacobs et al., 1992, 1993; Khuder et al., 2017; Kordatzis et al., 2003; Yamada et al., 2022; Yamazaki et al., 2013a), three studies were prospective (Amaral et al., 2019; Okuni et al., 2022; Tymstra et al., 2011), and one was a cross-sectional study (Muller et al., 2012).

3.3 | Risk of bias

The included RCT (Maniewicz et al., 2019) presented a low risk of bias for all the five domains analyzed (Table 5). On the other hand, most of the selected longitudinal studies presented an overall moderate risk of bias. For all three studied outcomes, the main areas for risk of bias within the observational studies were related to domain D1 (confounding factors) and domain D2 (selection of participants). Domain D5 (missing data) also represented an area of risk of bias for the outcome "effect on remaining teeth." One observational study (Jacobs et al., 1992) presented high risk of bias for domains D2 (selection of participants) and D3 (classification of interventions), which resulted in this study being classified with an overall high risk of bias (Table 6).

3.4 | Alveolar bone resorption

3.4.1 | Results of individual studies

Six observational studies assessed alveolar bone resorption in fully edentulous patients, five retrospective studies (Alrajhi et al., 2020; Jacobs et al., 1992, 1993; Khuder et al., 2017; Kordatzis et al., 2003), and one prospective study (Tymstra et al., 2011). The number of participating patients ranged between 30 and 140, totaling 453 individuals. All studies had removable complete dentures (RCD) as control groups, while the test groups were composed by implant-supported overdentures (I-OD) and/or implant-supported fixed complete dentures (I-FCD). Mean follow-up time was 6.3 ± 4.4 years for the groups with RCD, 6.4 ± 4.1 years for I-FCD, and 6.5 ± 3.2 years for I-OD. Alveolar bone measurements were conducted on panoramic

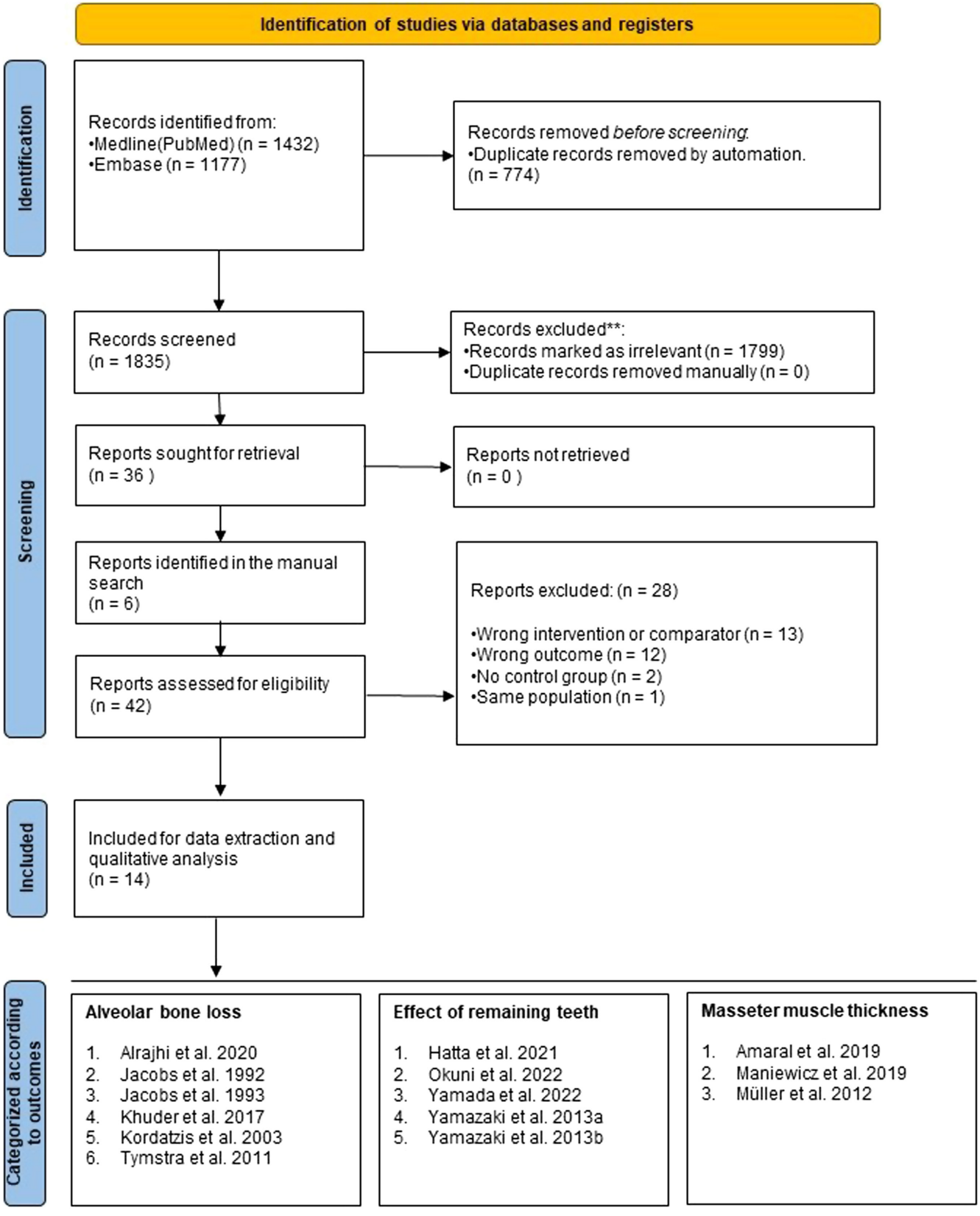


FIGURE 1 PRISMA flowchart for study selection.

radiographs in all studies. One study evaluated vertical bone resorption in the maxilla (Alrajhi et al., 2020), while two studies in the posterior area of the mandible (Jacobs et al., 1992; Kordatzis et al., 2003), and three studies in the posterior area of the mandible and the antagonist ridges (Jacobs et al., 1993; Khuder et al., 2017; Tymstra et al., 2011; Table 2).

TABLE 2 Summary of included articles on alveolar bone resorption in fully edentulous patients.

Authors (Year)	Study design	Patients (*n*)	Jaw	Age (years)	Time in function (years)	Control group (*n*)	Test group (*n*)	Outcomes
Jacobs et al. (1992)	RS	140	Man	RCD (59) I-OD (54) I-FCD (57)	RCD (13) I-OD (10) I-FCD (11)	RCD (85)	I-OD (30) I-FCD (25)	RBL[a]
Jacobs et al. (1993)	RS	44	Max/Man	RCD (56.0 ± 10) I-OD (61.0 ± 11.0) I-FCD (50.0 ± 6.0)	RCD (0.83) I-OD (3.6) I-FCD (3.1)	RCD (12)	I-OD (20) I-FCD (12)	RBL[a]
Kordatzis et al. (2003)	RS	73	Man	(54; 31–76)	(5)	RCD (34)	I-OD (39)	RBL[b]
Khuder et al. (2017)	RS	46	Max/Man	RCD (64.9 ± 9.7) I-OD (66.2 ± 8.4)	(4)	RCD (23)	I-OD (23)	RBL[c]
Tymstra et al. (2011)	PS	120	Max/Man	RCD (56.9) I-OD on two implants (54.0) I-OD on four implants (55.7)	(10)	RCD (60)	I-OD on two implants (30) I-OD on four implants (30)	RBL[d]
Alrajhi et al. (2020)	RS	30	Max	RCD (58.6 ± 3.0) I-FCD (59.2 ± 3.4)	(5)	RCD (15)	I-FCD on four implants (15)	RBL[d]

Abbreviations: I-OD, implant-supported Overdenture; loss I-FCD, implant-supported fixed complete denture; Man, mandible; Max, maxilla; PS, prospective study; RBL, radiographic alveolar bone; RCD, removable complete denture; RS, retrospective study.

[a]Wilding et al. (1987).

[b]Wright and Watson (1998).

[c]Kreisler et al. (2000) for maxillary arch and by Wilding et al. (1987) for posterior mandibular.

[d]Kreisler et al. (2000).

TABLE 3 Summary of included articles on the effect on remaining teeth in partially edentulous patients.

Authors (year)	Study design	Patients	Jaw	Age (years)	Time in function	Control group (*n*)	Test group (*n*)	Outcomes
Okuni et al. (2022)	PS	514	Max/Man (single bounded missing tooth)	I-FPD (51.9 ± 16.1) R-FPD (55.9 ± 15.1) T-FPD (61.2 ± 11.2)	10 years	R-FPD (216) T-FPD: (195)	I-FPD (103)	SR and other complications of remaining TAES.
Yamada et al. (2022)	RS	233	Max/Man	I-FPD (58.6 ± 8.8) T-RPD (66.9 ± 9.0)	55.6 ± 35.3 months	T-RPD (144)	I-FPD (89)	SR and other complications of remaining TAES, TNAES, TOES.
Yamazaki et al. (2013a)	RS	103	Max/Man (missing at least four continuous teeth)	I-FPD (46.4 ± 15.0) T-RPD (60.6 ± 12.7)	10 years	T-RPD (82)	I-FPD (21)	SR of remaining ART; TAES, TOES.
Yamazaki et al. (2013b)	RS	84	Max/Man (missing unilateral free-end 2 or 3 teeth)	(55.8 ± 9.4)	I-FPD 6.6 ± 4.1 years T-RPD 5.0 ± 3.4 years NR 6.0 ± 4.1 years	T-RPD (41) NR (10)	I-FPD (33)	SR and other complications of remaining ART, TAES, TOES
Hatta et al. (2021)	RS	56	Man (posterior unbonded unilateral)	51 subjects in the 70-year group and 5 subjects in the 80-year group	6 years	NR (28)	I-FPD (28)	SR of remaining TAES.

Abbreviations: ART, all remaining teeth; I-FPD, implant-supported fixed partial denture; Man, mandible; Max, maxilla; NR, no restoration; PS, prospective study; RCT, randomized controlled trial; R-FPD, resin-bounded fixed partial denture; RS, retrospective study; SR, survival rate; TAES, teeth adjacent to edentulous space; T-FPD, tooth-supported fixed partial denture; TNAES, teeth not adjacent to edentulous space; TOES, teeth opposing edentulous spaces; T-RPD, tooth-supported removable partial denture; TS, tooth survival.

TABLE 4 Summary of included articles on masseter muscle thickness in fully edentulous patients.

Authors (year)	Study design	Patients (*n*)	Jaw	Age (years)	Time in function	Control group (*n*)	Test group (*n*)	Outcomes
Amaral et al. (2019)	PS	12	Max/Man	(68.7 ± 5.2)	2 months	RCD (12)	I-OD (12)	MMT[a] (Highest value on either side)
Maniewicz et al. (2019)	RCT	32	Man	RCD (85.0 ± 6.2) I-OD (84.8 ± 5.4)	7 years	RCD (16)	I-OD (16)	MMT[a] (Mean of 2 readings on P-CS and NP-CS)
Müller et al. (2012)	CSS	80	Max/Man	RCD: (68.2 ± 6.2) Fully Dentate (66.0 ± 8) I-OD (68.1 ± 4.6) I-FPD (61.5 ± 8.3)	RCD (3.3 ± 3 years) I-OD (4.0 ± 2.6 years) I-FPD (3.9 ± 2.1 years)	RCD (20) Fully Dentate (20)	I-OD (20) I-FCD (20)	MMT[a] (Mean of 2 readings on both sides)

Abbreviations: CSS, cross-sectional study; I-FCD, implant-supported fixed complete denture; I-OD, implant-supported overdenture; RCD, removable complete denture; Man, mandible; Max, maxilla; MMT, masseter muscle thickness; NP-CS, not preferred chewing side; P-CS, preferred chewing side; PS, prospective study; RCT, randomized controlled trial.

[a]MMT measured with real-time linear ultrasound scanner and linear array transducer.

3.4.2 | Results of the qualitative synthesis

In rehabilitated ridge

Alrajhi et al. (2020) showed that patients rehabilitated with maxillary I-FCD opposed by remaining mandibular anterior teeth presented significantly less maxillary anterior and posterior alveolar bone resorption when compared with those rehabilitated with RCD. Similarly, when evaluating the mandibular posterior ridge, patients rehabilitated with I-OD demonstrated less alveolar bone resorption when compared with patients rehabilitated with RCD in two studies (Khuder et al., 2017; Kordatzis et al., 2003), but only one of them reaching statistical significance (Kordatzis et al., 2003). Jacobs et al. (1992) also demonstrated significantly less alveolar bone resorption in patients rehabilitated with I-FCD when compared to those rehabilitated with RCD. Conversely, two studies demonstrated slightly more posterior bone resorption in patients rehabilitated with I-OD when compared to those rehabilitated with RCD without, however, reaching statistical significance (Jacobs et al., 1992; Tymstra et al., 2011; Table 7).

In the antagonist ridge

Of the three studies reporting on maxillary alveolar bone resorption in the antagonistic ridge, two showed more bone resorption in patients rehabilitated with I-OD than those rehabilitated with RCD without, however, reaching statistical significance (Khuder et al., 2017; Tymstra et al., 2011). However, the third study showed significantly more bone resorption in patients rehabilitated with I-OD and RCD when compared to those rehabilitated with I-FCD (Jacobs et al., 1993; Table 7).

3.4.3 | Results of the quantitative synthesis

In the posterior mandible of the rehabilitated ridge

A meta-analysis was conducted with four studies (number of observations: $o = 324$) that compared alveolar bone resorption in the posterior mandible of the rehabilitated ridge between patients treated with RCD and those treated with I-OD (Jacobs et al., 1992; Khuder et al., 2017; Kordatzis et al., 2003; Tymstra et al., 2011). According to the pooled results of the meta-analysis, both fixed and random effects models yielded no benefit of rehabilitation with I-OD when compared to RCD. Additionally, Cochran's Q test ($p = .04$) also indicated heterogeneity among the pooled studies (Figure 2).

In the anterior maxilla of the antagonistic ridge

A meta-analysis was also conducted with three studies (number of observations: $o = 168$) that compared alveolar bone resorption in the anterior maxilla of the antagonistic ridge between patients rehabilitated with RCD and those rehabilitated with I-OD (Jacobs et al., 1993; Khuder et al., 2017; Tymstra et al., 2011). According to the pooled results, both fixed and random effects models yielded

TABLE 5 Risk of bias for the included randomized clinical trial.

Author (year)	D1	D2	D3	D4	D5	Overall risk of bias
Maniewicz et al. (2019)	Low	Low	Low	Low	Low	Low

Note: Domains of Bias: (D1) bias arising from the randomization process; (D2) bias due to deviations from intended interventions; (D3) bias due to missing outcomes; (D4) bias in measurement of the outcome; (D5) bias in selection of the reported result.

TABLE 6 Risk of bias for the included observational studies.

Author (year)	D1	D2	D3	D4	D5	D6	D7	Overall risk of bias
Alveolar bone resorption								
Alrajhi et al. (2020)	Moderate	Low	Moderate	Low	Low	Moderate	Low	Moderate
Jacobs et al. (1993)	Moderate	Moderate	Moderate	Low	Low	Moderate	Low	Moderate
Khuder et al. (2017)	Moderate	Moderate	Low	Low	Low	Moderate	Low	Moderate
Kordatzis et al. (2003)	Moderate	Moderate	Low	Low	Low	Low risk	Low	Moderate
Tymstra et al. (2011)	Moderate	Moderate	Moderate	Low	Moderate	Low risk	Low	Moderate
Jacobs et al. (1992)	Moderate	High risk	High	Low	Low	Moderate	Low risk	High
Effect on remaining teeth								
Okuni et al. (2022)	Moderate	Moderate	Low	Low	Moderate	Low	Low	Moderate
Yamada et al. (2022)	Moderate	Moderate	Moderate	Low	Moderate	Low	Low	Moderate
Yamazaki et al. (2013a)	Moderate	Moderate	Low	Low	Moderate	Low	Low	Moderate
Yamazaki et al. (2013b)	Moderate	Moderate	Low	Low	Moderate	Low	Low	Moderate
Hatta et al. (2021)	Moderate	Moderate	Low	Low	Moderate	Moderate	Low	Moderate
Masseter thickness								
Amaral et al. (2019)	Moderate	Moderate	Low	Low	Low	Low	Low	Moderate
Muller et al. (2012)	Moderate	Moderate	Low	Low	Low	Low	Low	Moderate

Note: Domains of Bias: (D1) bias due to confounding; (D2) bias in the selection of participants into the study; (D3) bias in classification of interventions; (D4) bias due to deviations from intended interventions; (D5) bias due to missing data; (D6) bias in measurement of outcomes; (D7) bias in selection of the reported results.

no benefit of rehabilitation with I-OD when compared to RCD. Additionally, Cochran's Q test ($p = .0001$) also indicated heterogeneity among the pooled studies (Figure 3).

3.5 | Effect on remaining teeth

3.5.1 | Results of individual studies

Five observational studies assessed the effect of different types of rehabilitation on the preservation of remaining teeth in partially edentulous patients, four retrospective studies (Hatta et al., 2021; Yamada et al., 2022; Yamazaki et al., 2013a, 2013b), and one prospective study (Okuni et al., 2022). The number of participants ranged between 24 and 514, totaling 1014 individuals. All studies presented I-FPDs in the test group, while the control groups were composed by resin-bonded fixed partial dentures (R-FPD), tooth-supported fixed partial dentures (T-FPD), tooth-supported removable partial dentures (T-RPD), and/or no restoration (NR). Time in function ranged from 3.4 to 10 years. Four studies evaluated both the maxilla and mandible (Okuni et al., 2022; Yamada et al., 2022; Yamazaki et al., 2013a, 2013b), and one study only assessed the mandible (Hatta et al., 2021). All five studies evaluated survival rates (SR) of remaining teeth adjacent to edentulous spaces (TAES). Three studies evaluated the SR of teeth opposing edentulous spaces (TOES; Yamada et al., 2022; Yamazaki et al., 2013a, 2013b). One study also evaluated survival rates (SR) of remaining teeth nonadjacent to edentulous spaces (TNAES) (Yamada et al., 2022), while two studies analyzed the SR of all remaining teeth (ART) (Yamazaki et al., 2013a, 2013b). Three studies also reported on teeth complications such as fracture or loss of cementation of prosthetic crowns, tooth fracture, caries, periapical lesions,

TABLE 7 Mean (±SD) alveolar bone resorption of residual ridge (in millimeters).

Authors (year)	Time in function (years)	Edentulism (years)	RCD	I-OD	I-FCD	*p*-value
Rehabilitated ridge						
Anterior maxilla						
Alrajhi et al. (2020)	5	3	0.51 ± 0.04	N/A	0.15 ± 0.02	<.001
Posterior maxilla						
Alrajhi et al. (2020)	5	3	0.30 ± 0.03	N/A	0.11 ± 0.02	<.001
Posterior mandible						
Jacobs et al. (1992)	I-OD: 2 I-FCD: 2.1	>10	0.10 ± 0.19	0.14 ± 0.2	0.04 ± 0.06	<.05
Kordatzis et al. (2003)	5	22	0.14 (−0.02–0.37)	0.06 (−0.12–0.24)	N/A	<.001
Tymstra et al. (2011)	10	>20	0.08 ± 0.11	2 implants 0.11 ± 0.07 4 implants 0.07 ± 0.08	N/A	>.05
Khuder et al. (2017)	1–7	5.8	0.12 ± 0.11	0.08 ± 0.07	N/A	=.116
Antagonistic ridge						
Anterior maxilla						
Jacobs et al. (1993)	2	>10	0.13 ± 0.13	0.04 ± 0.05	0.04 ± 0.06	<.05
Tymstra et al. (2011)	10	>20	0.04 ± 0.11	2 implants 0.12 ± 0.14 4 implants 0.11 ± 0.10	N/A	>.05
Khuder et al. (2017)	1–7	5.8	0.142 ± 0.102	0.074 ± 0.073	N/A	=.116

Abbreviations: I-FCD, implant-supported fixed complete denture; I-OD, implant-supported overdentures; N/A, nonapplicable; RCD, removable complete dentures.

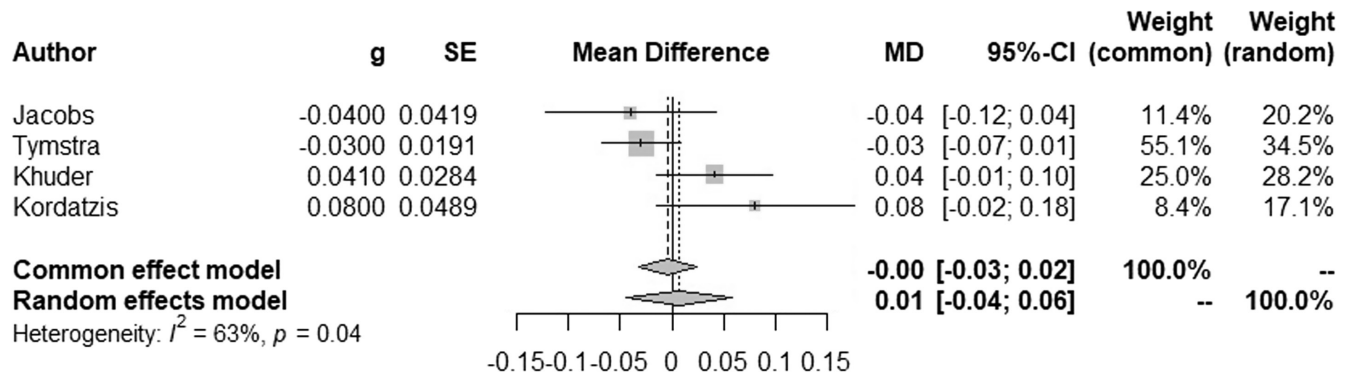


FIGURE 2 Forest plot of mean difference among the selected studies on posterior mandibular alveolar bone resorption.

and periodontal disease (Okuni et al., 2022; Yamada et al., 2022; Yamazaki et al., 2013a; Table 3).

3.5.2 | Results of the qualitative synthesis

Survival rates of teeth adjacent to edentulous spaces (TAES)

The study by Okuni et al., 2022 showed no statistical differences between patients rehabilitated with R-FPD and T-FPD and those rehabilitated with I-FPD. The study by Hatta et al., 2021 showed statistically higher SR of patients rehabilitated with I-FPD when compared with patients with NR. Conversely, three studies showed no statistically significant differences in the SR of patients rehabilitated with T-RPD and those rehabilitated with I-FPD (Yamada et al., 2022; Yamazaki et al., 2013a, 2013b; Table 8).

Survival rates of teeth nonadjacent to edentulous spaces (TNAES)

In the only study to clearly report on the SR of TNAES, a significant higher SR rate was observed in patients rehabilitated with I-FPD when compared with T-RPD (Table 8).

Survival rates of teeth opposing edentulous spaces (TOES)

Among the three studies to report the SR of TOES, one showed a significantly higher SR in patients rehabilitated with I-FPD when

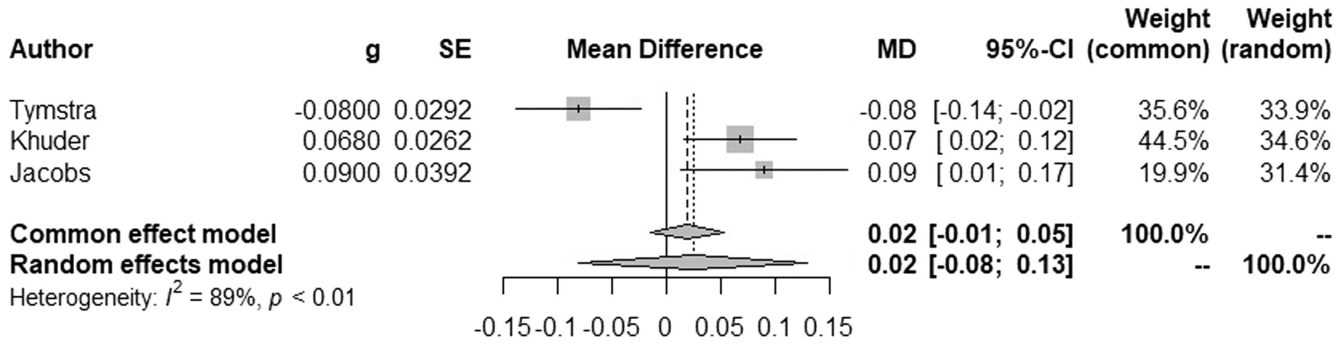


FIGURE 3 Forest plot of mean difference among the selected studies on anterior maxillary alveolar bone resorption.

TABLE 8 Survival rates (%) of remaining teeth of partially edentulous patients.

Authors (year)	Time in function (years)	R-FPD	T-FPD	T-RPD	NR	I-FPD	*p*-value
TAES							
Okuni et al. (2022)	10	89.0%	75.9%[a]	N/A	N/A	92.6%[a]	=.037[a]
Yamada et al. (2022)	4.6	N/A	N/A	89.7%	N/A	92.8%	=.567
Yamazaki et al. (2013a)	10	N/A	N/A	61.8%	N/A	62.2%	>.05
Yamazaki et al. (2013b)	10	N/A	N/A	80%	N/A	98%	>.05
Hatta et al. (2021)	6	N/A	N/A	NA	75%	100%	=.010
TNAES							
Yamada et al. (2022)	4.6	N/A	N/A	91.6%[a]	N/A	98.1%[a]	=.002[a]
TOES							
Yamada et al. (2022)	4.6	N/A	N/A	93.9%	N/A	97.5%	=.311
Yamazaki et al. (2013a)	10	N/A	N/A	83.8%	N/A	75%	>.05
Yamazaki et al. (2013b)	10	N/A	N/A	95%	75%	95%	>.05
ART							
Yamazaki et al. (2013a)	10	N/A	N/A	24.4%	N/A	40%	<.05
Yamazaki et al. (2013b)	10	N/A	N/A	50%	3%[a]	57%[a]	=.01[a]

Abbreviations: ART, all remaining teeth; I-FPD, implant-supported fixed partial denture; NR, no restoration; R-FPD, resin-bounded fixed partial denture; TAES, teeth adjacent to edentulous space; T-FPD, tooth-supported fixed partial denture; TNAES, teeth not adjacent to edentulous space; TOES, teeth opposing edentulous spaces; T-RPD, tooth-supported removable partial denture.

[a]Statistical difference between groups.

compared to those with NR, but no difference was observed with those rehabilitated with T-RPD (Yamazaki et al., 2013b). Two studies found no statistically significant differences between the SR in patients rehabilitated with I-FPD in comparison with those rehabilitated with T-RPD (Yamada et al., 2022; Yamazaki et al., 2013a; Table 8).

Survival rates of all remaining teeth (ART)

In the study by Yamazaki et al., 2013a, with a follow-up of 10 years, in patients with large partially edentulous areas (>3 missing teeth) the SR of ART was significantly higher in patients rehabilitated with I-FDP than those rehabilitated with T-RPD. Another retrospective study conducted by the same group demonstrated that in patients with short-span edentulous areas, the SR of ART in patients restored with I-FPD was comparable with those rehabilitated with T-RPD, but significantly higher when compared to those patients that received NR (Yamazaki et al., 2013b; Table 8).

Other complications in remaining teeth

Of the three studies that reported on the complications in the remaining teeth, the study of Yamada et al. (2022) showed significantly more complications in TAES, TNAES, and TOES in patients rehabilitated T-RPD when compared to those rehabilitated with I-FPD. Loss of retention was observed in 30 TAES (7.0% of the total subjects), and caries were observed in 80 TNAES (8.1% of the total subjects) and 46 TOES (7.3% of the total subjects). Caries was the most frequent complication in all patients, except for TAES in patients rehabilitated with T-RPD, in which loss of retention was the complication most frequently observed. The study by Yamazaki et al. (2013a) demonstrated that the incidence of complications in ART in patients rehabilitated with I-FPD (42%) was also lower than those rehabilitated with T-RPD (59%) and NR groups (90%). Patients treated with T-RPD lost approximately 80% of their TAES due to periodontal lesions. Regarding TOES, 4.8% of patients of patients rehabilitated with I-FPD, and 8.5% of patients

rehabilitated with T-RPD lost their teeth during the observation period. The cause for the only case of tooth loss in I-FPD group was periodontal lesion, whereas patients in T-RPD group mainly lost their teeth due to caries. Okuni et al. (2022) found no significant differences in the cumulative complication-free rates among patients treated with R-FPD, T-FPD, and I-FPD. Among the complications, the authors reported 87 cases of caries (79.1%), three cases of crown fracture (3.6%), and 19 cases of tooth extraction (17.3%) due to a periodontal lesion. They also showed that the main risk factors for the loss of TAES in patients treated with T-FDP in comparison to I-FPD in single-bounded edentulous spaces were the prosthetic material and deep periodontal probing depth.

3.5.3 | Results of the quantitative synthesis

Due to the heterogeneity of study designs, a meta-analysis could not be conducted with the studies that examined the effect of different types of prostheses on remaining teeth.

3.6 | Masseter muscle thickness

3.6.1 | Results of individual studies

Three studies evaluated jaw muscle thickness in fully edentulous patients, all of them specifically measuring masseter muscle thickness (MMT), one RCT (Maniewicz et al., 2019), one cross-sectional (Muller et al., 2012), and one prospective study (Amaral et al., 2019). The number of participating patients ranged between 12 and 80, totaling 158 individuals. All studies presented RCD, and one study also had fully dentate individuals as controls (Muller et al., 2012). The test groups were composed by I-OD in two studies, and I-OD and I-FCD in another (Muller et al., 2012). Time in function ranged from 2 months to 7 years. All studies evaluated MMT with the use of real-time linear ultrasound scanner and a linear array transducer (Table 4).

3.6.2 | Results of the qualitative synthesis

Although the three studies demonstrated more MMT in the I-OD groups when compared to the RCD groups, two studies reached statistical significance (Amaral et al., 2019; Muller et al., 2012). Maniewicz et al. (2019) showed no changes in MMT in the preferred chewing side (P-CS) and a nonsignificant increase of MMT in the not preferred chewing side (NP-CS; Table 9).

3.6.3 | Results of the quantitative synthesis

The meta-analysis was conducted with all three studies (number of observations: $o=108$) that compared masseter muscle thickness in patients rehabilitated with RCD and those rehabilitated with I-OD (Amaral et al., 2019; Maniewicz et al., 2019; Muller et al., 2012). According to the pooled results of the meta-analysis, both fixed and random effects models yielded a significant benefit of rehabilitation with I-OD when compared to RCD. Moreover, Cochran's Q test p-value = .5919 indicated no heterogeneity among the studies (Figure 4).

3.7 | Reporting biases

Egger's test indicated no publication bias of studies pooled to assess alveolar bone resorption in the posterior region of the mandible ($p=.4508$), in the anterior region of the maxilla ($p=.8719$), and masseter bone thickness ($p=.8013$). However, this meta-analysis contains a small number of studies, and Egger's test may lack the statistical power to detect bias when the number of studies is small (i.e., $k<10$).

4 | DISCUSSION

This review and meta-analysis provide a synthesis of the dental literature on the possible positive effect of interventions using implant-supported protheses on orofacial tissues over conventional prostheses or no treatment of fully and partially edentulous patients. From the 14 selected studies, three main outcomes emerged: alveolar bone resorption, effect on remaining teeth, and masseter muscle thickness. In this discussion, the main findings of each outcome and their possible implications to the clinical practice are highlighted.

4.1 | Bone resorption

Following tooth extraction, the alveolar process undergoes a series of physiological events that leads to a significant reduction in size

TABLE 9 Mean (±SD) of masseter muscle thickness during muscle contraction (in millimeters).

Authors (year)	Time in function	P-CS				NP-CS			
		RCD	I-OD	Diff	p- value	RCD	I-OD	Diff	p-value
Amaral et al. (2019)	2 months	9.8 ± 0.9	10.8 ± 1.0	+1.0	.01	N/A	N/A	N/A	—
Maniewicz et al. (2019)	7 years	11.0 ± 1.62	11.4 ± 2.10	0.0	.97	11.1 ± 1.0	11.4 ± 2.1	+0.3	.26
Muller et al. (2012)	At least 1 year	11.98 ± 1.84	13.29 ± 2.07	+1.3	.043	N/A	N/A	N/A	—

Abbreviations: Diff, difference between groups; I-OD, implant-supported overdenture; NP-CS, nonpreferred chewing side; P-CS, preferred chewing side; RCD, removable complete denture.

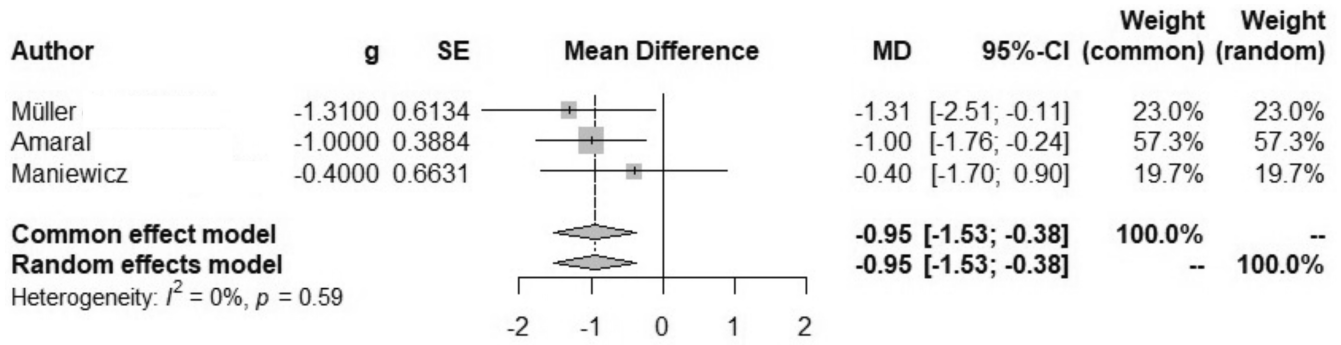


FIGURE 4 Forest plot of mean difference among the selected studies on masseter bone thickness.

and volume during and after healing (Araujo et al., 2006; Chappuis et al., 2017). When multiple adjacent teeth are extracted alveolar bone resorption is more significant, leading to horizontal and vertical deficiencies (Al-Askar et al., 2013). Even though it has been demonstrated that implant placement immediately after tooth extraction does not prevent the natural course of bone remodeling (Araujo et al., 2019), only a limited number of studies evaluated bone remodeling prospectively after functional oral rehabilitation with implants. In fully edentulous patients, it is believed that the constant compressive occlusal forces on the alveolar mucosa cause a gradual bone resorption of the underlying alveolar ridge (Ahmad et al., 2015; Carlsson, 2004; Maruo et al., 2010). In the long term, the occlusal stress on the alveolar ridge can lead to denture retention loss, and make implant rehabilitation more challenging (Huumonen et al., 2012).

This review has shown that adequate data on alveolar ridge resorption in fully edentulous patients following different rehabilitation modalities are still lacking. Although the qualitative analysis suggests that implant therapy may represent an advantage compared to conventional therapy, the meta-analysis of the pooled studies failed to show any such advantage. Differences in edentulism time may have had an important influence on the results. According to Jacobs et al. (1992), despite the more alveolar bone resorption observed in patients treated with I-OD when compared with RCD, when patients had been edentulous for more than 10 years, differences tended to disappear. This could be explained by the fact that after many years of edentulism, most of the alveolar bone process tends to resorb, leaving behind basal bone mostly. Moreover, alveolar bone resorption was also correlated with the status of the opposing arch (Jacobs et al., 1992; Khuder et al., 2017), a fact that may explain the reason why patients rehabilitated with I-OD presented similar bone resorption on the antagonistic ridge than those rehabilitated with RCD. These findings seem to reinforce the perception that regular maintenance appointments for the assessment of the occlusal adjustments can be fundamental in the prevention of maxillary bone resorption.

4.2 | Effect on remaining teeth

Failure to replace missing teeth can lead to a series of disruptions to the stomatognathic system (Shugars et al., 2000). It is a natural consequence of teeth adjacent to edentulous spaces to present extrusion and/or tilting, as well as occlusal disruptions over the years, which may lead to periodontal disease and an increased risk of caries (Aquilino et al., 2001; Shugars et al., 1998). It has been recently demonstrated that older patients with 4 or more missing teeth were more likely to experience multiple additional tooth loss, mainly caused by deeper probing pocket depth and lack of posterior support (Mihara et al., 2020). Several treatment modalities might be proposed for teeth or increasing partially edentulous patients. These individuals might be rehabilitated with conventional T-FPD, R-FPD, and T-RPD, or I-RPD and I-FPD, or even receive NR.

Not unexpectedly, the qualitative analysis showed that patients that received implant-supported therapy presented a tendency for higher SR and/or less tooth complications when compared to conventional therapy or no treatment. Nevertheless, care must be exercised, since significant differences exist in terms of the type of edentulism (single vs. multiple missing teeth; anterior vs. posterior; bounded vs. unbounded), treatment modalities, and the studied outcomes (TAES, TNAES, TOES, ART). Because of the diversity observed among studies, no meta-analysis could be conducted, clearly indicating the need for well-designed long-term prospective clinical studies that can permit comparisons between the effect of different types of restorations on the remaining dentition.

4.3 | Masseter muscle thickness

The consequences of age and full edentulism on masticatory masseter muscle atrophy and density have been previously demonstrated (Newton et al., 1987; Raustia et al., 1996). As the masseter muscle tissue age, a reduction in fiber diameter as well quantity seem to occur, being replaced by fat and connective tissue over time (Larsson, 1995). It has been demonstrated that overdentures supported by two to five teeth prevented the progress of masseter muscle atrophy when compared to completely edentulous patients that were rehabilitated with RCD (Newton et al., 2004). Moreover, in a case report that followed a 97-year-old patient during and after relining his mandibular RCD, MMT showed a 17% decrease during denture abstention and a significant increase beyond the preimplant level after I-OD insertion, suggesting that

masseter muscle bulk in old age may be dependable of denture function (Schimmel et al., 2010).

This review has shown that rehabilitation with I-OD may increase bite force and result in more masseter muscle thickness (Amaral et al., 2019; Muller et al., 2012). The only RCT included in this review, however, could not observe any significant differences in MMT either on the preferred chewing side or not preferred chewing side over a period of 7 years of observation (Maniewicz et al., 2019). A possible explanation is that aging might mask a possible training effect of the I-OD. Thus, although the meta-analysis of the pooled studies yielded a significant benefit for I-OD in comparison to RCD, the time factor seems to have an important effect in this type of analysis. Due to the differences observed in the results, MMT can only be properly assessed with long-term prospective clinical studies to better ascertain if the rehabilitation with I-OD actually offers an advantage over RCD.

4.4 | Limitations and future research directions

To the best of the authors' knowledge, this study represents the first attempt to systematically analyze the effect of implant therapy on the preservation of orofacial tissues. It remains unclear whether implant therapy has a positive effect in the sense of maintaining the alveolar ridge bone, preserving remaining teeth, or increasing/maintaining masseter muscle thickness in the long term when compared to conventional or no therapy. Therefore, due to a series of shortcomings involving study design and quality, definitive conclusions cannot be drawn.

Although efforts have been placed in making this review as comprehensively as possible, the gray literature was not consulted, and the search was restricted to articles in English published in journals available electronically, which may have resulted in some relevant studies being missed during the search procedure. Among the selected studies, only one was an RCT, which observed MMT over a period of 7 years, without finding any significant differences between treatment modalities. When contrasted with the work of Amaral et al. (2019), which found a significant MMT increase only 2 months after RCD had been relined into I-OD, it becomes clear that time emerges as a crucial factor in the analysis of the studied outcomes, which cannot be adequately dealt with by retrospective studies. Apart from that, in terms of quality, all the observational studies presented a moderate risk of bias, especially concerning confounding factors and the selection of participants in the study. Also, the diversity observed in the selected studies in terms of types of edentulism, populations, follow-up time and study designs all have a significant impact on the results, preventing a more consistent analysis. For instance, no comparative clinical study evaluating the effect of implant therapy on the course of bone remodeling in partially edentulous patients was found. On the other hand, no studies were found on the effect on the remaining teeth of patients that received complete restorations in the antagonistic arch.

Despite a tendency towards implant therapy, findings continue to be insufficient and controversial. It seems that this gap can only be overcome by the conduction of well-designed prospective comparatives studies, preferably RCT, so that the outcomes studied can be better ascertained in relation to the time factor. Nonetheless, while the therapeutical approach to a partially or fully edentulous patient may depend upon multiple factors such as individual anatomical features and overall treatment time and cost, the findings presented here should not discourage dentists from recommending implant-supported rehabilitation. This study has shown that implant-supported restorations, if not superior, they are at the very least equivalent to conventional rehabilitation in preserving orofacial tissues over time.

5 | CONCLUSIONS

This systematic review and meta-analysis were unable to unequivocally answer the focus question. While there are some indicators of the benefit of implant-supported prostheses over conventional prostheses or no therapy in preserving orofacial tissues, the evidence is still insufficient to confirm such perception. Long-term comparative longitudinal studies are strongly encouraged.

AUTHOR'S CONTRIBUTION

André B. De Souza and Flavia Matarazzo conceived the ideas, analysed the data, led the writing and reviewed the manuscript; Konstantinos Vazouras extracted the data and summarized the results; Panos Papaspyridakos and Hans-Peter Weber analysed the data and reviewed the manuscript.

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CONFLICT OF INTEREST STATEMENT

The authors declare no private or commercial competing interests.

DATA AVAILABILITY STATEMENT

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

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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CONSENSUS REPORT

CLINICAL ORAL IMPLANTS RESEARCH WILEY

Group 4 ITI Consensus Report: Patient benefits following implant treatment in partially and fully edentulous patients

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Abstract

Objectives: The aim of Working Group 4 was to address patient benefits associated with implant dentistry. Focused questions on (a) dental patient-reported outcomes (dPROs), (b) improvement in orofacial function, and (c) preservation of orofacial tissues in partially and fully edentulous patients following provision of implant-retained/supported dental prostheses were addressed.

Materials and Methods: Three systematic reviews formed the basis for discussion. Participants developed statements and recommendations determined by group consensus based on the findings of the systematic reviews. These were then presented and accepted following further discussion and modifications as required by the plenary of the 7th ITI Consensus Conference, taking place in 2023 in Lisbon, Portugal.

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Results: Edentulous patients wearing complete dentures (CD) experience substantial improvements in overall dPROs and orofacial function following treatment with either complete implant-supported fixed dental prostheses (CIFDP) or implant overdentures (IODs). With respect to dPROs, mandibular IODs retained by two implants are superior to IODs retained by one implant. However, increasing the number of implants beyond two, does not further improve dPROs. In fully edentulous patients, rehabilitation with CIFDP or IOD is recommended to benefit the preservation of alveolar bone and masseter muscle thickness.

Conclusions: Completely edentulous patients benefit substantially when at least the mandible is restored using an CIFDP or an IOD compared to CD. In fully edentulous patients, implant prostheses are the best option for tooth replacement. The availability of this treatment modality should be actively promoted in all edentulous communities, including those with limited access and means.

KEYWORDS
consensus report, dental patient-reported outcomes, meta-analysis, orofacial function, systematic review, tertiary prevention

1 | INTRODUCTION

The objectives of Group 4 of the 7th ITI Consensus Conference were to provide statements and recommendations for clinicians and researchers relating to patient benefits following implant treatment in partially and fully edentulous patients. Three systematic reviews, prepared and reviewed prior to the Consensus Conference, formed the basis for discussion within the working group. The working group formulated Consensus Statements and Clinical Recommendations that were then presented and accepted following further discussion and modifications when required by the plenary. Clinical Recommendations for future research were also prepared by the working group.

In addition, responses to questions considered relevant from a patient's perspective were made by the working group based on the findings of the systematic reviews.

The three systematic reviews are listed below:

1. Treatment effect of implant-supported fixed complete dentures and implant overdentures on patient-reported outcomes: A systematic review and meta-analysis (Abou-Ayash et al., n.d.)
2. Oral function in completely edentulous patients rehabilitated with implant-supported dental prostheses: A systematic review and meta-analysis (Srinivasan et al., n.d.)
3. Effect of dental implant therapy on the preservation of orofacial tissues: a systematic review and meta-analysis (De Souza et al., n.d.).

2 | SYSTEMATIC REVIEW 1

Treatment effect of implant-supported fixed complete dentures and implant overdentures on patient-reported outcomes: A systematic review and meta-analysis (Abou-Ayash et al., n.d.).

3 | PREAMBLE

The patient's perspective of treatment is a key factor in analyzing treatment success. Patient-reported outcomes (PROs) are commonly used for such patient-centered success analyses. In the medical field, PROs describe health outcomes that come directly from patients without interpretation by another person. Those PROs are recorded using different patient-reported outcome measures (PROMs), which represent the tools to record PROs. In dentistry, specific dental patient-reported outcome measures (dPROMs) are used that measure the patient-reported outcome of dental treatment (dPROs). However, the terms PROs and PROMs are often used as synonyms (Table 1).

The treatment of edentulous patients using dental implants is well established as a treatment alternative to conventional removable complete dentures (CDs) (Feine et al., 2002). The advantages of implant-supported or implant-retained overdentures (IODs), and complete implant-supported fixed dental prostheses (CIFDPs) over CDs in terms of parameters such as oral function, oral health or dPROs have been demonstrated in numerous studies and are therefore considered today to be evidence-based (Hartmann et al., 2020). However,

TABLE 1 List of abbreviations.

Complete implant-supported fixed dental prostheses	CIFDP
Dental patient-reported outcome	dPRO
Dental patient-reported outcome measure	PROM
Denture satisfaction score	DSS
Effect size	ES
Implant-supported or implant-retained overdenture	IOD
Muscosa-borne removable complete denture	CD
Oral health impact profile	OHIP
Oral impact on daily performance questionnaire	OIDP
Partial implant-supported fixed dental prosthesis	IFDP
Randomized controlled trials	RCT
Tooth-retained/supported removable partial dental prosthesis	RDP
Tooth-supported fixed dental prosthesis	FDP
Visual analog scale	VAS

it is unclear whether there is a difference between CIFDPs and IODs with regard to the benefits mentioned. Especially in the field of dPROs, this question could not be conclusively clarified. Attempts to summarize the existing evidence by a meta-analysis have so far failed due to the use of various dPROMs for the analysis of dPROs. In the present systematic review, we summarized the data from different dPROMs by calculating the effect size (ES), making the results obtained from different dPROMs comparable. The ES is a quantitative measure of the treatment effect. The larger the ES, the stronger the treatment effect. Generally, ES>0.8 are considered to be large. The main requirement for ES calculation was the availability of baseline (before implant therapy) and follow-up dPROs. The systematic literature search resulted in 1608 records, and 28 studies with dPROs of 1457 patients were finally included. This number was sufficient to perform a meta-analysis. The different dPROMs used in the included studies were different versions of the oral health impact profile (OHIP), different visual analog scales (VAS), the Short Form 36 questionnaire, the Oral Impact on Daily Performance questionnaire (OIDP), a patient satisfaction score, and the Denture Satisfaction Score (DSS; $n=2$).

The following limitations should be considered when interpreting the results of the present study: (1) only four of the included studies reported dPROs in CIFDPs, (2) among the 15 RCTs included, only 2 RCTs directly compared CIFDPs with IODs, (3) only three studies referred to treatment of the edentulous maxilla. Furthermore, the quality assessment of the literature included showed considerable variation with a high risk of bias and moderate-to-low certainty of evidence.

4 | CONSENSUS STATEMENTS

4.1 | Consensus statement 1

In fully edentulous patients wearing removable complete dentures (CD), the use of dental implants to retain/support dental prostheses in the maxilla and/or the mandible leads to an improvement in overall dental patient-reported outcomes (dPROs).

This statement is based on a descriptive analysis of 2 RCTs and 26 prospective case series (1457 patients).

4.2 | Consensus statement 2

Edentulous patients wearing complete dentures (CD) gain substantial improvements in overall dPROs following treatment which are comparable with either complete implant-supported fixed dental prostheses (CIFDPs) or implant overdentures (IODs).

This statement is based on a meta-analysis of 2 RCTs and 13 prospective case series (519 patients). Effect size (ES) CIFDPs: 1.68 [1.15, 2.20]; ES IODs: 1.26 [0.99, 1.52].

4.3 | Consensus statement 3

When restoring the edentulous mandible with an IOD, both bar and non-splinted attachments lead to a similar improvement in dPROs.

This statement is based on a meta-analysis of 2 RCTs and 18 prospective case series (639 patients). ES bars: 1.33 [0.37, 2.29]; ES non-splinted attachments: 1.38 [1.17, 1.58].

4.4 | Consensus statement 4

With respect to dPROs, mandibular IODs retained by two implants are superior to IODs retained by one implant.

This statement is based on a meta-analysis of 3 RCTs and 17 prospective case series (639 patients). ES difference: 0.72 [0.38, 1.06].

4.5 | Consensus statement 5

Increasing the number of implants to more than two implants to retain a mandibular IOD does not further improve dPROs.

TABLE 2 Effect size in respect to the increase in dPROs in relation to the number of implants to support/retain a mandibular IOD.

Implants per reconstruction	Patients (*n*)	Effect size (95%-CI)
1 Implant	304	0.67 [0.43, 0.91]
2 Implants	395	1.40 [1.18, 1.62]
3 Implants	135	1.46 [1.19, 1.73]
4 Implants	68	0.65 [−0.21, 1.50]

This statement is based on a meta-analysis of 2 RCTs and 18 prospective case series (598 patients), (Table 2).

5 | CLINICAL RECOMMENDATIONS

5.1 | Clinical recommendation 1

In fully edentulous patients can a CIFDP or an IOD be recommended to provide optimal stability and comfort?

In fully edentulous patients, based on dPROs, both CIFDPs and IODs result in an improvement in stability and comfort compared to CDs. For the highest levels of stability, retention, and comfort, CIFDPs may be recommended over IODs, whenever clinically indicated. Clinical decisions should also consider other relevant factors including speech, esthetic concerns, prosthetic space requirements, costs, stability, retention, maintenance requirements, and manual dexterity. Continuous assessment of the patient's ability to manage the prosthesis and maintain plaque control should be performed.

5.2 | Clinical recommendation 2

What is the ideal attachment for a mandibular IOD?

In fully edentulous patients, both splinted and unsplinted attachments are equally effective from a patient's perspective and can be recommended.

5.3 | Clinical recommendation 3

Based on dPROs, what is the ideal number of implants to retain/support a mandibular IOD?

In fully edentulous patients, mandibular IODs retained by one or two implants show positive effects on dPROs compared to a mandibular CD, with two implants being the optimal number. Additional implants do not offer further improvements in dPROs.

Based on expert opinion, if the opposing maxilla is dentate or restored with a fully implant-supported prosthesis, more than two standard-diameter implants in strategic positions are recommended to support the mandibular IOD to avoid complications and fractures of the implants and prosthetic components. More than two implants are also recommended to enable implant support over mucosal support in compromised anatomical situations (e.g., highly resorbed posterior mandible) and/or compromised mucosal conditions (e.g., hyposalivation).

6 | PATIENT PERSPECTIVES

For the Patient Perspectives, please refer to the section below.

7 | RECOMMENDATIONS FOR FUTURE RESEARCH

- In future studies on patient perspectives, a clear distinction should be made between the abbreviations dPROMs and dPROs.
- Based on the small number of studies on maxillary CIFDPs/IODs, as well as studies directly comparing the treatment effect of CIFDPs vs. IODs on dPROs, more research is needed. RCTs that include the rehabilitation of the edentulous maxilla and compare CIFDP and IOD treatment directly would be especially valuable to provide a conclusive assessment of the treatment effect on dPROs.
- For the analysis of dPROs, reporting of pre-treatment and follow-up scores (including measures for central tendency, e.g., means, and for score variability, e.g., standard deviations) should be mandatory.
- Future studies should use dPROMs with sufficient psychometric properties and several validated language versions available to ensure high methodological quality and comparability, such as the Oral Health Impact Profile (OHIP). The use of some type of OHIP questionnaire should therefore be the minimum standard for the collection of dPROs. For further assessment of specific treatment outcomes, individual questions or questionnaires can be added. To ensure comparability, questions should be chosen that were already applied in other studies on the same or similar topic. Answers to these questions should be collected on commonly accepted response scales, such as VAS, ordinal response scales, or Likert scales.

8 | SYSTEMATIC REVIEW 2

Oral function in completely edentulous patients rehabilitated with implant-supported dental prostheses: A systematic review and meta-analysis (Srinivasan et al., n.d.).

9 | PREAMBLE

The purpose of this systematic review was to evaluate the literature reporting on the short- to long-term effects of rehabilitation with implant-retained/supported prostheses on the components

of oral function in completely edentulous patients. The outcomes of oral function assessed in this systematic review and meta-analysis were:

- Bite force
- Masticatory performance
- Swallowing function
- Muscle activity
- Lip force
- Speech and articulation
- Oral tactile sensitivity
- Oral diadochokinesis
- Salivary flow

The findings of the systematic review and meta-analysis were based on 30 prospective studies comparing the oral function of completely edentate individuals rehabilitated with CDs in both jaws and those edentate individuals rehabilitated with a conventional maxillary CD opposing implant-retained/supported mandibular prothesis. The follow-up periods of the included studies ranged between 6 months and 10 years after implant loading. Sufficient data were available to perform a meta-analysis for evaluating bite force, masticatory performance (sieve method, colorimetric method, swallowing threshold), stimulated salivary flow rate, mandibular movement, and chewing pattern (area of chewing pattern, opening and closing velocity, masticatory cycle/second, and vertical height). The time points considered in the analyses were grouped into 6–12 months, 12–36 months, and > 36 months.

The review identified records evaluating the effects of implant rehabilitation on lip force, speech, and oral tactile threshold. These studies were however excluded from the meta-analysis as they were either retrospective in design, with follow-up periods below 6 months, or with inadequate sample sizes. The review did not identify records evaluating effects of implant rehabilitation on tongue function, swallowing function, oral stereognosis, and oral diadochokineses. The current review was unable to identify studies reporting on maxillary implant-retained/supported prostheses for edentate individuals that satisfied the scope and inclusion criteria of this review.

10 | CONSENSUS STATEMENTS

10.1 | Consensus statement 1

Overall oral function improves significantly in edentulous patients rehabilitated with mandibular IODs/CIFDPs opposing a conventional maxillary CD when compared to those rehabilitated with CDs in both jaws.

This statement is based on the overall results of the meta-analyses performed for the investigated time points at 6–12 months ($Z = -4.895$, $p < .001$; 10 studies: 2 RCTs, 8 prospective studies; 443 patients), at 12–36 months ($Z = -4.886$, $p < .001$; 14 studies: 3 RCTs, 11 prospective studies; 586 patients) and at more than 36 months ($Z = -9.108$, $p < .001$; 5 prospective studies; 179 patients) in function.

10.2 | Consensus statement 2

Bite force increases in edentulous patients rehabilitated with mandibular IODs/CIFDPs opposing a maxillary CD when compared to those rehabilitated with CDs in both jaws.

This statement is based on the meta-analysis performed for the investigated time points at 6–12 months ($Z = -3.788$, $p < .001$, 2 prospective studies, 52 patients), at 12–36 months ($Z = -4.041$, $p < .001$, 4 studies: 1 RCT and 3 prospective studies, 152 patients), and at more than 36 months ($Z = -8.061$, $p < .001$, 5 prospective studies, 179 patients).

10.3 | Consensus statement 3

Chewing (masticatory performance and efficiency) improves in edentulous patients rehabilitated with mandibular IODs/CIFDPs opposing a maxillary CD when compared to those rehabilitated with CDs in both jaws.

This statement is based on the meta-analysis of data provided by 7 studies (2 RCTs and 5 prospective studies; 327 patients) for the assessment of masticatory performance by mixing ability tests (variance of hue: $Z = -2.283$, $p < .022$, 5 studies: 2 RCTs and 3 prospective studies, 235 patients; mixing ability test: $Z = -4.711$, $p < .001$, 2 prospective studies, 92 patients) with a follow-up period of 12–36 months.

Assessment of chewing function using the sieving method (comminution tests) showed the largest effect size.

11 | CLINICAL RECOMMENDATIONS

11.1 | Clinical recommendation 1

With respect to oral function, should implant-retained/supported prostheses be considered the best treatment option in completely edentulous patients?

Oral function significantly improves in completely edentulous patients when the mandible is restored using an CIFDP or an IOD compared to CDs, therefore this should be recommended as the best treatment. The availability of this treatment modality should be actively promoted in all edentulous communities, including those with limited access and means.

12 | PATIENT PERSPECTIVES

In the following part, patient perspectives are formulated that are supported by the consensus statements from both systematic

reviews (Abou-Ayash et al., n.d.; Srinivasan et al., n.d.) and the clinical recommendations. The scenario below forms the basis for questions that an edentulous patient may pose when being considered for fixed or removable implant prostheses.

12.1 | Patient perspective 1

My upper denture fits well but I have problems with my lower denture, particularly when eating. Is there a better alternative than my current lower denture?

Response: Yes, there are removable dentures and fixed bridges attached to implants to replace your loose lower denture. There are many studies that show that these improve satisfaction and the ability to chew and bite. Implants will help to stabilize your dentures/bridges, making them more comfortable and less likely to move around.

12.2 | Patient perspective 2

As my upper denture fits well, should an implant denture/bridge be my first choice of treatment instead of a new lower full denture?

Response: Since you are not satisfied with your current lower denture, yes, a dental implant denture/bridge should be considered as your first option to help replace all of your missing lower teeth. Studies show that these are very beneficial to patients like you. However, a full assessment will be required to examine the amount of bone you have available to place implants and to consider your medical history.

12.3 | Patient perspective 3

If I keep my full denture as it is but want an implant denture in my lower jaw, how many implants will I need?

Response: If we are considering a removable implant denture, it is possible to use 1 implant, but we recommend 2, as the studies show us that this will provide you with greater satisfaction. Interestingly, the evidence also shows that putting in more than 2 implants will not lead to any improvements in your satisfaction.

12.4 | Patient perspective 4

Will I be happy with the removable implant denture in the long term?

Response: Yes, the majority of patients in your situation remain satisfied with their removable implant dentures for at least 10 years.

12.5 | Patient perspective 5

What if I would like to have a fixed solution, something that I do not have to remove?

Response: If you prefer to have a fixed denture, then you will require a minimum of 4 implants to provide you with a fixed implant bridge. Many patients have reported that this option provides the highest degree of stability and comfort. However, you must understand that the fixed option makes daily cleaning more challenging and will be more expensive.

13 | RECOMMENDATIONS FOR FUTURE RESEARCH

- Future clinical studies and trials on implant therapy should include appropriate parameters of oral function as outcome measures. This will generate valuable prospective data for evaluating the true significance of implant therapy in edentulous patients.
- Data on the measurement of masticatory performance/efficiency was very heterogenous as it was performed using many different techniques and interpretations. A consensus on a single, validated technique for measuring masticatory performance/efficiency that is easy to perform, without an elaborate armamentarium, and that is universally scalable with other methods is warranted.
- There is a paucity of scientific evidence on the effects of implant therapy on components of oral functions such as speech, lip force, oral tactile sensitivity, oral didochokinesis, and salivary flow. It is recommended that outcomes addressing these parameters are included in future clinical implant studies.

14 | SYSTEMATIC REVIEW 3

Effect of dental implant therapy on the preservation of orofacial tissues: a systematic review and meta-analysis (De Souza et al., n.d.).

15 | PREAMBLE

With the increase in life expectancy, more patients are bound to present with missing teeth due to periodontitis, caries, fracture, or a combination of these (Sarafidou et al., 2022). Clinicians may recommend fixed or removable conventional or implant-supported rehabilitations to treat both partially and fully edentulous spaces, or even no restoration. The treatment of choice must be carefully considered based on its long-term impact on function and esthetics and to preserve the health of remaining teeth (Okuni et al., 2022). Logically, it would be expected that rehabilitations with implant-supported prostheses may also help to preserve orofacial tissues such as the alveolar bone, remaining teeth, and jaw muscles when compared to conventional treatment modalities, or no treatment, but data remains controversial. Such information can assist clinicians in their therapeutic recommendations, and also patients when weighing the long-term benefits and limitations of each type of intervention.

The present systematic review and meta-analyses were conducted to answer the following question: In partially or fully edentulous

patients, do implant-supported dental prostheses preserve orofacial tissues when compared to conventional prostheses or no therapy?

The main goals and primary outcomes of this systematic review and meta-analysis were to comparatively analyze the effect of implant therapy on the following:

- Alveolar bone resorption—area measurements conducted on digital panoramic radiographs in relative terms (%), or changes in the area index over time;
- Remaining teeth—survival rate (%), complication rates (caries or other type of tooth structure loss, periodontal lesions, and crown fracture); and
- Masseter muscles thickness—measured, in millimeters, with real-time linear ultrasound scanner and linear array transducer.

16 | CONSENSUS STATEMENTS

16.1 | Consensus statement 1

Patients rehabilitated with IODs or CDs present similar bone resorption values in the posterior region of the mandible of fully healed ridges as assessed in panoramic radiographs.

This statement is based on a meta-analysis including four studies (three retrospective, one prospective; 324 patients) ([CI −0.04; 0.06], $p > .05$).

16.2 | Consensus statement 2

There is less alveolar bone resorption on the posterior mandible in patients with CIFDPs compared to CDs and IODs.

This statement is based on one retrospective study with 140 patients ($p < .05$).

16.3 | Consensus statement 3

Partially edentulous patients who are rehabilitated with tooth-supported removable dental prostheses (RDPs) present more tooth loss (mainly due to caries) than patients with implant-supported partial fixed partial dentures (IFPDs).

This statement is based on three retrospective studies (410 patients).

16.4 | Consensus statement 4

In fully edentulous patients using CDs, masseter muscle thickness increases after rehabilitation with mandibular IODs. The meta-analysis showed a significant benefit of IODs when compared to CDs.

This statement is based on three studies (one RCT, one cross-sectional, one prospective study; 108 patients). The effect size difference is 0.95 ([CI 1.53, 0.38], $p = .0012$).

17 | CLINICAL RECOMMENDATIONS

17.1 | Clinical recommendation 1

In edentulous patients, does implant treatment reduce alveolar bone resorption as compared to CD treatment?

Yes. In edentulous patients, rehabilitation with an CIFDP or IOD is also beneficial to reduce alveolar bone resorption. The evidence does not favor one treatment modality over another. Regular maintenance appointments to ensure peri-implant health and occlusal stability of the prosthesis are also recommended to minimize alveolar bone loss.

17.2 | Clinical recommendation 2

When tooth replacement is indicated in partially edentulous patients, can IFDPs be recommended over tooth-retained/supported removable partial dental prostheses (RDP) to preserve the health of the remaining teeth?

In periodontally stable, partially edentulous patients, when tooth replacement is indicated, treatment with IFDPs is recommended over the provision of RDPs to preserve the health of the remaining teeth.

17.3 | Clinical recommendation 3

In fully edentulous patients, can IODs/CIFDPs be recommended over CDs in the preservation of masticatory muscle?

In fully edentulous patients, rehabilitations with IODs/CIFDPs are recommended to increase masseter muscle thickness compared to CDs. It is plausible to infer that this may have a positive effect on chewing.

18 | PATIENT PERSPECTIVES

In the following part, patient perspectives are formulated that are supported by the consensus statements from both systematic reviews and the clinical recommendations. The scenario below forms the basis for questions that an edentulous patient may pose when being considered for fixed or removable implant prostheses.

18.1 | Patient perspective 1

Some of my teeth are missing, what will happen if I do not do anything?

Response: It depends on how many teeth are missing and where—functioning and esthetics may be impacted. Your teeth might move, and it might make it more difficult to clean them. Some studies show that not replacing missing teeth leads to bone loss. Furthermore, it may reduce the health of the remaining teeth and cause further

tooth loss. However, many patients are able to enjoy adequate function with some missing teeth.

18.2 | Patient perspective 2

I have complete dentures, and I heard about dental implants. I was wondering if those implants provide advantages related to the bone or the chewing muscles?

Response: Yes, many studies show that in patients without teeth, dental implants offer the advantage of preserving the jaw bone, as long as the implants are healthy. In addition, your chewing muscles become stronger compared to full dentures.

18.3 | Patient perspective 3

I have many missing teeth in my lower right jaw, and I would like to replace them. What is my best treatment option? Should I get a partial denture or a fixed implant bridge?

Response: Replacing the missing teeth with a fixed implant bridge will decrease the chances of further tooth loss when compared to a removable partial denture. With the partial denture in place, the remaining teeth are more prone to developing dental diseases. These partial dentures also require more maintenance. Therefore, I would advise you to get a fixed implant bridge.

19 | RECOMMENDATIONS FOR FUTURE RESEARCH

- Well-designed, clinical studies monitoring hard and soft tissue changes over time in partially and fully edentulous patients rehabilitated with an implant-supported prosthesis compared to a conventional fixed and removable prosthesis are strongly recommended. It is recommended that the alveolar bone dimensional changes should be evaluated by three-dimensional radiographs and include vertical, horizontal and bone volume alterations in both jaws. Soft tissue dimensional changes may be investigated by three-dimensional intra-oral surface scan-based imaging.
- Well-designed, clinical studies evaluating the effect of an implant-supported prosthesis compared to a conventional fixed or removable prosthesis or no treatment on remaining teeth should be investigated by means of periodontal health (e.g., periodontal bone level, periodontal disease), tooth health (e.g., incidence of caries, fracture, root canal treatment), tooth prognosis, and tooth survival.
- Well-designed prospective studies evaluating the effect of an implant-supported prosthesis compared to a conventional fixed or removable prosthesis or no treatment that analyzes the facial muscles of partially and fully edentulous patients.

AUTHOR CONTRIBUTIONS

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CONFLICT OF INTEREST STATEMENT

The authors of the group 4 Consensus Report declared no conflicts regarding the content of the 7th ITI Consensus Conference.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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REVIEW ARTICLE

CLINICAL ORAL IMPLANTS RESEARCH WILEY

Clinical performance of immediately placed and immediately loaded single implants in the esthetic zone: A systematic review and meta-analysis

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Abstract

Objectives: The aim of this study was to assess the following PIO question: In adult patients treated with an indication for single tooth extraction in the maxillary esthetic zone (15–25), what is the influence of an immediate implant placement and immediate loading protocol on the clinical performance (primary aim) and esthetic outcomes (secondary aim) focusing on investigations published after 2010.

Material and Methods: An electronic search in Medline (PubMed), the Cochrane Central Register of Controlled Trials, and EMBASE databases up to April 2022 was performed to identify clinical studies investigating the outcome of single implants subjected to immediate placement with immediate restoration/loading (Type 1A).

Results: Sixty-three studies (10 randomized controlled trials, 28 prospective and 25 retrospective cohort studies) were included with a follow-up ranging from 12 to 96 months. One thousand nine hundred sixty-one implants reported survival rates of 99.2 (98.6–99.5) % at 1 year, 97.5 (95.9–98.4) % after 3 years, and 95.8 (93.3–97.4) % after 5 years; 1064 immediately loaded restorations presented survival rates of 98.9 (97.8–99.5) % after 1 year, 96.8 (93.6–98.4) % after 2 years, and 94.8 (89.6–97.4) % after 5 years. Comparing baseline to 12-month data using the Hedges' g effect size (95% CI), papilla height presented an overall effect size of −0.71 (−1.25, −0.1) mm, mid-facial recession change of −0.15 (−0.66, 0.36) mm, and a 0.82 (0.37, 1.28) gain in PES.

Conclusions: Immediate implant placement and immediate loading can be considered a predictable and safe treatment option for single maxillary anterior restorations with adequate survival rates and favorable esthetics outcomes for up to 5 years.

KEYWORDS
dental implants, esthetic outcomes, immediate, papilla index, peri-implant soft tissue, pink esthetic score, provisional, white esthetic score

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1 | INTRODUCTION

Although partial edentulism is decreasing among industrialized countries due to improvements in oral health, this condition is still prevalent as a result of endodontic failures, trauma, and other causes (Schneider et al., 2017). Additionally, lifestyles are currently strongly influenced by esthetics; in this regard, anterior tooth loss and its associated esthetic impact can affect patients' satisfaction with their dentition in daily life (Al-Omiri et al., 2009).

Immediate implant placement and immediate loading/restoration (Type 1A) has become a popular and attractive treatment option for both dentists and patients. This implant protocol not only reduces the treatment time and clinical morbidity but also preserves the peri-implant mucosal tissue after tooth extraction, resulting in the best possible esthetic result (van Nimwegen et al., 2016; Yan et al., 2016). With increased publications reporting such interventions, Type 1A implant treatment has become a clinically documented protocol (Gallucci et al., 2018). With progressive advances in implant dentistry and high survival and success rates of immediate implants in recent years, there has been increased interest in esthetic evaluation on immediately placed and immediately loaded/restored implants (Mangano et al., 2017; Slagter et al., 2021; Vidigal et al., 2017). The demand for the optimal esthetic results observed when implementing the Type 1A protocol has increased, especially in the maxillary anterior area (Mangano et al., 2017; Slagter et al., 2021; Vidigal et al., 2017).

Immediate implant placement (Type 1) is the treatment of choice for carefully selected failing single teeth cases since local alveolar anatomy following tooth extraction has a large impact on the soft and hard tissue behavior around the future implant (Buser et al., 2017; Gallucci et al., 2018) and therefore in esthetics. Although the predictability of this approach has been widely described, to date, there is no review that evaluates the influence of the different treatment modalities on the esthetic outcomes and clinical performance of single implant treatments in the maxillary esthetic zone.

The primary aim of the present systematic review was to evaluate the clinical performance by means of implant and prosthetic survival and complication rates, and the secondary outcome was to assess the crestal bone loss and esthetic outcomes by means of esthetic indices of implants and their supported restorations inserted with Type 1A implant placement and loading (immediate placement + immediate restoration/loading) in the maxillary anterior zone, focusing on investigations published after 2010, answering the following PIO question: In adult patients treated with on indication for single tooth extraction in the maxillary esthetic zone (15–25), what is the influence of an immediate implant placement and immediate loading protocol on the clinical performance and esthetic outcomes.

2 | MATERIALS AND METHODS

2.1 | Study protocol

The present systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (Page et al., 2021) and the Cochrane Handbook for Systematic Reviews of Interventions (Deeks et al., 2021). The protocol and the review were designed according to the PIO (Population, Intervention, Outcome) model:

- Population: Adult patients with indication for single tooth extraction and immediate single implant and immediate loaded implant-supported crown protocol in the esthetic anterior maxilla 15–25 (FDI).
- Intervention or exposure: Immediate implant placement and immediate loading of single implants using modern dental implants after 2010 with no particular surgical or restorative procedure.
- Outcome: Clinical performance as primary outcome (Implant and prosthetic survival rates), and as secondary aim, crestal bone loss, esthetic outcomes by means of esthetic indices (papilla height, papilla index and heights), midfacial/buccal recession in soft tissue level, pink esthetic score (PES) (Belser et al., 2009), pink esthetic score (Fürhauser et al., 2005), white esthetic score (WES).

Therefore, the PIO question was as follows: In adult patients treated with an indication for single tooth extraction in the maxillary esthetic zone (15–25), what is the influence of an immediate implant placement and immediate loading protocol on the clinical performance and esthetic outcomes.

In the present review, there was no comparison with other loading and placement protocols. Subgroup analyses were made with respect to flap versus flapless implant placement, screw-retained versus cement-retained restorations.

2.2 | Eligibility criteria

2.2.1 | Inclusion criteria

- Clinical studies of single implants and implant-supported crowns using an immediate implant placement and immediate loading protocol in the anterior maxilla 15–25 (FDI), including objective esthetic outcomes, implant information, surgical procedures, and the restorative procedure.
- Studies published after 2010 will only include modern surface implants and updated protocols. Older studies may include smooth surface implants and older protocols and as such introduce a research bias. As we cannot differentiate between the implant surfaces and the followed protocols in the older studies, we have chosen for this approach as we expect that these studies will provide us with the information we seek.
- Randomized and controlled clinical trials, cross-sectional studies, cohort studies, case–control studies, case series including at least 10 participants.
- Studies including clearly documented clinical procedures (implant design, surface, implant material; surgical procedures: GBR, soft tissue grafting, extraction socket grafting, no augmentation procedures; flapless, flap implant surgery; restorative procedures:

type of provisional, type of definitive crown including abutment types and material).
- Studies including clearly documented objective esthetic outcomes on esthetic indices.
- Minimum follow-up period of 12 months.
- Publications written in English, German, or Spanish.

2.2.2 | Exclusion criteria

- Review articles, chart reviews, case reports, and/or questionnaires.
- In vitro or animal studies.
- Implants supporting full-arch restorations or partial restorations replacing more than one missing tooth and implants supporting removable prostheses.
- Fully edentulous patients, implants placed in irradiated bone or alveolar clefts.
- Studies including soft tissue, peri-implant, and/or esthetic evaluations that do not use objective esthetic outcomes on esthetic indexes in implant dentistry.
- Insufficient documentation regarding implant placement and loading, objective clinical outcomes, esthetic outcome assessments, implant design, surgical procedures, and/or the restorative procedure.
- Inability to separate data for sites in the esthetic zone from posterior and mandibular sites or across intervention groups.

2.3 | Search strategy

An electronic search from January 1, 2010, to April 1, 2022, in three databases – National Library of Medicine (MEDLINE [PubMed]) (applying Textwords), the Cochrane Central Register of Controlled Trials (CENTRAL) (applying only trials, there were no reviews), and EMBASE (Elsevier) – was performed without applying any additional time or language restrictions and with the assistance of a medical information specialist at the Medicine University Library of the University of Bern. The search strategy is shown in Table 1. In addition, a literature hand searches from January 1, 2010, to April 1, 2022, was performed. References of the included studies and previous systematic reviews on loading protocols for single implants (Zhou et al., 2021) were screened. Reviewer agreement during the study selection process was estimated using Cohen's kappa statistics (*k*-score).

2.4 | Study selection process and data collection

References were imported to a reference manager software program (EndNote, Thomson Reuters), and duplicates were removed via the Leads method. Following this, a Research Information Systems (RIS) file with the obtained references was imported to Covidence (Veritas Health Innovation, Melbourne, Australia; available at www.covidence.org) and two independently calibrated reviewers (J.G.W. and P.M-M.) performed title, abstract, and full-text screening. Disagreement regarding inclusion was resolved by reviewer discussion. If a comparison arm or multiple cohorts were identified in the same study, data from Type 1A implant placement and loading protocol from each group were recorded separately. If an article reported longitudinal data from the same cohort, information from the longest follow-up was included.

2.5 | Data items

Data extracted and collected from each included article were recorded in an Excel spreadsheet (Version 15.17, Microsoft) by four calibrated reviewers (J.W., P.M-M., B.O. and M.A.), and any potential disagreement was resolved by consensus. The following items were recorded and analyzed: author, year of publication, number of participants, sex, age, follow-up, number of dropouts, number of implants, implant design/surface, surgical procedure (bone and soft tissue augmentation procedure), restorative procedure (provisional restoration, definitive restoration material), biological complications, technical complications, and esthetic index information.

2.6 | Summary measures, synthesis of results, data, and statistical analysis

In the present systematic review, the primary outcome was to evaluate the clinical performance by means of implant and restoration failure and survival rates as well as the rates of surgical, technical, and biological complications.

Regarding clinical performance subgroup analyses were made according to the following:

- Implant design: tapered versus parallel and active versus passive threads, surface, implant material.
- Surgical procedures: GBR versus soft tissue grafting versus extraction socket grafting versus no augmentation procedures; flapless versus flap implant surgery.
- Restorative procedures: Screw retained versus cement retained type of provisional, type of definitive crown.

The secondary outcome was to assess the esthetic outcomes of immediate implant placement and immediate loading of single implants regarding the esthetic indices (Papilla height, papilla index), midfacial/buccal recession in soft tissue level, pink esthetic score (PES) (Belser et al., 2009), pink esthetic score (Fürhauser et al., 2005), white esthetic score (WES) following a recent review of esthetic assessments in implant dentistry (Cosyn et al., 2017). For comparability of PES Belser and PES Fürhauser, mean and standard deviation of the two scores were transformed into percentages of the maximum of the score (PES Belser: maximum 10, PES Fürhauser maximum 14).

TABLE 1 Systematic search strategy for the focus question.

Focused question	In adult patients with indication for single tooth extraction in the maxillary esthetic zone (15–25), what is the influence of an immediate implant placement and immediate loading protocol on the clinical performance and esthetic outcomes	
PIO	Population	Adult patients with indication for single tooth extraction and immediate single implant and immediate loaded implant-supported crown protocol in the esthetic anterior maxilla 15–25 (FDI).
	Intervention	Immediate implant placement and immediate loading of single implants using modern dental implants after 2010 with different surgical and restorative procedures.
	Outcome	Clinical performance and esthetic outcomes: Implant and prosthetic survival rates, papilla heights, crestal bone loss, Esthetic indices (Papilla height, papilla index), midfacial/buccal recession in soft tissue level, pink esthetic score (PES) (Belser et al., 2009), pink esthetic score (Fürhauser et al., 2005), white esthetic score (WES), implant and prosthetic survival rates, papilla heights, crestal bone loss.
Search Strategy	Pubmed	((“dental implantation, endosseous”[MeSH Terms] OR “dental implants”[MeSH Terms] OR “implantation*”[Text Word] OR “implant”[Text Word] OR “implants”[Text Word]) AND (“dental prosthesis, implant supported”[MeSH Terms] OR “crown*”[Text Word] OR “single crown”[Text Word] OR “single unit*”[Text Word]) AND (“immediate implant*”[Text Word] OR “immediate implant placement”[Text Word] OR “immediate placement*”[Text Word] OR “immediate”[Text Word] OR “fresh extraction socket*”[Text Word] OR “immediate extraction socket*”[Text Word]) AND (“immediate dental implant loading”[MeSH Terms] OR “immediate”[Text Word]) AND (“esthetics”[MeSH Terms] OR “esthetic*”[Text Word] OR “aesthetic*”[Text Word] OR “esthetic indices”[Text Word] OR “esthetic index”[Text Word] OR “esthetic assessment*”[Text Word] OR “esthetic outcome*”[Text Word] OR “white esthetic score*”[Text Word] OR “wes”[Text Word] OR “pink esthetic score*”[Text Word] OR “pes”[Text Word] OR “complex esthetic index”[Text Word] OR “copenhagen index score”[Text Word] OR “recession*”[Text Word] OR “mucosal recession*”[Text Word] OR “midfacial recession*”[Text Word] OR “mucosal change*”[Text Word] OR “soft tissue*”[Text Word])) AND (english[Filter])
	Embase	(implant* OR “implant”/exp OR “endosseous implant”/exp OR “tooth implant”/exp OR “tooth implantation”/exp) AND (“implant-supported denture”/exp OR “tooth crown”/exp OR crown* OR “single crown*” OR “single unit*”) AND (“immediate implant*” OR “immediate implant placement*” OR “immediate placement*” OR “immediate” OR “fresh extraction socket*” OR “immediate extraction socket*” OR immediate) AND (“esthetics”/exp OR esthetic* OR aesthetic* OR “esthetic indices” OR “aesthetic indices” OR “esthetic index” OR “aesthetic index” OR “esthetic assessment*” OR “aesthetic assessment*” OR “esthetic outcome*” OR “aesthetic outcome*” OR “white esthetic score*” OR wes OR “pink esthetic score*” OR pes OR “implant crown esthetic index” OR “implant crown esthetic indices” OR “complex esthetic index” OR “copenhagen index score*” OR recession* OR “mucosal recession*” OR “midfacial recession*” OR “mucosal change*” OR “soft tissue*”) AND [english]/lim
	Cochrane	[Dental Implantation, Endosseous] OR [Dental Implants] OR (implantation* OR implant OR implant*) AND [Dental Prosthesis, Implant-Supported] OR (crown* OR “single crown*” OR “single unit*”) AND (“immediate implant*” OR “immediate implant placement” OR “immediate placement*” OR “immediate” OR “fresh extraction socket*” OR “immediate extraction socket*”) AND [Immediate Dental Implant Loading] AND [Esthetics] OR (Esthetic* OR aesthetic* OR “esthetic indices” OR “esthetic index” OR “esthetic assessment*” OR “esthetic outcome*” OR “white esthetic score*” OR wes OR “pink esthetic score*” OR pes OR “implant crown esthetic index” OR “implant crown esthetic indices” OR “complex esthetic index” OR “copenhagen index score” OR recession* OR “mucosal recession*” OR “midfacial recession*” OR “mucosal change*” OR “soft tissue*”)
Database Search	MEDLINE (PubMed), Embase, and Cochrane.	

Implant placement and implant loading were assessed following definitions from the 6th Consensus Conference of the International Team for Implantology (Gallucci et al., 2018): Type 1 implant placement; immediate implant placement: dental implants are placed in the fresh socket on the same day of tooth extraction (Chen et al., 2004; Chen & Buser, 2009; Hämmerle et al., 2004). Type A implant loading; immediate loading: dental implants are connected to the prosthesis within 1 week of implant placement. Type 1A: immediate placement with immediate restoration/loading (Gallucci et al., 2018).

Surgical and implant complications were assessed individually between studies according to each study's own assessment, definition, and description. Biological complications were evaluated based on the specific assessment of each study following the Lang criteria (Lang et al., 2000). Technical complications were assessed following the definitions reported at the 4th Consensus Conference of the International Team of Implantology (Salvi & Bragger, 2009).

Failure and survival rates of implants and restorations, as well as surgical, technical, and biological complications rates, were estimated assuming Poisson distributed failures. The Poisson

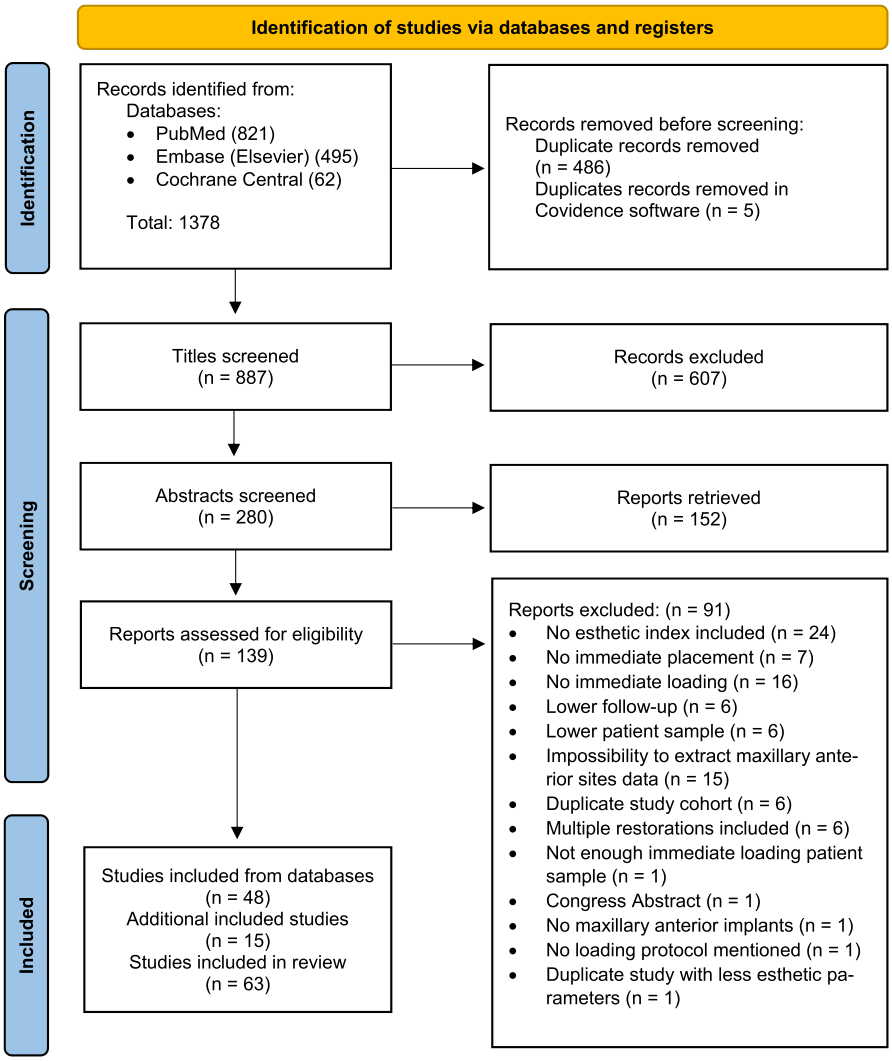


FIGURE 1 Flowchart.

distribution describes the probability of a given number of events during a fixed period of time assuming that events occur independently and that the mean event rate is constant. Overall failure, survival, and complication rates were estimated using a random-effects Poisson regression. For the estimation of failure, survival, technical, and biological complication rates, the cumulated follow-up time of implants or restorations was taken as the exposure variable. To estimate the surgical complication rates of implants and restorations, the total number implants or restorations were taken as the exposure variable. A random-effects Poisson regression was used to analyze whether restoration survival rates were dependent on the retention type (screw/cement). The same method was applied to estimate the effect of the surgical complication rate of implants on the rate of technical and biological complications of restorations.

The secondary outcome was to assess the esthetic outcomes by using weighted means of papilla height, papilla index, midfacial/buccal recession at the soft tissue level, and PES (%) and WES were estimated with a random effects model using a restricted maximum likelihood estimator for inter-study variance (REML). Since esthetic scores of studies were reported for baseline and mixed follow-up times, meta-analysis regression adjusted for time was used to compare the overall mean esthetic score of subgroups (flap vs. no flap, type of implant (parallel-walled/tapered walled), implementation of a soft tissue procedure, and the implant connection were extracted). Based on baseline and follow-up data after 12 months, Hedges' *g* effect sizes (ES) were calculated for those esthetic outcomes with sufficient data for a baseline versus follow-up comparison (Goulet-Pelletier & Cousineau, 2018). Hedges' *g* is calculated by multiplying Cohen's *d* by a so-called correction factor, which is based on the number of observations and the Gamma function. Since cross-measurement correlations between baseline and follow-up data of the studies were not known, Hedges' *g* was calculated assuming independent data. A random effects model (REML) was used to estimate overall ES and 95% confidence intervals. All *p*-values are two-sided with a significance threshold of .05. Stata/IC 16.1 for Unix was used for statistical analysis.

2.7 | Risk of bias

To assess the methodological quality of the selected studies, the ROB 2 risk of bias tool for randomized controlled trials (RCTs) and

the Newcastle-Ottawa-Scale (NOS) (Wells et al., 2013) for observational and case–control studies were used, and the evaluation was performed by three independent and calibrated reviewers (P.M-M., B.O. and M.A.). The ROB 2 risk of bias tool is a domain-based tool in which critical assessments are evaluated independently for each domain. This tool is based on five domains that can be qualified as "Low" or "High" risk of bias or can express "some concerns". The NOS is a quality assessment tool for nonrandomized trials, in which included studies can receive a maximum of 9 stars. A classification of 7–9 points corresponds to a low risk of bias, 5–6 points to a medium risk of bias, and fewer than 5 points to a high risk of bias.

3 | RESULTS

3.1 | Search results

The initial electronic search of the three databases resulted in a total of 1378 references, from which 486 duplicate records were removed via EndNote and 5 using the Covidence software. A total of 887 potential references were selected, of which the authors screened 280 abstracts; from these, 139 references were included for full-text evaluation. Following this, a total of 48 articles were included and 91 were excluded based on the selection criteria. In addition, the hand search identified 15 additional studies, yielding a final total of 63 articles included in the present systematic review (Figure 1 and Table S1).

Regarding inter-reviewer agreement, Cohen's kappa statistic ± standard deviation (SD) range was: 0.567 ± 0.030 (95% confidence interval [CI]: 0.626–0.508) (moderate agreement) for title selection, 0.978 ± 0.059 (95% confidence interval CI: 1.095–0.861) for abstract selection (excellent agreement), and 0.799 ± 0.798 (95% CI: 0.961–0.635) (excellent agreement) for full-text assessment.

3.2 | Description of included studies

Among the included references, 63 studies (10 randomized controlled trials, 28 prospective cohort, and 25 retrospective cohort studies) were included with follow-up periods that ranged from 12 to 96 months (Table 2a–f).

Although including a greater number of implants can provide stronger evidence due the representativity of the sample, overall, the included studies showed a substantial between-study heterogeneity, for most of the analysis the fraction of variance that is due to heterogeneity (I^2) is over 50%. Therefore, a supplement analysis was performed only focusing on the RCT studies.

3.3 | Risk of bias within studies

The risk of bias for the included randomized clinical trial showed eight trials with low risk and one with some concerns. Considering the quality assessment of the included cohort studies reported nine stars in three studies, eight stars in six, seven stars in five, six stars in 10, five stars in 20, four stars in eight, and finally three stars in two studies (Table 3a,b).

3.4 | Implants and restoration survival meta-analysis

Focusing on implant survival, data extracted from 61 studies (encompassing 1961 implants) were obtained. A detailed overview of the individual studies is given in Table 4. A total of 35 failures occurred, with survival rates of 99.2 (98.6–99.5) % at 1 year, 97.5 (95.9–98.4) % after 3 years, and 95.8 (93.3–97.4) % after 5 years (Table 4 and Table S2). Restoration survival data were obtained from 35 studies, covering 1064 immediately loaded restorations. Failure rates per study are presented in Table 5. The overall restoration survival rates were 98.9 (97.8–99.5) % after 1 year, 96.8 (93.6–98.4) % after 2 years, and 94.8 (89.6–97.4) % after 5 years (Table 5). Restoration survival rates on study type are displayed in Tables S3 and S4. Data assessing the influence of the individual retention type – screw versus cement retention – with respect to restoration survival were analyzed; both retention types presented similar survival rates calculated up to 5 years; ranged from 99.0% to 95.0% for screw-retained restorations and from 98.7% to 93.4% for cement-retained (Table 6).

3.5 | Surgical complications of implants, biological and technical complications of restorations

Of 63 included articles, 38 reported any complication, and therefore the analysis and sub-analysis were based on these studies follow-up and related information. An overview of reported surgical complications in the included studies is given in Table 7. The estimated surgical complication rate calculated per 100 implants (95% CI [confidence interval]) of the 1281 immediately placed implants reported across 38 studies was 5.86 (3.40–10.11) %. Focusing on the included studies, an overview of technical and biological complications is presented in Tables 8 and 9. According to random-effects Poisson regression analysis, individual complication rates per 100 restorations were estimated (95% CI) to be 3.27 (1.51–7.07) technical and 2.18 (0.91–5.23) biological complications per restoration year. To evaluate the influence of surgical complications on the rate of technical and biological complications, an incidence rate analysis was performed. The outcome was that neither complication rate (technical or biological) was significantly influenced by surgical complications (Tables S4–S6).

3.6 | Esthetic outcome meta-analysis

Esthetic outcomes were documented using the retrieved data including the following indices: papilla height (mm), papilla index,

TABLE 2A General characteristics of the included studies.

Author (year)	Country	Type of study	Clinical settting	Total number of patients	Patients included for assessment	Gender	Patients age (SD)	Follow-up (SD) in months
Arora et al. (2017)	Australia	Prospective study	Private practice	20	20	13 females, 3 males	44.7 (12.7)	37 (14)
Arora and Ivanovski (2018)	Australia	Retrospective study	University	30	30	21 females, 9 males	NM	47 (15)
Barone et al. (2016)	Italy	Prospective study	NM	32	30	21 females, 16 males	40.1 (13.3)	84
Bonnet et al. (2018)	France	Retrospective study	Private practice	39	39	27 females, 16 males	37.6	12
Bruno et al. (2014)	Intaly	Prospective study	Private practice	28	12	11 females, 12 males	59.9 (12.2)	12
Cabello et al. (2013)	Spain	Prospective study	Private practice	14	14	7 females, 7 males	52	12
Cardaropoli et al. (2015)	Italy	Prospective study	Private practice	26	26	14 females, 12 males	42.35 (9.41)	12
Cardaropoli et al. (2019)	Italy	Prospective study	Private practice	20	20	13 females, 7 males	58.5 (11.03)	12
Chan et al. (2019)	USA	RCT	University	20	18	8 females, 10 males	60.4 (12)	12
Cooper et al. (2014)	USA	Prospective study	University	55	45	33 females, 22 males	45 (14)	60
Cosyn et al. (2011)	Belgium	RCT	University	32	25	16 females, 14 males	54	36
Cosyn et al. (2013)	Belgium	Retrospective study	University	28	28	15 females, 13 males	51 (15)	33 (8)
Cosyn et al. (2016)	Belgium	Prospective study	Private practice	22	17	10 females, 12 males	50	60
Cristalli et al. (2015)	Italy	Prospective study	Private practice	60	60	15 females, 9 males	47.27 (8.25)	48
Crespi et al. (2018)	Italy	RCT	MN	28	24	15 females, 15 males	55.6	12
D'Avenia et al. (2019)	Italy	Retrospective study	University	20	20	7 females, 13 males	50.42 (11.35)	16
Degidi et al. (2014)	Italy	RCT	Private practice	91	53	NM	40.1 (12.5) 37.7 (14.3)	24
Esposito et al. (2015)	Italy	RCT	Private practice	106	54	32 females, 22 males	48	12
Felice et al. (2015)	Italy	RCT	Private practice	50	25	13 females, 12 males	51.32	12
Fürhauser et al. (2016)	Austria	Prospective study	Academy	77	77	46 females, 31 males	48.8 (16.1)	60
Ganeles et al. (2017)	USA	Prospective study	Private practice	15	11	6 females, 9 males	68.33 (14.4)	24
Guarnieri et al. (2016)	Italy	Retrospective study	Private practice	25	25	5 females, 7 males	42	36
Groenendijk et al. (2020)	The Netherland	Prospective study	Private practice	100	98	57 females, 41 males	45.8	12
Hartlev et al. (2014)	Denmark	Prospective study	University	68	54	21 females, 33 males	43	33
Hassani et al. (2021)	Iran	Retrospective study	University	20	20	13 females, 7 males	38.1	12
Kan et al. (2011)	USA	Prospective study	University	35	35	NM	36.8	48
Khzam et al. (2014)	Australia	Retrospective study	University	13	13	9 females, 4 males	44.7 (18.7)	23.2 (7.6)
Kniha et al. (2017)	Germany	Prospective study	Hopsital	16	16	NM	55	12
Kolerman et al. (2016)	Israel	Retrospective study	University	34	34	20 females, 14 males	52.68 (14.35)	12–48
Kolerman et al. (2017)	Israel	Retrospective study	University	39	39	23 females, 16 males	47.51 (18.09)	44.82 (28)
Lombardo et al. (2016)	Italy	Retrospective study	University	16	16	11 females, 5 males	44	23.3 (14.8)
Ma et al. (2019)	New Zeeland	Prospective study	University	27	16	12 females, 4 males	NM	60
Malchiodi et al. (2013)	Italy	Prospective study	University	58	58	26 females, 32 males	39.9	36
Mangano et al. (2012)	Italy	Prospective study	NM	26	26	8 females, 18 males	48.7	24

TABLE 2A (Continued)

Author (year)	Country	Type of study	Clinical settting	Total number of patients	Patients included for assessment	Gender	Patients age (SD)	Follow-up (SD) in months
Mangano et al. (2013)	Italy	Retrospective study	NM	40	40	8 females, 10 males	44.9	31.09 (5.27)
Mangano et al. (2017)	Italy and Brazil	Retrospective study	Private practice	103	103	27 females, 15 males	46.5 (15.1)	36
Migliorati et al. (2015)	Italy	Prospective study	University	50	48	25 females, 23 males	47.5	24
Noelken et al. (2011)	Germany	Retrospective study	University	16	16	11 females, 5 males	43	22
Noelken et al. (2018) (2)	Germany	Retrospective study	University	26	26	12 females, 14 males	48.4	45 (23)
Östman et al. (2020)	USA	Prospective study	Private practice	19	19	11 females, 8 males	NM	19
Paul and Held (2012)	Switzerland	Retrospective study	NM	28	26	16 females, 10 males	44.8	40.8
Pieri et al. (2011)	Italy	RCT	University	40	38	23 females, 15 males	45.8 46.6	12
Puisys et al. (2022)	Lithuania	RCT	University	52	52	15 females, 10 males	45.8 (13.63)	12
Raes et al. (2018)	Belgium	Prospective study	Private practice	39	29	6 females, 10 males	45	96
da Rosa et al. (2014)	Brazil	Prospective study	Private practice	24	18	8 females, 10 males	52.4	58.56 (8.19)
Ross et al. (2014)	USA	Retrospective study	Private practice	47	47	28 females, 19 males	47.4	60
Saedi Germi et al. (2020)	Iran	Retrospective study	Private practice	18	18	10 females, 8 males	NM	12
Sicilia-Felechosa et al. (2020)	Spain	Retrospective study	University	40	40	23 females, 17 males	58.7	41.28
Slagter et al. (2021)	The Netherlands	Retrospective study	University	40	40	15 females, 5 males	39 (16.9)	60
Spinato et al. (2012)	Italy	Retrospective study	NM	41	41	30 females, 11 males	42.5	32
Stoupel et al. (2016)	USA	RCT	University	39	39	25 females, 14 males	54 46	12
Sun et al. (2020)	China	Prospective study	Hospital	30	30	23 females, 37males	NM	24
Takeshita et al. (2015)	Japan	Retrospective study	Private practice	18	18	NM	48	18
Tian et al. (2019)	China	Prospective study	Hospital	30	27	14 females, 16 males	34.6 (12)	12
Tortamano et al. (2010)	Brazil	Prospective study	University	12	12	3 females, 10 males	NM	18
Tsuda et al. (2011)	USA	Retrospective study	University	10	10	6 females, 4 males	48	12
Valentini et al. (2010)	France	Retrospective study	NM	90	40	NM	NM	12
van Nimwegen et al. (2016)	The Netherlands	Retrospective study	Private practice	64	51	23 females, 26 males	50	48
van Nimwegen et al. (2018)	The Netherlands	RCT	University	60	50	17 females, 13 males	45.5 (15.5)	12
Vidigal et al. (2017)	Brazil	Retrospective study	NM	53	53	31 females, 22 males	46	51
Yang et al. (2019)	China	Prospective study	University	40	40	18 females, 22 males	38.31 (11.23)	12
Yoshino et al. (2014)	USA	Prospective study	University	20	20	13 females, 6 males	52.6	12
Zuiderveld et al. (2018)	The Netherlands	Prospective study	University	60	58	32 females, 28 males	45.5 (15.5) 47.8 (15.3)	12

Abbreviations: NM, not mentioned; RCT, randomized clinical trial; SD, standard deviation.

TABLE 2B Implant characteristics of the included studies.

Author (year)	Total number of implants	Implants included for assessment	Implant failed	Implant material	Implant manufacturer	Implant type	Implant surface	Implant connection type
Arora and Ivanovski (2018)	20	20	0	1	Osseospeed Dentsply (AstraTech)	1	4	6
Arora et al. (2017)	30	30	0	1	Osseospeed Dentsply (AstraTech)	1	4	6
Barone et al. (2016)	37	35	2	1	Premium/Khono, Sweden & Martina	1	8	2
Bonnet et al. (2018)	39	39	0	1	Nobel Replace/Nobel Actuve	1/2	3	7/3
Bruno et al. (2014)	36	17	0	1	NobelActive, NobelReplace Select, NobelPerfect	1/2	3	7/3
Cabello et al. (2013)	14	14	0	1	Straumann	1	1	9/10
Cardaropoli et al. (2015)	26	26	0	1	T3 Biomet 3i	3	5	2
Cardaropoli et al. (2019)	20	20	0	1	Straumann BLT	1	2	9
Chan et al. (2019)	20	18	2	1	IS II active, Neobiotech	2	1	2
Cooper et al. (2014)	55	52	3	1	OsseoSpeed. Dentsply Implants.	1	4	6
Cosyn et al. (2011)	32	25	1	1	Nobel Replace tapared	2	3	2
Cosyn et al. (2013)	28	26	3	1	Nobel Replace tapared	2	3	7
Cosyn et al. (2016)	22	17	NM	1	Nobel Replace tapared	2	3	7
Crespi et al. (2018)	30	30	0	1	Outlink, Sweden & Martin	2	7	1
Cristalli et al. (2015)	23	23	2	1	Nobel Active	2	3	3
D'Avenia et al. (2019)	20	20	NM	1	Nobel Active	2	3	3
Degidi et al. (2014)	53	53	0	1	ANKYLOS, DENTSPLY	2	1	4
Esposito et al. (2015)	54	54	2	1	V3 Mis Implants	2	11	3
Felice et al. (2015)	50	50	2	1	MegaGen implant	1	10	3
Fürhauser et al. (2016)	77	77	0	1	XiVE S Plus	2	9	3
Ganeles et al. (2017)	15	11	0	1	75 Nobel Replace; 2 Astra Osseospeed	1/2	3/4	6
Guarnieri et al. (2016)	12	12	0	1	Laser-lok, Biohorizon	2	13	2
Groenendijk et al. (2020)	98	98	0	1	Nobel Active	2	3	3
Hartlev et al. (2014)	68	54	1	1	Nobel replace select	2	3	7
Hassani et al. (2021)	20	20	0	1	Superline. Dentium	1	1	2
Kan et al. (2011)	35	35	0	1	Nobel replace	2	3	7
Khzam et al. (2014)	15	15	0	1	Nobel Active	2	3	3
Kniha et al. (2017)	16	16	0	2	Straumann PURE Ceramic Implant	1	12	8
Kolerman et al. (2016)	34	34	0	1	Seven MIS Implants	2	1	2
Kolerman et al. (2017)	39	39	1	1	Lans or Seven, MIS Implants	2	11	2
Lombardo et al. (2016)	21	21	1	1	Bicon dental implant	1	14	5
Ma et al. (2019)	28	17	2	1	Co-Axis 12d, Southern Implants	1	6	1
Malchiodi et al. (2013)	64	64	0	1	NM	2		NM
Mangano et al. (2012)	21	21	1	1	Bicon dental implant	1	14	5

TABLE 2B (Continued)

Author (year)	Total number of implants	Implants included for assessment	Implant failed	Implant material	Implant manufacturer	Implant type	Implant surface	Implant connection type
Mangano et al. (2013)	26	26	0	1	Leone implant system	1	15	4
Mangano et al. (2017)	40	22	0	1	Leone implant system	1	15	4
Migliorati et al. (2015)	48	47	0	1	Straumann.BLTI.	2	2	9
Noelken et al. (2011)	18	18	0	1	Nobel Biocare. Nobel Perfect (3) Nobel perfect groovy (15)	2	2	3
Noelken et al. (2018) (2)	26	26	0	1	AstraTech	1	4	6
Östman et al. (2020)	19	19	0	1	Southerm Implants of North America	3	6	1
Paul and Held (2012)	33	31	0	1	Nobel Biocare. Nobel Perfect.	2	3	6
Pieri et al. (2011)	38	37	1	1	Samo Smiler Implants, Biospark	2	5	2
Puisys et al. (2022)	50	50	0	1	Straumann. BLT.	2	2	9
Raes et al. (2018)	11	11	0	1	AstraTech Osseospeed	1	4	6
da Rosa et al. (2014)	18	18	0	1	Nobel Replace tapred	2	3	7
Ross et al. (2014)	47	47	0	1	Nobel Biocare	NM	3	NM
Saedi Germi et al. (2020)	18	18	0	1	NM	NM	NM	NM
Sicilia-Felechosa et al. (2020)	40	40	1	1	Zimmer Biomet. Nobel Biocare Speedy	1/2	3	1
Slagter et al. (2021)	18	18	0	1	Nobel Biocare Nobel Active	2	3	3
Spinato et al. (2012)	45	45	0	1	Screw-Vent, Zimmer	2	1	2
Stoupel et al. (2016)	39	39	0	1	3i Biomet	2	16	2
Sun et al. (2020)	30	30	0	1	Nobel Replace	2	3	6
Takeshita et al. (2015)	21	21	0	1	OsseoSpeed. Dentsply implants	1	4	6
Tian et al. (2019)	30	27	0	1	Nobel Active, Nobel Biocare (18). Camlog Screw Line (12)	2	3	3
Tortamano et al. (2010)	12	12	0	1	Straumann, Tapered effect	2	1	2
Tsuda et al. (2011)	10	10	0	1	OsseoSpeed. Astra Tech	1	4	6
Valentini et al. (2010)	94	43	2	1	Astra Tech ST implants	2	4	2
van Nimwegen et al. (2016)	51	51	2	1	3i Osseotite	1	16	2
van Nimwegen et al. (2018)	60	58	1	1	Nobel Biocare. Nobel Active.	2	3	3
Vidigal et al. (2017)	53	53	2	1	NM	NM	NM	NM
Yang et al. (2019)	50	50	0	1	Straumann. Nobel Active. Osstem. Apollo. Dentium	2	2/3	2/3
Yoshino et al. (2014)	20	20	0	1	Straumann. Bone Level.	1	2	9
Zuiderveld et al. (2018)	60	58	2	1	Nobel Active. Nobel Biocare.	2	3	3

Note: Implant material: 1-Titanium; 2-Zirconia. Implant type: 1. Parallel-walled; 2. Tapered-walled; 3. Hybrid conical. Implant surface: 1-SLA; 2-SLActive; 3-TiUnite; 4-TiOblast; 5-Dual acid-etched, calcium phosphate; 6-Alumina particles; 7-Titanium-plasma sprayed; 8-Zirconia-Titanium; 9-Friadent plus; 10-Ca2 ions SLA; 11-phosphonated molecules of B+; 12-ZLA; 13-Laser lock; 14-Integra-Ti; 15-HRS Surface; 16-Dual acid-etched fine-micron topography. Implant connection type: 1-External hex; 2-Internal hex; 3- Connical hex; 4-Morse Taper; 5-Loking-Taper; 6-Connical connection; 7-Tri-channel; 8-internatl connection pure; 9-Internal Octogon-Crossfit; 10-Internal Octogon-Synocta.

Abbreviation: NM, Not mentioned.

TABLE 2C Surgical characteristics of the included studies.

Author (year)	Total number of implants	Implants included for assessment	Bone augmentation procedure	Bone augmentation material	Soft tissue augmentation procedure	Soft tissue augmentation material	Flap or flapless implant surgery
Arora and Ivanovski (2018)	20	20	2	Xenograft Bovine, Bio-OSS	NM	NM	1
Arora et al. (2017)	30	30	1	xenograft (Bio-Oss)	No	NM	1
Barone et al. (2016)	37	35	1	Zenograft Porcine, MP3, Osteobiol-Tecnoss	NM	NM	1
Bonnet et al. (2018)	39	39	1	Xenograft Bovine, Bio-OSS	Free CGT	NM	1
Bruno et al. (2014)	36	17	1	Xenograft Bovine, Bio-OSS	NM	NM	1
Cabello et al. (2013)	14	14	0	NM	NM	NM	1
Cardaropoli et al. (2015)	26	26	1	Xenograft Bovine, Bio-OSS	NM	NM	1
Cardaropoli et al. (2019)	20	20	1	; Botiss Biomaterials	NM	NM	1
Chan et al. (2019)	20	18	1	Human allograft, Puros	NM	NM	1
Cooper et al. (2014)	55	52	0	0	NM	NM	1
Cosyn et al. (2011)	32	25	1	Human allograft, Puros	NM	NM	2
Cosyn et al. (2013)	28	26	1	Xenograft Bovine, Bio-OSS	NM	NM	2
Cosyn et al. (2016)	22	17	1	Xenograft Bovine, Bio-OSS	NM	NM	2
Crespi et al. (2018)	30	30	0	0	NM	NM	1
Cristalli et al. (2015)	23	23	1	Xenograft Bovine, Bio-OSS	CGT	CGT	2
D'Avenia et al. (2019)	20	20	1/2	Xenograft Bovine, Bio-OSS	NM	NM	1
Degidi et al. (2014)	53	53	NM	NM	NM	NM	1
Esposito et al. (2015)	54	54	1	Xenograft Bovine, Bio-OSS	NM	NM	2
Felice et al. (2015)	50	50	1	Xenograft Bovine, Bio-OSS	NM	NM	2
Fürhauser et al. (2016)	77	77	1	Algae derived bone, Algipore Frios	NM	NM	1
Ganeles et al. (2017)	15	11	NM	NM	NM	NM	1/2
Guarnieri et al. (2016)	12	12	NM	NM	NM	NM	1
Groenendijk et al. (2020)	98	98	1	Autogenous bone graft	4 of 98	CGT	1
Hartlev et al. (2014)	68	54	NM	NM	NM	NM	NM
Hassani et al. (2021)	20	20	1	Biphasic calcium phosphate (Osteon II, Genoss)	NM	NM	1
Kan et al. (2011)	35	35	0	0	0	0	1
Khzam et al. (2014)	15	15	1	Xenograft Bovine, Bio-Oss, Geistlich	NM	NM	1
Kniha et al. (2017)	16	16	1	NM	NM	NM	1
Kolerman et al. (2016)	34	34	1	Xenograft Bovine, Bio-OSS Collagen	NM	NM	2
Kolerman et al. (2017)	39	39	1	Allograft (FDBA)	NM	NM	1

TABLE 2C (Continued)

Author (year)	Total number of implants	Implants included for assessment	Bone augmentation procedure	Bone augmentation material	Soft tissue augmentation procedure	Soft tissue augmentation material	Flap or flapless implant surgery
Lombardo et al. (2016)	21	21	1	Autogenous bone and beta-tricalcium phosphate	NM	NM	1
Ma et al. (2019)	28	17	NM	NM	NM	NM	1
Malchiodi et al. (2013)	64	64	1	Autogenous	NM	NM	1
Mangano et al. (2012)	21	21	1	Biphasic calcium phosphate granules (MBCPR; Biomatlante, Vigneux de Bretagne, France)	NM	NM	2
Mangano et al. (2013)	26	26	NM	NM	NM	NM	2
Mangano et al. (2017)	40	22	2	Calcium phosphate granules (Biocer)	9 of 42	CTG	2
Migliorati et al. (2015)	48	47	1	Xenograft Bovine, Bio-Oss, Geistlich	24 (yes) 24 (no)	CTG Palate	1
Noelken et al. (2011)	18	18	1	Autogenous	NM	NM	1
Noelken et al. (2018) (2)	26	26	1	Autogenous	13 (yes) 13 (no)	CTG palate	1
Östman et al. (2020)	19	19	1	Xenograft, mp3, Osteobiol, Tecnoss. Allograft, Zimmer Biomet	NM	NM	1
Paul and Held (2012)	33	31	1	Xenograft Bovine, Bio-Oss, Geistlich	Yes	CTG	1
Pieri et al. (2011)	38	37	1	Autogenous + xenograft, Bio-Oss	NM	NM	1
Puisys et al. (2022)	50	50	1	(A) allogenic; (B) allogenic + autogenous + collagen membrane	Yes	CTG tuberosity	1
Raes et al. (2018)	11	11	NM	NM	NM	NM	1
da Rosa et al. (2014)	18	18	1	Autogenous bone graft	NM	NM	1
Ross et al. (2014)	47	47	1	Cortical Allograft. Puros, Zimmer.	NM	NM	1
Saedi Germi et al. (2020)	18	18	1	Allograft	NM	NM	1
Sicilia-Felechosa et al. (2020)	40	40	1	Autogenous + xenograft, DBBM, Bio-Oss	Yes	Allogenic dermis	1
Slagter et al. (2021)	18	18	1	Autogenous + xenograft (Bio-Oss)	NM	NM	1
Spinato et al. (2012)	45	45	23 (0) 22 (1)	Autogenous, Xenograft bovine, Alograft, Combination	No	No	NM
Stoupel et al. (2016)	39	39	0	0	0	0	
Sun et al. (2020)	30	30	1	Xenograft Bovine, Bio-Oss, Geistlich	No	No	1
Takeshita et al. (2015)	21	21	1	Beta tricalcium phospate	No	No	1
Tian et al. (2019)	30	27	1	Xenograft (Bio-Oss)	No	No	1

(Continues)

TABLE 2C (Continued)

Author (year)	Total number of implants	Implants included for assessment	Bone augmentation procedure	Bone augmentation material	Soft tissue augmentation procedure	Soft tissue augmentation material	Flap or flapless implant surgery
Tortamano et al. (2010)	12	12	No	No	No	No	1
Tsuda et al. (2011)	10	10	1	Xenograft (Bio-Oss)	CTG	CTG	1
Valentini et al. (2010)	94	43	2	Xenograft (Bio-Oss)	NM	NM	2
van Nimwegen et al. (2016)	51	51	1	Autogenous + xenograft (endobon)	NM	NM	1
van Nimwegen et al. (2018)	60	58	1	Autogenous + xenograft bovine, Bio-Oss, Geistlich	30 (yes) 30 (no)	CTG tuberosity	1
Vidigal et al. (2017)	53	53	1	Xenograft (Bio-Oss)	16 of 53	CTG	1
Yang et al. (2019)	50	50	1	Xenograft, bovine, Bio-Oss. Artificial: Beta-TCP	No	No	1
Yoshino et al. (2014)	20	20	1	Autogenous + xenograft bovine, Bio-Oss, Geistlich	10 (yes) 10 (no)	CTG tuberosity	1
Zuiderveld et al. (2018)	30	58	1	Autogenous + xenograft, DBBM, Bio-Oss	30 (yes) 30 (no)	CTG tuberosity	1

Note: Bone augmentation procedure: 0-No bone augmentation; 1-Bone to implant gap, 2-GBR. Flap or Flapless implant surgery: 1-Flapless; 2. Flap.

midfacial recession, pink esthetic score (PES), and white esthetic score (WES). The follow-up times for the analysis were defined as 0 (baseline), 1–6, 12, 18–24, 33–44, and 48–96 months.

A summary of the meta-analysis focusing on esthetic outcomes providing the included study and implant counts and the measured heterogeneity of the individual studies is presented in Table 10. Table S7a–f presents the individual data of each index with respect to follow-up time, including the individual weight of each study. Available data were extracted for comparison between timepoints baseline and 12 months. Here, Table 11a summarizes the papilla height outcome, observed to be an overall effect size of −0.71 (−1.25, −0.17) mm after 1 year with respect to all included studies (Table 11a, Figure 2). For midfacial recession, an overall effect size (baseline to 12 months) of −0.15 (−0.66, 0.36) mm was estimated with Hedges' *g* effect size (Table 11b, Figure 3). PES index in the retrieved data reported an overall effect size of 0.82 (0.37–1.28) comparing baseline data to 12-month follow-up (Table 11c, Figure 4).

3.7 | Esthetic outcome – influence of individual groups – meta-analysis

During data extraction, groups were used to document the influence of individual treatment procedure characteristics. These data were compared within the individual index. Study inclusion depended on the individual information available in each study. The following characteristics could be included in the analysis: flap or flapless; type of implant (parallel or tapered walled), soft tissue procedure (yes or no), and implant connection (internal or conical hex). Use (or not) of a flap had no significant influence on the outcome of the papilla height, PES, or WES indices (Table 12). The type of implant used was differentiated into "parallel walled" and "tapered walled". The WES index was significantly influenced by the type of implant ($p = .049$), with the parallel-walled design outperforming the tapered one (Table 12). However, papilla height, midfacial recession, and PES were not influenced by the type of implant. Soft tissue procedures reported in the studies did not influence the outcome of the midfacial recession or the PES score (Table 12). The implant connection did not have an impact on the esthetic outcome or the PES/ WES (Table 12).

3.8 | Supplementary analysis – data extraction only focusing on RCTs

Additional data analysis was performed to describe the outcomes separating the RCTs from the other studies and comparing to prospective and retrospective investigations. Here, the failure rate of implants was higher reported in the RCTs (2.36 per 100 years) compared to less than 1 in observational studies. Similar results were obtained with the survival of restoration the RCTs had higher failure rate (4.07 per 100 years) compared with 0.71 for prospective and 0.51 retrospective studies. Overall, a similar trend was observed with surgical, technical, and biological complications. Here, especially the

TABLE 2D Restorative characteristics of the included studies.

Author (year)	Total number of implants	Implants included for assessment	Implant survival (number)	Type of occlusion in provisional	Provisional restoration retention system	Abutment provisional material	Definitive restoration retention system	Definitive abutment material	Restoration material	Restoration survival
Arora and Ivanovski (2018)	20	20	20	1	1	NM	1	4/5	4	20
Arora et al. (2017)	30	30	30	1	1	3	NM	NM	NM	30
Barone et al. (2016)	37	35	35	1	2	3	2	1	1	35
Bonnet et al. (2018)	39	39	39	1	1	3	2	1	1/5	39
Bruno et al. (2014)	36	17	17	3	1	3	NM	NM	NM	NM
Cabello et al. (2013)	14	14	14	1	1/2	NM	1	1/4	1/5	14
Cardaropoli et al. (2015)	26	26	26	1	1	2	2	NM	NM	26
Cardaropoli et al. (2019)	20	20	20	1	1	2	1	NM	4	20
Chan et al. (2019)	20	18	18	1	1	3	2	5	4	18
Cooper et al. (2014)	55	52	52	1	2	3	2	5	4	NM
Cosyn et al. (2011)	32	25	30	1	1	3	2	5	1	25
Cosyn et al. (2013)	28	26	28	1	1	3	2	5	NM	28
Cosyn et al. (2016)	22	17	17	1	1	2	1	NM	1/4	17
Crespi et al. (2018)	30	30	30	2	2	4	2	1	5	30
Cristalli et al. (2015)	23	23	23	2	1	3	2	5	1	23
D'Avenia et al. (2019)	20	20	20	NM	1	NM	NM	NM	5	20
Degidi et al. (2014)	53	53	53	1	2	3	2	5	1	53
Esposito et al. (2015)	54	54	52	1	NM	NM	2	NM	1	50
Felice et al. (2015)	50	50	23	1	2	NM	2	5	1	23
Fürhauser et al. (2016)	77	77	77	1	1	5	2	7	8	77
Ganeles et al. (2017)	15	11	15	1	NM	NM	NM	4/5	NR	15
Guarnieri et al. (2016)	12	12	12	1	2	3	2	5	NM	12
Groenendijk et al. (2020)	98	98	98	1	NM	3	NM	5	NM	98
Hartlev et al. (2014)	68	54	54	1	2	6	2	4/5	4/5	54
Hassani et al. (2021)	20	20	20	1	1	3	1/2	5	4/5	NM
Kan et al. (2011)	35	35	35	1	2	3	2	3	1	35
Khzam et al. (2014)	15	15	15	1	1	NM	NM	4	4	NM
Kniha et al. (2017)	16	16	16	1	2	NM	2	4	4	16
Kolerman et al. (2016)	34	34	34	0	NM	3	2	5	34	34
Kolerman et al. (2017)	39	39	39	1	2	NM	2	4	5	39
Lombardo et al. (2016)	21	21	20	NM	2	4	2	1	4	
Ma et al. (2019)	28	17	17	1	1	3	1	6	4	17
Malchiodi et al. (2013)	64	64	64	1	2	3	2	5	1/5	NM
Mangano et al. (2012)	21	21	26	2	2	3	2	1	1	26

(Continues)

TABLE 2D (Continued)

Author (year)	Total number of implants	Implants included for assessment	Implant survival (number)	Type of occlusion in provisional	Provisional restoration retention system	Abutment provisional material	Definitive restoration retention system	Definitive abutment material	Restoration material	Restoration survival
Mangano et al. (2013)	26	26	22	2	2	3	2	1	1	22
Mangano et al. (2017)	40	22	42	1	2	2	2	NM	1	42
Migliorati et al. (2015)	48	47	47	1	1	NM	NM	NM	NM	NM
Noelken et al. (2011)	18	18	18	1	2	3	2	NM	1.5	NM
Noelken et al. (2018) (2)	26	26	26	1	1/2	3	2	5	5	NM
Östman et al. (2020)	19	19	19	1	1	2/3	1	NM	4	NM
Paul and Held (2012)	33	31	31	1	1	3	2	5	4	NM
Pieri et al. (2011)	38	37	37	1	1	3	2	4/5	1/4	37
Puisys et al. (2022)	50	50	25	1	1	3	1	5	5	NM
Raes et al. (2018)	11	11	11	1	2	3	2	5	4	11
da Rosa et al. (2014)	18	18	18	NM	1	3	2	4	4	18
Ross et al. (2014)	47	47	47	1	2	3	2	4/5	1/4	NM
Saedi Germi et al. (2020)	18	18	18	NM	NM	NM	NM	NM	NM	NM
Sicilia-Felechosa et al. (2020)	40	40	39	1	1	3	NM	NM	NM	NM
Slagter et al. (2021)	18	18	18	NM	1	NM	1/2	4	4	18
Spinato et al. (2012)	45	45		1	1		NM	NM	NM	45
Stoupel et al. (2016)	39	39	38	1	1	3	NM	NM	NM	NM
Sun et al. (2020)	30	30	30	1	2	NM	2	NM	5	NM
Takeshita et al. (2015)	21	21	21	1	2	3	2	1/4/5	1/4	NM
Tian et al. (2019)	30	27	27	1	1	NM	NM	NM	NM	NM
Tortamano et al. (2010)	12	12	12	1	1	3	1	NM	1	12
Tsuda et al. (2011)	10	10	10	1	2	3	2	4	4	NM
Valentini et al. (2010)	94	43	41	1	2	NM	2	NM	NM	41
van Nimwegen et al. (2016)	51	51	49	1	1	2	2	5	4	49
van Nimwegen et al. (2018)	60	58	58	1	1	NM	1/2	4	5	NM
Vidigal et al. (2017)	53	53	51	1	2	3	NM	NM	NM	51
Yang et al. (2019)	50	50	50	1	1	NM	NM	NM	NM	NM
Yoshino et al. (2014)	20	20	20	1	1	3	2	4	4	NM
Zuiderveld et al. (2018)	30	58	58	1	1	3	1/2	4	4	NM

Note: Type of occlusion in provisional: 1-Nonfunctional occlusion; 2-Full contact in centric occlusion; 3-Maximum intercuspation. Provisional restoration retention system: 1-Screw retained; 2-Cement retained. Abutment provisional material: 1-Plastic; 2-PEEK; 3-Titanium; 4-Metal; 5-Titanium-Zirconia; 6-Zirconia. Definitive restoration retention system: 1-Screw retained; 2-Cement retained. Definitive abutment material: 1-Metal; 2-Co-Cr; 3-Gold; 4-Zirconia; 5-Titanium; 6-Gold-Zirconia; 7-Titanium-Zirconia. Restoration material: 1-Metal-Ceramic; 2-Titanium; 3-Gold; 4-Ceramic; 5-Zirconia; 6-Cr-Co; 7-Metal; 8-leucite glass- ceramic; 9-Lithium disilicate; 10-zirconia-veneering porcelain; 11-zirconia-based.

Abbreviation: NM, Not mentioned.

TABLE 2E Complications and marginal/crestal bone loss of the included studies.

Author (year)	Total number of implants	Implant and surgical complications		Biological complications		Technical complications		Marginal/crestal bone loss	
		Type	Number of implants	Type	Number of implants	Type	Number of implants	Mesial	Distal
Arora and Ivanovski (2018)	20	5	2	6	1	0	0	0.05 ± 0.65	0.06 ± 0.52
Arora et al. (2017)	30	NM	NM	7	1	0	0	0.18 ± 1.38	0.34 ± 1.40
Barone et al. (2016)	37	11	2	0	0	NM	NM	1.00 ± 0.00	
Bonnet et al. (2018)	39	NM	NM	8	2	0	0	NM	NM
Bruno et al. (2014)	36	6	3	NM	NM	NM	NM	NM	NM
		7	2						
Cabello et al. (2013)	14	NM	NM	0	0	1	3	NM	NM
						5	1		
						6	1		
Cardaropoli et al. (2015)	26	0	0	NM	NM	NM	NM	NM	NM
Cardaropoli et al. (2019)	20	0	0	0	0	0	0	NM	NM
Chan et al. (2019)	20	14	2	NM	NM	NM	NM	0.7 ± 0.6	
Cooper et al. (2014)	55	11	3	NM	NM	NM	NM	0.43 ± 1.00	
Cosyn et al. (2011)	32	0	0	0	0	5	1	1.13 ± 0.43	0.86 ± 0.54
Cosyn et al. (2013)	28	NM	5	NM	NM	NM	NM	NM	NM
Cosyn et al. (2016)	22	8	2	3	1	4	1	0.19 ± 0.30	
						5	1		
						7	1		
Crespi et al. (2018)	30	0	0	NM	NM	NM	NM	NM	NM
Cristalli et al. (2015)	23	0	0	0	0	0	0	0.383 ± 0.512	0.278 ± 0.595
D'Avenia et al. (2019)	20	NM	NM	NM	NM	NM	NM	0.59 ± 1.04	0.63 ± 1.18
Degidi et al. (2014)	53	0	0	4	3	NM	NM	NM	NM
Esposito et al. (2015)	54	7	19	4	1	7	4	0.23 ± 0.11	
				5	1				
Felice et al. (2015)	50	NM	NM	NM	NM	8	2	0.15 ± 0.10	
Fürhauser et al. (2016)	77	NM	NM	NM	NM	NM	NM	NM	NM
Ganeles et al. (2017)	15	NM	NM	0	0	0	0	−1.40 ± 1.89	
Guarnieri et al. (2016)	12	NM	NM	NM	NM	NM	NM	0.35 ± 0.18	
Groenendijk et al. (2020)	98	10	1	2	1	1	1	NM	NM

(Continues)

TABLE 2E (Continued)

Author (year)	Total number of implants	Implant and surgical complications		Biological complications		Technical complications		Marginal/crestal bone loss	
		Type	Number of implants	Type	Number of implants	Type	Number of implants	Mesial	Distal
Hartlev et al. (2014)	68	NM	NM	NM	NM	NM	NM	NM	NM
Hassani et al. (2021)	20	0	0	0	0	0	0	1.53 ± 0.10	
Kan et al. (2011)	35	NM	NM	0	0	0	0	0.72 ± 0.27	−0.63 ± 0.21
Khzam et al. (2014)	15	NM	NM	NM	NM	NM	NM	1.20 ± 1.01	0.80 ± 1.14
Kniha et al. (2017)	16	0	0	0	0	0	0	NM	NM
Kolerman et al. (2016)	34	NM	2	0	0	0	0	3.82 ± 0.87	
Kolerman et al. (2017)	39	NM	NM	NM	NM	NM	NM	1.90 ± 0.54	1.50 ± 0.51
Lombardo et al. (2016)	21	3	1	0	0	5	3	NM	NM
Ma et al. (2019)	28	5 6 7	3 4 2	NM	NM	0	0	−0.1 ± −0.25	
Malchiodi et al. (2013)	64	0	0	0	0	0	0	0.70 ± 0.50	0.90 ± 0.70
Mangano et al. (2012)	21	0	0	0	0	0	0	0.44 ± 0.14	
Mangano et al. (2013)	26	0	0	0	0	0	0	0.45 ± 0.15	
Mangano et al. (2017)	40	NM	NM	5	3	1 4 6	2 2 5	NM	NM
Migliorati et al. (2015)	48	0	0	NM	NM	NM	NM	−0.115 ± 0.162 −0.165 ± 0.055	−0.005 ± 0.021 −0.167 ± 0.072
Noelken et al. (2011)	18	NM	NM	1	1	NM	NM	1.30	1.00
Noelken et al. (2018) (2)	26	0	0	NM	NM	NM	NM	0.00 ± 0.70 0.10 ± 0.30	
Östman et al. (2020)	19	NM	NM	NM	NM	NM	NM	NM	NM
Paul and Held (2012)	33	NM	NM	0	0	NM	NM	NM	NM
Pieri et al. (2011)	38	5	1	NM	NM	NM	NM	0.2 ± 0.17 0.51 ± 0.24	
Puisys et al. (2022)	50	0	0	0	0	0	0	0.1 ± 0.21	0.2 ± 0.25
Raes et al. (2018)	11	NM	NM	NM	NM	NM	NM	NM	NM
da Rosa et al. (2014)	18	NM	NM	NM	NM	NM	NM	NM	NM

TABLE 2E (Continued)

Author (year)	Total number of implants	Implant and surgical complications		Biological complications		Technical complications		Marginal/crestal bone loss	
		Type	Number of implants	Type	Number of implants	Type	Number of implants	Mesial	Distal
Ross et al. (2014)	47	NM	NM	NM	NM	NM	NM	NM	NM
Saedi Germi et al. (2020)	18	NM	NM	NM	NM	NM	NM	NM	NM
Sicilia-Felechosa et al. (2020)	40	10	1	NM	NM	NM	NM	0.2 ± 0.16	
Slagter et al. (2021)	18	NM	NM	NM	NM	NM	NM	0.71 ± 0.68	0.71 ± 0.71
Spinato et al. (2012)	45	NM	NM	NM	NM	NM	NM	0.94 ± 0.51	
								0.90 ± 0.49	
Stoupel et al. (2016)	39	14	1	6	7	NM	NM	0.47 ± 0.98	0.59 ± 1.05
				1	2			0.73 ± 1.18	1.33 ± 1.23
Sun et al. (2020)	30	0	0	NM	NM	NM	NM	NM	NM
Takeshita et al. (2015)	21	NM	NM	NM	NM	NM	NM	0.56 ± 1.28	
Tian et al. (2019)	30	NM	NM	NM	NM	6	1	NM	NM
Tortamano et al. (2010)	12	NM	NM	NM	NM	NM	NM	NM	NM
Tsuda et al. (2011)	10	3	3	1	1	NM	NM	−0.14 ± 0.33	−0.14 ± 0.30
Valentini et al. (2010)	94	NM	NM	5	2	NM	NM	0.18 ± 0.66	0.43 ± 0.95
van Nimwegen et al. (2016)	51	14	2	NM	NM	NM	NM	NM	NM
van Nimwegen et al. (2018)	60	10	1	NM	NM	NM	NM	NM	NM
Vidigal et al. (2017)	53	14	2	NM	NM	1	1	NM	NM
						2	1		
						5	7		
Yang et al. (2019)	50	NM	NM	NM	NM	NM	NM	1.21 ± 1.44	
Yoshino et al. (2014)	20	3	1	1	1	5	1	−0.07 ± 0.16	
				2	1	7	1	−0.31 ± 0.41	
Zuiderveld et al. (2018)	30	NM	NM	NM	NM	NM	NM	0.04 ± 0.46	0.02 ± 0.37
								0.06 ± 0.42	0.03 ± 0.38

Note: Implant and surgical complications. 3: lack of stability; 5: draining sinus/bone dehiscence; 6: bone fenestration; 7: lack of stability; 8: midfacial recession; 10: soft tissue complication; 11: implant loss; 14: osteointegration failure. Biological complications: 1: periimplantitis; 2: fistula; 3: esthetic complications; 4: discomfort; 5: pain; 6: mucosal inflammation; 7: draining sinus; 8: acute infection. Technical complications: 1: screw loosening; 2: screw fracture; 4: chipping; 5: decementation; 6: crown loosening; 7: provisional crown broken; 8: loss of retention.

Abbreviation: NM: Not mentioned.

TABLE 2F Esthetic outcomes characteristics of the included studies.

Author (year)	Papilla height		Papilla index		Mid-facial/mid-buccal soft tissue recession	Pink esthetic score (Belser)	Pink esthetic score (Fürhauser)	White esthetic score
	Mesial	Distal	Mesial	Distal				
Arora and Ivanovski (2018)	NM	NM	NM	NM	NM	NM	11.1	8.4
Arora et al. (2017)	0.06 ± 0.66	0.06 ± 0.58	NM	NM	−0.23 ± 0.69	NM	11.25 ± 1.36	NM
Barone et al. (2016)	NM	NM	2.71 ± 0.45	2.71 ± 0.45	NM	7.71 ± 0.72	NM	NM
Bonnet et al. (2018)	NM	NM	NM	NM	NM	7.07 ± 1.328	NM	NM
Bruno et al. (2014)	NM	NM	2.00	1.82	NM	NM	NM	NM
Cabello et al. (2013)	−0.38 ± 0.68	−0.80 ± 0.96	NM	NM	−0.45 ± 0.25	NM	NM	NM
Cardaropoli et al. (2015)	−0.17 ± 0.28	−0.08 ± 0.18	NM	NM	−0.21 ± 0.32	NM	11.45 ± 1.45	NM
Cardaropoli et al. (2019)	−0.03 ± 0.34	−0.03 ± 0.34	NM	NM	0.08 ± 0.49	NM	12.55 ± 1.00	NM
Chan et al. (2019)	0.4 ± 1.00	0.5 ± 1.4	NM	NM	−0.10 ± 0.9	NM	NM	NM
Cooper et al. (2014)	−0.13 ± 1.61	−0.21 ± 1.61	NM	NM	0.06 ± 0.98	NM	NM	NM
Cosyn et al. (2011)	−0.05 ± 0.83	−0.08 ± 1.24	NM	NM	−0.34 ± 0.80	NM	10.48 ± 2.7	8.17 ± 1.52
Cosyn et al. (2013)	NM	NM	NM	NM	NM	NM	10.88 ± 2.41	NM
Cosyn et al. (2016)	0.09 ± 0.33	−0.25 ± 0.45	NM	NM	−0.53 ± 0.53	NM	11.18 ± 1.38	NM
Crespi et al. (2018)	NM	NM	NM	NM	−0.30	NM	10.88 ± 2.41	NM
Cristalli et al. (2015)	NM	NM	NM	NM	NM	7.96 ± 1.19	NM	9.00 ± 1.22
D'Avenia et al. (2019)	NM	NM	NM	NM	NM	NM	8.90 ± 1.20	NM
Degidi et al. (2014)	0.01 ± 0.18	−0.03 ± 0.13	NM	NM	−0.59 ± 0.21	NM	NM	NM
	0.08 ± 0.16	0.10 ± 0.17	NM	NM	−0.35 ± 0.12	NM		
Esposito et al. (2015)	NM	NM	NM	NM	NM	NM	13 ± 1.5	NM
Felice et al. (2015)	NM	NM	NM	NM	NM	NM	12.78 ± 0.42	NM
Fürhauser et al. (2016)	NM	NM	NM	NM	NM	NM	12.60	NM
Ganeles et al. (2017)	NM	NM	2.45	2.64	NM	NM	10	NM
Guarnieri et al. (2016)	0.41 ± 0.41	0.35 ± 0.83	NM	NM	−0.06 ± 0.61	NM	11.06 ± 0.63	7.32 ± 0.71
Groenendijk et al. (2020)	NM	NM	NM	NM	NM	NM	12 ± 2.0	NM
Hartlev et al. (2014)	NM	NM	NM	NM	NM	NM	9.9	7.70
Hassani et al. (2021)	NM	NM	NM	NM	NM	NM	11.2 ± 1.1	8.00 ± 1.02
Kan et al. (2011)	−0.22 ± 0.34	−0.21 ± 0.41	NM	NM	−1.13 ± 0.87	NM	NM	NM
Khzam et al. (2014)	−0.50 ± 1.12	−0.30 ± 0.82	NM	NM	−0.20 ± 0.78	NM	NM	NM
Kniha et al. (2017)	0.83 ± 0.65		NM	NM	NM	NM	NM	NM
Kolerman et al. (2016)	NM	NM	NM	NM	−0.54	7.12 ± 1.89	NM	7.32 ± 1.25
Kolerman et al. (2017)	NM	NM	NM	NM	−0.41	7.92 ± 1.6	NM	7.66 ± 1.48

TABLE 2F (Continued)

Author (year)	Papilla height		Papilla index		Mid-facial/mid-buccal soft tissue recession	Pink esthetic score (Belser)	Pink esthetic score (Fürhauser)	White esthetic score
	Mesial	Distal	Mesial	Distal				
Lombardo et al. (2016)	NM	NM	NM	NM	NM	7.86±0.8	NM	9.50±0.8
Ma et al. (2019)	NM	NM	2.29	2.12	0.28±0.20	NM	NM	NM
Malchiodi et al. (2013)	0.60±0.50	0.80±0.60	NM	NM	0.50±0.60	NM	NM	NM
Mangano et al. (2012)	NM	NM	NM	NM	NM	7.3±1.17	NM	7.00±1.35
Mangano et al. (2013)	NM	NM	NM	NM	NM	7.45±1.63	NM	7.04±1.29
Mangano et al. (2017)	NM	NM	NM	NM	NM	7.8±1.8	NM	8.60±1.7
Migliorati et al. (2015)	0.8	0.6	NM	NM	−0.41±0.38 −0.22±0.24	7.15±1.75	NM	7.98±0.99
	0.8	0.7			−0.93±0.58 −0.35±0.36			
Noelken et al. (2011)	NM	NM	NM	NM	NM	NM	12.5	NM
Noelken et al. (2018) (2)	NM	NM	NM	NM	−1.00±0.70 −0.40±0.70	NM	12.2±0.6 13.0±1.20	NM
Östman et al. (2020)	NM	NM	NM	NM	NM	NM	13.0	NM
Paul and Held (2012)	NM	NM	NM	NM	NM	8.39±1.33	NM	9.50±0.65
Pieri et al. (2011)	−0.24±0.21 −0.33±0.19	−0.28±0.19 −0.33±0.23	NM	NM	−0.61±0.54 −0.73±0.52	NM	NM	NM
Puisys et al. (2022)	NM	NM	NM	NM	0.0±0.1	NM	12.8±1.19	NM
Raes et al. (2018)	NM	NM	NM	NM	NM	NM	10.63±2.11	NM
da Rosa et al. (2014)	0.20	0.30	NM	NM	0.6	NM	NM	NM
Ross et al. (2014)	NM	NM	NM	NM	−0.30	NM	NM	NM
Saedi Germi et al. (2020)	NM	NM	NM	NM	NM	8.58±1.003	NM	NM
Sicilia-Felechosa et al. (2020)	NM	NM	NM	NM	NM	NM	12.43±2.13	NM
Slagter et al. (2021)	NM	NM	2.56±0.78	2.5±0.79	NM	7.83±1.69	NM	7.50±2.12
Spinato et al. (2012)	NM	NM	NM	NM	−0.40±0.60 −0.30±0.36	NM	NM	NM
Stoupel et al. (2016)	−0.09±0.27 −0.22±0.43	−0.06±0.25 −0.28±0.39	NM	NM	−0.22±0.31 −0.42±0.52	NM	NM	NM

(Continues)

TABLE 2F (Continued)

Author (year)	Papilla height		Papilla index		Mid-facial/mid-buccal soft tissue recession	Pink esthetic score (Belser)	Pink esthetic score (Fürhauser)	White esthetic score
	Mesial	Distal	Mesial	Distal				
Sun et al. (2020)	−0.59 ± 0.13	−0.58 ± 0.13	NM	NM	−0.59 ± 0.09	NM	12.07 ± 1.62	NM
	−1.17 ± 0.19	−1.22 ± 0.33			−1.09 ± 0.22		11.33 ± 1.76	
Takeshita et al. (2015)	NM	NM	NM	NM	NM	NM	10.24 ± 2.39	8.29 ± 1.62
Tian et al. (2019)	NM	NM	NM	NM	−0.24 ± 0.37	NM	NM	NM
Tortamano et al. (2010)	−0.14	−0.03	NM	NM	−0.03	NM	NM	NM
Tsuda et al. (2011)	NM	NM	2.00	2.60	−2.25 ± 1.21	NM	NM	NM
Valentini et al. (2010)	NM	NM	2.81 ± 0.50	2.81 ± 0.50	NM	NM	NM	NM
van Nimwegen et al. (2016)	NM	NM	NM	NM	NM	7.35 ± 1.23	NM	9.14 ± 0.94
van Nimwegen et al. (2018)	NM	NM	NM	NM	0.20 ± 0.70	NM	11.28 ± 1.67	NM
					−0.48 ± 1.13		11.36 ± 1.65	
Vidigal et al. (2017)	NM	NM	NM	NM	NM	NM	8.63 ± 2.40	6.92 ± 1.67
Yang et al. (2019)	−0.21 ± 0.80	−0.36 ± 0.79	1.9 ± 0.74	2.16 ± 0.76	−0.05 ± 0.92	NM	NM	NM
Yoshino et al. (2014)	NM	NM	2.1	2.2	−0.25 ± 0.35	NM	NM	NM
			2.4	1.9	−0.70 ± 0.48			
Zuiderveld et al. (2018)	−0.3 ± 0.7	−0.4 ± 0.7	NM	NM	0.10 ± 0.80	6.4 ± 1.5	NM	7.40 ± 1.3
	−0.4 ± 1.0	−0.6 ± 0.6			−0.50 ± 1.1	6.8 ± 1.5		
					−0.52 ± 1.16			

Abbreviation: NM, Not mentioned.

TABLE 3A Quality assessment of cohort included studies using the Newcastle-Ottawa scale.

Study	Selection				Comparability		Outcome			Number of stars (out of 9)
	S1	S2	S3	S4	C1	C2	E1	E2	E3	
Arora et al. (2017)	★	0	★	★	0	0	★	★	★	6
Arora and Ivanovski (2018)	★	0	★	★	★	0	★	★	★	6
Barone et al. (2016)	★	0	★	★	0	0	★	★	★	6
Bonnet et al. (2018)	★	0	★	★	0	0	0	★	★	5
Bruno et al. (2014)	★	0	★	★	0	0	0	★	★	5
Cabello et al. (2013)	★	0	0	★	0	0	0	★	★	4
Cardaropoli et al. (2015)	★	0	★	★	0	0	0	★	★	5
Cardaropoli et al. (2019)	★	0	★	★	0	0	0	★	★	5
Cooper et al. (2014)	★	★	0	★	★	★	0	★	★	7
Cosyn et al. (2011)	★	0	★	★	0	0	★	★	★	7
Cosyn et al. (2013)	★	★	★	★	★	★	★	★	★	9
Cosyn et al. (2016)	★	0	★	★	0	0	0	★	★	5
Cristalli et al. (2015)	★	0	★	★	0	0	★	★	★	6
D'Avenia et al. (2019)	★	0	★	★	0	0	0	★	★	5
Fürhauser et al. (2016)	★	0	★	★	0	0	★	★	★	7
Ganeles et al. (2017)	★	0	★	★	0	0	★	★	★	6
Guarnieri et al. (2016)	★	★	★	★	★	★	★	★	★	9
Groenendijk et al. (2020)	★	0	★	★	0	0	0	★	★	5
Hartlev et al. (2014)	★	0	★	★	0	0	0	★	0	4
Hassani et al. (2021)	★	0	0	★	★	★	0	★	★	6
Kan et al. (2011)	★	0	★	★	★	★	0	★	★	7
Khzam et al. (2014)	★	0	★	★	0	0	0	★	★	5
Kniha et al. (2017)	★	0	★	★	★	★	0	★	★	7
Kolerman et al. (2016)	★	0	★	0	0	0	0	★	★	4
Kolerman et al. (2017)	★	0	★	★	0	0	0	★	★	5
Lombardo et al. (2016)	★	0	0	★	0	0	0	★	★	4
Ma et al. (2019)	★	0	★	★	0	0	★	★	★	6
Malchiodi et al. (2013)	★	0	0	★	0	0	0	★	★	4
Mangano et al. (2012)	★	0	★	★	0	0	0	★	★	5
Mangano et al. (2013)	★	0	★	★	★	0	0	★	★	6
Mangano et al. (2017)	★	0	★	★	0	0	0	★	★	5
Migliorati et al. (2015)	★	★	★	★	★	★	★	★	★	9
Noelken et al. (2011)	★	0	★	★	0	0	0	★	★	5
Noelken et al. (2018)	★	★	★	★	★	★	0	★	★	8
Östman et al. (2020)	★	0	★	★	0	0	0	★	★	5
Paul and Held (2012)	★	0	★	★	0	0	0	★	★	5
Ross et al. (2014)	★	0	0	★	0	0	0	★	★	4
Raes et al. (2018)	★	★	★	★	★	★	0	★	★	8
da Rosa et al. (2014)	★	0	★	★	0	0	0	★	★	5
Saedi Germi et al. (2020)	★	0	0	★	0	0	0	★	★	4
Sicilia-Felechosa et al. (2020)	★	0	★	★	0	0	0	★	★	6
Slagter et al. (2021)	★	★	★	★	★	★	0	★	★	8
Spinato et al. (2012)	★	0	0	★	★	★	0	★	★	6
Sun et al. (2020)	★	★	★	★	★	★	0	★	★	8
Takeshita et al. (2015)	★	0	0	★	0	0	0	★	★	4
Tian et al. (2019)	★	0	★	★	0	0	0	★	★	5
Tortamano et al. (2010)	★	0	★	★	0	0	0	★	★	5
Tsuda et al. (2011)	★	0	★	★	0	0	0	★	★	5
Valentini et al. (2010)	★	0	0	★	0	0	0	★	0	3
van Nimwegen et al. (2016)	★	0	★	★	0	0	0	★	★	5
Vidigal et al. (2017)	★	0	★	★	0	0	0	★	★	3
Yang et al. (2019)	★	0	★	★	0	0	0	★	★	5
Yoshino et al. (2014)	★	★	★	★	★	★	0	★	★	8

TABLE 3B Quality assessment of randomized clinical trials, according to RoB 2 bias tool (risk of bias).

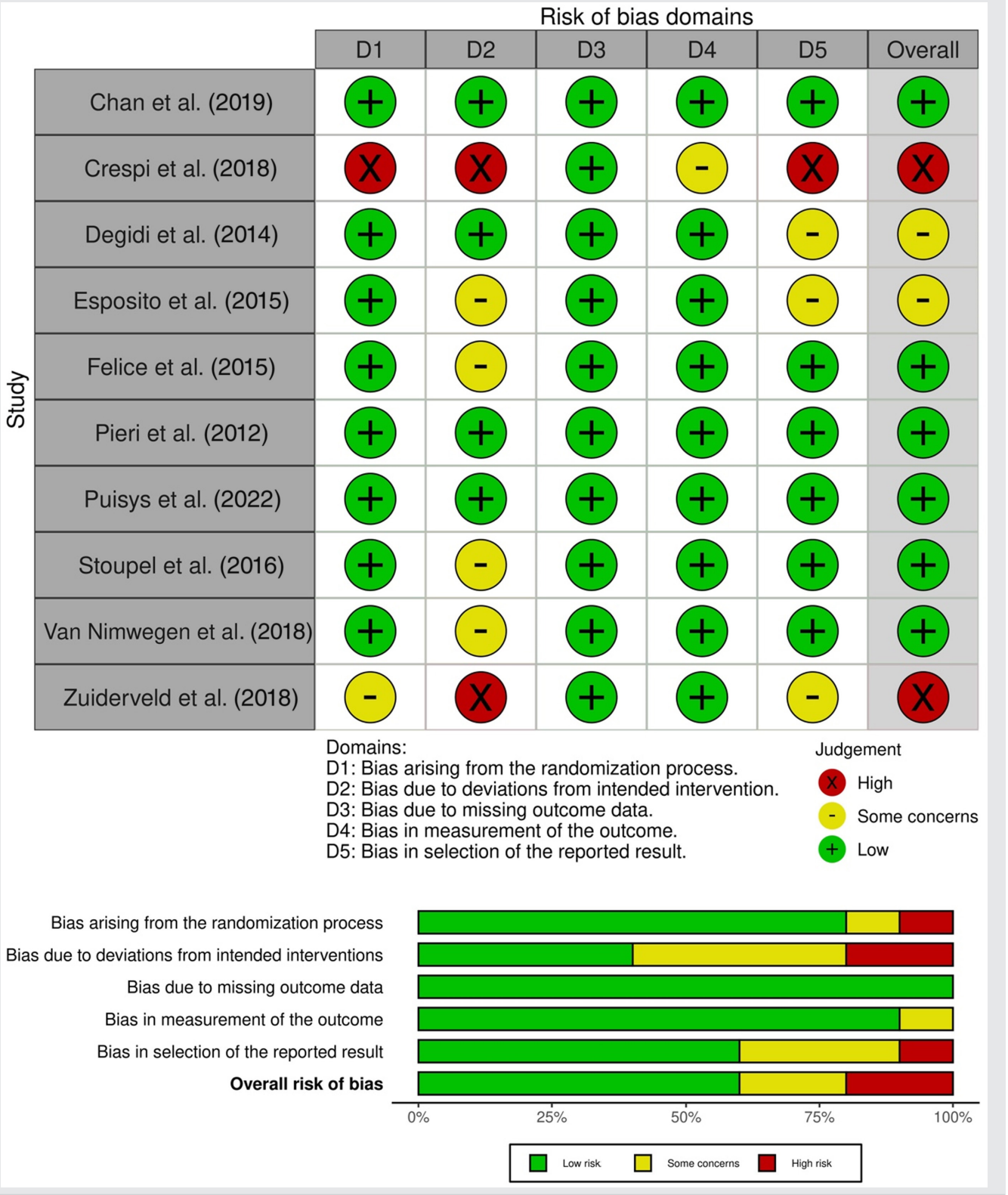


TABLE 4 Survival of implants (failures [X] of immediate implants [U]) – failure rates of studies.

Study ID	Author (year)	Patients included	Mean exposure time (months)	Immediate implants	Failures	Failure rate per year (95% CI)[a]
1	Arora et al. (2017)	30	47	30	0	0 (0–3.1[b])
2	Arora and Ivanovski (2018)	20	37	40	0	0 (0–3.0[b])
3	Barone et al. (2016)	30	84	37	2	0.8 (0.1–2.8)
4	Bonnet et al. (2018)	39	12	39	0	0 (0–9.5[b])
5	Bruno et al. (2014)	12	12	36	0	0 (0–10.2[b])
6	Cabello et al. (2013)	14	12	14	0	0 (0–26.3[b])
7	Cardaropoli et al. (2015)	26	12	26	0	0 (0–14.2[b])
8	Cardaropoli et al. (2019)	20	12	20	0	0 (0–18.4[b])
9	Chan et al. (2019)	18	12	20	2	10.0 (1.2–36.1)
10	Cooper et al. (2014)	45	60	55	3	1.1 (0.2–3.2)
11	Cosyn et al. (2011)	25	36	32	1	1.0 (0.0–5.8)
12	Cosyn et al. (2013)	28	33	28	3	3.9 (0.8–11.4)
14	Crespi et al. (2018)	60	48	30	0	0 (0–3.1[b])
15	Cristalli et al. (2015)	24	12	25	2	8.0 (1.0–28.9)
17	Degidi et al. (2014)	53	24	53	0	0 (0–3.5[b])
18	Esposito et al. (2015)	54	12	54	2	3.7 (0.4–13.4)
19	Felice et al. (2015)	25	12	25	2	8.0 (1.0–28.9)
20	Fürhauser et al. (2016)	77	60	77	0	0 (0–1.0[b])
21	Ganeles et al. (2017)	11	24	15	0	0 (0–12.3[b])
22	Guarnieri et al. (2016)	25	36	12	0	0 (0–10.2[b])
23	Groenendijk et al. (2020)	98	12	98	0	0 (0–3.8[b])
24	Hartlev et al. (2014)	54	33	54	1	0.7 (0.0–3.8)
25	Hassani et al. (2021)	20	12	20	0	0 (0–18.4[b])
26	Kan et al. (2011)	35	48	35	0	0 (0–2.6[b])
27	Khzam et al. (2014)	13	23.2	15	0	0 (0–12.7[b])
28	Kniha et al. (2017)	16	12	16	0	0 (0–23.1[b])
30	Kolerman et al. (2017)	39	44.82	39	1	0.7 (0.0–3.8)
31	Lombardo et al. (2016)	16	23.3	21	1	2.5 (0.1–13.7)
32	Ma et al. (2019)	16	60	28	2	1.4 (0.2–5.2)
33	Malchiodi et al. (2013)	58	36	64	0	0 (0–1.9[b])
34	Mangano et al. (2012)	26	24	26	1	1.9 (0.0–10.7)
35	Mangano et al. (2013)	40	31.09	22	0	0 (0–6.5[b])
36	Mangano et al. (2017)	103	36	42	0	0 (0–2.9[b])
37	Migliorati et al. (2015)	48	24	48	0	0 (0–3.8[b])
38	Noelken et al. (2011)	16	22	18	0	0 (0–11.2[b])
39	Noelken et al. (2018), ABG	14	61	13	0	0 (0–5.6[b])
39	Noelken et al. (2018), ABG + CTG	13	29	13	0	0 (0–11.7[b])
40	Östman et al. (2020)	19	19	19	0	0 (0–12.3[b])
41	Paul and Held (2012)	26	40.8	31	0	0 (0–3.5[b])
42	Pieri et al. (2011), T: Platform switch abutment	19	12	19	1	5.3 (0.1–29.3)
42	Pieri et al. (2011), C: Conventional abutment	19	12	19	0	0 (0–19.4[b])
43	Puisys et al. (2022)	25	12	25	0	0 (0–14.8[b])
44	Raes et al. (2018)	29	96	11	0	0 (0–4.2[b])
45	da Rosa et al. (2014)	18	58.56	18	0	0 (0–4.2[b])
46	Ross et al. (2014)	47	60	47	0	0 (0–1.6[b])

(Continues)

TABLE 4 (Continued)

Study ID	Author (year)	Patients included	Mean exposure time (months)	Immediate implants	Failures	Failure rate per year (95% CI)[a]
47	Saedi Germi et al. (2020)	18	12	18	0	0 (0–20.5[b])
48	Sicilia-Felechosa et al. (2020)	40	41.28	40	1	0.7 (0.0–4.0)
49	Slagter et al. (2021)	40	60	18	0	0 (0–4.1[b])
50	Spinato et al. (2012)	41	32	45	0	0 (0–3.1[b])
51	Stoupel et al. (2016), Flap	21	12	21	1	4.8 (0.1–26.5)
53	Takeshita et al. (2015)	18	18	21	0	0 (0–11.7[b])
54	Tian et al. (2019)	27	12	30	0	0 (0–12.3[b])
55	Tortamano et al. (2010)	12	18	12	0	0 (0–20.5[b])
56	Tsuda et al. (2011)	10	12	10	0	0 (0–36.9[b])
57	Valentini et al. (2010)	40	12	43	2	4.7 (0.6–16.8)
58	van Nimwegen et al. (2016)	51	48	51	2	1.0 (0.1–3.5)
59	van Nimwegen et al. (2018)	60	12	60	1	1.7 (0.0–9.3)
60	Vidigal et al. (2017)	53	51	53	2	0.9 (0.1–3.2)
61	Yang et al. (2019)	40	12	50	0	0 (0–7.4[b])
63	Zuiderveld et al. (2018), T: with CTG	29	12	30	1	3.3 (0.1–18.6)
63	Zuiderveld et al. (2018), C: without CTG	29	12	30	1	3.3 (0.1–18.6)

[a]Assuming poisson distributed failures.

[b]One-sided confidence interval.

biological complications present different findings when RCT studies are analyzed separately with a value of 6.22 in RCTs compared to 0.60 in prospective and 1.70 in retrospective studies.

4 | DISCUSSION

Treatment approaches in the field of oral implantology should be evaluated by combining the surgical and prosthetic phases and evaluating the overall outcome of the combined pathway. The goal of achieving a successful, long-lasting, and esthetic outcome is dependent on both the surgical and prosthetic phase and should therefore be evaluated from an objective view with respect to their combined treatment. Gallucci et al. (2018) emphasized the importance of assessing outcomes considering the implant-prosthetic concept as a single variable (Gallucci et al., 2018; Papaspyridakos et al., 2012). Immediate placement is defined as Type 1 treatment, placing the implant on the day of dental extraction (Chen et al., 2004; Chen & Buser, 2009; Hämmerle et al., 2004).

Within the evolution of results published by the ITI (International Team of Implantology) Consensus Conferences, the definition of immediate loading has been modified over the years. The latest version is that the restoration (provisional or final) is loaded in the first week following implant placement (Gallucci et al., 2014; Weber et al., 2009). In the last ITI Consensus Conference, a novel classification of combining immediate implant placement and immediate loading was proposed and defined as Type 1A (Gallucci et al., 2018).

With the data from the 63 studies published since 2010 and included here (10 randomized controlled trials, 28 prospective cohort and 25 retrospective cohort studies), a meta-analysis could be performed to evaluate the esthetic outcome and clinical performance of implants and their supported restorations inserted with Type 1A implant placement and loading in the maxillary anterior zone.

The overall survival rate of the implants calculated up to 5 years (95.8 (93.3–97.4) %) are similar to other implant placement concepts, and the survival of the restorations was also acceptable after 5 years (94.8%). 10-year data on the outcome of fixed implant-supported restorations presented survival rates of 95.5% in the literature (Wittneben, Buser, et al., 2014; Wittneben, Millen, et al., 2014) with a 98.8% implant survival rate (Buser et al., 2012). No influence of the retention type (screw vs. cement) on survival rate was observed. This has been confirmed in a specific meta-analysis focusing on this topic (Wittneben et al., 2017; Wittneben, Buser, et al., 2014; Wittneben, Millen, et al., 2014). Complications during the surgical phase were more frequent than the incidence of biological and technical complications of the restorations.

Multiple tools have been introduced to evaluate esthetic outcomes in implant treatment. Two of the most commonly used and accepted subjective tools currently available are the pink (PES) and white (WES) esthetic scores. PES was initially proposed by Fürhauser et al. (2005) to evaluate the peri-implant mucosa using seven distinct peri-implant soft tissue parameters. These parameters are the presence and absence of mesial and distal papillae, level of the facial mucosal margin, soft tissue contour, alveolar process deficiency (facial convexity), soft tissue color, and soft tissue texture. Each parameter has a score ranging from 0 to 2 with two being the best score and zero the poorest score, for a total possible score of 14. Belser et al. (2009) proposed a modification to

TABLE 5 Survival of restorations – (failure/survival [BB] of immediate loading [AO]) – failure rate per study.

Study ID	Author (year)	Patients included	Mean exposure time (months)	Immediate loadings	Failures	Failure rate per year (95% CI)[a]
1	Arora et al. (2017)	30	47	30	0	0 (0–3.1[b])
2	Arora and Ivanovski (2018)	20	37	20	0	0 (0–6.0[b])
3	Barone et al. (2016)	30	84	37	2	0.8 (0.1–2.8)
4	Bonnet et al. (2018)	39	12	39	0	0 (0–9.5[b])
6	Cabello et al. (2013)	14	12	14	0	0 (0–26.3[b])
7	Cardaropoli et al. (2015)	26	12	26	0	0 (0–14.2[b])
8	Cardaropoli et al. (2019)	20	12	20	0	0 (0–18.4[b])
9	Chan et al. (2019)	18	12	18	0	0 (0–20.5[b])
11	Cosyn et al. (2011)	25	36	32	7	7.3 (2.9–15.0)
12	Cosyn et al. (2013)	28	33	28	0	0 (0–4.8[b])
13	Cosyn et al. (2016)	17	60	22	5	4.5 (1.5–10.6)
14	Crespi et al. (2018)	60	48	30	0	0 (0–3.1[b])
15	Cristalli et al. (2015)	24	12	25	2	8.0 (1.0–28.9)
16	D'Avenia et al. (2019)	20	16	20	0	0 (0–13.8[b])
19	Felice et al. (2015)	25	12	25	2	8.0 (1.0–28.9)
20	Fürhauser et al. (2016)	77	60	77	0	0 (0–1.0[b])
21	Ganeles et al. (2017)	11	24	15	0	0 (0–12.3[b])
22	Guarnieri et al. (2016)	25	36	12	0	0 (0–10.2[b])
23	Groenendijk et al. (2020)	98	12	98	0	0 (0–3.8[b])
24	Hartlev et al. (2014)	54	33	54	0	0 (0–2.5[b])
26	Kan et al. (2011)	35	48	35	0	0 (0–2.6[b])
28	Kniha et al. (2017)	16	12	16	0	0 (0–23.1[b])
30	Kolerman et al. (2017)	39	44.82	39	0	0 (0–2.5[b])
32	Ma et al. (2019)	16	60	17	0	0 (0–4.3[b])
34	Mangano et al. (2012)	26	24	26	0	0 (0–7.1[b])
35	Mangano et al. (2013)	40	31.09	22	0	0 (0–6.5[b])
36	Mangano et al. (2017)	103	36	42	0	0 (0–2.9[b])
42	Pieri et al. (2011), T: Platform switch abutment	19	12	19	1	5.3 (0.1–29.3)
44	Raes et al. (2018)	29	96	11	0	0 (0–4.2[b])
45	da Rosa et al. (2014)	18	58.56	18	0	0 (0–4.2[b])
49	Slagter et al. (2021)	40	60	18	0	0 (0–4.1[b])
55	Tortamano et al. (2010)	12	18	12	0	0 (0–20.5[b])
57	Valentini et al. (2010)	40	12	43	2	4.7 (0.6–16.8)
58	van Nimwegen et al. (2016)	51	48	51	2	1.0 (0.1–3.5)
60	Vidigal et al. (2017)	53	51	53	2	0.9 (0.1–3.2)

[a]Assuming poisson distributed failures.
[b]One-sided confidence interval.

TABLE 6 Survival of restorations – retention – failure rate and survival rates.

Retent. type	No. of studies	No. of imm. implants	Exp. time (years)	Failures	Failure rate[a] per 100 years	Survival rates[a]		
						1 year	3 years	5 years
Screw	6	105	309	5	1.0 (0.2–6.3)	99.0 (93.7–99.8)	97.0 (82.3–99.5)	95.0 (72.2–99.2)
Cement	23	725	2233	18	1.3 (0.6–3.0)	98.7 (97.0–99.4)	96.0 (91.3–98.2)	93.4 (85.9–97.0)

[a]Random-effects Poisson regression, screw versus cement: IRR (95% CI): 1.3 (0.2–7.2), $p = .743$.

TABLE 7 Surgical complications of implants – complication rate per study.

Study ID	Author (year)	Patients included	Immediate implants	No. of complications	Complications per 100 implants (95% CI)[a]
2	Arora and Ivanovski (2018)	20	40	2	5.0 (0.6–18.1)
3	Barone et al. (2016)	30	37	2	5.4 (0.7–19.5)
4	Bonnet et al. (2018)	39	39	0	0 (0–9.5[b])
5	Bruno et al. (2014)	12	36	5	13.9 (4.5–32.4)
6	Cabello et al. (2013)	14	14	0	0 (0–26.3[b])
7	Cardaropoli et al. (2015)	26	26	0	0 (0–14.2[b])
8	Cardaropoli et al. (2019)	20	20	0	0 (0–18.4[b])
9	Chan et al. (2019)	18	20	2	10.0 (1.2–36.1)
10	Cooper et al. (2014)	45	55	3	5.5 (1.1–15.9)
11	Cosyn et al. (2011)	25	32	0	0 (0–11.5[b])
12	Cosyn et al. (2013)	28	28	5	17.9 (5.8–41.7)
13	Cosyn et al. (2016)	17	22	7	31.8 (12.8–65.6)
14	Crespi et al. (2018)	60	30	0	0 (0–12.3[b])
15	Cristalli et al. (2015)	24	25	0	0 (0–14.8[b])
17	Degidi et al. (2014)	53	53	0	0 (0–7.0[b])
18	Esposito et al. (2015)	54	54	19	35.2 (21.2–54.9)
23	Groenendijk et al. (2020)	98	98	1	1.0 (0.0–5.7)
25	Hassani et al. (2021)	20	20	0	0 (0–18.4[b])
28	Kniha et al. (2017)	16	16	0	0 (0–23.1[b])
29	Kolerman et al. (2016)	34	34	2	5.9 (0.7–21.2)
31	Lombardo et al. (2016)	16	21	1	4.8 (0.1–26.5)
32	Ma et al. (2019)	16	28	9	32.1 (14.7–61.0)
33	Malchiodi et al. (2013)	58	64	0	0 (0–5.8[b])
34	Mangano et al. (2012)	26	26	0	0 (0–14.2[b])
35	Mangano et al. (2013)	40	22	0	0 (0–16.8[b])
37	Migliorati et al. (2015)	48	48	0	0 (0–7.7[b])
39	Noelken et al. (2018)	26	26	0	0 (0–14.2[b])
42	Pieri et al. (2011)	19	19	1	5.3 (0.1–29.3)
43	Puisys et al. (2022)	25	25	0	0 (0–14.8[b])
48	Sicilia-Felechosa et al. (2020)	40	40	1	2.5 (0.1–13.9)
51	Stoupel et al. (2016), Flapless	18	18	0	0 (0–20.5[b])
51	Stoupel et al. (2016), Flap	21	21	1	4.8 (0.1–26.5)
52	Sun et al. (2020)	30	30	0	0 (0–12.3[b])
56	Tsuda et al. (2011)	10	10	3	30.0 (6.2–87.7)
58	van Nimwegen et al. (2016)	51	51	2	3.9 (0.5–14.2)
59	van Nimwegen et al. (2018)	60	60	1	1.7 (0.0–9.3)
60	Vidigal et al. (2017)	53	53	2	3.8 (0.5–13.6)
62	Yoshino et al. (2014)	20	20	1	5.0 (0.1–27.9)

[a]Assuming Poisson distributed complications.

[b]One-sided confidence interval.

PES scoring by combining three less important parameters (facial contour, soft tissue color and texture) into one variable, resulting in only five parameters and a maximum possible score of 10. The WES index was also proposed by Belser et al. (2009) and focuses on the esthetic evaluation of an implant restoration. WES is based on five parameters, each also receiving a score between 0 and 2 for a maximum possible score of 10. These variables are tooth form, outline, color, surface texture, and translucency. Tettamanti et al. (2016) concluded in a comparison investigation of these and other esthetic indices that PES/WES and peri-implant–crown index (PICI) were

TABLE 8 Technical complications of restorations – complication rate per study.

ID	Author (year)	Patients included	Immediate loadings	Exposure time (years)	No. of complications	Complications per 100 years (95% CI)[a]
1	Arora et al. (2017)	30	30	117.5	0	0 (0–3.1[b])
2	Arora and Ivanovski (2018)	20	20	61.7	0	0 (0–6.0[b])
4	Bonnet et al. (2018)	39	39	39	0	0 (0–9.5[b])
6	Cabello et al. (2013)	14	14	14	5	35.7 (11.6–83.3)
8	Cardaropoli et al. (2019)	20	20	20	0	0 (0–18.4[b])
11	Cosyn et al. (2011)	25	32	96	1	1.0 (0.0–5.8)
13	Cosyn et al. (2016)	17	22	110	3	2.7 (0.6–8.0)
15	Cristalli et al. (2015)	24	25	25	0	0 (0–14.8[b])
18	Esposito et al. (2015)	54	35	35	4	11.4 (3.1–29.3)
19	Felice et al. (2015)	25	25	25	2	8.0 (1.0–28.9)
21	Ganeles et al. (2017)	11	15	30	0	0 (0–12.3[b])
23	Groenendijk et al. (2020)	98	98	98	1	1.0 (0.0–5.7)
25	Hassani et al. (2021)	20	20	20	0	0 (0–18.4[b])
26	Kan et al. (2011)	35	35	140	0	0 (0–2.6[b])
28	Kniha et al. (2017)	16	16	16	0	0 (0–23.1[b])
31	Lombardo et al. (2016)	16	20	38.8	3	7.7 (1.6–22.6)
32	Ma et al. (2019)	16	17	85	0	0 (0–4.3[b])
33	Malchiodi et al. (2013)	58	64	192	0	0 (0–1.9[b])
34	Mangano et al. (2012)	26	26	52	0	0 (0–7.1[b])
35	Mangano et al. (2013)	40	22	57	0	0 (0–6.5[b])
36	Mangano et al. (2017)	103	42	126	9	7.1 (3.3–13.6)
43	Puisys et al. (2022)	25	25	25	0	0 (0–14.8[b])
54	Tian et al. (2019)	27	30	30	1	3.3 (0.1–18.6)
60	Vidigal et al. (2017)	53	53	225.2	9	4.0 (1.8–7.6)
62	Yoshino et al. (2014)	20	20	20	2	10.0 (1.2–36.1)

[a]Assuming Poisson distributed complications.
[b]One-sided confidence interval.

TABLE 9 Biological complications of restorations – complication rate per study.

ID	Author (year)	Patients included	Immediate loadings	Exposure time (years)	No. of complications	Complications per 100 years (95% CI)[a]
1	Arora et al. (2017)	30	30	117.5	0	0 (0–3.1[b])
2	Arora and Ivanovski (2018)	20	20	61.7	2	3.2 (0.4–11.7)
3	Barone et al. (2016)	30	37	259	2	0.8 (0.1–2.8)
4	Bonnet et al. (2018)	39	39	39	0	0 (0–9.5[b])
6	Cabello et al. (2013)	14	14	14	0	0 (0–26.3[b])
8	Cardaropoli et al. (2019)	20	20	20	0	0 (0–18.4[b])
11	Cosyn et al. (2011)	25	32	96	0	0 (0–3.8[b])
13	Cosyn et al. (2016)	17	22	110	1	0.9 (0.0–5.1)
15	Cristalli et al. (2015)	24	25	25	0	0 (0–14.8[b])
17	Degidi et al. (2014)	29	53	106	3	2.8 (0.6–8.3)
18	Esposito et al. (2015)	54	35	35	2	5.7 (0.7–20.6)
21	Ganeles et al. (2017)	11	15	30	0	0 (0–12.3[b])
23	Groenendijk et al. (2020)	98	98	98	1	1.0 (0.0–5.7)
25	Hassani et al. (2021)	20	20	20	0	0 (0–18.4[b])
26	Kan et al. (2011)	35	35	140	0	0 (0–2.6[b])
28	Kniha et al. (2017)	16	16	16	0	0 (0–23.1[b])
31	Lombardo et al. (2016)	16	20	38.8	0	0 (0–9.5[b])

TABLE 9 (Continued)

ID	Author (year)	Patients included	Immediate loadings	Exposure time (years)	No. of complications	Complications per 100 years (95% CI)[a]
33	Malchiodi et al. (2013)	58	64	192	0	0 (0–1.9[b])
34	Mangano et al. (2012)	26	26	52	0	0 (0–7.1[b])
35	Mangano et al. (2013)	40	22	57	0	0 (0–6.5[b])
36	Mangano et al. (2017)	103	42	126	3	2.4 (0.5–7.0)
38	Noelken et al. (2011)	16	18	33	1	3.0 (0.1–16.9)
41	Paul and Held (2012)	26	31	105.4	0	0 (0–3.5[b])
43	Puisys et al. (2022)	25	25	25	0	0 (0–14.8[b])
51	Stoupel et al. (2016), Flapless	18	18	18	5	27.8 (9.0–64.8)
51	Stoupel et al. (2016), Flap	21	21	21	4	19.0 (5.2–48.8)
56	Tsuda et al. (2011)	10	10	10	1	10.0 (0.3–55.7)
57	Valentini et al. (2010)	40	43	43	2	4.7 (0.6–16.8)
62	Yoshino et al. (2014)	20	20	20	2	10.0 (1.2–36.1)

[a]Assuming Poisson distributed complications.

[b]One-sided confidence interval.

TABLE 10 Esthetic outcomes – weighted mean scores – meta-regression, random-effects model (REML).

	Month	No. of studies/ subgroups	Implants included	EWM	95% CI	I^2	τ^2
Papilla (mm)	0	11	303	−0.3	−0.5; −0.1	0.83	0.03
	1–6	26	566	−0.4	−0.5; −0.3	0.92	0.05
	12	37	866	−0.3	−0.4; −0.1	0.95	0.13
	18–24	4	54	−0.0	−0.7; 0.7	0.69	0.13
	33–44	8	306	0.3	−0.0; 0.6	0.86	0.11
	48–96	8	268	−0.1	−0.2; 0.0	0.62	0.02
PI	0	4	94	0.9	−1.2; 2.9	0.97	1.63
	1–6	4	136	2.1	1.8; 2.4	0.52	0.02
	12	6	244	1.6	0.1; 3.0	0.99	1.96
	48–96	3	71	2.7	2.4; 2.9	0.00	0.00
Midfacial	0	17	393	−0.5	−0.9; −0.1	0.96	0.56
	1–6	26	493	−0.5	−0.7; −0.3	0.91	0.16
	12	30	631	−0.3	−0.5; −0.2	0.96	0.13
	18–24	8	149	−0.4	−0.7; −0.2	0.83	0.07
	33–44	6	179	−0.2	−0.7; 0.4	0.93	0.26
	48–96	5	151	−0.3	−1.0; 0.4	0.96	0.29
PES (%)	0	15	417	73.2	66.4; 80.0	0.96	141.64
	1–6	11	306	83.1	78.9; 87.3	0.86	31.27
	12	19	583	83.1	79.2; 87.0	0.95	61.31
	18–24	9	167	79.1	73.9; 84.3	0.84	37.96
	33–44	7	150	81.7	75.7; 87.6	0.88	34.22
	48–96	9	281	76.9	71.8; 82.1	0.90	38.33
WES	0	7	246	6.2	4.6; 7.9	0.99	2.95
	1–6	5	182	8.2	7.1; 9.2	0.85	0.57
	12	3	158	7.5	6.0; 9.1	0.91	0.33
	18–24	5	111	8.2	7.0; 9.3	0.94	0.76
	33–44	4	98	7.9	7.0; 8.8	0.75	0.23
	48–96	4	153	8.3	6.3; 10.3	0.97	1.53

Abbreviation: EWM, estimated weighted mean.

TABLE 11A Papilla height (mm) – baseline and 12 month, Random-effects model (REML).

	Implants included	Baseline Mean, SD	12 month Mean, SD	Effect size[a] Hedges' *g* [95% CI]	Weight (%)
Cabello et al. (2013), mesial	14	−0.06, 0.49	−0.38, 0.68	−0.52 [−1.31, 0.26]	8.05
Cabello et al. (2013), distal	14	−0.19, 0.54	−0.8, 0.96	−0.76 [−1.56, 0.04]	7.99
Chan et al. (2019), mesial	18	0.3, 1	0.4, 1	0.10 [−0.58, 0.77]	8.43
Chan et al. (2019), distal	18	0.3, 1.3	0.5, 1.4	0.14 [−0.53, 0.82]	8.43
Pieri et al. (2011), T: Platform switch abutment, mesial	18	0, 0	−0.24, 0.21	−1.58 [−2.36, −0.80]	8.06
Pieri et al. (2011), T: Platform switch abutment, distal	18	0, 0	−0.28, 0.19	−2.04 [−2.88, −1.19]	7.84
Pieri et al. (2011), C: Conventional abutment, mesial	19	0, 0	−0.33, 0.19	−2.40 [−3.28, −1.53]	7.72
Pieri et al. (2011), C: Conventional abutment, distal	19	0, 0	−0.33, 0.23	−1.99 [−2.80, −1.17]	7.95
Zuiderveld et al. (2018), T: with CTG, mesial	29	−0.4, 0.7	−0.3, 0.7	0.14 [−0.38, 0.67]	8.88
Zuiderveld et al. (2018), T: with CTG, distal	29	−0.4, 0.6	−0.4, 0.7	0.00 [−0.52, 0.52]	8.89
Zuiderveld et al. (2018), C: without CTG, mesial	29	−0.3, 0.8	−0.4, 1	−0.11 [−0.63, 0.42]	8.89
Zuiderveld et al. (2018), C: without CTG, distal	29	−0.6, 0.7	−0.6, 0.6	0.00 [−0.52, 0.52]	8.89
Overall				−0.71 [−1.25, −0.17]	
$I^2 = 87.37\%$, $H^2 = 7.92$, $\tau^2 = 0.78$					

[a]Assuming a correlation of 0 between baseline and 12 month.

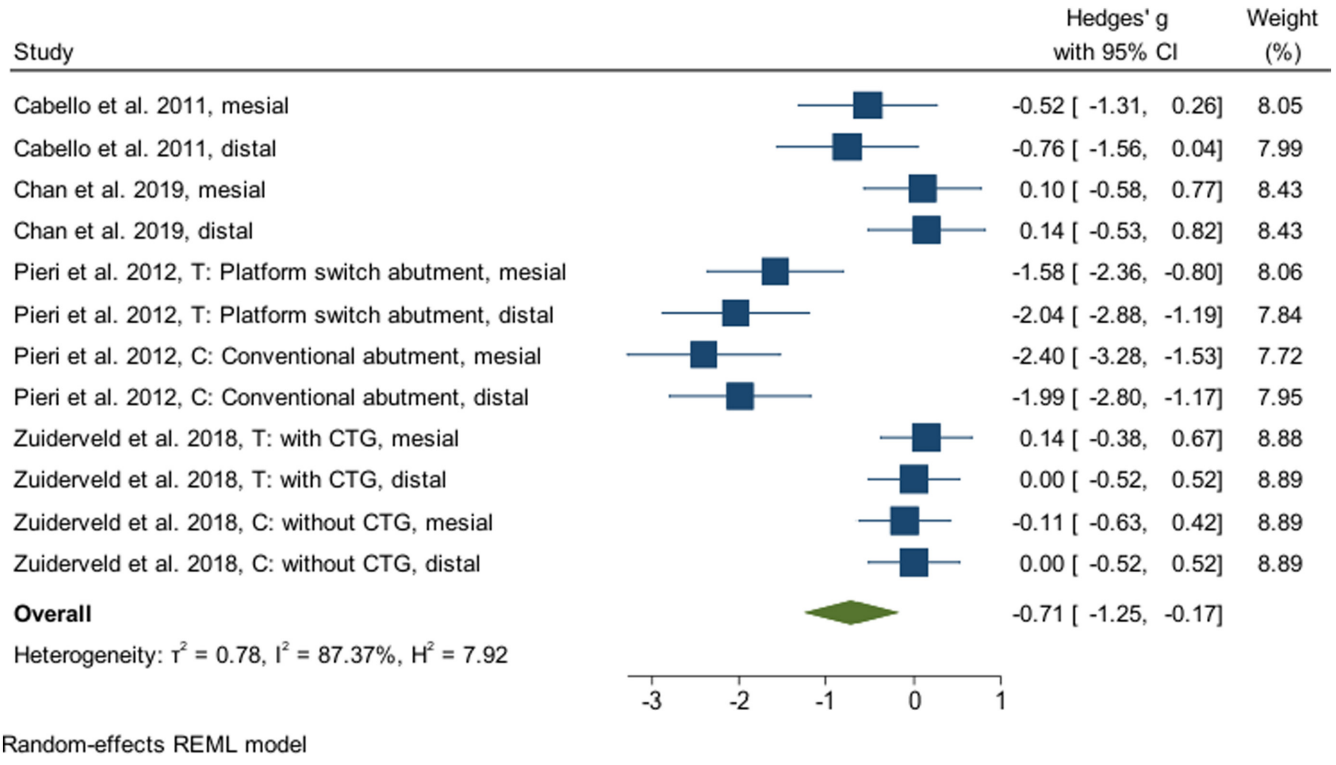


FIGURE 2 Forest plot: Papilla height (mm) – baseline and 12 month, random-effects model (REML).

TABLE 11B Midfacial – baseline and 12 month, Random-effects model (REML).

	Implants included	Baseline Mean, SD	12 month Mean, SD	Effect size[a] Hedges' *g* [95% CI]	Weight (%)
Cabello et al. (2013), mesial	14	−0.16, 0.4	−0.45, 0.25	−0.84 [−1.65, −0.03]	5.40
Chan et al. (2019), mesial	18	−0.2, 0.8	−0.1, 0.9	0.11 [−0.56, 0.79]	5.64
Ma et al. (2019), mesial	17	0, 0	0.36, 0.4	1.24 [0.48, 2.01]	5.48
Migliorati et al. (2015), CGT, mesial	24	−0.14, 0.36	−0.13, 0.44	0.02 [−0.55, 0.60]	5.79
Migliorati et al. (2015), CGT, distal	24	0, 0	−0.13, 0.24	−0.75 [−1.35, −0.15]	5.76
Migliorati et al. (2015), without CTG, mesial	24	−0.08, 0.29	−0.73, 0.51	−1.54 [−2.21, −0.88]	5.65
Migliorati et al. (2015), without CTG, distal	24	−0.18, 0.4	−0.24, 0.58	−0.12 [−0.70, 0.46]	5.79
Noelken et al. (2018), ABG	13	−1.8, 0.6	−0.8, 0.7	1.49 [0.56, 2.41]	5.19
Noelken et al. (2018), ABG + CTG	13	−2.3, 0.7	−0.3, 0.4	3.40 [2.08, 4.71]	4.41
Pieri et al. (2011), T: Platform switch abutment, mesial	18	0, 0	−0.61, 0.54	−1.56 [−2.34, −0.78]	5.46
Pieri et al. (2011), C: Conventional abutment, mesial	19	0, 0	−0.73, 0.52	−1.94 [−2.75, −1.14]	5.41
Puisys et al. (2022), mesial	25	0.2, 0.37	0, 0.1	−0.73 [−1.31, −0.14]	5.78
Spinato et al. (2012), Bone graft	22	−0.23, 0.53	−0.4, 0.6	−0.29 [−0.90, 0.31]	5.74
Spinato et al. (2012), No Bone graft	23	−0.15, 0.32	−0.3, 0.36	−0.43 [−1.03, 0.17]	5.76
Tian et al. (2019)	27	−0.26, 0.41	−0.24, 0.37	0.05 [−0.49, 0.59]	5.84
Tsuda et al. (2011), mesial	10	−2.2, 0.59	−2.25, 1.21	−0.05 [−0.98, 0.88]	5.18
Zuiderveld et al. (2018), T: with CTG, mesial	29	0.1, 0.9	0.1, 0.8	0.00 [−0.52, 0.52]	5.87
Zuiderveld et al. (2018), C: without CTG, mesial	29	−0.5, 1	−0.5, 1.1	0.00 [−0.52, 0.52]	5.87
Overall				−0.15 [−0.66, 0.36]	
$I^2 = 90.47\%$, $H^2 = 10.49$, $\tau^2 = 1.08$					

[a]Assuming a correlation of 0 between baseline and 12 month.

significantly more reproducible than the traditional implant crown aesthetic index.

This meta-analysis only included clinical studies with data available for esthetic outcome indices. Not all studies included baseline information; however, an effect size comparison was performed with Hedges' *g* and estimated a loss of papilla height (−0.71 mm) between baseline and 12 months, midfacial recession of −0.15 mm, and a gain of 0.82 in PES. The loss of papilla height and minor midfacial recession are influenced by the local alveolar anatomy following tooth extraction. Dimensional changes following tooth extraction can occur and have been described as the "bundle bone effect" (Araújo et al., 2005; Misawa et al., 2016). Ridge alteration and bone remodeling processes occur exactly in the first 12 months. However, there was an increase in PES, which may suggest that although these bone modifications occur, they are not clinically evident. Individual characteristics of each study were documented, and groups were created to measure the influence of treatment approaches within the esthetic outcome results. Data regarding flap versus no flap, type of implant (parallel-walled/tapered walled), implementation of a soft tissue procedure, and the implant connection were extracted. Today, the flapless approach is advantageous because it maintains the vascular supply to the peri-implant mucosa; however, flap use offers the possibility of implementing bone or contour augmentation procedures and provides better access. In the present investigation, the presence or absence of a flap, implementation of soft tissue procedures, and implant connection type had no influence on the result of the included esthetic outcome indices. Only the implant type had a statistically significant influence on WES, favoring a parallel-walled implant type.

Reduced treatment time and fewer dental appointments, no need for removable provisional prostheses, and patient expectations have encouraged the combined treatment of immediate implant insertion and loading in oral implantology. Future studies should be designed using validated and standardized esthetic indices assessed before treatment, immediately after completion of treatment, and repeated at regular follow-up intervals to accurately gauge the treatment outcome from an esthetic point of view and provide long-term success for patients.

Considering the limitations of the present review, the chosen languages were those that reviewers could speak, read, and write correctly. Although this could be a potential limitation, some authors have been suggested that the English language is sufficient for systematic reviews; nevertheless, the use of other languages may widen the scope of possible studies to be included (Morrison et al., 2012).

Another limitation was the present heterogeneity of different study types that were included (randomized and controlled clinical trials, cross-sectional studies, cohort studies, case–control studies, case series); therefore, a supplement analysis was performed only including RCT studies that have a lower risk of bias.

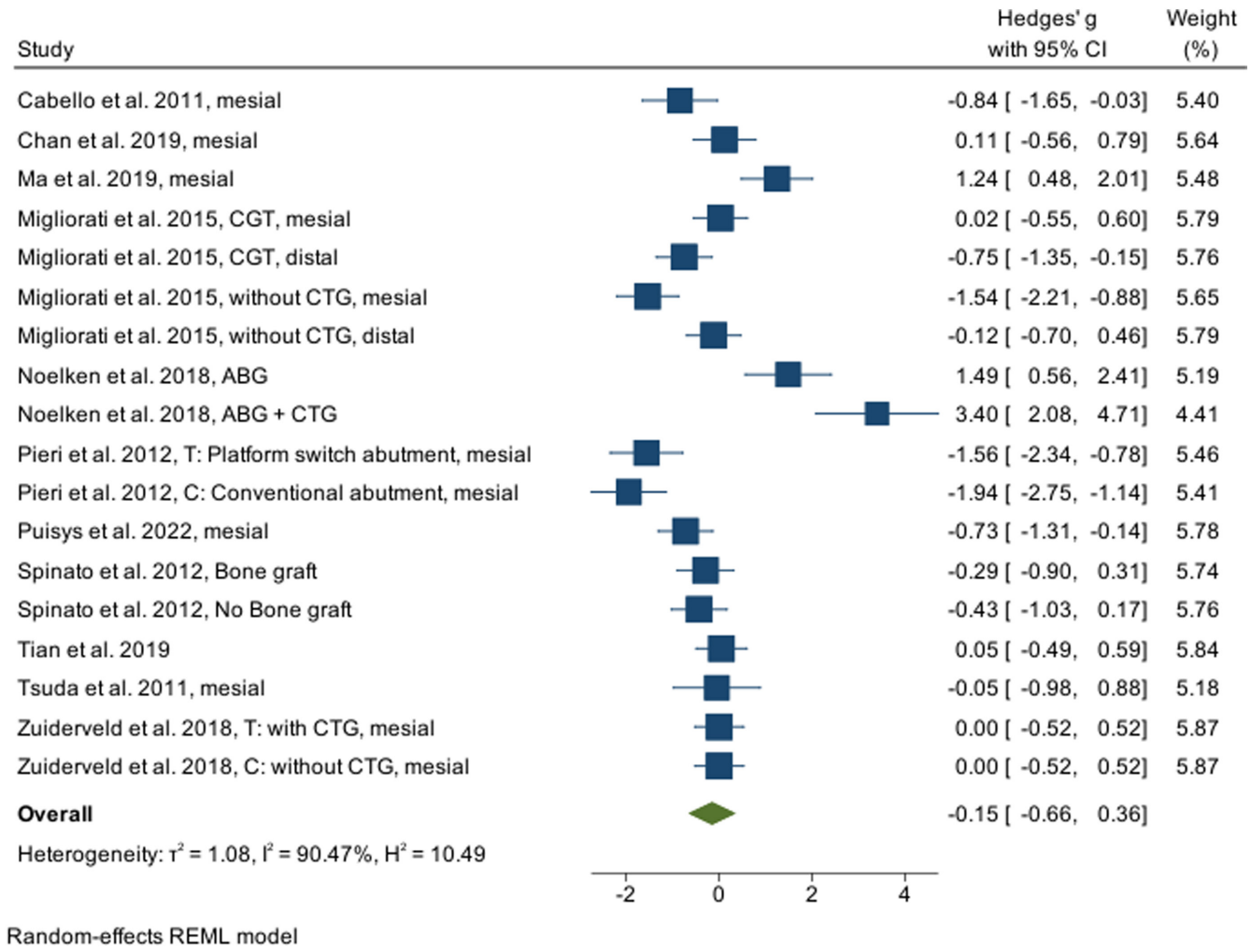


FIGURE 3 Forest plot: Midfacial – baseline and 12 month, random-effects model (REML).

TABLE 11C PES (%) – baseline and 12 month, Random-effects model (REML).

	Implants included	Baseline Mean, SD	12 month Mean, SD	Effect size[a] Hedges' *g* [95% CI]	Weight (%)
Bonnet et al. (2018)	39	56.5, 14.2	70.7, 13.3	1.02 [0.54, 1.50]	14.05
Cardaropoli et al. (2015), mesial	26	84.1, 8.9	81.8, 10.4	−0.23 [−0.79, 0.32]	13.33
Cardaropoli et al. (2019), mesial	20	87.5, 8.9	89.6, 7.1	0.26 [−0.38, 0.90]	12.54
D'Avenia et al. (2019), mesial	20	48.2, 12.5	63.6, 8.6	1.41 [0.69, 2.13]	11.78
Groenendijk et al. (2020)	98	70.5, 17.1	86.3, 11.7	1.07 [0.77, 1.38]	15.51
Noelken et al. (2018), ABG	13	73.6, 10.7	88.6, 8.6	1.50 [0.57, 2.42]	9.89
Noelken et al. (2018), ABG + CTG	13	62.1, 18.6	85.7, 6.4	1.64 [0.69, 2.59]	9.69
Puisys et al. (2022), mesial	25	88.6, 9.4	91.4, 8.5	0.31 [−0.26, 0.88]	13.21
Overall				0.82 [0.37, 1.28]	
I^2 = 79.93%, H^2 = 4.98, τ^2 = 0.33					

[a]Assuming a correlation of 0 between baseline and 12 month.

Although the data analysis was performed by time stratification considering the short-, medium- and long-term follow-up, it should be noted that the follow-up heterogeneity may limit the obtained results. These limitations should be considered when the results shall be applied for further subjects.

5 | CONCLUSION

Immediate implant placement and immediate loading in the maxillary esthetic zone presents excellent clinical performance by means of high survival rates for both implants and reconstructions, and

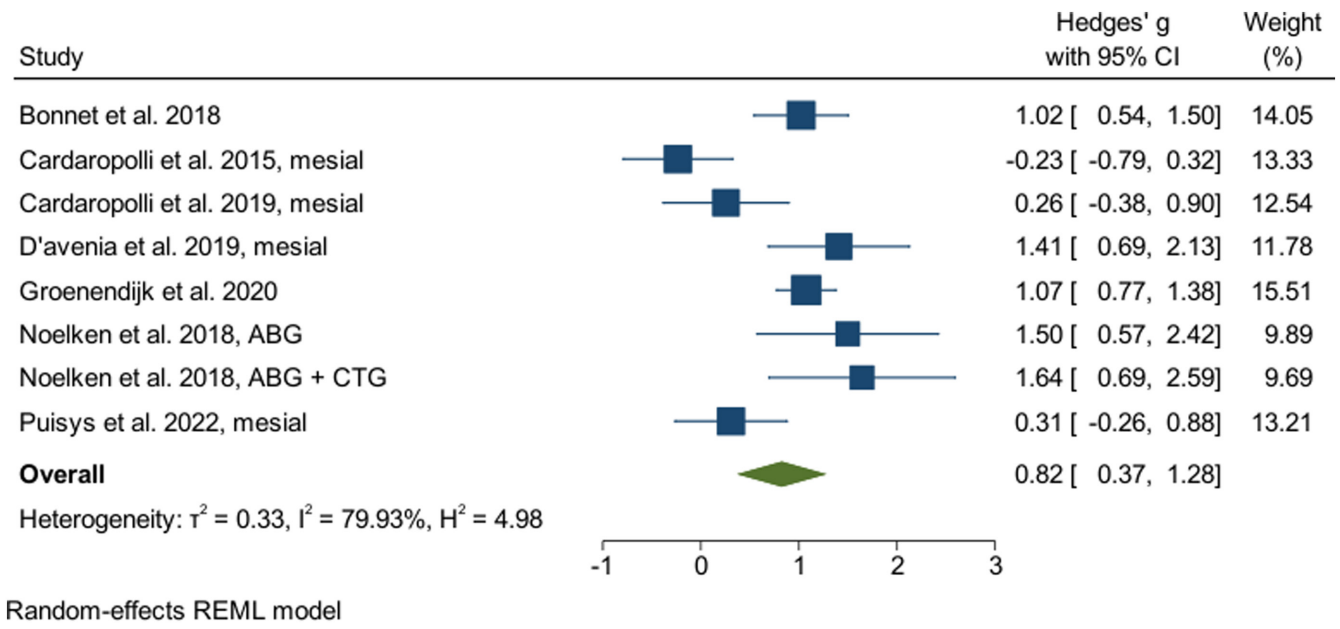


FIGURE 4 Forest plot: PES (%) – baseline and 12 month, random-effects model (REML).

TABLE 12 Esthetic outcomes – weighted mean scores in groups.

	Studies/Subgroup	Implants included	Weighted mean[a]	95% CI[a]	*p*-value[a]
Papilla (mm)					
Flap					
Flapless	9	182	−0.1	−0.6; 0.4	
Flap	3	94	−0.1	−3.9; 3.6	
Difference			−0.2	−0.8; 0.4	.494
Type of implant					
Parallel-walled	3	60	−0.1	−10.6; 10.4	
Tapered-walled	5	87	0.3	−0.5; 1.0	
Difference			−0.2	−1.1; 0.7	.601
Midfacial					
Type of implant					
Parallel-walled	3	54	−1.2	−14.1; 11.8	
Tapered-walled	7	139	−0.1	−0.4; 0.2	
Difference			0.6	−0.5; 1.7	.235
Soft tissue procedure					
No	7	168	−0.5	−1.2; 0.2	
Yes	5	101	−0.5	−1.8; 0.8	
Difference			0.0	−1.1; 1.1	.999
PES (%)					
Flap					
Flapless	23	697	76.2	70.5; 81.9	
Flap	8	219	80.0	70.3; 89.8	
Difference			2.9	−6.0; 11.8	.510
Type of implant					
Parallel-walled	11	293	80.3	75.6; 85.0	
Tapered-walled	11	361	73.3	63.8; 82.9	
Difference			−1.6	−6.4; 3.3	.507

TABLE 12 (Continued)

	Studies/Subgroup	Implants included	Weighted mean[a]	95% CI[a]	*p*-value[a]
Soft tissue procedure					
No	4	93	72.0	62.5; 81.6	
Yes	5	138	73.4	53.6; 93.2	
Difference			3.3	−11.8; 18.4	.610
Implant connection					
Internal hex	5	170	80.0	69.8; 90.3	
Conical hex	5	209	63.9	40.8; 87.0	
Difference			−6.8	−28.1; 14.5	.474
WES					
Flap					
Flapless	11	410	6.4	5.0; 7.9	
Flap	5	126	8.4	5.5; 11.3	
Difference			1.1	−0.8; 2.9	.230
Type of implant					
Parallel-walled	7	182	7.8	6.7; 8.9	
Tapered-walled	6	243	5.6	2.9; 8.3	
Difference			−1.8	−3.6; −0.0	.049
Implant connection					
Internal hex	4	144	7.6	4.7; 10.5	
Conical hex	3	139	4.5	1.8; 7.3	
Difference			−1.2	−6.1; 3.8	.548

[a]Meta-analysis regression adjusted for time, Random-effects model (REML).

therefore it can be concluded as a viable treatment option under specific conditions. These conditions are healthy adjacent teeth, intact facial bone, no acute infection present, ability to place the implant in the correct 3-dimensional position for an optimal restoration, and anticipated primary stability of the implant to allow immediate restoration.

Another conclusion was that esthetic outcome measured by individual parameters resumed stable results over time.

AUTHOR CONTRIBUTIONS

Julia-Gabriela Wittneben, Pedro Molinero-Mourelle and Adam Hamilton were involved in the concept and design of the study, data collection, analyzed and interpreted data, drafted the article and approved the final version of the manuscript; Barbara Obermaier and Muhsen Alnasser were involved in the data collection and approved the final version. Dean Morton, German O. Gallucci and Daniel Wismeijer were involved in the concept and design of the study, data analysis, critical revision of the manuscript and approved the final version.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

None declared.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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REVIEW ARTICLE

CLINICAL ORAL IMPLANTS RESEARCH WILEY

Selection criteria for immediate implant placement and immediate loading for single tooth replacement in the maxillary esthetic zone: A systematic review and meta-analysis

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Abstract

Objectives: The aim of this study was to review available evidence for Type 1A (immediate implant placement and immediate loading) of single tooth replacement in the maxillary esthetic zone.

Materials and Methods: An electronic search was conducted utilizing the databases of MEDLINE, Embase, and Cochrane to identify publications reporting on the outcomes of Type 1A for single tooth replacement in the maxillary esthetic zone. The success and survival rates of the included articles were reported, which were further categorized according to the clinical criteria reported in Type 1A. Mean survival rates were univariately compared between risk groups and additionally between studies published before and since 2012 using bias-corrected and study size-weighed bootstrap tests. A study time-correcting meta-analysis was then performed to obtain an overall effect for the study pool.

Results: A total of 3118 publications were identified in the search, with a total of 68 articles included. A mean number of implants per study were 37.2 and mean follow-up was 2.8 years. All the included studies utilizing Type 1A report highly selective inclusion and exclusion criteria. Univariate risk group comparison determined that studies before 2012 report a significantly lower mean survival rate (difference of −1.9 percentage points [PP], 95% CI: [−0.3, −4.0], $p = .02$), facial gap dimension had an impact on survival rates (+3.1 PP [0.2, 5.3] for width >2 mm, $p = .04$), as well as presence of endodontic infection (+2.6 PP [0.9, 5.1], $p = .004$).

Conclusions: Type 1A has a high survival rate in studies reporting strict patient and site selection criteria. Further research is required to assess esthetic and functional success with Type 1A treatments.

KEYWORDS
dental implants, immediate dental implant loading, immediate dental implant placement, meta-analysis, systematic review

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1 | INTRODUCTION

The use of dental implants for the replacement of missing or failing teeth in partially edentulous patients has been shown to be a clinically predictable option (Jung et al., 2012). Original protocols recommended the placement of dental implants in healed alveolar ridges coupled with long healing periods prior to restoration and loading of the dental implant (Albrektsson et al., 1981). The current body of evidence provides encouraging data on the placement of implants at the time of tooth extraction and, in some situations, in conjunction with the connection of an immediately delivered implant-supported prosthesis (Buser et al., 2017; Gallucci et al., 2018; Kan et al., 2018; Seyssens et al., 2021, 2022; Zhou et al., 2021).

Dating back to 2003, the International Team for Implantology (ITI) has periodically revisited the classification for timing of implant placement and loading protocols (Chen et al., 2004; Chen & Buser, 2009; Hämmerle et al., 2004) in preparation for their consensus conferences. In the most recent consensus conference, a systematic review highlighted the connection and inseparability of outcomes with regard to implant placement and loading protocols (Gallucci et al., 2018). With this, Type 1A implant protocols are defined as immediate placement of an implant on the same day of tooth extraction and immediate restoration/loading on the same day or up to 1 week following implant placement (Gallucci et al., 2018).

Immediate placement and loading of an implant are most desirable as it has significant patient-centered advantages in reducing the overall treatment time as well as reducing the number of interventions and associated morbidity (Chen & Buser, 2009; Cosyn et al., 2019; Noelken et al., 2014; Slagter et al., 2014). Furthermore, it may assist in preserving the hard and soft tissue morphology through the use of a provisional restoration, aiding in achieving an ideal esthetic outcome (De Rouck et al., 2009; Kan et al., 2018; Kan & Rungcharassaeng, 2001; Puisys et al., 2022; Zhou et al., 2021).

However, Type 1A protocols can be challenging due to the complexity and technique sensitivity of the surgical procedures (Cosyn et al., 2019; Levine et al., 2017; Morton et al., 2018). There is evidence that shows there is a higher risk for early implant loss when an implant is immediately loaded (Schrott et al., 2014). It is common to find suggestions in the literature of factors that would contraindicate using Type 1A protocols, such as the presence of an active infection, soft tissue defects, thin tissue phenotype, lack of the socket's facial bone wall following extraction, and the absence of a facial gap between the implant and facial bone wall often known as the horizontal defect dimension (HDD; Araújo et al., 2022; Cochran & Douglas, 1993; Levine et al., 2022). Additionally, inferior outcomes related to the clinical, radiographic, and esthetic results can be obtained when those factors are present at the implant site (Chen et al., 2019; Cosyn et al., 2019; Sanz-Sánchez et al., 2015; Zhang et al., 2017).

Due to the available evidence from systematic reviews reporting on the success of Type 1A implant protocols, conservative criteria for their predictable implementation of Type 1A protocols were recommended (Morton et al., 2018). When following the recommended criteria, very few patients and sites would be classified as suitable, therefore alternative protocols would be indicated. The scientific evidence to support such criteria requires periodic review to provide guidelines in managing sites that may present compromises in any of the individual criteria. It has also been reported that adjunctive procedures such as simultaneous socket grafting and/or connective tissue grafting in conjunction with Type 1A implant protocols could mitigate the associated esthetic risks following tooth extraction, however, these procedures carry their own inherent technical challenges (Araújo et al., 2022; Seyssens et al., 2021, 2022).

The complexity of treatment increases with the added risks associated with immediate loading; therefore, it is generally recommended to select this protocol only when patient-centered benefits are present (Morton et al., 2018). This is supported by the majority of literature that focuses on Type 1A protocols reported on implants placed in the anterior maxilla (Zhou et al., 2021). This has patient-centered advantages in addressing the psychosocial and esthetic effects of having a missing tooth in the esthetic zone (Gotfredsen et al., 2021; Huynh-Ba et al., 2018).

Despite the significant volume of literature addressing immediate implant placement and immediate loading, the survival rate of Type 1A protocols with regard to the characteristics of the patients and sites where the implant was placed and loaded has not been systematically reviewed. This systematic review aims to identify, review, analyze, and summarize the available evidence on the survival rate of immediate loading of an immediately placed implant in the maxillary esthetic zone. Furthermore, two approaches are shown and discussed on how to assess survival rates based on studies with different study duration. The null hypothesis for this study is that the patient and site selection criteria do not influence the overall survival rate of Type 1A implant protocols.

2 | MATERIALS AND METHODS

This systematic review was conducted following PRISMA (Preferred Reporting for Systematic Reviews and Meta-Analyses) guidelines (Liberati et al., 2009; Page et al., 2021). The study was registered with the International Prospective Register of Systematic Reviews (PROSPERO) database (CRD42021292749).

2.1 | Focus question

To identify studies for this review, the PICO question (population, intervention, comparison, and outcome) was formulated with patients who require replacement of a single tooth in the anterior maxilla (15–25 FDI) as the population; immediate implant placement and immediate loading with specific site selection criteria, such as intact socket walls, facial bone of at least 1 mm in thickness, no acute infection at the site, the availability of at least 3 mm of bone apical and lingual to the socket to provide primary stability, at least 35 Ncm insertion torque, and/or ISQ of 70; thick soft tissue phenotype as

the intervention; immediate implant placement and immediate loading without one or more site-specific factors for selection criteria as the comparison; and survival rate as the outcome. Thus, the PICO question was formulated: "In patients who require replacement of a single tooth in the anterior maxilla (15–25), does specific site selection criteria influence the survival outcome of an immediate implant placed with immediate loading?" The following sections provide a concise description of the specific methodological aspects of the study.

2.2 | Search strategy

The search strategy was developed using keywords and Mesh terms (Table 1). The electronic search was conducted utilizing the databases MEDLINE (PubMed), Embase, and Cochrane to identify publications in English up to January 14th, 2022. Due to the specificity of the PICO regarding the site selection, a comprehensive search strategy was formulated encompassing a complete list of articles for manual screening.

TABLE 1 Systematic search strategy for the focus question.

Focused question	**Does the site selection influence the outcome of an immediate implant placed with immediate loading?**	
PICO	Population	Patients who require replacement of a single tooth in the anterior maxilla 15–25 (FDI)
	Intervention	Immediate implant placement and immediate loading of single implant restorations using modern dental implants with a micro-rough surface with specific site selection criteria, including: • Intact socket walls; • Facial bone of at least 1 mm in thickness; • No acute infection at the site; • The availability of at least 3 mm of bone apical and lingual to the socket to provide primary stability; • At least 35 Ncm insertion torque and/or ISQ of 70; and • Thick soft tissue phenotype
	Comparison	Immediate implant placement and immediate loading of single implant restorations using modern dental implants with a micro-rough surface without one or more site-specific factors in the selection criteria
	Outcome	Evaluate the implants after a minimum follow-up of 12 months regarding: • Proportion of procedures that are executed successfully on selected patients vs. those that are moved to an alternate implant placement/loading protocol; • Survival of implants/ implant-supported crowns; and • Criteria influencing the survival/success of implants placed immediately and loaded immediately
Search Strategy	PubMed	(dental implantation, endosseous[MeSH] OR dental implants[MeSH] OR implantation OR implant OR implants) AND (dental prostheses, implant supported[MeSH] OR crown OR single crown OR single unit) AND (immediate implant OR immediate implantation OR immediate implant placement OR immediate placement OR immediate OR fresh extraction sockets OR immediate extraction sockets) AND (immediate dental implant loading[MeSH] OR immediate) AND (English[Language])
	Embase	("dental implantation, endosseous"/exp OR "dental implantation, endosseous" OR (("dental"/exp OR dental) AND ("implantation,"/exp OR implantation,) AND endosseous AND ("mesh"/exp OR mesh)) OR "dental implants"/exp OR "dental implants" OR (("dental"/exp OR dental) AND ("implants"/exp OR implants) AND ("mesh"/exp OR mesh)) OR "implantation"/exp OR implantation OR "implant"/exp OR implant OR "implants"/exp OR implants) AND ("dental prostheses, implant supported" OR (("dental"/exp OR dental) AND ("prostheses,"/exp OR prostheses,) AND ("implant"/exp OR implant) AND supported AND ("mesh"/exp OR mesh)) OR "crown"/exp OR crown OR "single crown" OR (single AND ("crown"/exp OR crown)) OR "single unit" OR (single AND ("unit"/exp OR unit))) AND ("immediate implant" OR (immediate AND ("implant"/exp OR implant)) OR "immediate implantation" OR (immediate AND ("implantation"/exp OR implantation)) OR "immediate implant placement" OR (immediate AND ("implant"/exp OR implant) AND placement) OR "immediate placement" OR (immediate AND placement) OR immediate OR "fresh extraction sockets" OR (fresh AND ("extraction"/exp OR extraction) AND sockets) OR "immediate extraction sockets" OR (immediate AND ("extraction"/exp OR extraction) AND sockets)) AND ("immediate dental implant loading"/exp OR "immediate dental implant loading" OR (immediate AND ("dental"/exp OR dental) AND ("implant"/exp OR implant) AND ("loading"/exp OR loading) AND ("mesh"/exp OR mesh)) OR immediate) AND ("English"/exp OR English) AND ("language"/exp OR language)
	Cochrane	(dental implantation, endosseous[MeSH] OR dental implants[MeSH] OR implantation OR implant OR implants) AND (dental prostheses, implant supported[MeSH] OR crown OR single crown OR single unit) AND (immediate implant OR immediate implantation OR immediate implant placement OR immediate placement OR immediate OR fresh extraction sockets OR immediate extraction sockets) AND (immediate dental implant loading[MeSH] OR immediate) AND (English[Language])
Database Search	MEDLINE (PubMed), Embase, and Cochrane	

Reference lists of the studies that had been included by the electronic search were screened and checked for cross-references. An attempt was made to identify gray literature by searching through the database of the U.S. National Library of Medicine (www.clinicaltrials.gov). In addition, the following journals were hand searched up to January 2022: Clinical Implant Dentistry and Related Research, Clinical Oral Implants Research, Clinical Oral Investigations, International Journal of Oral & Maxillofacial Implants, International Journal of Oral & Maxillofacial Surgery, Journal of Clinical Periodontology, and the Journal of Periodontology.

The search results were exported and imported on Covidence (Melbourne, Australia), a systematic review management, to organize and evaluate the papers.

2.3 | Selection criteria

All types of study designs were included, provided they met the following criteria:
Inclusion criteria:

- Studies on humans;
- At least 10 participants;
- Studies that report immediate implant placement with immediate loading (Type 1A);
- Modern, rough surface implants;
- Single implants placed in the esthetic zone, from 15 to 25 (FDI);
- Implant survival rate and Number of implant failures reported; and
- Minimal follow-up evaluation of 12 months.

Exclusion criteria:

- Animal or in-vitro studies;
- Studies using zirconia implants;
- Review articles;
- Implants with machine surfaces or hydroxyapatite (HA) coatings;
- Implant supporting fixed or removable, partial or full-arch reconstructions with multiple implants;
- Insufficient information on defined outcome criteria;
- Studies that did not report on both the implant placement and implant loading protocols;
- Implant placement and loading protocols other than Type 1A immediate implant placement and immediate loading;
- Studies containing data on several implant placement and loading protocols where the data on Type 1A was not able to be clearly separated;
- Studies with less than 12-month follow-up period; and
- Multiple publications on the same patient population.

Furthermore, only the study with the most extended follow-up was included in multiple publications with the same study population. However, previous studies were consulted only to retrieve information not provided in the most recent publication.

2.4 | Screening of studies and data collection

After duplicate records exclusion, two reviewers (L.H.G. and K.P.A.) independently screened the title and abstract to the outcomes. Then, the full texts were screened for meeting the inclusion criteria. Disagreements were resolved by discussion between reviewers and consultation with a third reviewer (A.H.) when required.

Data were extracted manually independently by the three reviewers (L.H.G., K.P.A., and A.H.) from the included studies and recorded on standardized forms. The following information was collected for further analysis:

- Author(s), year of publication, and study designs: randomized/nonrandomized controlled trial, retrospective study, case series, and experimental study;
- Number of implants and location;
- Follow-up in months;
- Survival rate, success rate, and patient dropout(s)/number of implant failures;
- Implant brand, implant dimensions, implant lengths, and implant design; and
- Inclusion and procedural criteria reported for Type 1A protocols.

Included studies were analyzed according to the risk assessment Tables 2 and 3 for Type 1A immediate implant placement and immediate restoration/loading in single tooth sites (Lambert et al., 2023); the selection criteria of each study were assessed regarding low-, medium-, or high-risk inclusions.

Data on noncompliance to the planned Type 1A treatment protocol were identified in prospective studies to perform an intention-to-treat analysis, which for the purpose of this review described the number of sites that were selected and/or included for Type 1A treatment that were not able to be completed as planned. The reasons for deviation from the originally planned treatment protocol were also collated.

2.5 | Quality assessment

The quality assessment of all the included studies was analyzed by two reviewers (L.H.G. and K.P.A.). The risk of bias was assessed in randomized controlled trials (RCT) using the Cochrane quality assessment tool RoB2 (Higgins et al., 2022; Sterne et al., 2019). For nonrandomized studies, the Newcastle–Ottawa Assessment Scale (http://www.ohri.ca/pro-grams/clinical_epidemiology/oxford.asp) was applied to evaluate the selection of the study groups, the comparability of the groups, and the ascertainment of the outcome of interest converting the Newcastle–Ottawa scales to Agency for

TABLE 2 Risk assessment for immediate implant placement in single tooth sites (Lambert et al., 2023).

	Low risk	Medium risk	High risk
Preoperative assessment			
Patient related			
Medical Status	Healthy, Uneventful healing		Compromised healing
Esthetic risk	Low/Medium esthetic risk	High esthetic risk	Significant esthetic compromise expected
Site related			
Gingival margin position	Absence of recession	Minor Gingival recession	Gingival recession ≥2 mm
Soft tissue quality	Thick gingival phenotype	Thin gingival phenotype or limited keratinized gingivae	Absence of keratinized gingivae
Bone anchorage	Sufficient bone anchorage to achieve primary stability		Lack of bone anchorage to achieve primary stability
Facial bone wall	≥1 mm facial bone thickness	Facial bone plate <1 mm thickness, or small fenestration or dehiscence defect	Significant fenestration or dehiscence of facial bone
Mucoperiosteal Flap	Sufficient alveolar bone for a flapless approach		Need for a flapped bone augmentation procedure
Socket position within alveolar envelope	Socket within the alveolar bone envelope		Socket and facial bone wall protruding out of the bone envelope
Presence of endodontic infection	Absence of infection	Chronic peri-apical infection	Acute infection
Presence of periodontal disease	Periodontally healthy	Controlled periodontal disease	Active periodontal disease
Planning Implant position	Ideal three-dimensional position with axis exiting through the cingulum or incisal edge		Facially positioned or over-angulated implant or excessive implant depth
Gap between facial bone and planned implant position	>2 mm	1–2 mm	<1 mm
Intra-operative assessment			
Extraction	Minimally invasive tooth extraction	Damage to surrounding soft tissue including severed/detached papillae	Significant damage to soft tissue and surrounding bone
Primary Implant Stability	Primary stability achieved		Lack of primary stability
Final implant position	Ideal three-dimensional position achieved		Facially positioned or over-angulated implant or excessive implant depth

Healthcare Research and Quality (AHRQ) standards (good, fair, and poor).

2.6 | Statistical analysis

Cohen's kappa statistical analysis was performed to assess the level of agreement between the reviewers in the article screening process. Descriptive statistics such as mean and standard deviation (continuous data), percentages (count data), and data range were used to summarize demographics, number of implants, survival rates, success rates, study duration, failure time, and study dropouts.

2.6.1 | Main analysis

Survival rates were compared by inclusion criteria groups formed after the risk assessment. For interpretation of survival rates, one must always consider (average) study duration and study size, therefore the statistical assessment was done in two steps. First, mean survival rates and average study duration (both weighed by study sizes) were univariately compared between risk groups and additionally between studies published before and since 2012. As the distribution of the survival rates was skewed, non-normal, and with a lot of identical values (many having 100%), *p*-values for both survival rates and average study duration comparisons were calculated with the

TABLE 3 Risk assessment for immediate loading of an immediately placed single implant (Lambert et al., 2023).

	Low risk	Medium risk	High risk
Preoperative assessment			
Patient related			
Occlusal Scheme	No direct occlusal contacts	Minimal occlusal contact and/or shared guidance	Main determinant of anterior guidance
Occlusal Parafunction	Absent		Present
Site related			
Bone anchorage	Sufficient bone anchorage to resist loading forces		Insufficient bone anchorage to resist loading forces
Tooth Position	Incisor and premolars	Canine	Molars
Intra-operative assessment			
Primary Implant Stability	30–45 Ncm insertion torque	20–30 Ncm insertion torque	<20 Ncm insertion torque

help of bias-corrected and study size-weighed Bootstrap tests (Efron & Tibshirani, 1994) and presented with bias-corrected and study size-weighed bootstrap confidence intervals. In a second step, survival rates within the first 6 months, labeled as "early survival rates," were assessed using the very same techniques as from the first step and then compared to the previously obtained results. Roughly 90% of all implant losses occurred within the first 6 months so the results regarding early and overall survival rates should be comparable. Note that due to a non-negligible degree of missing observations, inclusion criteria could only be assessed in a univariate context.

2.6.2 | Secondary analysis

Survival rates were transformed in order to obtain comparable measures over time (i.e., study duration) and a meta-analysis was then performed to obtain an overall effect for the study pool. For the transformation of survival rates, an approach from epidemiology was used: For each study, incidence and survival rates, I_Y and S_Y, per observed implant-year were calculated as follows:

$$\text{Incidence rate per observed implant year} = I_Y = \frac{\text{Number of observed losses}}{\text{Total observed years in situ, all Impl.}}$$

$$\text{Survival rate per observed implant year} = S_Y = 1 - I_Y$$

For example, study A observing 10 implants with an average study time of 10 years, reported 1 loss after 9 years, that is, with reported survival of 90%, has an I_Y of 1/99 ≈ 1% (1 loss and 9 implants were observed 10 years in situ, and 1 was observed 9 years in situ), and thus an S_Y of ≈99%. Note that this approach is more accurate than simply reweighing raw survival rates by the product of implant x average study duration as the latter approach would put on par study A to a study B that observed 100 implants 1 year long with 10 losses (which would be clinically unacceptable). Observed implant-years had to be estimated by considering study dropouts and late implant losses (6+ months). If the timepoint of a loss or a dropout was unknown, it was assumed to have happened in the middle of the study duration.

Following the hands-on guide for meta-analysis (Harrer et al., 2021) and the suggestions from Spittal et al. (2015) to account for excessive zeros, a Poisson random-effects meta-analysis was used to systematically assess the transformed I_Y (and thus, S_Y) from all 68 studies. Notice that in order to obtain a better model fit, incidence rates were first logarithmized (using a continuity correction) and the resulting means and confidence intervals were re-transformed to the original scale. The Knapp–Hartung correction (Knapp & Hartung, 2003) was further applied to correct potential biases from small-sample studies. Mean S_Y as obtained from meta-analysis is then graphically presented along with its 95% confidence interval. In addition, a 95% prediction interval for the survival rate per observed implant-year of a single study is drawn. Between-study heterogeneity is then assessed using Higgins & Thompsons' I^2 statistic (Higgins & Thompson, 2002). An I^2 of 50%, for example, means that 50% of the total variance is caused by study heterogeneity. If all studies were comparable (and thus exchangeable), one would expect an I^2 of 0%.

An exact binomial test was used to assess the proportion of early and late failures.

All analyses in this report were performed with the statistics software R, version 4.0.2 (R Development Core Team, 2020). Throughout, *p*-values less than .05 were considered statistically significant. No correction for multiple comparisons was applied.

3 | RESULTS

3.1 | Study collection and study descriptives

A total number of 3118 publications were identified by the search. Following the title screening, 606 abstracts and 241 full-text articles were evaluated for inclusion (Figure 1). A Kappa score of 0.63 was obtained for eligibility assessment of full-text articles, which indicates a substantial interrater agreement. A total of 173 articles were excluded from the full-text screening for not meeting the inclusion criteria, with the reasons for exclusion listed in Table 4. A total of 68 articles were included for data extraction

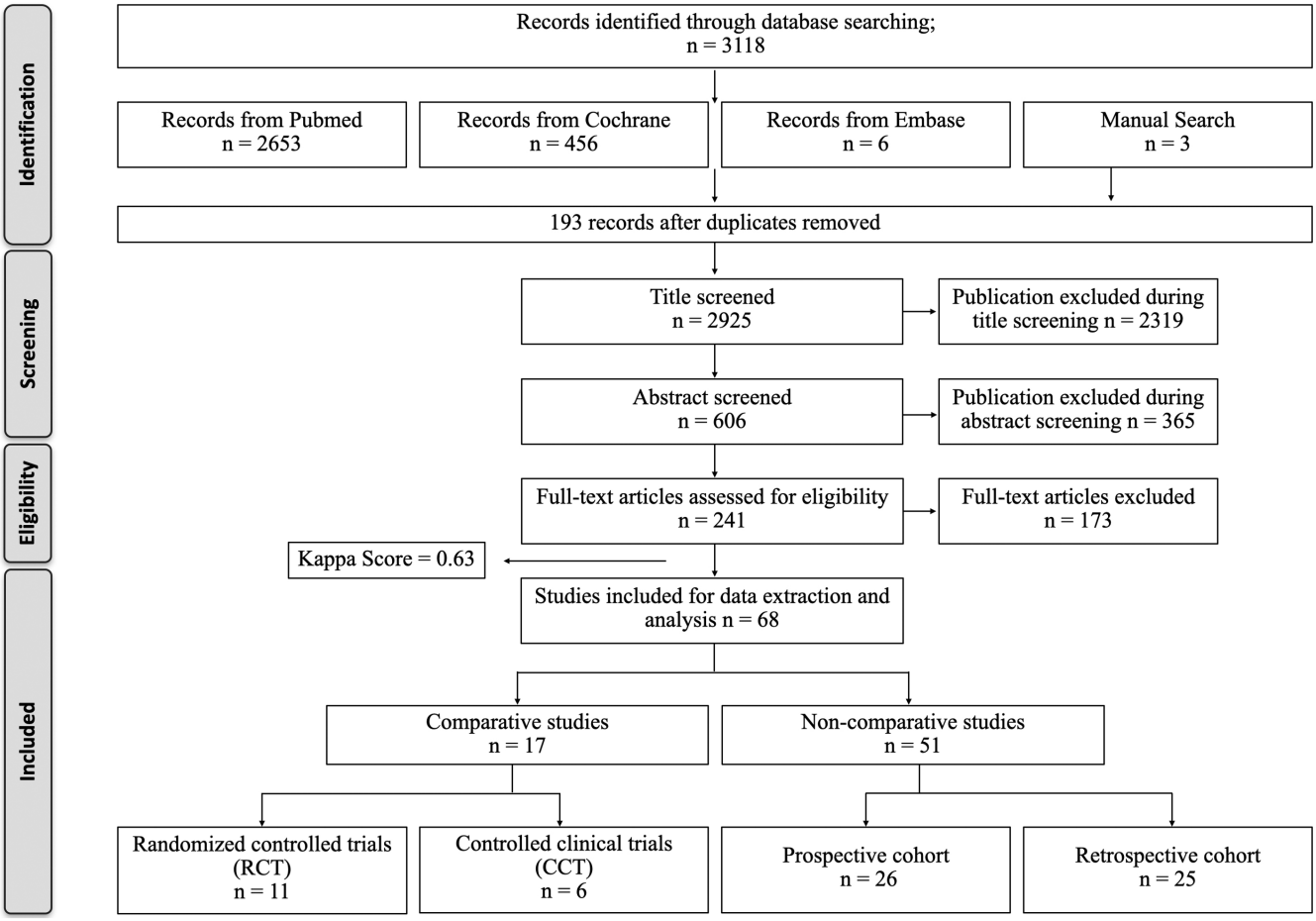


FIGURE 1 Search results and screening.

which comprised 11 randomized control trials (RCTs), six controlled clinical trials (CCTs), 26 prospective cohort studies, and 25 retrospective cohort studies.

The main characteristics of the included studies are reported in Table 5. Mean number of implants per study were 37.2 (SD: 22.9) and mean follow-up time was 2.8 years (SD: 2.3). Fifty-three implant failures were reported leading to survival rates ranging from 86.7% to 100% and 23 of the included 68 studies reported success rates ranging from 88.0% to 100%. Regarding the time of implant loss, the failure time is reported in 67 of 68 papers: From a total of 49 reported losses with known failure time, 43 (87.8%) are early losses compared to 6 losses later than 6 months (12.2%) (significantly more early failures, $p < .0001$). One paper reported four losses without further information regarding failure time. Dropout rates were reported in 25 papers ranging from 0% to 41.8%.

3.2 | Main analysis: Comparison of survival rates

The estimated weighed mean overall survival rate for implants placed with a Type 1A protocol is 97.7% (95% CI: 96.9%–98.4%) and weighed mean early survival rate is slightly higher with 98.3% (95% CI: 97.6%–98.8%), see Table 6.

Table 6 also presents the results of the univariate comparisons of inclusion criteria groups regarding survival rates, average study durations, and early survival rates.

Gap dimension showed a statistically significant impact on survival rates as weighed group means significantly differed: 95.9% of implants survived for gaps smaller than 2 mm versus 99.0% for gaps more than 2 mm ($p = .04$). Weighed early survival rates also statistically significantly differed (96.5% vs. 99.2%, $p = .04$) and weighed average study duration was comparable (2.5 years vs. 2.6 years, $p = .85$). The second significant impact was found for publication year: Before 2012 weighed mean survival rate was 96.3%, and since 2012, it raised to 98.2% ($p = .02$), even though publications from 2012 or later reported significantly larger study durations (2.9 years vs. 2.0 years before 2012, $p = .005$). Similar results were found regarding early mean survival rates (97.2% pre-2012 vs. 98.6% 2012 and later, $p = .04$). This might be an indicator that surgeons are getting more experienced with immediate implant placement over time, together with advances in implant technology, materials, surfaces, and surgical techniques. Studies including smokers had unexpectedly higher weighed mean survival rates than those excluding

TABLE 4 Full-text articles excluded.

Exclusion reason	Number of articles	References
Wrong study design	2	Brignardello-Petersen (2017)—review Locante (2001)—technique
Less than 1-year follow-up	11	Bavetta et al. (2019), Bell and Bell (2014), Calvo Guirado et al. (2007), Chu et al. (2020), Felice et al. (2011), Hui et al. (2001), Kotb et al. (2020), Rungcharassaeng et al. (2012), Saito et al. (2016), van Kesteren et al. (2010), Yoo et al. (2006)
Less than 10 sites	8	Carini et al. (2014), Crespi et al. (2007), Crespi et al. (2019), Juodzbalys and Wang (2010), Lorenzoni et al. (2003), Palattella et al. (2008), Peron and Romanos (2020), Shibly, Kutkut, and Albandar (2012)
Not single crowns	6	Anitua et al. (2016), Crespi et al. (2010b), Crespi et al. (2012), Degidi and Piattelli (2005), Miyamoto and Obama (2011), Nikellis et al. (2004)
Not separated Type 1a	14	Berberi (2021), Berberi, Tehini, et al. (2014), Boardman et al. (2016), Cannizzaro et al. (2016), Crespi et al. (2009), Esposito et al. (2015), Guarnieri et al. (2020), Locante (2004), Milillo et al. (2016), Norton (2004), Petrungaro (2017), Pozzi et al. (2015), Raes, Cosyn, et al. (2018), Testori et al. (2007)
Not separated sites(anterior/posterior/maxilla/mandible)	59	Aguirre-Zorzano et al. (2011), Amato et al. (2020), Amato et al. (2018), Avvanzo et al. (2009), Barone et al. (2016), Barone et al. (2006), Barone et al. (2015), Becker et al. (2011), Block et al. (2004), Blus and Szmukler-Moncler (2010), Chaushu et al. (2001), Clauser et al. (2020), Cornelini et al. (2008), Cornelini et al. (2005), Covani et al. (2004), Crespi et al. (2010a), de Carvalho et al. (2013), Degidi et al. (2008), Drago and Lazzara (2004), El-Chaar (2011), Ferrantino et al. (2021), Galli et al. (2008), Givens Jr. et al. (2015), Glauser et al. (2004), Grandi, Garuti, Guazzi, et al. (2012), Grandi et al. (2014), Grandi et al. (2015), Grunder et al. (1999), Horwitz et al. (2008), Hosseini et al. (2015), Hruska et al. (2002), Kniha et al. (2017), Kolinski et al. (2014), Kopp et al. (2013), Laviv et al. (2010), Levin (2011), Levin and Wilk (2013), Luongo et al. (2014), Malchiodi et al. (2010), Malchiodi et al. (2011), Maló et al. (2015), Meltzer (2012), Mura (2012), Noelken, Moergel, Kunkel, et al. (2018), Noelken et al. (2007), Noelken et al. (2014), Peñarrocha-Diago et al. (2012), Peron and Romanos (2016), Pozzi et al. (2021), Schwartz-Arad et al. (2007), Shibly, Kutkut, Patel, and Albandar (2012), Shibly et al. (2010), Siebers et al. (2010), Siormpas et al. (2014), Soardi et al. (2012), Vanden Bogaerde et al. (2005), Velasco-Ortega et al. (2018), Zafiropoulos et al. (2010), Zembić et al. (2012)
Immediate placement but not immediate loading	22	Arora and Ivanovski (2018b), Aslroosta et al. (2021), Benic et al. (2012), Bianchi and Sanfilippo (2004), Bilhan et al. (2011), Cecchinato et al. (2015), Covani et al. (2012), Evans and Chen (2008), Felice et al. (2015), Fugazzotto (2012), Garcia-Sanchez et al. (2021), Guarnieri et al. (2015), Heinemann et al. (2013), Hof et al. (2015), Jung et al. (2013), Koh et al. (2011), Lee et al. (2012), Malchiodi et al. (2016), Polizzi et al. (2000), Shi et al. (2020), Tadi et al. (2014), Wagenberg et al. (2013)
Immediate loading but not immediate placement	27	Anitua et al. (2008), Boedeker et al. (2011), Donos et al. (2019), Ericsson et al. (2000), Glibert et al. (2016), Hall et al. (2006), Kim et al. (2015), Lang et al. (2014), Lindeboom et al. (2006), Maló et al. (2003), Meizi et al. (2014), Mertens and Steveling (2011), Nissan et al. (2008), Ostman et al. (2010), Parel and Schow (2005), Proussaefs et al. (2002), Proussaefs and Lozada (2004), Rai et al. (2020), Rizkallah et al. (2013), Ryser et al. (2005), Sarnowski and Paul (2012), Simmons et al. (2016), Stacchi et al. (2018), Stanley et al. (2017), Vandeweghe et al. (2012), Vandeweghe et al. (2013), Vervaeke et al. (2013)
Survival rate not reported	4	Fürhauser et al. (2017), Groenendijk et al. (2021), Mangano et al. (2016), Roe et al. (2012)
Longer follow-up reported in a subsequently included publication	12	Brown and Payne (2011), Chan et al. (2019), Cooper et al. (2010), Cosyn et al. (2013), De Bruyn et al. (2013), De Rouck et al. (2008), De Rouck et al. (2009), Kan et al. (2003), Mijiritsky et al. (2009), Raes et al. (2011), Raes et al. (2012), Slagter et al. (2017)
Multiple publications with the same patient data	7	Canullo, Iurlaro, and Iannello (2009), Chu et al. (2018), Chu et al. (2015), Hartlev et al. (2014), Kolerman, Nissan, Mijiritsky, et al. (2016), van Nimwegen et al. (2018), Wang et al. (2020)
Socket shield technique	1	Hinze et al. (2018)
Included	68	Aguilar-Salvatierra et al. (2016), Arora and Ivanovski (2018a), Berberi, Noujeim, et al. (2014), Berberi, Sabbagh, et al. (2014), Bittner et al. (2020), Block et al. (2009), Bonnet et al. (2018), Bruno et al. (2014), Bushahri et al. (2021), Cabello et al. (2013), Calvo-Guirado et al. (2015), Calvo-Guirado et al. (2009), Canullo et al. (2010), Canullo, Goglia, et al. (2009), Canullo and Rasperini (2007), Cardaropoli et al. (2019), Cardaropoli et al. (2015), Cooper et al. (2014), Cosyn et al. (2011), Cosyn et al. (2016), Crespi et al. (2008), Cristalli et al. (2015), Degidi et al. (2013), Degidi et al. (2014), Di Alberti et al. (2012), Ferrara et al. (2006), Ganeles et al. (2017), Grandi, Garuti, Samarani, et al. (2012), Grandi et al. (2013), Groenendijk et al. (2020), Groenendijk et al. (2017), Groisman et al. (2003), Hartlev et al. (2013), Kan et al. (2011), Khzam et al. (2014), Kolerman, Nissan, Rahmanov, et al. (2016), Lombardo et al. (2016), Ma et al. (2019), Malchiodi et al. (2013), Mangano et al. (2012), Mangano et al. (2013), McAllister et al. (2012), Menchini-Fabris et al. (2019), Migliorati et al. (2015), Mijiritsky et al. (2021), Noelken et al. (2011), Noelken, Moergel, Pausch, et al. (2018), Norton (2011), Paul and Held (2013), Pieri et al. (2011), Raes, Eghbali, et al. (2018), Raes et al. (2017), Ribeiro et al. (2008), Rosa et al. (2014), Ross et al. (2014), Saedi Germi et al. (2020), Sato et al. (2017), Seyssens et al. (2020), Shanelec (2005), Slagter et al. (2021), Spinato et al. (2012), Tarnow et al. (2014), Tortamano et al. (2010), Valentini et al. (2010), Van Nimwegen et al. (2016), Vidigal Jr. et al. (2017), Yang et al. (2019), Zuiderveld et al. (2018)

smokers, however, this was not statistically significant (98.8% vs. 97.4%, $p = .06$). Studies with nonsmokers are of significantly larger weighed duration which is a possible confounding variable (3.2 years vs. 2.0 years, $p < .001$). The presence of chronic endodontic infection did not appear to negatively affect implant survival in Type 1A protocols with higher survival rates reported compared to those studies which excluded all endodontic infections (98.8% vs. 96.2%, $p = .004$). Weighed study duration in the analysis of endodontic infection was comparable (2.3 vs. 2.2 years, $p = .88$).

3.3 | Meta-analysis

A Poisson random-effects meta-analysis was used to systematically assess the survival rates per observed implant-year S_Y from all 68 studies. An image of the result is shown in Figure 2 and a summary is shown in the first line of Table 7 (main model).

Forty-two studies reported an S_Y of 100% without losses compared to 26 studies with at least one loss. The lowest S_Y was reported in the study of Grandi et al., 2013 (91.3%).

The estimated mean survival rate per observed implant-year is 99.4% with a 95% CI of 99.0% to 99.7%. The estimated 95% prediction interval of a single study ranges from 95.3% to 100%. Finally, the measure of heterogeneity I^2 is 53% and significantly higher than zero ($p = .002$), indicating a "moderate level of heterogeneity" (Higgins & Thompson, 2002).

Further sensitivity analysis showed that estimation of mean survival rate per observed implant-year is quite robust to outliers. A recalculation removing influential studies of Groisman et al., 2003, Block et al., 2009, Grandi et al., 2013, and Cristalli et al., 2015 yielded a slightly higher mean S_Y of 99.5%, a narrower prediction interval of 97.5% to 100%, and a reduced measure of heterogeneity I^2 of 34% (line 2 in Table 7).

3.4 | Quality assessment

Figure 3 summarizes the risk for bias for the included RCTs. Most of the studies have some concern or high risk with regard to the randomization process, which is largely due to the time of the randomization and the concealment of allocation. Due to the nature of treatment, it is not possible to blind the patients or the clinicians delivering care. Another important aspect was the team involved in collecting and analyzing the final data, and most of the included articles had blinded outcome assessors. The outcome data are well reported in all included studies, demonstrating a low risk of bias.

The risk of bias for nonrandomized studies is presented in Table 8. Twenty of the 57 evaluated studies were qualified with good quality, and 35 articles were identified as fair. Additionally, two articles were qualified with poor quality. Most of the studies have some concerns regarding the selection of the patients with the outcome of interest not defined at the start of the study.

3.5 | Outcome analysis based on study inclusion criteria

Selection criteria that were found to be reported in each study and the corresponding risk assessments are summarized in Table 9 and included:

- Medical status;
- Gingival margin position;
- Soft tissue quality;
- Bone anchorage;
- Facial bone wall;
- Mucoperiosteal flap;
- Presence of endodontic infection;
- Presence of periodontal disease;
- Gap between the facial bone and implant;
- Damage during tooth extraction;
- Primary implant stability;
- Occlusal scheme; and
- Signs of parafunction.

3.5.1 | Medical status

The medical status of the patient as an inclusion or exclusion criterion for Type 1A protocols was reported in 63 of the included articles. Forty-one studies (Berberi, Noujeim, et al., 2014; Berberi, Sabbagh, et al., 2014; Bittner et al., 2020; Block et al., 2009; Bonnet et al., 2018; Bushahri et al., 2021; Canullo et al., 2010; Canullo, Goglia, et al., 2009; Cardaropoli et al., 2019; Cooper et al., 2014; Cosyn et al., 2011, 2016; Crespi et al., 2008; Ferrara et al., 2006; Grandi, Garuti, Samarani, et al., 2012; Groenendijk et al., 2017; Kan et al., 2011; Khzam et al., 2014; Lombardo et al., 2016; Ma et al., 2019; Mangano et al., 2013; McAllister et al., 2012; Menchini-Fabris et al., 2019; Migliorati et al., 2015; Mijiritsky et al., 2021; Noelken et al., 2011; Raes et al., 2017; Raes, Eghbali, et al., 2018; Ribeiro et al., 2008; Rosa et al., 2014; Saedi Germi et al., 2020; Sato et al., 2017; Seyssens et al., 2020; Spinato et al., 2012; Tarnow et al., 2014; Tortamano et al., 2010; Valentini et al., 2010; Van Nimwegen et al., 2016; Vidigal Jr. et al., 2017; Yang et al., 2019; Zuiderveld et al., 2018) included only healthy patients with no medical conditions and excluded patients with any smoking degree. All studies excluded heavy smokers (>10–15 cigarettes/day). Twenty studies (Arora & Ivanovski, 2018a, 2018b; Bruno et al., 2014; Cabello et al., 2013; Calvo-Guirado et al., 2009, 2015; Canullo & Rasperini, 2007; Cardaropoli et al., 2015; Cristalli et al., 2015; Degidi et al., 2013; Ganeles et al., 2017; Groenendijk et al., 2021; Hartlev et al., 2013; Kolerman, Nissan, Rahmanov, et al., 2016; Malchiodi et al., 2013; Mangano et al., 2012; Noelken, Moergel, Pausch, et al., 2018; Norton, 2011; Paul & Held, 2013; Pieri et al., 2011) allowed for patients categorized as light smokers

(<10–15 cigarettes/day) to be included. Three studies included patients with controlled diabetes (HbA1c < 7; Aguilar-Salvatierra et al., 2016; Grandi et al., 2013; Norton, 2011), with one of these studies (Aguilar-Salvatierra et al., 2016) also having patients with an HbA1c of up to 10 demonstrating lower implant survival and higher marginal bone loss in patients with poorly controlled diabetes.

3.5.2 | Gingival margin position

Gingival recession was reported as an exclusion criterion for Type 1A implant treatment protocol in 22 studies (Bittner et al., 2020; Block et al., 2009; Bruno et al., 2014; Cabello et al., 2013; Canullo et al., 2010; Cardaropoli et al., 2015, 2019; Cosyn et al., 2011, 2016; Cristalli et al., 2015; Di Alberti et al., 2012; Groisman et al., 2003; Kan et al., 2011; Khzam et al., 2014; Mangano et al., 2013; Migliorati et al., 2015; Raes, Eghbali, et al., 2018; Ross et al., 2014; Saedi Germi et al., 2020; Seyssens et al., 2020; Tarnow et al., 2014; Vidigal Jr. et al., 2017). Only two studies (Noelken, Moergel, Pausch, et al., 2018; Shanelec, 2005) reported that preoperative labial tissue deficiencies were present, and for which sub-epithelial connective tissue grafting was performed in some of them.

3.5.3 | Soft tissue quality

Soft tissue phenotype was considered as part of the inclusion criteria or study outcomes analysis in 25 studies (Bittner et al., 2020; Bushahri et al., 2021; Cabello et al., 2013; Calvo-Guirado et al., 2009, 2015; Canullo et al., 2010; Canullo, Goglia, et al., 2009; Canullo & Rasperini, 2007; Cosyn et al., 2011, 2016; Groenendijk et al., 2021; Kan et al., 2011; Malchiodi et al., 2013; Mangano et al., 2012, 2013; Migliorati et al., 2015; Raes, Eghbali, et al., 2018; Rosa et al., 2014; Ross et al., 2014; Saedi Germi et al., 2020; Shanelec, 2005; Spinato et al., 2012; Vidigal Jr. et al., 2017; Zuiderveld et al., 2018), of which eight studies excluded (Cosyn et al., 2011, 2016; Malchiodi et al., 2013; Mangano et al., 2012, 2013; Raes, Eghbali, et al., 2018; Saedi Germi et al., 2020; Spinato et al., 2012) sites with thin gingival phenotype. A minimum height of keratinized tissues ranging from 2 to 3 mm was required in four studies (Block et al., 2009; Calvo-Guirado et al., 2009, 2015; Cristalli et al., 2015). Sites with a thin soft tissue phenotype were included in 17 studies (Bittner et al., 2020; Bushahri et al., 2021; Cabello et al., 2013; Calvo-Guirado et al., 2009, 2015; Canullo et al., 2010; Canullo, Goglia, et al., 2009; Canullo & Rasperini, 2007; Groenendijk et al., 2021; Kan et al., 2011; Migliorati et al., 2015; Noelken, Moergel, Pausch, et al., 2018; Rosa et al., 2014; Ross et al., 2014; Shanelec, 2005; Vidigal Jr. et al., 2017; Zuiderveld et al., 2018). Connective tissue grafting in conjunction with Type 1A implant treatment protocols for phenotype modification and compensation for anticipated alveolar ridge dimensional changes associated with tooth extraction was reported in seven studies (Bonnet et al., 2018; Kolerman, Nissan, Rahmanov, et al., 2016; Migliorati et al., 2015; Noelken, Moergel, Pausch, et al., 2018; Shanelec, 2005; Vidigal Jr. et al., 2017; Zuiderveld et al., 2018).

3.5.4 | Bone anchorage

Sufficient bone anchorage for primary stability as a preoperative assessment and inclusion criteria with Type 1A protocols was reported in 37 studies. Nineteen of these studies specified a minimum distance of bone apical to the socket to allow for engagement with the implant beyond the apex of the tooth ranging from 3 to 5 mm (Aguilar-Salvatierra et al., 2016; Berberi, Noujeim, et al., 2014; Berberi, Sabbagh, et al., 2014; Bushahri et al., 2021; Calvo-Guirado et al., 2015; Canullo et al., 2010; Canullo, Goglia, et al., 2009; Cosyn et al., 2011, 2016; Crespi et al., 2008; Cristalli et al., 2015; Groenendijk et al., 2017, 2021; Kolerman, Nissan, Rahmanov, et al., 2016; Ma et al., 2019; Menchini-Fabris et al., 2019; Pieri et al., 2011; Ribeiro et al., 2008; Seyssens et al., 2020). A requirement for sufficient bone to be present but did not provide any indication of the preoperative assessment criteria to determine suitability was reported in 18 studies (Arora & Ivanovski, 2018a, 2018b; Block et al., 2009; Bruno et al., 2014; Cardaropoli et al., 2019; Degidi et al., 2014; Ferrara et al., 2006; Migliorati et al., 2015; Noelken, Moergel, Pausch, et al., 2018; Raes, Eghbali, et al., 2018; Rosa et al., 2014; Saedi Germi et al., 2020; Sato et al., 2017; Spinato et al., 2012; Tarnow et al., 2014; Tortamano et al., 2010; Valentini et al., 2010; Vidigal Jr. et al., 2017; Yang et al., 2019).

3.5.5 | Facial bone wall

The presence of an intact facial bone wall following tooth extraction was required in 42 studies (Arora & Ivanovski, 2018a, 2018b; Berberi, Noujeim, et al., 2014; Berberi, Sabbagh, et al., 2014; Bittner et al., 2020; Block et al., 2009; Cabello et al., 2013; Canullo et al., 2010; Canullo, Goglia, et al., 2009; Canullo & Rasperini, 2007; Cardaropoli et al., 2015, 2019; Cosyn et al., 2011, 2016; Crespi et al., 2008; Cristalli et al., 2015; Degidi et al., 2013; Ferrara et al., 2006; Grandi et al., 2013; Grandi, Garuti, Samarani, et al., 2012; Groenendijk et al., 2017; Kan et al., 2011, 2003; Khzam et al., 2014; Lombardo et al., 2016; Mangano et al., 2012, 2013; Menchini-Fabris et al., 2019; Paul & Held, 2013; Pieri et al., 2011; Raes, Eghbali, et al., 2018; Ribeiro et al., 2008; Ross et al., 2014; Saedi Germi et al., 2020; Sato et al., 2017; Seyssens et al., 2020; Shanelec, 2005; Spinato et al., 2012; Tarnow et al., 2014; Tortamano et al., 2010; Van Nimwegen et al., 2016; Vidigal Jr. et al., 2017; Yang et al., 2019). Seven studies allowed for small facial dehiscence or fenestration defects of up to 3 mm (Bonnet et al., 2018; Bruno et al., 2014; Bushahri et al., 2021; Hartlev et al., 2013; Ma et al., 2019; McAllister et al., 2012; Migliorati et al., 2015). Larger defects or complete lack of facial bone was reported in 11 studies (Calvo-Guirado et al., 2009; Cooper et al., 2014; Groenendijk et al., 2021; Kolerman, Nissan, Rahmanov, et al., 2016; Noelken et al., 2011; Noelken,

TABLE 5 Included study characteristics.

Study	Type of study	Comparison	Number of implant sites	Lost to follow-up	Excluded due to procedural complications	Intention to treat	Number of implants included
Bittner et al. (2020)	Randomized control trial	Bone Graft vs. No Graft	22	0	0	100	22
Block et al. (2009)	Randomized control trial	Type 1a vs. 4a	38	7	1	97	30
Bushahri et al. (2021)	Randomized control trial	Type 1a vs. 1c	20	2	0	100	18
(Canullo, Goglia, et al., 2009)	Randomized control trial	Platform match vs. platform shift	22	0	0	100	22
Canullo et al. (2010)	Randomized control trial	Disconnection vs. one abutment one time	32	0	7	78	25
Crespi et al. (2008)	Randomized control trial	Type 1a vs. 1c	20	0	0	100	20
Degidi et al. (2014)	Randomized control trial	Disconnection vs. one abutment one time	91	25	13	86	53
Migliorati et al. (2015)	Randomized control trial	SCTG vs. No SCTG	48	1	0	100	47
Pieri et al. (2011)	Randomized control trial	Platform match vs. platform shift	40	1	1	98	38
Slagter et al. (2021)	Randomized Control Trial	Type 1a vs. 1c	20	2	0	100	18
Zuiderveld et al. (2018)	Randomized Control Trial	SCTG vs. No SCTG	60	0	0	100	60
Berberi, Sabbagh, et al. (2014)	Controlled clinical trial	Type 1a vs. 4a	22	NR	NR	-	22
Cooper et al. (2014)	Controlled clinical trial	Type 1a vs. 4a	63	7	8	87	48
Di Alberti et al. (2012)	Controlled clinical trial	Type 1a vs. 4a	25	0	NR	-	25
Grandi et al. (2013)	Controlled clinical trial	Type 1a vs. 4a	25	0	0	100	25
Raes et al. (2017)	Controlled clinical trial	Type 1a vs. 4a	48	NR	NR	-	48
Raes, Eghbali, et al. (2018)	Controlled clinical trial	Type 1a vs. 4a	16	4	NR	-	12
Aguilar-Salvatierra et al. (2016)	Prospective cohort	Healthy vs. Diabetic	85	0	NR	-	85
Berberi, Noujeim, et al. (2014)	Prospective cohort	No comparison	20	NR	NR	-	20
Cabello et al. (2013)	Prospective cohort	No comparison	14	NR	NR	-	14
Calvo-Guirado et al. (2009)	Prospective cohort	No comparison	61	1	NR	-	60
Calvo-Guirado et al. (2015)	Prospective cohort	No comparison	71	NR	NR	-	71
Canullo and Rasperini (2007)	Prospective cohort	No comparison	10	0	NR	-	10
Cardaropoli et al. (2015)	Prospective cohort	No comparison	26	0	0	100	26
Cardaropoli et al. (2019)	Prospective cohort	No comparison	20	0	0	100	20
Cosyn et al. (2011)	Prospective cohort	No comparison	32	4	2	94	26
Cosyn et al. (2016)	Prospective cohort	No comparison	22	4	0	100	18
Cristalli et al. (2015)	Prospective cohort	No comparison	29	0	4	86	25
Ferrara et al. (2006)	Prospective cohort	No comparison	39	0	6	85	33
Ganeles et al. (2017)	Prospective cohort	No comparison	15	4	NR	-	11

Mean follow-up (months)	Total number of failures	Early failures <6 m	Late failures 6 m+	Survival rate (%)	Success rate (%)	Success criteria reported	Implant details	Implant diameters	Implant lengths	Implant design
12	0	0	0	100	NR	N	BioMet 3i Certain	3.25–5 mm	8.5–15 mm	BL, T
24	4	NR	NR	86.7	NR	N	BioMet 3i Certain	3.25–4 mm	11.5–13 mm	BL, T
30	2	2	0	88.9	NR	N	Neobiotech IS II active	3.5–4.5 mm	11.5–13 mm	BL, T
25	0	0	0	100	NR	N	Sweden & Martina Global	5.5 mm		BL, T
36	0	0	0	100	100	N	Sweden & Martina Global	5.5 mm	13 mm	BL, T
24	0	0	0	100	NR	Y	Sweden & Martina Outlink	3.75–5 mm	13 mm	BL, T
24	0	0	0	100	NR	N	Dentsply Ankylos	3.5–4.5 mm	14–17 mm	BL, T
24	0	0	0	100	NR	N	Straumann Tapered Effect	NR	NR	TL, T
12	1	1	0	97.4	97.35	Y	Samo Biomedica Smiler Cone	NR	NR	BL, T
60	0	0	0	100	NR	N	Nobel Active	NR	NR	BL, T
12	2	2	0	96.7	96.7	Y	Nobel Active	3.5–4.3 mm	15–18 mm	BL, T
60	2	2	0	90.9	NR	N	Dentsply Astra Tech TX	3.5–5 mm	11–15 mm	BL, P
60	3	3	0	93.8	NR	N	Dentsply Astra Tech TX	3.5–5 mm	11–17 mm	BL, P
12	0	0	0	100	100	Y	MIS Seven	3.3–4.2 mm	11.5–16 mm	BL, T
12	2	2	0	92	NR	N	JDentalCare, JDEvolution	3.7–5 mm	11.5–15 mm	BL, T
60	1	1	0	97.9	NR	N	Dentsply Astra Tech TX	3.5–5 mm	11–19 mm	BL, P
96	1	1	0	91	NR	N	Dentsply Astra Tech TX	3.5–5 mm	13–17 mm	BL, P
24	4	0	4	95.3	NR	N	Straumann Bone Level	3.3–4.1 mm	10–14 mm	BL, P
36	0	0	0	100	NR	N	Dentsply Astra Tech TX	NR	NR	BL, P
12	0	0	0	100	NR	N	Straumann, Bone Level/ Tissue Level	NR	NR	BL or TL, P
12	1	1	0	96.7	NR	N	Biomet 3i Certain	4–5 mm	13–15 mm	BL, P
36	0	0	0	100	NR	N	MIS Seven	4.2–5 mm	11.5–13 mm	BL, T
21.9	0	0	0	100	NR	N	Def Con TSATM	4 mm	13 mm	TL, T
12	0	0	0	100	NR	N	BioMet 3i T3	4–5 mm	11.5–15 mm	BL, T
12	0	0	0	100	NR	N	Straumann Bone Level Tapered	3.3–4.8 mm	10–14 mm	BL, T
36	1	1	0	96	NR	N	Nobel Replace	NR	NR	BL, T
60	1	1	0	94.4	NR	N	Nobel Active	NR	NR	BL, T
12	2	2	0	91.6	91.6	Y	Nobel Active	3.5–5 mm	11.5–18 mm	BL, T
28.1	2	2	0	94	NR	N	Friadent Frialit	3.8–5.5 mm	13–15 mm	BL, T
24	0	0	0	100	100	Y	Nobel Active	3.5–5 mm	10–15 mm	BL, T

(Continues)

TABLE 5 (Continued)

Study	Type of study	Comparison	Number of implant sites	Lost to follow-up	Excluded due to procedural complications	Intention to treat	Number of implants included
Grandi, Garuti, Samarani, et al. (2012)	Prospective cohort	No comparison	36	NR	NR	-	36
Groenendijk et al. (2021)	Prospective cohort	No comparison	100	2	NR	-	98
Groisman et al. (2003)	Prospective cohort	No comparison	92	NR	NR	-	92
Kan et al. (2011)	Prospective cohort	Thick vs. Thin Biotype	35	NR	NR	-	35
Ma et al. (2019)	Prospective cohort	No comparison	28	9	2	93	17
Malchiodi et al. (2013)	Prospective cohort	No comparison	64	0	NR	-	64
McAllister et al. (2012)	Prospective cohort	No comparison	61	13	2	97	46
Noelken et al. (2011)	Prospective cohort	No comparison	18	0	0	100	18
Rosa et al. (2014)	Prospective cohort	No comparison	24	6	NR	-	18
Sato et al. (2017)	Prospective cohort	No comparison	16	0	NR	-	16
Seyssens et al. (2020)	Prospective cohort	No comparison	22	3	NR	-	19
Tortamano et al. (2010)	Prospective cohort	No comparison	12	0	0	100	12
Yang et al. (2019)	Prospective cohort	Thin vs. Thick Facial Bone	50	0	NR	-	50
Arora and Ivanovski (2018a)	Retrospective cohort	Type 1a vs. 1c	20	-	-	-	20
Bonnet et al. (2018)	Retrospective cohort	No comparison	39	-	-	-	39
Bruno et al. (2014)	Retrospective cohort	No comparison	17	-	-	-	17
Degidi et al. (2013)	Retrospective cohort	No comparison	10	-	-	-	10
Groenendijk et al. (2017)	Retrospective cohort	No comparison	16	-	-	-	16
Hartlev et al. (2013)	Retrospective cohort	No comparison	55	-	-	-	55
Khzam et al. (2014)	Retrospective cohort	No comparison	15	-	-	-	15
Kolerman, Nissan, Rahmanov, et al. (2016)	Retrospective cohort	No comparison	34	-	-	-	34
Lombardo et al. (2016)	Retrospective cohort	No comparison	21	-	-	-	21
Mangano et al. (2012)	Retrospective cohort	No comparison	26	-	-	-	26
Mangano et al. (2013)	Retrospective cohort	No comparison	22	-	-	-	22
Menchini-Fabris et al. (2019)	Retrospective cohort	No comparison	76	-	-	-	76
Mijiritsky et al. (2021)	Retrospective cohort	No comparison	23	-	-	-	23
Noelken, Moergel, Pausch, et al., 2018	Retrospective cohort	No comparison	26	-	-	-	26
Norton (2011)	Retrospective cohort	No comparison	68	-	-	-	68
Paul and Held (2013)	Retrospective cohort	No comparison	31	-	-	-	31
Ribeiro et al. (2008)	Retrospective cohort	No comparison	46	-	-	-	46
Ross et al. (2014)	Retrospective Cohort	No comparison	47	-	-	-	47
Saedi Germi et al. (2020)	Retrospective Cohort	No comparison	18	-	-	-	18
Shanelec (2005)	Retrospective Cohort	No comparison	100	-	-	-	100
Spinato et al. (2012)	Retrospective Cohort	No comparison	45	-	-	-	45
Tarnow et al. (2014)	Retrospective Cohort	No comparison	34	-	-	-	34
Valentini et al. (2010)	Retrospective Cohort	No comparison	24	-	-	-	24
Van Nimwegen et al. (2016)	Retrospective Cohort	No comparison	51	-	-	-	51
Vidigal Jr. et al. (2017)	Retrospective Cohort	No comparison	53	-	-	-	53

Abbreviations: BL, bone level; NR, not reported; P, parallel/cylindrical; T, tapered; TL, tissue level.

Mean follow-up (months)	Total number of failures	Early failures <6 m	Late failures 6 m+	Survival rate (%)	Success rate (%)	Success criteria reported	Implant details	Implant diameters	Implant lengths	Implant design
12	1	1	0	97.2	97.2	Y	JDentalCare, JDEvolution	4.3–5 mm	13–15 mm	BL, T
12	0	0	0	100.0	93	Y	Nobel Active	3–4.3 mm	11.5–18 mm	BL, T
24	6	5	1	93.5	NR	N	Nobel Replace	3.5–6 mm	13–16 mm	BL, T
48	0	0	0	100	100	Y	Nobel Replace	NR	NR	BL, T
60	0	0	0	100	NR	N	Southern Co-Axis	4 mm	13–15 mm	BL, T
36	0	0	0	100	100	Y	NR	3.25–4.9 mm	10–16 mm	BL, T
24	1	1	0	97.8	NR	N	Nobel Active	4.3–5 mm	10–15 mm	BL, T
22	0	0	0	100	94	Y	Nobel Perfect	3.5–5 mm	16 mm	TL, P
58.56	0	0	0	100	100	Y	Nobel replace	3.5–5 mm		BL, T
12	0	0	0	100	NR	N	Neodent CM drive	3.5–5 mm	13–16 mm	BL, T
120	2	1	1	91	NR	N	Nobel Active	NR	NR	BL, T
18	0	0	0	100	NR	N	Straumann tapered effect	4.1 mm	12 mm	TL, P
12	0	0	0	100	NR	N	Nobel active, straumann bone level, dentium	NR	NR	BL, P or T
36	0	0	0	100	95	Y	Dentsply Astra Tech TX	NR	NR	BL, P
48	0	0	0	100	100	Y	Nobel Replace/Active	NR	NR	BL, T
12	0	0	0	100	NR	N	Nobel Replace	NR	NR	BL, T
18	0	0	0	100	NR	N	Dentsply Ankylos	3.5–4.5 mm	14-17 mm	BL, T
25	0	0	0	100	NR	N	Nobel Active	3.5–4.3 mm	NR	BL, T
33	1	1	0	98	NR	N	Nobel Replace	3.5–6 mm	13–16 mm	BL, T
23	0	0	0	100	NR	Y	Dentsply Astra Tech TX	3.5–5 mm	13–15 mm	BL, P
29	0	0	0	100	88	Y	MIS Seven	3.3–5 mm	13–16 mm	BL, T
24	1	1	0	95.2	NR	N	Bicon	NR	NR	BL, T
24	0	0	0	100	100	Y	Leone Implant System	4.1–4.8 mm	NR	BL, T
31.09	0	0	0	100	100	Y	Leone Implant System	3.3–4.8 mm	NR	BL, P
36	0	0	0	100	NR	N	Sweden & Martina, Outlink	3.75–4.1 mm	NR	BL, T
187.37	0	0	0	100	100	Y	Dentsply Xive, Frialit 2, MIS Seven	3.3–5.5 mm	13–15 mm	BL, T
30	0	0	0	100	100	Y	Dentsply, Astra Tech TX	3.5–5 mm	15–17 mm	BL, P
24	3	3	0	95.5	NR	N	Dentsply, Astra Tech TX	3.5–5 mm	11–17 mm	BL, P
40.8	0	0	0	100	100	Y	Nobel Perfect	NR	16 mm	BL, T
27.1	3	3	0	93.5	93.5	Y	Conexão	3.5–6 mm	10–15 mm	BL, T
60	0	0	0	100	100	Y	Nobel Replace	3.5–4.3 mm	13–16 mm	TL, T
12	0	0	0	100	NR	N	NR	NR	NR	NR
18	2	2	0	98	98	Y	Bränemark Mark IV	4 mm	13–18 mm	BL, P
32	0	0	0	100	NR	N	Zimmer Screw-Vent	3.7–4.7 mm	11.5–16 mm	BL, P
27	0	0	0	100	NR	N	NR	NR	NR	NR
34	0	0	0	100	NR	N	Dentsply, Astra Tech TX	4.5–5 mm	13 mm +	BL, P
48	2	2	0	96.9	NR	Y	BioMet 3i, Certain	3.25–4.5 mm	10-15 mm	BL, P
51	2	2	0	96.2	NR	N	NR	NR	NR	NR

TABLE 6 Comparison of weighed survival rates and weighed average study time by inclusion criteria and publication year.

	Entire timeline						Within first 6 months			
	Analyzed sample						Analyzed sample			
	Number of Studies	Number of Implants	Survival % (Overall survival)		Avg. study time (years)		Number of studies	Number of implants	Survival % (early survival)	
Overall	68	2531	97.708 (96.911; 98.442)		2.665 (2.272; 3.136)		67	2493	98.275 (97.571; 98.819)	
Medical status										
Healthy	41	1329	97.413 (96.026; 98.353)	p = .06	3.212 (2.706; 4.114)	p < .001*	40	1291	97.986 (97.117; 98.764)	p = .14
Smokers	20	808	98.806 (97.454; 99.578)		1.967 (1.513; 2.350)		20	808	99.010 (97.826; 99.660)	
Occlusal scheme										
Contacts	10	337	97.498 (95.142; 99.359)	p = .94	2.294 (1.722; 2.983)	p = .23	10	337	98.813 (95.763; 100.00)	p = .42
No contacts	47	1746	97.410 (96.322; 98.280)		2.861 (2.392; 3.565)		46	1708	97.892 (97.099; 98.584)	
Facial bone wall										
Defects	17	698	98.200 (96.543; 99.149)	p = .52	2.484 (1.773; 3.358)	p = .85	17	698	98.567 (97.228; 99.381)	p = .56
Intact	42	1342	97.660 (96.311; 98.576)		2.581 (2.160; 3.144)		41	1304	98.160 (97.253; 98.876)	
Soft tissue quality										
Excluded	8	245	98.387 (95.901; 99.590)	p = .83	3.155 (2.532; 4.567)	p = .10	8	245	98.776 (96.954; 99.682)	p = .98
Included	17	745	98.627 (97.538; 99.459)		2.293 (1.630; 3.051)		17	745	98.792 (97.751; 99.538)	
Gap dimension										
Less than 2 mm	8	341	95.918 (94.167; 97.838)	p = .04*	2.491 (2.084; 3.841)	p = .91	8	341	96.481 (95.125; 98.138)	p = .04*
More than 2 mm	12	472	99.014 (96.589; 100.00)		2.322 (1.433; 5.195)		12	472	99.153 (97.056; 100.00)	
Mucoperiosteal flap										
Flap	14	482	97.067 (95.355; 98.605)	p = .37	2.851 (1.996; 3.938)	p = .63	14	482	97.718 (96.230; 98.930)	p = .44
Flapless	49	1763	97.928 (96.733; 98.727)		2.601 (2.185; 3.275)		48	1725	98.319 (97.417; 98.994)	
Endodontic infection										
No Infection	18	618	96.162 (93.930; 97.851)	p = .004*	2.287 (1.869; 2.761)	p = .88	17	580	97.069 (95.644; 98.404)	p = .007*
Incl. chronic / excl. acute	24	910	98.892 (97.806; 99.579)		2.168 (1.674; 3.644)		24	910	99.121 (98.064; 99.663)	
Periodontal disease										
Excluded	43	1435	97.387 (96.113; 98.370)	p = .46	2.479 (2.035; 3.004)	p = .33	41	1397	98.210 (97.183; 98.995)	p = .87
Included	10	374	98.202 (95.781; 99.512)		3.201 (2.111; 6.526)		10	374	98.396 (96.154; 99.525)	
Insertion torque										
35 and more	24	841	97.517 (96.447; 98.485)	p = .54	2.541 (1.912; 3.422)	p = 34	24	841	98.216 (97.225; 99.041)	p = .99
Less than 35	19	575	98.117 (96.352; 99.218)		3.089 (2.297; 5.169)		19	575	98.261 (96.593; 99.302)	

TABLE 6 (Continued)

	Entire timeline						Within first 6 months				
	Analyzed sample						Analyzed sample				
	Number of Studies	Number of Implants	Survival % (Overall survival)		Avg. study time (years)		Number of studies	Number of implants	Survival % (early survival)	
Bone graft										
Autogenous	11	378	97.269 (94.778; 99.322)	p = .49	3.655 (2.642; 6.937)	p = .11	11	378	97.619 (95.455; 99.392)	p = .44
Xenograft	21	617	98.063 (96.614; 99.255)		2.481 (1.755; 3.459)		21	617	98.379 (97.116; 99.372)	
Soft tissue graft										
No	61	2171	97.604 (96.566; 98.407)	p = .31	2.723 (2.332; 3.296)	p = .44	60	2133	98.265 (97.530; 98.877)	p = .96
Yes	7	360	98.335 (97.224; 99.380)		2.318 (1.609; 3.376)		7	360	98.333 (97.222; 99.381)	
Publication year										
Before 2012	17	689	96.262 (94.270; 97.620)	p = .02*	2.028 (1.700; 2.460)	p = .005*	16	651	97.235 (95.878; 98.294)	p = .04*
From 2012	51	1842	98.249 (97.425; 98.912)		2.904 (2.416; 3.620)		51	1842	98.643 (97.951; 99.200)	

Note: Values are presented as means (95% CI). Comparisons as of bootstrap tests. Statistically significant p-values are marked with an asterisk ("*").

Moergel, Pausch, et al., 2018; Norton, 2011; Rosa et al., 2014; Slagter et al., 2021; Valentini et al., 2010; Zuiderveld et al., 2018). The thickness of facial bone was only considered in eight studies (Bittner et al., 2020; Bushahri et al., 2021; Cardaropoli et al., 2019; Groenendijk et al., 2017; Kolerman, Nissan, Rahmanov, et al., 2016; Noelken, Moergel, Pausch, et al., 2018; Seyssens et al., 2020; Yang et al., 2019), with thicknesses ranging from 0 to 1.6 mm, and no studies reported a minimum of 1 mm facial bone thickness as an inclusion criterion.

3.5.6 | Mucoperiosteal flap

Flapless immediate implant placement was performed in 49 of the included studies (Arora & Ivanovski, 2018a, 2018b; Berberi, Sabbagh, et al., 2014; Bittner et al., 2020; Block et al., 2009; Bonnet et al., 2018; Bruno et al., 2014; Bushahri et al., 2021; Cabello et al., 2013; Canullo et al., 2010; Canullo, Goglia, et al., 2009; Canullo & Rasperini, 2007; Cardaropoli et al., 2015, 2019; Cosyn et al., 2016; Crespi et al., 2008; Degidi et al., 2013; Ferrara et al., 2006; Grandi et al., 2013; Grandi, Garuti, Samarani, et al., 2012; Groenendijk et al., 2017, 2021; Groisman et al., 2003; Hartlev et al., 2013; Kan et al., 2011; Khzam et al., 2014; Ma et al., 2019; Malchiodi et al., 2013; Menchini-Fabris et al., 2019; Migliorati et al., 2015; Mijiritsky et al., 2021; Noelken et al., 2011; Noelken, Moergel, Pausch, et al., 2018; Paul & Held, 2013; Pieri et al., 2011; Ribeiro et al., 2008; Rosa et al., 2014; Saedi Germi et al., 2020; Sato et al., 2017; Seyssens et al., 2020; Shanelec, 2005; Slagter et al., 2021; Spinato et al., 2012; Tarnow et al., 2014; Tortamano et al., 2010; Van Nimwegen et al., 2016; Vidigal Jr. et al., 2017; Yang et al., 2019; Zuiderveld et al., 2018). The use of a minimal mucoperiosteal flap was reported in three studies (Berberi, Noujeim, et al., 2014; Cosyn et al., 2011; Cristalli et al., 2015), with a further 11 studies reporting raising a full-thickness mucoperiosteal flap for the purpose of extraction and immediate implant placement (Calvo-Guirado et al., 2009; Cooper et al., 2014; Di Alberti et al., 2012; Ganeles et al., 2017; Kolerman, Nissan, Rahmanov, et al., 2016; Mangano et al., 2012, 2013; Norton, 2011; Raes, Eghbali, et al., 2018; Ross et al., 2014; Valentini et al., 2010).

3.5.7 | Presence of endodontic infection

Eighteen studies reported the presence of endodontic infection as an exclusion criteria (Berberi, Noujeim, et al., 2014; Berberi, Sabbagh, et al., 2014; Block et al., 2009; Canullo & Rasperini, 2007; Cosyn et al., 2016; Degidi et al., 2013; Ferrara et al., 2006; Groisman et al., 2003; Hartlev et al., 2013; Khzam et al., 2014; Kolerman, Nissan, Rahmanov, et al., 2016; Pieri et al., 2011; Ribeiro et al., 2008; Spinato et al., 2012; Tarnow et al., 2014; Tortamano et al., 2010; Valentini et al., 2010; Zuiderveld et al., 2018), with eight studies excluding acute infection (Canullo et al., 2010; Canullo, Goglia, et al., 2009; Cardaropoli et al., 2015, 2019; Cosyn et al., 2011; Degidi et al., 2014;

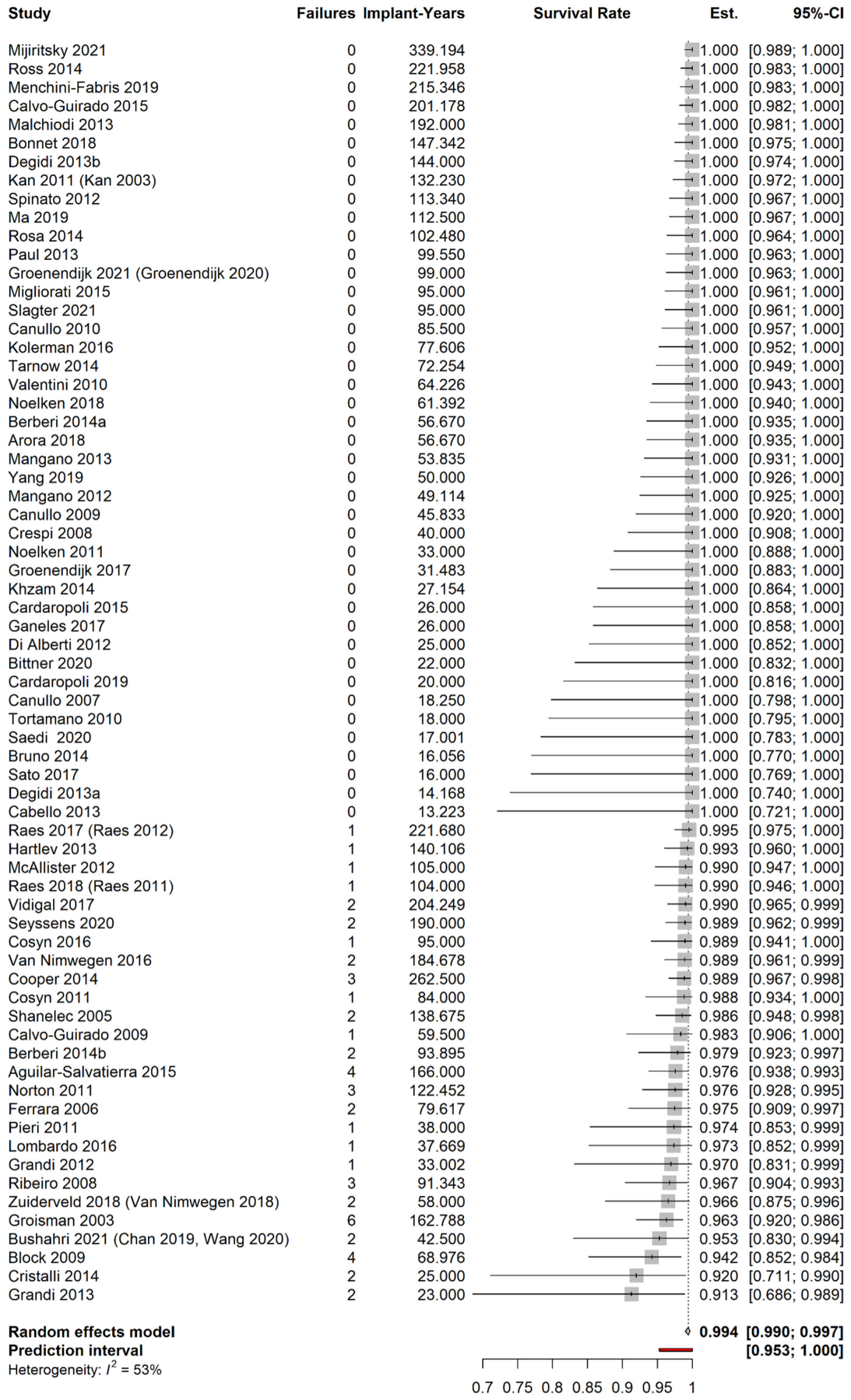


FIGURE 2 Estimated survival rate per observed implant-years for each study with calculated mean survival rate and prediction interval from meta-analysis.

TABLE 7 Results of the meta-analysis (first line) with an additional sensitivity analysis. Influential studies removed: Groisman et al. (2003), Block et al. (2009), Grandi et al. (2013), and Cristalli et al. (2015).

Analysis	Mean S_Y + 95% CI	PI	Heterogeneity I^2 + 95% CI
Main model	99.4% (99.0%; 99.7%)	(95.3%; 100%)	53% (25%; 74%)
Influential studies removed	99.5% (99.1%; 99.7%)	(97.5%; 100%)	34% (0%; 64%)

Note: Mean S_Y = Estimated mean survival rate per observed implant-year.
Abbreviations: I^2 = heterogeneity measure; PI, prediction interval.

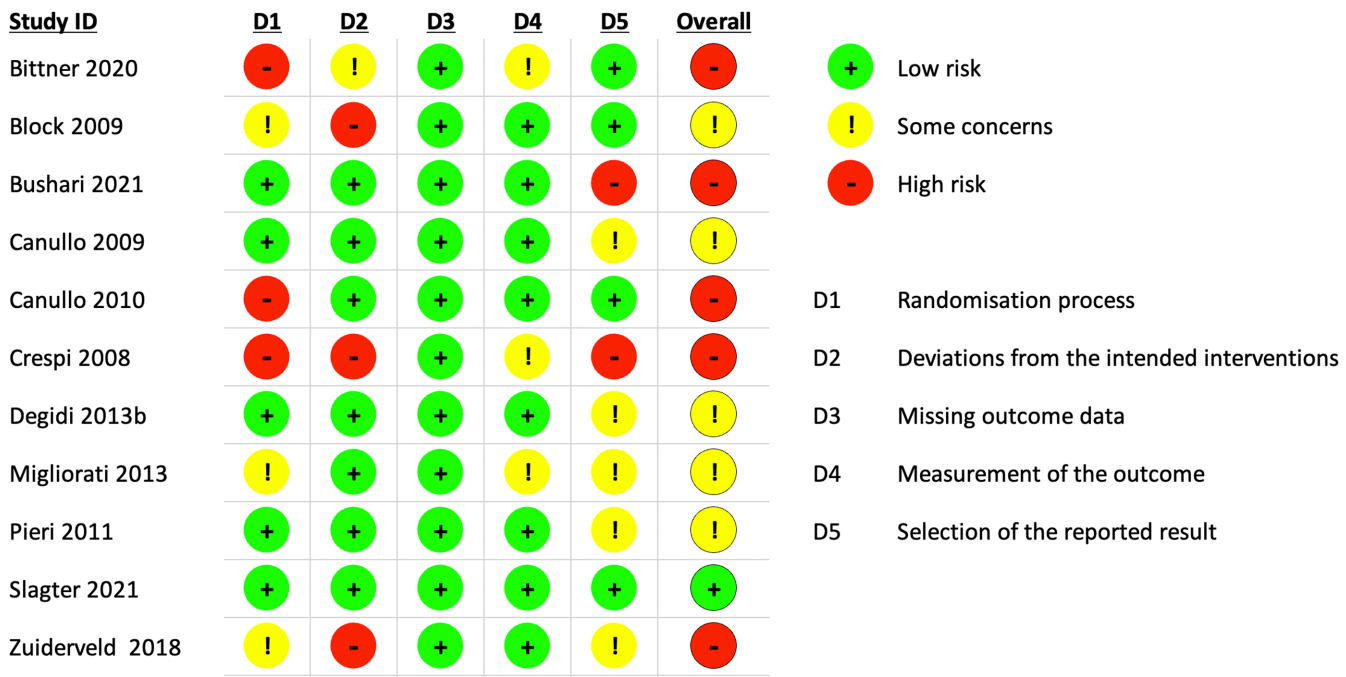


FIGURE 3 Risk of bias assessment for randomized control trials using the Cochrane RoB2 tool.

McAllister et al., 2012; Yang et al., 2019) and sixteen studies included sites with chronic infection and only excluded acute endodontic infection (Arora & Ivanovski, 2018a, 2018b; Bittner et al., 2020; Calvo-Guirado et al., 2009; Crespi et al., 2008; Cristalli et al., 2015; Di Alberti et al., 2012; Grandi et al., 2013; Grandi, Garuti, Samarani, et al., 2012; Groenendijk et al., 2017, 2021; Kan et al., 2011; Malchiodi et al., 2013; Mangano et al., 2012; Migliorati et al., 2015; Mijiritsky et al., 2021; Noelken, Moergel, Pausch, et al., 2018). Studies including chronic endodontic infection often reported that some sites with apical fenestration of the labial cortical bone were included. However, no reports mentioned the presence of a chronic draining fistula and breach of the labial mucosa as being included.

3.5.8 | Presence of periodontal disease

The presence of periodontal disease was an exclusion criterion in 43 studies (Aguilar-Salvatierra et al., 2016; Arora & Ivanovski, 2018a, 2018b; Berberi, Noujeim, et al., 2014; Berberi, Sabbagh, et al., 2014; Bittner et al., 2020; Block et al., 2009; Bonnet et al., 2018; Bushahri et al., 2021; Cabello et al., 2013; Canullo et al., 2010; Canullo & Rasperini, 2007; Cardaropoli et al., 2019; Cosyn et al., 2016; Degidi et al., 2013; Ferrara et al., 2006; Groenendijk et al., 2017, 2021; Groisman et al., 2003; Hartlev et al., 2013; Khzam et al., 2014; Lombardo et al., 2016; Ma et al., 2019; Mangano et al., 2012, 2013; McAllister et al., 2012; Migliorati et al., 2015; Noelken, Moergel, Pausch, et al., 2018; Pieri et al., 2011; Raes et al., 2017; Raes, Eghbali, et al., 2018; Ribeiro et al., 2008; Rosa et al., 2014; Saedi Germi et al., 2020; Sato et al., 2017; Seyssens et al., 2020; Spinato et al., 2012; Tarnow et al., 2014; Tortamano et al., 2010; Valentini et al., 2010; Vidigal Jr. et al., 2017; Yang et al., 2019; Zuiderveld et al., 2018), with only 10 studies including patients with a history of treated periodontal disease (Calvo-Guirado et al., 2015; Cosyn et al., 2011; Cristalli et al., 2015; Di Alberti et al., 2012; Grandi et al., 2013; Grandi, Garuti, Samarani, et al., 2012; Kan et al., 2011; Kolerman, Nissan, Rahmanov, et al., 2016; Malchiodi et al., 2013; Mijiritsky et al., 2021) and 1 study excluding periodontal acute infection (Cardaropoli et al., 2015).

TABLE 8 Risk of bias assessment for nonrandomized studies using the Newcastle–Ottawa scale.

Authors & Year	Type of study	Selection	Comparability	Outcome	AHRQ
Berberi, Tehini, et al. (2014)	Controlled clinical trial	**	*	**	Fair
Cooper et al. (2014)	Controlled clinical trial	***	**	***	Good
Di Alberti et al. (2012)	Controlled clinical trial	*	*	**	Poor
Grandi et al. (2013)	Controlled clinical trial	**	*	**	Fair
Raes et al. (2017)	Controlled clinical trial	***	**	**	Good
Raes, Eghbali, et al. (2018)	Controlled clinical trial	**	*	**	Fair
Aguilar-Salvatierra et al. (2016)	Prospective cohort	**	*	**	Fair
Berberi, Noujeim, et al. (2014)	Prospective cohort	**	*	**	Fair
Cabello et al. (2013)	Prospective cohort	**	*	**	Fair
Calvo-Guirado et al. (2009)	Prospective cohort	**	*	**	Fair
Calvo-Guirado et al. (2015)	Prospective cohort	**	*	**	Fair
Canullo and Rasperini (2007)	Prospective cohort	**	*	**	Fair
Cardaropoli et al. (2015)	Prospective cohort	**	*	**	Fair
Cardaropoli et al. (2019)	Prospective cohort	**	*	**	Fair
Cosyn et al. (2011)	Prospective cohort	**	*	***	Fair
Cosyn et al. (2016)	Prospective cohort	**	*	**	Fair
Cristalli et al. (2015)	Prospective cohort	**	*	**	Fair
Ferrara et al. (2006)	Prospective cohort	**	*	***	Fair
Ganeles et al. (2017)	Prospective cohort	**	*	***	Fair
Grandi, Garuti, Samarani, et al. (2012)	Prospective cohort	**	*	**	Fair
Groenendijk et al. (2021)	Prospective cohort	***	*	**	Good
Groisman et al. (2003)	Prospective cohort	**	*	***	Fair
Kan et al. (2011)	Prospective cohort	***	*	***	Good
Ma et al. (2019)	Prospective cohort	**	*	**	Fair
Malchiodi et al. (2013)	Prospective cohort	***	*	***	Good
McAllister et al. (2012)	Prospective cohort	**	*	***	Fair
Noelken et al. (2011)	Prospective cohort	**	*	***	Fair
Rosa et al. (2014)	Prospective cohort	**	*	**	Fair
Sato et al. (2017)	Prospective cohort	**	*	**	Fair
Seyssens et al. (2020)	Prospective cohort	***	*	***	Good
Tortamano et al. (2010)	Prospective cohort	***	*	***	Good
Yang et al. (2019)	Prospective cohort	***	**	**	Good
Arora and Ivanovski (2018a)	Retrospective cohort	***	*	***	Good
Bonnet et al. (2018)	Retrospective cohort	**	*	***	Fair
Bruno et al. (2014)	Retrospective cohort	***	*	**	Good
Degidi et al. (2013)	Retrospective cohort	*	*	***	Poor
Groenendijk et al. (2017)	Retrospective cohort	**	*	**	Fair
Hartlev et al. (2013)	Retrospective cohort	***	*	**	Good
Khzam et al. (2014)	Retrospective cohort	***	*	**	Good
Kolerman, Nissan, Rahmanov, et al. (2016)	Retrospective cohort	***	*	***	Good
Lombardo et al. (2016)	Retrospective cohort	***	*	***	Good
Mangano et al. (2012)	Retrospective cohort	**	*	***	Fair
Mangano et al. (2013)	Retrospective cohort	**	*	***	Fair
Menchini-Fabris et al. (2019)	Retrospective cohort	***	**	***	Good

TABLE 8 (Continued)

Authors & Year	Type of study	Selection	Comparability	Outcome	AHRQ
Mijiritsky et al. (2021)	Retrospective cohort	***	*	***	Good
Noelken, Moergel, Pausch, et al., 2018	Retrospective cohort	***	**	***	Good
Norton (2011)	Retrospective cohort	**	*	***	Fair
Paul and Held (2013)	Retrospective cohort	**	*	***	Fair
Ribeiro et al. (2008)	Retrospective cohort	***	*	***	Good
Ross et al. (2014)	Retrospective cohort	**	*	***	Fair
Saedi Germi et al. (2020)	Retrospective cohort	***	*	***	Good
Shanelec (2005)	Retrospective cohort	**	*	***	Fair
Spinato et al. (2012)	Retrospective cohort	**	*	***	Fair
Tarnow et al. (2014)	Retrospective cohort	**	**	***	Fair
Valentini et al. (2010)	Retrospective cohort	**	*	***	Fair
Van Nimwegen et al. (2016)	Retrospective cohort	***	**	***	Good
Vidigal Jr. et al. (2017)	Retrospective cohort	**	**	***	Fair

Note: The asterisks are part of the Newcastle Ottowa Scale (NOS) for risk of bias assessment, so are described in the manual for NOS: https://www.ohri.ca/programs/clinical_epidemiology/oxford.asp

3.5.9 | Facial gap (horizontal defect dimension—HDD)

The presence of a gap between the implant and facial bone wall was reported in 56 studies (Arora & Ivanovski, 2018a, 2018b; Berberi, Noujeim, et al., 2014; Berberi, Sabbagh, et al., 2014; Bittner et al., 2020; Block et al., 2009; Bonnet et al., 2018; Bruno et al., 2014; Bushahri et al., 2021; Cabello et al., 2013; Calvo-Guirado et al., 2009; Canullo et al., 2010; Canullo, Goglia, et al., 2009; Canullo & Rasperini, 2007; Cardaropoli et al., 2015, 2019; Cosyn et al., 2016; Cristalli et al., 2015; Degidi et al., 2013; Di Alberti et al., 2012; Ferrara et al., 2006; Grandi et al., 2013; Grandi, Garuti, Samarani, et al., 2012; Groenendijk et al., 2017, 2021; Groisman et al., 2003; Hartlev et al., 2013; Kan et al., 2011; Khzam et al., 2014; Kolerman, Nissan, Rahmanov, et al., 2016; Lombardo et al., 2016; Ma et al., 2019; Mangano et al., 2012; Migliorati et al., 2015; Mijiritsky et al., 2021; Noelken et al., 2011; Noelken, Moergel, Pausch, et al., 2018; Norton, 2011; Paul & Held, 2013; Pieri et al., 2011; Raes, Eghbali, et al., 2018; Rosa et al., 2014; Ross et al., 2014; Saedi Germi et al., 2020; Sato et al., 2017; Seyssens et al., 2020; Shanelec, 2005; Slagter et al., 2021; Spinato et al., 2012; Tarnow et al., 2014; Tortamano et al., 2010; Valentini et al., 2010; Van Nimwegen et al., 2016; Vidigal Jr. et al., 2017; Yang et al., 2019; Zuiderveld et al., 2018). The size of the gaps varied between 1 and 4 mm, with most studies reporting placing biomaterial into the gap. Biomaterials utilized for socket grafting in conjunction with Type 1A protocols included deproteinized bovine bone mineral xenograft (22 studies—Arora & Ivanovski, 2018a; Arora & Ivanovski, 2018b; Bittner et al., 2020; Bonnet et al., 2018; Bruno et al., 2014; Canullo, Goglia, et al., 2009; Canullo & Rasperini, 2007; Cardaropoli et al., 2015; Cardaropoli et al., 2019; Cosyn et al., 2011; Cosyn et al., 2016; Cristalli et al., 2015; Degidi et al., 2013; Grandi et al., 2013; Grandi, Garuti, Samarani, et al., 2012; Groenendijk et al., 2017; Groenendijk et al., 2021; Khzam et al., 2014; Migliorati et al., 2015; Paul & Held, 2013; Seyssens et al., 2020; Valentini et al., 2010; Vidigal Jr. et al., 2017), autogenous bone (11 studies—Berberi, Noujeim, et al., 2014; Berberi, Sabbagh, et al., 2014; Ferrara et al., 2006; Ganeles et al., 2017; Groisman et al., 2003; Kan et al., 2011; Malchiodi et al., 2013; Mijiritsky et al., 2021; Noelken et al., 2011; Noelken, Moergel, Pausch, et al., 2018; Rosa et al., 2014), autogenous bone and xenograft mixture (six studies—Norton, 2011; Pieri et al., 2011; Shanelec, 2005; Slagter et al., 2021; Van Nimwegen et al., 2016; Zuiderveld et al., 2018), human allograft (six studies—Block et al., 2009; Bushahri et al., 2021; Kolerman, Nissan, Rahmanov, et al., 2016; Ross et al., 2014; Saedi Germi et al., 2020; Tarnow et al., 2014), alloplastic graft materials (three studies—Canullo et al., 2010; Lombardo et al., 2016; Mangano et al., 2012), and alloplastic/allograftor/xenograft on the same study (three studies—McAllister et al., 2012; Sato et al., 2017; Yang et al., 2019). Only one study reported placing large implants to minimize the gap between the implant and the extraction socket's facial bone wall (Ferrara et al., 2006).

3.5.10 | Extraction

Minimally traumatic extraction techniques to minimize damage to the surrounding alveolar bone and soft tissues were reported in 59 studies (Arora & Ivanovski, 2018a, 2018b; Berberi, Noujeim, et al., 2014; Bittner et al., 2020; Block et al., 2009; Bonnet et al., 2018; Bruno et al., 2014; Bushahri et al., 2021; Cabello et al., 2013; Canullo et al., 2010; Canullo, Goglia, et al., 2009; Canullo & Rasperini, 2007; Cardaropoli et al., 2015, 2019; Cosyn et al., 2011, 2016; Crespi et al., 2008; Cristalli et al., 2015; Degidi et al., 2013, 2014; Di Alberti et al., 2012; Ferrara et al., 2006; Grandi et al., 2013; Grandi, Garuti,

TABLE 9 Reported study criteria for inclusion/exclusion categorized based on risk assessment.

Authors & year	Medical status—standardized reporting	Occlusal scheme	Occlusal parafunction included or excluded (I/E/NR)	Pre-op gingival margin position	Soft tissue quality (thin phenotype)—include I or exclude E	CTG performed at time of implant placement (Y/N)	Bone Anchorage standardized	Facial Bone Wall presence—small defects up to 3 mm, large 3 mm +	Facial Bone Wall thickness
Bittner et al. (2020)	Healthy Patients	No Contacts	NR	E	I	N	NR	Intact Facial Bone	0.8 mm
Block et al. (2009)	Healthy Patients	No Contacts	NR	E	NR	N	Sufficient Bone	Intact Facial Bone	NR
Bushahri et al. (2021)	Healthy Patients	No Contacts	NR	NR	I	N	≥4 mm bone height	Small Defects Included	1 mm
Canullo, Goglia, et al. (2009)	Healthy Patients	No Contacts	NR	NR	I	N	≥3 mm bone height	Intact Facial Bone	NR
Canullo et al. (2010)	Healthy Patients	No Contacts	NR	E	I	N	≥4 mm bone height	Intact Facial Bone	NR
Crespi et al. (2008)	Healthy Patients	Limited Contacts	E	NR	NR	N	≥4 mm bone height	Intact Facial Bone	NR
Degidi et al. (2014)	Light Smokers	No Contacts	E	NR	NR	N	Sufficient Bone	Intact Facial Bone	NR
Migliorati et al. (2015)	Healthy Patients	No Contacts	NR	E	I	Y	Sufficient Bone	Small Defects Included	NR
Pieri et al. (2011)	Light Smokers	No Contacts	E	NR	NR	N	≥4 mm bone height	Intact Facial Bone	NR
Slagter et al. (2021)	NR	NR	NR	NR	NR	N	NR	Large defects Included	NR
Zuiderveld et al. (2018)	Healthy Patients	No Contacts	NR	NR	I	Y	NR	Large defects Included	NR
Berberi, Sabbagh, et al. (2014)	Healthy Patients	Limited Contacts	NR	NR	NR	N	≥5 mm bone height	Intact Facial Bone	NR
Cooper et al. (2014)	Healthy Patients	No Contacts	NR	NR	NR	N	NR	Large defects Included	NR
Di Alberti et al. (2012)	NR	Full Contact	NR	E	NR	N	NR	NR	NR
Grandi et al. (2013)	Diabetes and Light Smokers	No Contacts	NR	NR	NR	N	NR	Intact Facial Bone	NR

Mucoperiosteal flap	Presence of endodontic infection	Presence of periodontal disease	Presence of buccal gap (Y/N)	Gap dimensions (mm)	Graft material (none, auto, allo, xeno)	Extraction	Primary implant stability—insertion torque	Primary implant stability—resonance frequency analysis
Flapless	Chronic Infection Included	Periodontal disease excluded	Y	$\bar{x}$ =2.9 mm	Xenograft or None	Flapless	>20Ncm	NR
Flapless	Absence of infection	Periodontal disease excluded	Y	NR	Allograft	Minimally traumatic using periotomes	NR	>71 ISQ
Flapless	NR	Periodontal disease excluded	Y	$\bar{x}$ =2.7 mm	Allograft	Minimally traumatic	≥30	NR
Flapless	Absence of Acute Infection	NR	Y	>1 mm	Xenograft	Minimally traumatic using periotomes	32-45Ncm	NR
Flapless	Absence of Acute Infection	Periodontal disease excluded	Y	>1 mm	Alloplastic	Minimally traumatic using periotomes	32-45Ncm	NR
Flapless	Chronic Infection Included	NR	NR	NR	NR	Minimally traumatic	>25Ncm	>60 ISQ
Flapless	Absence of Acute Infection	NR	Y	2 mm	NR	Minimally traumatic	≥25Ncm	≥60 ISQ
Flapless	Chronic Infection Included	Periodontal disease excluded	Y	NR	Xenograft	Minimally traumatic	NR	NR
Flapless	Absence of infection	Periodontal disease excluded	Y	NR	Autogenous and Xenograft mix	Minimally traumatic using periotomes	≥40Ncm	NR
Flapless	NR	NR	Y	NR	Autogenous and Xenograft mix	Minimally traumatic using periotomes	NR	NR
Flapless	Absence of infection	Periodontal disease excluded	Y	NR	Autogenous and Xenograft mix	Minimally traumatic	≥45Ncm	NR
Flapless	Absence of infection	Periodontal disease excluded	Y	NR	Autogenous	NR	≥32Ncm	NR
Full-Thickness Flap	NR	NR	NR	NR	None	NR	NR	NR
Full-Thickness Flap	Chronic Infection Included	Treated Periodontal Disease Included	Y	2 mm	NR	Minimally traumatic using periotomes	≥40Ncm	>60 ISQ
Flapless	Chronic Infection Included	Treated Periodontal Disease Included	Y	NR	Xenograft	Minimally traumatic	≥45Ncm	NR

TABLE 9 (Continued)

Authors & year	Medical status—standardized reporting	Occlusal scheme	Occlusal parafunction included or excluded (I/E/NR)	Pre-op gingival margin position	Soft tissue quality (thin phenotype)—include I or exclude E	CTG performed at time of implant placement (Y/N)	Bone Anchorage standardized	Facial Bone Wall presence—small defects up to 3 mm, large 3 mm +	Facial Bone Wall thickness
Raes et al. (2017)	Healthy Patients	No Contacts	NR	NR	NR	N	NR	NR	NR
Raes, Eghbali, et al. (2018)	Healthy Patients	No Contacts	NR	E	E	N	Sufficient Bone	Intact Facial Bone	NR
Aguilar-Salvatierra et al. (2016)	Diabetes	Limited Contacts	NR	NR	NR	N	≥5 mm bone height	NR	NR
Berberi, Noujeim, et al. (2014)	Healthy Patients	Limited Contacts	NR	NR	NR	N	≥5 mm bone height	Intact Facial Bone	NR
Cabello et al. (2013)	Light Smokers	No Contacts	I	E	I	N	NR	Intact Facial Bone	NR
Calvo-Guirado et al. (2009)	Light Smokers	NR	I	NR	I	N	NR	Large defects Included	NR
Calvo-Guirado et al. (2015)	Light Smokers	Limited Contacts	NR	NR	I	N	≥5 mm bone height	NR	NR
Canullo and Rasperini (2007)	Light Smokers	No Contacts	NR	NR	I	N	NR	Intact Facial Bone	NR
Cardaropoli et al. (2015)	Light Smokers	No Contacts	NR	E	NR	N	NR	Intact Facial Bone	NR
Cardaropoli et al. (2019)	Healthy Patients	No Contacts	NR	E	NR	N	Sufficient Bone	Intact Facial Bone	0.8 mm
Cosyn et al. (2011)	Healthy Patients	No Contacts	E	E	E	N	≥5 mm bone height	Intact Facial Bone	NR
Cosyn et al. (2016)	Healthy Patients	No Contacts	E	E	E	N	≥5 mm bone height	Intact Facial Bone	NR
Cristalli et al. (2015)	Light Smokers	Limited Contacts	E	E	NR	N	≥4 mm bone height	Intact Facial Bone	NR
Ferrara et al. (2006)	Healthy Patients	No Contacts	E	NR	NR	N	Sufficient Bone	Intact Facial Bone	NR
Ganeles et al. (2017)	Light Smokers	No Contacts	E	NR	NR	N	NR	NR	NR

Mucoperiosteal flap	Presence of endodontic infection	Presence of periodontal disease	Presence of buccal gap (Y/N)	Gap dimensions (mm)	Graft material (none, auto, allo, xeno)	Extraction	Primary implant stability—insertion torque	Primary implant stability—resonance frequency analysis
NR	NR	Periodontal disease excluded	NR	NR	NR	NR	NR	NR
Full-Thickness Flap	NR	Periodontal disease excluded	Y	<2 mm or >2 mm	None	Minimally traumatic	≥25Ncm	NR
NR	NR	Periodontal disease excluded	NR	NR	NR	NR	≥35Ncm	>60 ISQ
Minimal Mucoperiosteal Flap	Absence of infection	Periodontal disease excluded	Y	NR	Autogenous	Minimally traumatic using periotomes	≥32Ncm	NR
Flapless	NR	Periodontal disease excluded	Y	NR	None	Minimally traumatic with Benex	NR	NR
Full-Thickness Flap	Chronic Infection Included	NR	Y	1 mm	None	NR	NR	>64 ISQ
NR	NR	Treated Periodontal Disease Included	NR	NR	NR	NR	NR	>60 ISQ
Flapless	Absence of infection	Periodontal disease excluded	Y	NR	Xenograft	Minimally traumatic using periotomes	32-45Ncm	NR
Flapless	Absence of Acute Infection	Acute periodontal infection excluded	Y	NR	Xenograft	Minimally traumatic	≥50Ncm	NR
Flapless	Absence of Acute Infection	Periodontal disease excluded	Y	≥2 mm	Xenograft	Minimally traumatic	≥35Ncm	NR
Minimal Mucoperiosteal Flap	Absence of Acute Infection	Treated Periodontal Disease Included	NR	NR	Xenograft	Minimally traumatic using periotomes	≥35Ncm	NR
Flapless	Absence of infection	Periodontal disease excluded	Y	NR	Xenograft	Minimally traumatic using periotomes	≥35Ncm	NR
Minimal Mucoperiosteal Flap	Chronic Infection Included	Treated Periodontal Disease Included	Y	$\bar{x}$ =2.73 mm	Xenograft	Minimally traumatic using periotomes	≥35Ncm	NR
Flapless	Absence of infection	Periodontal disease excluded	Minimal	<1 mm	Autogenous	Minimally traumatic	NR	NR
Full-Thickness Flap	NR	NR	NR	NR	Autogenous	NR	≥35Ncm	NR

TABLE 9 (Continued)

Authors & year	Medical status—standardized reporting	Occlusal scheme	Occlusal parafunction included or excluded (I/E/NR)	Pre-op gingival margin position	Soft tissue quality (thin phenotype)—include I or exclude E	CTG performed at time of implant placement (Y/N)	Bone Anchorage standardized	Facial Bone Wall presence—small defects up to 3 mm, large 3 mm +	Facial Bone Wall thickness
Grandi, Garuti, Samarani, et al. (2012)	Healthy Patients	No Contacts	NR	NR	NR	N	NR	Intact Facial Bone	NR
Groenendijk et al. (2021)	Light Smokers	NR	E	NR	I	N	≥5 mm bone height	Large defects Included	NR
Groisman et al. (2003)	NR	No Contacts	NR	E	NR	N	NR	NR	NR
Kan et al. (2011)	Healthy Patients	NR	E	E	I	N	NR	Intact Facial Bone	NR
Ma et al. (2019)	Healthy Patients	No Contacts	E	NR	NR	N	≥4 mm bone height	Small Defects Included	NR
Malchiodi et al. (2013)	Light Smokers	No Contacts	E	NR	E	N	NR	NR	NR
McAllister et al. (2012)	Healthy Patients	NR	E	NR	NR	N	NR	Small Defects Included	NR
Noelken et al. (2011)	Healthy Patients	No Contacts	NR	NR	NR	N	NR	Large Defects Included	NR
Rosa et al. (2014)	Healthy Patients	NR	NR	NR	I	N	Sufficient Bone	Large Defects Included	Missing
Sato et al. (2017)	Healthy Patients	NR	E	NR	NR	N	Sufficient Bone	Intact Facial Bone	NR
Seyssens et al. (2020)	Healthy, excluded smokers	No Contacts		E	NR	N	≥5 mm bone height	Intact Facial Bone	0.8 mm
Tortamano et al. (2010)	Healthy Patients	No Contacts	NR	NR	NR	N	Sufficient Bone	Intact Facial Bone	NR
Yang et al. (2019)	Healthy Patients	No Contacts	NR	NR	NR	N	Sufficient Bone	Intact Facial Bone	0 to >1 mm
Arora and Ivanovski (2018a)	Light Smokers	No Contacts	NR	NR	NR	N	Sufficient available bone	Intact Facial Bone	NR
Bonnet et al. (2018)	Healthy Patients	No Contacts	NR	NR	NR	Y	NR	Small Defects Included	NR

Mucoperiosteal flap	Presence of endodontic infection	Presence of periodontal disease	Presence of buccal gap (Y/N)	Gap dimensions (mm)	Graft material (none, auto, allo, xeno)	Extraction	Primary implant stability—insertion torque	Primary implant stability—resonance frequency analysis
Flapless	Chronic Infection Included	Treated Periodontal Disease Included	Y	NR	Xenograft	Minimally traumatic	≥30Ncm	NR
Flapless	Chronic Infection Included	Periodontal disease excluded	Y	≥2 mm	Xenograft	Minimally traumatic	NR	NR
Flapless	Absence of infection	Periodontal disease excluded	Y	>1 mm	Autogenous	Minimally traumatic using periotomes	NR	NR
Flapless	Chronic Infection Included	Treated Periodontal Disease Included	Y	NR	Autogenous	Minimally traumatic	NR	NR
Flapless	NR	Periodontal disease excluded	Y	1.5–3	None	Flapless	NR	Mean of 65.1 ISQ + -4.38
Flapless	Chronic Infection Included	Treated Periodontal Disease Included	NR	NR	Autogenous	Minimally traumatic using periotomes	NR	NR
NR	Absence of Acute Infection	Periodontal disease excluded	NR	NR	Xenograft, Allograft or Alloplastic	NR	≥35Ncm	NR
Flapless	NR	NR	Y	NR	Autogenous	Minimally traumatic	NR	NR
Flapless	NR	Periodontal disease excluded	Y	NR	Autogenous	Minimally traumatic using periotomes	≥35Ncm	NR
Flapless	NR	Periodontal disease excluded	Y	NR	Alloplastic or Xenograft	Minimally traumatic	NR	NR
Flapless	NR	Periodontal disease excluded	Y	NR	Xenograft	Minimally traumatic using periotomes	≥35Ncm	NR
Flapless	Absence of infection	Periodontal disease excluded	Y	NR	NR	Minimally traumatic	NR	NR
Flapless	Absence of Acute Infection	Periodontal disease excluded	Y	2 mm	Xenograft or Alloplastic	Minimally traumatic	≥35Ncm	NR
Flapless	Chronic Infection Included	Periodontal disease excluded	Y	NR	Xenograft	Minimally traumatic using periotomes	≥30Ncm	NR
Flapless	NR	Periodontal disease excluded	Y	NR	Xenograft	Minimally traumatic using periotomes	≥30Ncm	NR

TABLE 9 (Continued)

Authors & year	Medical status—standardized reporting	Occlusal scheme	Occlusal parafunction included or excluded (I/E/NR)	Pre-op gingival margin position	Soft tissue quality (thin phenotype)—include I or exclude E	CTG performed at time of implant placement (Y/N)	Bone Anchorage standardized	Facial Bone Wall presence—small defects up to 3 mm, large 3 mm +	Facial Bone Wall thickness
Bruno et al. (2014)	Light Smokers	Limited Contacts	E	E	NR	N	Sufficient available bone	Small Defects Included	
Degidi et al. (2013)	Light Smokers	No Contacts	E	NR	NR	N	NR	Intact Facial Bone	NR
Groenendijk et al. (2017)	Healthy Patients	NR	E	NR	NR	N	≥4 mm bone height	Intact Facial Bone	0.9 mm
Hartlev et al. (2013)	Light Smokers	No Contacts	E	NR	NR	N	NR	Small Defects Included	NR
Khzam et al. (2014)	Healthy Patients	No Contacts	NR	E	NR	N	NR	Intact Facial Bone	NR
Kolerman, Nissan, Rahmanov, et al. (2016)	Light Smokers	No Contacts	E	NR	NR	Y	≥5 mm bone height	Large defects Included	<1 mm or deficient
Lombardo et al. (2016)	Healthy Patients	NR	E	NR	NR	N	NR	Intact Facial Bone	NR
Mangano et al. (2012)	Light Smokers	Limited Contacts	E	NR	E	N	NR	Intact Facial Bone	
Mangano et al. (2013)	Healthy Patients	Limited Contacts	NR	E	E	N	NR	Intact Facial Bone	NR
Menchini-Fabris et al. (2019)	Healthy Patients	NR	E	NR	NR	N	≥4 mm bone height	Intact Facial Bone	NR
Mijiritsky et al. (2021)	Healthy Patients	No Contacts	E	NR	NR	N	NR	NR	NR
Noelken, Moergel, Pausch, et al. 2018	Light Smokers	No Contacts	NR	I	I	Y	Sufficient Bone	Large defects Included	0–1.5 mm
Norton (2011)	Diabetes & Light Smoker	No Contacts	NR	NR	NR	N	NR	Defects Included	NR
Paul and Held (2013)	Light Smokers	No Contacts	NR	NR	NR	N	NR	Intact Facial Bone	NR
Ribeiro et al. (2008)	Healthy Patients	No Contacts	NR	NR	NR	N	≥3 mm bone height & ≥5 mm Bone Width	Intact Facial Bone	NR

Mucoperiosteal flap	Presence of endodontic infection	Presence of periodontal disease	Presence of buccal gap (Y/N)	Gap dimensions (mm)	Graft material (none, auto, allo, xeno)	Extraction	Primary implant stability—insertion torque	Primary implant stability—resonance frequency analysis
Flapless	NR	NR	Y	$\bar{x}$ =1.5 mm	Xenograft	Minimally traumatic	≥35Ncm	≥65 ISQ
Flapless	Absence of infection	Periodontal disease excluded	Y	NR	Xenograft	Minimally traumatic	≥25Ncm	>60 ISQ
Flapless	Chronic Infection Included	Periodontal disease excluded	Y	2 mm	Xenograft	Minimally traumatic	≥40Ncm	NR
Flapless	Absence of infection	Periodontal disease excluded	Y	<2 mm	None	Minimally traumatic using periotomes	≥30Ncm	NR
Flapless	Absence of infection	Periodontal disease excluded	Y	NR	Xenograft	Minimally traumatic	≥30Ncm	NR
Full-Thickness Flap	Absence of infection	Treated Periodontal Disease Included	Y	NR	Allograft	Minimally traumatic using periotomes	≥32Ncm	NR
NR	NR	Periodontal disease excluded	Y	NR	Alloplastic	Minimally traumatic	NR	NR
Full-Thickness Flap	Chronic Infection Included	Periodontal disease excluded	Y	NR	Alloplastic	Minimally traumatic	NR	NR
Full-Thickness Flap	NR	Periodontal disease excluded	NR	NR	NR	Minimally traumatic	NR	NR
Flapless	NR	NR	NR	NR	None	Minimally traumatic using magnetic mallet	NR	NR
Flapless	Chronic Infection Included	Treated Periodontal Disease Included	Y	2 mm	Autogenous	Minimally traumatic using periotomes	≥32Ncm	NR
Flapless	Chronic Infection Included	Periodontal disease excluded	Y	NR	Autogenous	Minimally traumatic	NR	NR
Full-Thickness Flap	NR	NR	Y	1 mm	Autogenous and Xenograft mix	Minimally traumatic using periotomes	≤25Ncm	NR
Flapless	NR	NR	Y	1.5–2.5 mm	Xenograft	Flapless	NR	NR
Flapless	Absence of infection	Periodontal disease excluded	NR	NR	NR	Flapless	NR	NR

TABLE 9 (Continued)

Authors & year	Medical status—standardized reporting	Occlusal scheme	Occlusal parafunction included or excluded (I/E/NR)	Pre-op gingival margin position	Soft tissue quality (thin phenotype)—include I or exclude E	CTG performed at time of implant placement (Y/N)	Bone Anchorage standardized	Facial Bone Wall presence—small defects up to 3 mm, large 3 mm +	Facial Bone Wall thickness
Ross et al. (2014)	NR	No Contacts	NR	E	I	N	NR	Intact Facial Bone	NR
Saedi Germi et al. (2020)	Healthy Patients	NR	NR	E	E	N	Sufficient Bone	Intact Facial Bone	NR
Shanelec (2005)	NR	No Contacts	NR	I	I	Y	NR	Intact Facial Bone	NR
Spinato et al. (2012)	Healthy Patients	No Contacts	NR	NR	E	N	Sufficient Bone	Intact Facial Bone	NR
Tarnow et al. (2014)	Healthy Patients	No Contacts	E	E	NR	N	Sufficient Bone	Intact Facial Bone	NR
Valentini et al. (2010)	Healthy Patients	No Contacts	NR	NR	NR	N	Sufficient Bone	Large defects Included	NR
Van Nimwegen et al. (2016)	Healthy Patients	No Contacts	NR	NR	NR	N	NR	Intact Facial Bone	NR
Vidigal Jr. et al. (2017)	Healthy Patients	No Contacts	E	E	I	Y	Sufficient Bone	Intact Facial Bone	NR

Risk Categorization:

	Low Risk
	Medium Risk
	High Risk

Abbreviations: E, excluded; I, included; N, no; NR, not reported; Y, yes.

Samarani, et al., 2012; Groenendijk et al., 2017, 2021; Groisman et al., 2003; Hartlev et al., 2013; Kan et al., 2011; Khzam et al., 2014; Kolerman, Nissan, Rahmanov, et al., 2016; Lombardo et al., 2016; Ma et al., 2019; Malchiodi et al., 2013; Mangano et al., 2012, 2013; Menchini-Fabris et al., 2019; Migliorati et al., 2015; Mijiritsky et al., 2021; Noelken et al., 2011; Norton, 2011; Paul & Held, 2013; Pieri et al., 2011; Raes, Eghbali, et al., 2018; Ribeiro et al., 2008; Rosa et al., 2014; Ross et al., 2014; Saedi Germi et al., 2020; Sato et al., 2017; Seyssens et al., 2020; Shanelec, 2005; Slagter et al., 2021; Spinato et al., 2012; Tarnow et al., 2014; Tortamano et al., 2010; Van Nimwegen et al., 2016; Vidigal Jr. et al., 2017; Yang et al., 2019; Zuiderveld et al., 2018). Six Studies (Bittner et al., 2020; Ma et al., 2019; Paul & Held, 2013; Ribeiro et al., 2008; Ross et al., 2014; Spinato et al., 2012) reported that the extractions were performed via a flapless approach, while only one study reported that a mucoperiosteal flap was raised prior to tooth extraction (Valentini et al., 2010). The use of periotomes for syndesmotomy as part of the extraction process was reported in 24 studies (Arora & Ivanovski, 2018a, 2018b; Berberi, Noujeim, et al., 2014; Block et al., 2009; Bonnet et al., 2018; Canullo et al., 2010; Canullo, Goglia, et al., 2009; Canullo & Rasperini, 2007; Cosyn et al., 2011, 2016; Cristalli et al., 2015; Di Alberti et al., 2012; Groisman et al., 2003; Hartlev et al., 2013; Kolerman, Nissan, Rahmanov, et al., 2016; Malchiodi et al., 2013; Mijiritsky et al., 2021; Norton, 2011; Pieri et al., 2011; Rosa et al., 2014; Saedi Germi et al., 2020; Seyssens et al., 2020; Shanelec, 2005; Slagter et al., 2021; Van Nimwegen et al., 2016), with one study reporting the use of a magnetic mallet (Menchini-Fabris et al., 2019) and another utilizing a vertical extraction system (Cabello et al., 2013). No studies reported the use of piezo surgery as part of the extraction process.

3.5.11 | Primary stability

The implant insertion torque value was the most commonly reported criteria for evaluation of primary implant stability in 42 of the included

Mucoperiosteal flap	Presence of endodontic infection	Presence of periodontal disease	Presence of buccal gap (Y/N)	Gap dimensions (mm)	Graft material (none, auto, allo, xeno)	Extraction	Primary implant stability—insertion torque	Primary implant stability—resonance frequency analysis
Full-Thickness Flap	NR	NR	Y	NR	Allograft	Flapless	≥35Ncm	NR
Flapless	NR	Periodontal disease excluded	Y	NR	Allograft	Minimally traumatic using periotomes	≥35Ncm	NR
Flapless	NR	NR	Y	NR	Autogenous and Xenograft mix	Minimally traumatic using periotomes	NR	NR
Flapless	Absence of infection	Periodontal disease excluded	Y	$\bar{x}$ = 2.14 mm	None	Flapless	≥35Ncm	NR
Flapless	Absence of infection	Periodontal disease excluded	Y	NR	Allograft	Minimally traumatic	≥35Ncm	NR
Full-Thickness Flap	Absence of infection	Periodontal disease excluded	Y	NR	Xenograft	Flap elevation	≥40Ncm	NR
Flapless	NR	NR	Y	NR	Autogenous and Xenograft mix	Minimally traumatic using periotomes	≥35Ncm	NR
Flapless	NR	Periodontal disease excluded	Y	NR	Xenograft	Minimally traumatic	≥35Ncm	NR

studies (Aguilar-Salvatierra et al., 2016; Arora & Ivanovski, 2018a, 2018b; Berberi, Noujeim, et al., 2014; Berberi, Sabbagh, et al., 2014; Bittner et al., 2020; Bonnet et al., 2018; Bruno et al., 2014; Bushahri et al., 2021; Canullo et al., 2010; Canullo, Goglia, et al., 2009; Canullo & Rasperini, 2007; Cardaropoli et al., 2015, 2019; Cosyn et al., 2011, 2016; Crespi et al., 2008; Cristalli et al., 2015; Degidi et al., 2013, 2014; Di Alberti et al., 2012; Ganeles et al., 2017; Grandi et al., 2013; Grandi, Garuti, Samarani, et al., 2012; Groenendijk et al., 2017; Hartlev et al., 2013; Khzam et al., 2014; Kolerman, Nissan, Rahmanov, et al., 2016; McAllister et al., 2012; Mijiritsky et al., 2021; Norton, 2011; Pieri et al., 2011; Raes, Eghbali, et al., 2018; Rosa et al., 2014; Ross et al., 2014; Saedi Germi et al., 2020; Seyssens et al., 2020; Spinato et al., 2012; Tarnow et al., 2014; Valentini et al., 2010; Van Nimwegen et al., 2016; Vidigal Jr. et al., 2017; Yang et al., 2019; Zuiderveld et al., 2018). A minimum insertion torque threshold of 30–45 Ncm was used for immediate loading in 34 studies (Aguilar-Salvatierra et al., 2016; Arora & Ivanovski, 2018a, 2018b; Berberi, Noujeim, et al., 2014; Berberi, Sabbagh, et al., 2014; Bonnet et al., 2018; Bruno et al., 2014; Bushahri et al., 2021; Canullo et al., 2010; Canullo, Goglia, et al., 2009; Canullo & Rasperini, 2007; Cardaropoli et al., 2019; Cosyn et al., 2011, 2016; Cristalli et al., 2015; Di Alberti et al., 2012; Ganeles et al., 2017; Grandi, Garuti, Samarani, et al., 2012; Groenendijk et al., 2017; Hartlev et al., 2013; Khzam et al., 2014; Kolerman, Nissan, Rahmanov, et al., 2016; McAllister et al., 2012; Mijiritsky et al., 2021; Pieri et al., 2011; Rosa et al., 2014; Ross et al., 2014; Saedi Germi et al., 2020; Seyssens et al., 2020; Spinato et al., 2012; Tarnow et al., 2014; Valentini et al., 2010; Van Nimwegen et al., 2016; Vidigal Jr. et al., 2017; Yang et al., 2019). Five studies used 20–25 Ncm as the minimum insertion torque threshold for immediate loading (Crespi et al., 2008; Degidi et al., 2013, 2014; Norton, 2011; Raes, Eghbali, et al., 2018). One study assessed Type 1A with a relatively low insertion torque of less than 25 Ncm (Bittner et al., 2020). Three studies reported a relatively high minimum insertion torque at or above 45 Ncm (Cardaropoli et al., 2015; Grandi et al., 2013; Zuiderveld et al., 2018). Resonance frequency analysis (RFA) for determination of primary stability and suitability for loading

was reported in 10 studies (Aguilar-Salvatierra et al., 2016; Block et al., 2009; Bruno et al., 2014; Calvo-Guirado et al., 2009, 2015; Crespi et al., 2008; Degidi et al., 2013, 2014; Di Alberti et al., 2012; Ma et al., 2019), with minimum thresholds ranging from 60 to 71 ISQ (implant stability quotient).

3.5.12 | Occlusion

Occlusal criteria for immediate loading was reported in 57 studies, with 47 studies reporting no occlusal contacts on immediately loaded restorations (Arora & Ivanovski, 2018a, 2018b; Bittner et al., 2020; Block et al., 2009; Bonnet et al., 2018; Bushahri et al., 2021; Cabello et al., 2013; Canullo et al., 2010; Canullo, Goglia, et al., 2009; Canullo & Rasperini, 2007; Cardaropoli et al., 2015, 2019; Cooper et al., 2014; Cosyn et al., 2011, 2016; Degidi et al., 2013, 2014; Ferrara et al., 2006; Ganeles et al., 2017; Grandi et al., 2013; Grandi, Garuti, Samarani, et al., 2012; Groisman et al., 2003; Hartlev et al., 2013; Khzam et al., 2014; Kolerman, Nissan, Rahmanov, et al., 2016; Ma et al., 2019; Malchiodi et al., 2013; Migliorati et al., 2015; Mijiritsky et al., 2021; Noelken et al., 2011; Noelken, Moergel, Pausch, et al., 2018; Norton, 2011; Paul & Held, 2013; Pieri et al., 2011; Raes et al., 2017; Raes, Eghbali, et al., 2018; Ribeiro et al., 2008; Ross et al., 2014; Seyssens et al., 2020; Shanelec, 2005; Spinato et al., 2012; Tarnow et al., 2014; Tortamano et al., 2010; Valentini et al., 2010; Van Nimwegen et al., 2016; Vidigal Jr. et al., 2017; Yang et al., 2019; Zuiderveld et al., 2018). Limited occlusal contacts were reported in nine studies (Aguilar-Salvatierra et al., 2016; Berberi, Noujeim, et al., 2014; Berberi, Sabbagh, et al., 2014; Bruno et al., 2014; Calvo-Guirado et al., 2015; Crespi et al., 2008; Cristalli et al., 2015; Mangano et al., 2012, 2013), with only one study (Di Alberti et al., 2012) reporting that the immediate restorations were in full occlusal contact.

3.6 | Intention-to-treat analysis

Only 23 studies reported whether all included patients were able to complete the prospectively assigned treatment protocol, or whether treatment protocols had to be varied due to intra-operative criteria not being met (Bittner et al., 2020; Block et al., 2009; Bushahri et al., 2021; Canullo et al., 2010; Canullo, Goglia, et al., 2009; Cardaropoli et al., 2015, 2019; Cooper et al., 2014; Cosyn et al., 2011, 2016; Crespi et al., 2008; Cristalli et al., 2015; Degidi et al., 2014; Ferrara et al., 2006; Grandi et al., 2013; Ma et al., 2019; McAllister et al., 2012; Migliorati et al., 2015; Noelken et al., 2011; Pieri et al., 2011; Slagter et al., 2021; Tortamano et al., 2010; Zuiderveld et al., 2018). The most common reasons for not completing the planned Type 1A protocol were fracture of the facial bone during extraction and lack of desired insertion torque during immediate implant placement. The successful completion of the intention to treat with a Type 1A protocol ranged from 85% to 100%. The intention-to-treat analysis is hampered by the heterogeneity in the timepoint in which studies consider a patient/site to be included as a prospective participant of a Type 1A protocol.

4 | DISCUSSION

4.1 | Quality of included studies and validity of methods

This report summarizes the results and comparisons regarding reported survival rates from 68 included papers. Of the 68 studies, 11 RCTs were included for review. This systematic review aimed to assess the impact-specific patient and site characteristics reported for a single intervention, Type 1A immediate implant placement, and immediate loading of single implants in the maxillary esthetic zone. When assessing the impact of patient characteristics, an RCT study design is not directly applicable with only the treatment groups which were of Type 1A treatment protocol included in this analysis and carry the same weight as a prospective cohort study. The inclusion of study designs other than RCTs is appropriate within the design of this systematic review and provides clinically relevant data for descriptive reporting. The authors acknowledge that with the inclusion of lower-quality case series and retrospective studies, there is an inherent risk of bias; however, even these studies report using strict patient and site selection criteria.

Statistical assessment of survival rates from studies with different time horizons without detailed information on failures and dropouts and with missing data is not an easy task as there are multiple pitfalls. Performing a meta-analysis on raw survival rates without any correction for study duration would yield an easily interpretable, but highly problematic outcome as studies lasting 10 years would be put on the same level as studies lasting 1 year (same study size). On the other hand, performing a meta-analysis with study duration correction as presented in this paper—it has its origins in epidemiology—, the corrected outcomes ensure a fair comparison, but may feel strange as they are not in the usually reported spheres. In an iterative procedure, the authors thus agreed to additionally assess data in a simpler way in form of univariate (multivariate was not possible due to the small database) group-wise mean comparisons with cautious interpretation and to present these results in the first place along with the results from the time-corrected meta-analysis as complementary analysis.

As the distribution of the survival rates was skewed, non-normal, and with a lot of identical values (many having 100%), *p*-values for comparisons of both survival rates and average study duration were calculated with the help of bias-corrected bootstrap tests and presented with bias-corrected bootstrap confidence intervals. Bootstrap tests are tests that are based on resampling and are superior to common mean tests as they have a bias correction and do not follow parametric distributions. However, as it is common for nonparametric/semi-parametric methods, bootstrap tests lack statistical power compared to parametric alternatives, and also, study heterogeneity is not specifically modeled. Due to missing

combinations, a multivariate analysis was not possible so further confounding effects cannot be ruled out, as discussed further below.

Coming back to the here presented meta-analysis, the obtained heterogeneity measure I^2 of 53% can be interpreted as "moderate" (Higgins & Thompson, 2002) and is particularly low for a meta-analysis of this size. Eliminating the four most influential studies leads to an even lower I^2 of 34%.

Another limitation of this design and results, which may be an indicator for the lack of statistically significant differences, is that although the criteria reported have different thresholds, which formed the basis of our analysis, many patients in the study may be quite far beyond the threshold values, that is, the study may report a minimum threshold of 25 Ncm insertion torque, however, one site may have been at 25 Ncm, with the remaining sites all above 40 Ncm and this would not be reported. The search strategy used in this study limited the results to publications in English only which may exclude some relevant data.

4.2 | Implant survival with type 1A treatment protocols

The estimated weighed mean overall survival rate for Type 1A protocols for single implants in the maxillary esthetic zone is 97.7%, which is consistent with other systematic reviews (Atieh et al., 2009; Chen & Buser, 2014; Cosyn et al., 2019; Gallucci et al., 2018; Garcia-Sanchez et al., 2022; Pommer et al., 2021; Slagter et al., 2014; Zhou et al., 2021).

The short-term mean follow-up time of all included studies at 32 months or 2.7 years (2.3; 3.1) should be considered when assessing the survival outcomes of Type 1A protocols. The rate of failures is also not linear, with the majority of failures occurring during the initial healing period prior to osseointegration. This may be related to immediate loading protocols employed, and this is often attributed to the patients who experience early failures, however, similar rates of early implant failures are reported with unloaded implants as a result of surgical- and patient-related factors (Clauser et al., 2022).

Systematic reviews which only included longer studies with longer follow-up durations include very few studies and report comparable survival rates with Type 1A protocols (Pommer et al., 2021). As the vast majority of failures with Type 1A protocols reported within the study timeframes occurred early within the first 6 months, it could be questioned as to whether the treatment protocol will continue to have an outcome effect in the long term once osseointegration has been established (Schrott et al., 2014).

Univariate bootstrap tests show that studies before 2012 report a significantly lower survival rate. This is not surprising when looking at the proportions of studies reporting incidences. Before 2012, 9 of 17 or 52.9% report a loss, while since 2012, only 17 of 51 = 33.3% report a loss. A reason is surely that clinicians have grown in experience and the technology and clinical techniques have advanced, however, one should not forget the impact of publication bias, that is, studies that are not published due to "inadequate" results due to increasing commercial pressures.

4.3 | Reported patient and site selection criteria for type 1A treatment protocols

All the included studies utilizing a Type 1A treatment protocol report highly selective inclusion and exclusion criteria. The only site-specific criteria which were found to influence survival in this systematic review was the size of the facial gap, however, this is based on only 20 of the included 68 studies, and the presence of chronic endodontic infection. Sites that presented with a gap of over 2 mm between the socket facial bone wall and implant at the time of implant placement were associated with higher implant survival rates (99.0% vs. 95.9%, $p = .04$). This finding may be related to the negative effects of facial implant positioning and using wider implant diameters that completely fill the socket. On the other hand, all studies reporting gaps ≥2 mm were published from 2012 and later so the higher survival rates here might also be related to advances in implant technology and more proficient surgery experience.

The significantly lower survival rate in studies that did not include patients with endodontic infections (96.2% vs. 98.9% for studies with patients with infections) is surprising and unexpected. Although the parameter may be slightly confounded with publication year and gap dimension as most studies including infection have a gap dimension ≥2 mm, there may be other, unknown associated factors that might affect implant survival. Current evidence indicates that placement of immediate dental implants into extraction sites with chronic peri-apical infections, provided appropriate clinical procedures are performed to debride the socket prior to implant placement (Chen et al., 2018; Chrcanovic et al., 2015; Fugazzotto, 2012; Waasdorp et al., 2010; Zuffetti et al., 2017).

Statistically significant differences were not found between survival rates for all the other reported patient and site characteristics. This can indicate that the site characteristics may not influence to a large degree the survival of implants. It also must be considered that survival is a relatively weak outcome measure and does not give an indication of clinically significant parameters such as esthetics, peri-implant tissue health, surrounding bone volume, alveolar ridge dimensions, and patient-reported outcome measures.

Few studies reported individual inclusion criteria which are considered higher risk for complications with Type 1A protocols.

Where higher-risk anatomical criteria were included, such as large defects of the facial bone wall and gingival recession, there was a tendency toward performing adjunct procedures such as connective tissue grafting, and/or raising full-thickness mucoperiosteal flaps to facilitate guided bone regeneration procedures.

4.4 | Intention-to-treat analysis (ITT) for type 1A treatment protocols

The intention-to-treat analysis is important for understanding how often can a chosen procedure be successfully completed in a given site/patient (Hollis & Campbell, 1999). As also reported in previous systematic reviews (Schrott et al., 2014), most studies did not include patients until the intervention has been successfully completed. As

such they do not report sites in which the intervention was aborted due to procedural complications or intra-operative assessments that deemed the site no longer suitable to continue with immediate implant placement or immediate loading. It is also not reported how many patients were screened as potential participants that did not meet the inclusion criteria and the reasons for exclusion.

Two studies reported a relatively high proportion of sites that did not meet the procedural criteria to continue with a Type 1A protocol. Cristalli et al., 2015 reported 4 of 28 sites having defects in the facial plates following extraction rendering an intention to treat of 86% (Cristalli et al., 2015). Ferrara et al., 2006 reported 6 of 39 implants that did not have sufficient primary stability to continue with immediate loading with an ITT of 85%, which may be related to the implant design utilized in the study (Ferrara et al., 2006).

4.5 | Clinical significance

This article highlights the importance of strict patient and site selection for Type 1A implant protocols since the literature on compromised sites is lacking. The risk assessment table provides a framework for clinicians to identify when sites may be indicated for Type 1A protocols when low-risk factors are present. The assessment categories and thresholds are based on the current knowledge and understanding of the clinical and preclinical literature regarding implant survival, as well as esthetic and biological outcomes (Araújo et al., 2022; Buser et al., 2017; Chappuis et al., 2013; Levine et al., 2022). Several of the risk assessment criteria for Type 1A, such as thickness of facial bone, soft tissue phenotype, esthetic risk, gingival margin position, and presence of a facial gap, are specifically targeted at achieving optimal esthetics in recognition of the dimensional alveolar ridge changes that occur following tooth extraction that can lead to compromised esthetic outcomes (Chen & Buser, 2009, 2014; den Hartog et al., 2008; Morton et al., 2014; Yang et al., 2019), and are unlikely to be influential in survival outcomes.

The risk thresholds are slightly more conservative than those reported as minimum inclusion criteria in the literature in recognition that the studies may include only very few patients who were close to this threshold, and the mean values in these studies, which the success and survival are based on, may be considerably higher. The risk assessment table should be periodically reviewed, and thresholds updated as new literature becomes available.

4.6 | Clinical recommendations

The studies included in this review on Type 1A immediate implant placement and loading protocols demonstrated high- to short-medium-term survival rates. The quantity and quality of evidence appear to be sufficient to justify these protocols as routine in sites and patients can be considered as low risk of complications. According to previously published validation criteria (Gallucci et al., 2009, 2018; Zhou et al., 2021), the literature included in the current systematic review would support that Type 1A protocols in the anterior maxilla can be considered clinically and scientifically validated when strict selection criteria are followed. Since the reported studies all had strict patient- and site-specific selection criteria for Type 1A protocols, the patient population and sites that this literature is applicable to may be limited, and further studies are required to expand upon the indications for this protocol.

Survival rates were used in this systematic review as they are the most commonly reported outcome measure in the dental literature. However, clinical decision-making needs to encompass factors that can influence implant success including the potential for esthetic, biological, mechanical, and technical complications. Until literature is present to demonstrate acceptable implant esthetic and survival outcomes of Type 1A implant treatment in compromised sites, to obtain predictable results it would be recommended to follow strict patient and site selection.

Where sites are presenting with local anatomical characteristics which are considered moderate-risk factors, such as thin facial bone, thin soft tissue phenotype, and minor gingival recession, adjunctive treatments such as connective tissue grafting (CTG) tend to be used, which suggests that they may be required to provide successful esthetic outcomes. Several systematic reviews have specifically assessed the influence of CTG on esthetic parameters reporting an improvement in soft tissue profile and less mucosal recession where CTG is used in conjunction with Type 1A protocols (Atieh & Alsabeeha, 2020; Seyssens et al., 2021).

Due to the lack of published studies, where patients and sites are identified as having high-risk factors, Type 1A protocols cannot be recommended for routine use.

Type 1A protocols are technically challenging and this may influence the ability to achieve the necessary procedural criteria to successfully complete the planned intervention. The experience of the clinician should be taken into consideration when electing to underate a Type 1A protocol, and should only be performed by experienced clinicians, particularly if sites present with any moderate-risk factors.

In this systematic review, 51 of the 68 included studies included reported grafting the gap between the implant and the facial bone wall when it was greater than 1 mm. The presence of a facial gap larger than 2 mm was univariately associated with increased survival rate and greater facial bone thickness when filled with bone substitutes, which is consistent with other literature (Atieh et al., 2009; Levine et al., 2022). Although regeneration of bone can occur without the placement of biomaterials into the gap, grafting is recommended to minimize the postextraction dimensional alveolar ridge changes (Araújo et al., 2022).

5 | CONCLUSION

Within the limitation of the present systematic review and range of studies included, Type 1A immediate implant placement and immediate loading for single implants in the maxillary esthetic zone has a

high survival rate. All the included studies demonstrated strict inclusion and exclusion criteria which highlights the importance of appropriate patient and site selection. A risk assessment tool is proposed based on the reported inclusion criteria, which can assist clinicians in identifying suitable sites indicated for Type 1A implant placement and loading protocols. Due to the limitations in using survival analysis for clinical decision-making, further research is required to assess esthetic and functional success with Type 1A protocols.

AUTHOR CONTRIBUTIONS

AH, LG, KA, JW, DM, WM, GG, and DW conceived the ideas and developed the methodology; LG and KA performed title and abstract screening; AH assisted in the screening as the third reviewer; AH, LG, and KA performed the full-text screening and data extraction; LM performed the statistical analysis; AH, LG, KA, JW, DM, WM, GG, and DW reviewed the statistical analysis; AH, LG, and KA lead the writing; AH, LG, KA, JW, LM, DM, WM, GG, and DW revised the manuscript critically for important intellectual content; and AH gave the final approval of the version to be submitted.

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CONFLICT OF INTEREST STATEMENT

The authors report no conflicts of interest related to this research.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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CONSENSUS REPORT

CLINICAL ORAL IMPLANTS RESEARCH WILEY

Group 5 ITI Consensus Report: Implant placement and loading protocols

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International Team for Implantology

Abstract

Objectives: Working Group 5 was convened to discuss and find consensus on the topics of implant placement and loading protocols associated with single missing teeth in the anterior maxilla (aesthetic zone). Consensus statements, clinical recommendations, patient perspectives and future research suggestions were developed and presented to the plenary for discussion and approval.

Materials and Methods: Two systematic reviews were developed and submitted prior to the conference. The group considered in detail the systematic reviews and developed statements, clinical recommendations, patient perspectives and future research suggestions based on the findings of the reviews and experience of group members. Definitive versions were developed after presentation to and discussion by the plenary.

Results: Five consensus statements were developed and approved from each systematic review. Twelve clinical recommendations were developed by the group based on both reviews and experience. Three patient perspectives were developed, and five suggestions made for future research.

Conclusions: Based on the findings of the systematic reviews and experience of group members, the Type 1A protocol (immediate placement and immediate loading), when

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utilized in the anterior maxilla under favorable conditions, is considered predictable and is associated with high survival rates. The procedure is considered clinically viable and is associated with aesthetic outcomes, although surgical, technical, and biological complications can occur.

KEYWORDS
bone implant interactions, clinical assessment, diagnosis, loading, placement, prosthodontics, surgical techniques

1 | INTRODUCTION

Patients and clinicians desire increasingly rapid treatment options that maintain expected success and survival rates without increasing the risk of complications. The ITI has for more than two decades evaluated and reported on evolving protocols relating to implant placement and loading, objectively reviewing the state of the science and clinical practice. The developing knowledge base and volume of clinical expertise have been reported and updated regularly (Benic et al., 2014; Chen & Buser, 2009; Chen et al., 2004; Chiapasco, 2004; Cochran et al., 2004; Cordaro et al., 2009; Gallucci et al., 2009, 2014, 2018; Ganeles & Wismeijer, 2004; Grutter & Belser, 2009; Hammerle et al., 2004; Morton et al., 2004, 2014, 2018; Papaspyridakos et al., 2014; Roccuzzo et al., 2009; Schimmel et al., 2014; Schrott et al., 2014; Weber et al., 2009).

At the Third ITI Consensus Conference held in Gstaad, Switzerland (2003), consensus was found regarding terminology and classification of procedures relating to both the surgical and restorative phases of patient care (Chen et al., 2004; Chiapasco, 2004; Cochran et al., 2004; Ganeles & Wismeijer, 2004; Hammerle et al., 2004; Morton et al., 2004). Five years later (2008) at the Fourth ITI Consensus Conference held in Stuttgart, Germany, concepts relating to risk factors for complications were introduced and discussed (Chen & Buser, 2009; Cordaro et al., 2009; Gallucci et al., 2009; Grutter & Belser, 2009; Roccuzzo et al., 2009; Weber et al., 2009). By 2013 and the Fifth ITI Consensus Conference (Bern, Switzerland), the ITI was able to find and publish agreement regarding patient and site selection and provide recommendations relating to time points post-extraction (Benic et al., 2014; Gallucci et al., 2014; Morton et al., 2014; Papaspyridakos et al., 2014; Schimmel et al., 2014; Schrott et al., 2014).

It is important to note that many of these protocol changes were taking place in a fluid patient care environment. Dental implant macromorphology and surfaces, implant alloys, connections, abutments and restorative materials were becoming more conducive to success when incorporating accelerated treatment protocols. Knowledge regarding biomaterials, with respect to the relevance of specific site-related parameters, led to pivotal statements and recommendations being made at the Sixth ITI Consensus Conference (2018) in Amsterdam (Gallucci et al., 2018; Morton et al., 2018). Of great significance was consensus being found for treatment planning to be finalized for both implant placement and loading when the indication for extraction is confirmed and not after tooth removal. A classification system for placement and loading protocols for partially edentulous patients published as part of the proceedings brought treatment considerations together under a single umbrella for patients (Gallucci et al., 2018).

As part of the Seventh Consensus Conference in Lisbon (2023), Group 5 continued the above focus, specifically the Type 1A protocol (immediate placement and immediate loading) for the replacement of single maxillary anterior teeth (15–25 FDI). Immediate placement and loading of a single tooth, first reported by Wohrle (1998), has received a great deal of attention over the last 20 plus years as it is desirable to clinicians and associated with high patient-centred benefits.

Two systematic reviews were prepared for Group 5 to consider:

1. Hamilton A, Gonzaga L, Amorim K, Wittneben J, Martin L, Morton D, Martin W, Gallucci GO, and Wismeijer D. Selection criteria for type 1A (immediate implant placement and immediate loading) for single tooth replacement in the maxillary aesthetic zone: a systematic review and meta-analysis. (Hamilton et al., 2023).
2. Wittneben JG, Molinero-Mourelle P, Hamilton A, Alnasser M, Obermaier B, Morton D, Gallucci GO, and Wismeijer D. Clinical performance of immediately placed and immediately loaded single implants in the aesthetic zone. A systematic review and meta-analysis. (Wittneben et al., 2023).

2 | DEFINITIONS OF TERMS

Type 1A – immediate implant placement and immediate restoration/loading

- Immediate implant placement
  - Dental implants are placed in the fresh socket on the same day of tooth extraction, as part of the same procedure.
- Immediate loading
  - Dental implants are connected to a prosthesis in occlusion with the opposing arch within 1 week subsequent to implant placement.

- Immediate restoration
  - Dental implants are connected to a prosthesis held out of occlusion with the opposing arch within 1 week subsequent to implant placement.
- Survival
  - The presence of an implant in situ at the follow-up examination (Papaspyridakos et al., 2014).
- PES
  - Pink esthetic score (PES) (Belser et al., 2009; Fürhauser et al., 2005).
- WES
  - White esthetic score (WES) (Belser et al., 2009).

These definitions are in accordance with publications from previous ITI Consensus Conferences and ITI Treatment Guides (Benic et al., 2014; Chen et al., 2004, 2009; Chiapasco, 2004; Cochran et al., 2004; Cordaro et al., 2009; Gallucci et al., 2009, 2014, 2018; Ganeles & Wismeijer, 2004; Grutter & Belser, 2009; Hammerle et al., 2004; Morton et al., 2004, 2014, 2018; Papaspyridakos et al., 2014; Roccuzzo et al., 2009; Schimmel et al., 2014; Schrott et al., 2014; Weber et al., 2009; Chen & Buser, ITI Treatment Guide Volume 3., 2008).

Proceedings. ITI Consensus Conferences.

ITI Treatment Guide Volume 3.

The following consensus statements were developed from the two previously mentioned systematic reviews that assessed selection criteria and implant survival (Hamilton et al., 2023) and clinical performance (Wittneben et al., 2023) of immediately placed and immediately loaded dental implants (Type 1A) for single tooth replacement in the anterior maxilla (15–25 FDI) (region of aesthetic significance). All implants included in the two reviews exhibited a minimum of 12 months follow-up.

3 | SYSTEMATIC REVIEW PAPER 1

3.1 | Manuscript title

Selection criteria for Type 1A (immediate implant placement and immediate loading) for single tooth replacement in the maxillary aesthetic zone: a systematic review and meta-analysis.

3.2 | Preamble

The following consensus statements are based on a systematic review that assessed implant survival with Type 1A (immediate implant placement and immediate restoration/loading) protocol for implant replacement of single teeth in the anterior maxilla (15–25 FDI), with a minimum of 12 months follow-up. The review also assessed the reported patient and site-specific selection criteria that may influence survival outcomes. The review is based on data from 43 prospective (11 randomized control trials [RCTs] and 6 clinical controlled trials [CCTs]) and 25 retrospective studies with a total of 2531 implants with a mean follow-up of 2.6 years.

3.3 | Consensus statements

3.3.1 | Consensus statements 1

The Type 1A protocol for replacement of a single tooth in the anterior maxilla (15–25 FDI) is predictable with high implant survival rates. This is based on studies with highly selective populations, with favourable patient and site-specific characteristics. When failures occur, the majority are within the first 6 months of implant placement. This statement is supported by 43 prospective (including data from 11 RCTs and 6 CCTs) and 25 retrospective studies.

3.3.2 | Consensus statements 2

Multiple patient and site-specific factors are relevant in the selection and completion of a Type 1A protocol for the replacement of a single tooth in the anterior maxilla (15–25 FDI). These include:

a) General factors:

- Medical status (63 studies)
- Periodontal disease (54 studies)
- Occlusal scheme (57 studies)
- Parafunction (26 studies)

b) Site-specific factors:

- Facial bone wall (60 studies)
- Endodontic infection (42 studies)
- Bone for anchorage (37 studies)
- Soft tissue quality (25 studies)
- Gingival margin position (22 studies)

c) Treatment factors:

- Mucoperiosteal flap (63 studies)
- Damage during tooth extraction (59 studies)
- Gap between the facial bone and implant (56 studies)
- Primary implant stability (42 studies)

3.3.3 | Consensus statements 3

The Type 1A protocol may not be able to be completed in all selected sites due to intra-operative procedural events mostly related to the extraction of the tooth or lack of primary implant stability. This statement is supported by 23 prospective studies (including data from 11 RCTs and 2 CCTs).

3.3.4 | Consensus statements 4

A chronic periapical infection associated with the tooth to be extracted is not a contraindication for the Type 1A protocol provided there is sufficient bone to achieve primary implant stability. This statement is supported by 29 prospective (including data from 9 RCTs and 3 CCTs) and 13 retrospective studies.

3.3.5 | Consensus statements 5

With regards to implant position, the presence of at least a 2 mm gap between the implant and the facial bone increases implant survival when the Type 1A protocol is utilized. This statement is supported by 13 prospective (including data from 5 RCTs and 2 CCTs) and 7 retrospective studies.

4 | SYSTEMATIC REVIEW PAPER 2

4.1 | Manuscript title

Clinical performance of immediately placed and immediately loaded single implants in the aesthetic zone. A systematic review and meta-analysis.

4.2 | Preamble

The following consensus statements are based on a systematic review that assessed the clinical performance of dental implants used according to the Type 1A (immediate implant placement and immediate restoration/loading) protocol for replacement of single teeth in the aesthetic zone (anterior maxilla 15–25 FDI).

The statements are based on up to 38 prospective (including 10 RCTs) and 25 retrospective studies with a follow-up of 12 and 96 months.

4.3 | Consensus statements

4.3.1 | Consensus statements 1

The Type 1A protocol, when utilized in the aesthetic zone, is a clinically viable treatment option. However surgical, technical and biological complications can occur. This statement is supported by 63 studies (10 randomized controlled trials, 28 prospective and 25 retrospective studies) with a follow-up ranging from 12 to 96 months. Surgical complications (mean per year 5.86%; 38 clinical studies) and technical (mean 3.27%; 25 clinical studies) and biological (mean 2.18%; 29 clinical studies) complications may occur.

4.3.2 | Consensus statements 2

For the Type 1A protocol, survival is not influenced by the type of implant (bone level vs. parallel walled vs. tapered design). This statement is supported by 63 studies (10 randomized controlled trials, 28 prospective and 25 retrospective studies) with a follow-up ranging from 12 to 96 months.

4.3.3 | Consensus statements 3

For the Type 1A protocol, there was an increase in PES when the space between the implant and the facial bone of the residual socket was grafted with autogenous bone or bone substitute. This statement is supported by 35 studies (7 randomized controlled trials, 12 prospective and 16 retrospective studies) with follow-up ranging from 12 to 96 months.

4.3.4 | Consensus statements 4

For the Type 1A protocol, the flapless approach provides good aesthetic outcomes (papilla height, PES and WES). This statement is supported by 11 clinical studies for papilla height, 31 clinical studies for PES and 16 clinical studies for WES.

4.3.5 | Consensus statements 5

For the Type 1A protocol, differences in survival are not influenced by type of retention (screw or cement retained) when focusing on the final restoration. This statement is supported by 29 clinical studies.

5 | CLINICAL RECOMMENDATIONS

The following clinical recommendations are based on the consensus statements from both systematic reviews.

5.1 | Preamble

The replacement of a single tooth in the anterior maxilla (15–25 FDI) with the Type 1A protocol is a complex procedure with high patient-centred benefits. It should be considered as the treatment

of choice when ideal conditions are present. Ideal site conditions include:

- Healthy adjacent teeth
- Intact facial bone
- No acute infection
- Ability to place the implant in the correct three-dimensional (3D) position for restoration
- Anticipated stability of the implant to allow immediate restoration

Multiple patient and site-related factors need to be considered for this treatment in order to achieve predictable long-term functional and aesthetic outcomes. If the criteria for the Type 1A protocol are not met, alternative treatment options must be considered.

Patients undergoing implant therapy should have no medical or psychological contraindications to complex oral surgical and restorative procedures. Patients should have realistic expectations about the final outcomes, be fully informed and have consented to undergo the Type 1A protocol.

1. **What clinical experience is recommended for the Type 1A protocol?**
   The Type 1A protocol is classified as a complex procedure (ITI SAC Classification, 2nd Edition, 2021) and should be performed by clinicians experienced in surgical and restorative implant procedures. These clinicians should have skills specific to tooth extraction and immediate implant placement, hard and soft tissue augmentation procedures and immediate loading/restoration of implants. A team approach is often needed.

   Dawson A, Martin WC, and Polido W. The SAC Classification in Implant Dentistry. 2nd Edition. Quintessence.

2. **How should a patient be clinically assessed for the Type 1A protocol?**
   A thorough clinical examination should be performed for the proper assessment of the patient and site. The patient should be assessed with the Esthetic Risk Assessment (ITI TG 10, SAC 2nd Edition) and risk assessment for immediate implant placement in single tooth sites (Hamilton et al. 2023, ITI TG 14) to determine the patient and site-specific risk factors for immediate implant placement.

3. **What radiographs are recommended to properly assess a site for the Type 1A protocol?**
   Radiographic assessment of the site and relevant surrounding tissues with a good-quality periapical radiograph and a cone-beam computed tomography (CBCT) scan is strongly recommended. The following radiographic criteria should be fulfilled:
   - An intact or minimally damaged facial bone plate
   - Sufficient bone available to provide primary stability in an ideal 3D position
   - Health of the adjacent teeth

4. **Is software planning recommended for the Type 1A protocol?**
   When a CBCT (digital volume) has been captured, the use of implant planning software is strongly recommended in order to evaluate the site and simulate the ideal 3D implant position. This allows the following to be analysed:
   - The tooth–alveolus axis relationship allows planning for optimal 3D restoration-driven implant placement.
   - The gap between the implant and the facial bone wall is at the level of the planned implant shoulder position.
   - Abutment options.

5. **What restorative preparation should there be prior to commencing treatment?**
   The prior fabrication and use of a traditional or computer-guided surgical template is highly recommended to achieve an optimal restoratively driven 3D implant position. A provisional crown, shell crown or matrix should be prepared prior to tooth extraction according to the desired method for fabrication of the planned immediate implant restoration. An alternative provisional prosthetic replacement of the tooth should be prepared and available in the event the treatment cannot be completed due to intra-operative events.

6. **How should the tooth be extracted when utilizing the Type 1A protocol?**
   A minimally traumatic tooth extraction with a flapless approach is recommended and all efforts should be made to preserve bone and soft tissue integrity. Special instrumentation may be required to achieve this goal. Debridement of the socket should be performed. The integrity of the socket walls should be confirmed following extraction.

7. **What should be done if the facial bone is compromised when the tooth is extracted?**
   If the facial bone is compromised during and following tooth extraction, the extent of the defect must be assessed. If a minor defect in the facial bone is present, the Type 1A protocol may still be considered. However, the risk of aesthetic complications is increased and additional adjunctive hard and soft

tissue regenerative procedures may be required. In larger defects, alternative treatment protocols to Type 1A must be considered.

8. **Can the Type 1A protocol be done in the presence of chronic periapical infection?**
   The Type 1A protocol can be selected for teeth presenting with chronic periapical infections. However, it is recommended that this is only considered when the following conditions exist:
   - Absence of a fistula
   - Infection can be completely debrided
   - There is sufficient bone remaining to provide primary implant stability

9. **How big should the facial gap be?**
   The facial gap should ideally be >2 mm in width at the level of the implant shoulder. However, this may not always be possible and ultimately needs to be considered in relation to the likely functional loading, implant diameter and the dimensions of the socket.

10. **What should be done when the facial bone or soft tissues are thin?**
    The following treatment can be considered:
    - In thin-tissue phenotype situations, or when facial bone is thin (less than 1 mm), the Type 1A protocol can still be considered. However, in addition to grafting of the gap, adjunctive soft tissue grafting may be required to compensate for anticipated post-extraction dimension changes. This will increase the complexity of the procedure and the risk of adverse outcomes.
    - Alternative implant placement and loading protocols may also be considered to reduce the risk.

11. **What steps should be taken for connection of the provisional crown to the implant?**
    Immediate placement of a provisional restoration is well documented. This can be performed according to previously published consensus statements. The following factors should be considered:
    - Screw retention is recommended.
    - Emergence profile should be appropriate (not over- or under-contoured).
    - Timeframe should be from implant placement to 1-week post placement.
    - A highly polished surface of the provisional is required.
    - The occlusion scheme should be without any eccentric contacts.
    - Light proximal contacts should be present.
    - The provisional restoration should be inserted and the retaining screw (abutment or prosthetic) torqued according to guidelines published by each manufacturer.

12. **What should be done if the Type 1A protocol cannot be completed at the time of surgery?**
    If the Type 1A protocol cannot be completed, the implant can be placed with simultaneous grafting and allowed to heal without loading the implant. If the implant cannot be placed, an early placement protocol can be considered. Alternatively, the socket may be grafted and followed by late implant placement.

5.2 | Patient perspectives

The following patient scenario, associated questions and answers were developed by Group 5, and are based on the consensus statements, clinical recommendations and expert opinion. The scenario forms the basis for questions that a patient may pose when being considered for the Type 1A protocol to replace a maxillary anterior tooth.

5.3 | Scenario

'My dentist told me that I have an infection located around the root of one of my front teeth. My dentist also told me that the tooth cannot be saved and needs to be extracted. My dentist mentioned that a dental implant with a crown could provide a long-term solution for replacement of this tooth'.

5.3.1 | Patient perspective 1: Can you remove the tooth and place a dental implant and crown at the same time?

We need to perform an examination of your mouth and make an assessment of important clinical aspects. We will need to take X-rays, which will most likely include a 3D scan known as a CBCT. If conditions are favourable, we can consider removing the tooth, placing the implant and a crown at the same time. This response is based on scientific evidence.

5.3.2 | Patient perspective 2: What could go wrong during the procedure?

Every effort is made to avoid complications and risks. Even so, unforeseen problems can arise during the procedure. Complications that occur during the procedure will most likely be related to one or more of the following three things:

- Complications resulting from the extraction (removal) of the tooth

- Inability to properly place a stable dental implant or place the implant in the ideal restoratively driven 3D position
- Inability to place a restoration (crown) on the dental implant at the same appointment, requiring an alternative option to be considered

This response is based on scientific evidence and expert opinion.

5.3.3 | Patient perspective 3: What could go wrong after the procedure?

Minor postoperative discomfort and swelling are expected and can usually be managed with over-the-counter medications. Postoperative complications are relatively rare but possible. Most postoperative complications can be related to one or more of the following four things:

- Postoperative pain and/or bleeding
- Postoperative infection
- Postoperative loosening and/or failure (loss) of the implant
- Undesirable aesthetic outcomes

This response is based on scientific evidence and expert opinion.

6 | RECOMMENDATIONS FOR FUTURE RESEARCH

Recommendation 1: Current studies report on outcomes for the Type 1A protocol used in highly controlled situations. It is recommended that future research report on the number of patients screened for inclusion, the number subsequently excluded and why. Survival, site-specific and aesthetic data from larger samples in less restricted populations should be gathered, with both practice and patient-centred clinical evaluation advisable.

Recommendation 2: Detailed reporting on treatments not able to be completed as a result of intra-operative variables (intention-to-treat analysis) should be undertaken. It is recommended that as a result of regional variations in the nature of soft tissues and the facial bone plate in the maxilla, reporting should differentiate between the premolars and the canine-to-canine region. Furthermore, future papers should identify immediate implant placement and/or immediate loading and/or type 1A protocols in the title and abstract to facilitate screening for future systematic reviews.

Recommendation 3: Future research should focus on outcomes, survival and success of procedures provided once failure and complications as a result of the Type 1A protocol are observed. Clinical and patient-centred outcomes should be reported.

Recommendation 4: The choice of augmentation materials used in conjunction with the Type 1A protocol has not been investigated adequately. Specifically, it is recommended that the choice of hard tissue graft material, in conjunction with the grafting of the space between the implant and facial bone (HDD – horizontal defect dimension) be investigated specifically with regard to long-term clinical and aesthetic outcomes.

Recommendation 5: The choice of soft tissue grafting procedures and materials used in conjunction with the Type 1A protocol has not adequately investigated, specifically when these procedures are indicated and when they should be utilized in conjunction with hard tissue augmentation options. Site-specific indication for use, along with long-term clinical and aesthetic outcomes, should be evaluated.

AUTHOR CONTRIBUTIONS

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CONFLICT OF INTEREST STATEMENT

All authors and participants in Group 5 declared no conflicts regarding the content of the Seventh ITI Consensus Conference or subsequent articles developed from the proceedings.

DATA AVAILABILITY STATEMENT

The data that supports the findings of this study are available in the supplementary material of this article.

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